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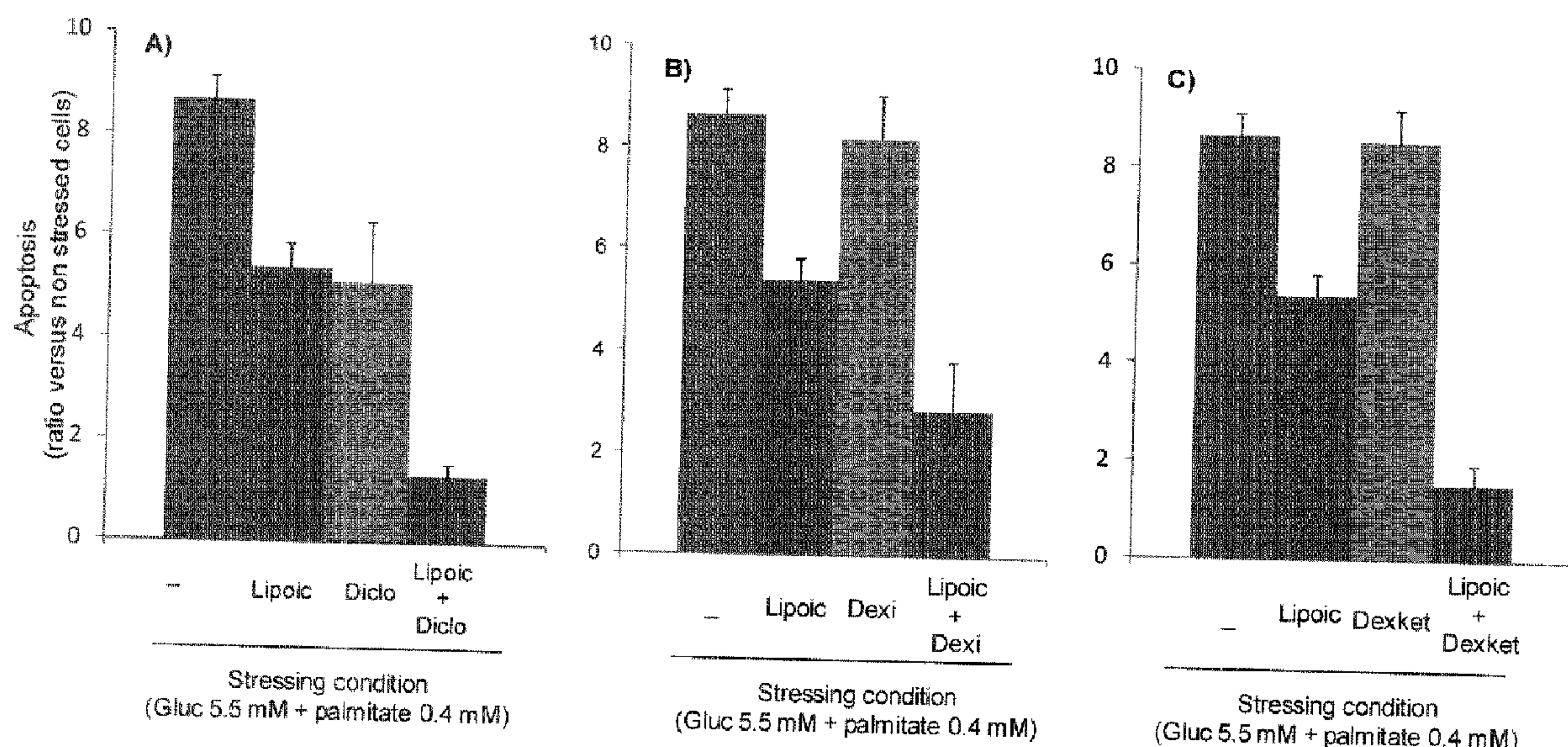
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(54) Titre : THERAPIES COMBINATOIRES POUR LE TRAITEMENT DE TROUBLES METABOLIQUES
(54) Title: COMBINATION THERAPIES FOR TREATING METABOLIC DISORDERS

The combination of (R) Lipoic Acid and diclofenac, dexibuprofen, or dexketoprofen protects beta-cells from cellular stress implicated in diabetes related pancreas dysfunction



INS-1E β -cells were pretreated overnight with lipoic acid 100 μ M, diclofenac 100 μ M (Diclo), dexibuprofen 500 μ M (Dexi) and Dexketoprofen 500 μ M (Dexket) alone or in combination as indicated in graphics A, B and C.

Figure 1

(57) Abrégé/Abstract:

This invention is directed to pharmaceutical combinations comprising an antioxidant agent, an anti-inflammatory agent, and optionally at least one other anti-diabetic agent useful for treating metabolic disorders. This invention also encompasses

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pharmaceutically acceptable compositions comprising an antioxidant agent, an anti-inflammatory agent, optionally at least one other anti-diabetic agent, and at least one pharmaceutically acceptable earner. The combinations and compositions of this invention are useful as methods for treating metabolic disorders including diabetes, particularly Type I and Type II diabetes, as well as diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular disease, inflammatory disorders, nephropathy, neuropathy, retinopathy, β -cell dysfunction, dyslipidemia, LADA, metabolic syndrome, hyperglycemia, insulin resistance, and/or chronic obstructive pulmonary disease in a mammal, particularly a diabetic mammal, and specifically a human patient. This invention is particularly directed to pharmaceutical compositions comprising an lipoic acid, one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, and optionally one or more pharmaceutically acceptable carriers. The compositions of this invention are useful as methods for treating metabolic disorders including type II diabetes, insulin resistance, beta-cell dysfunction, and hyperglycemia in a patient, particularly a diabetic patient.

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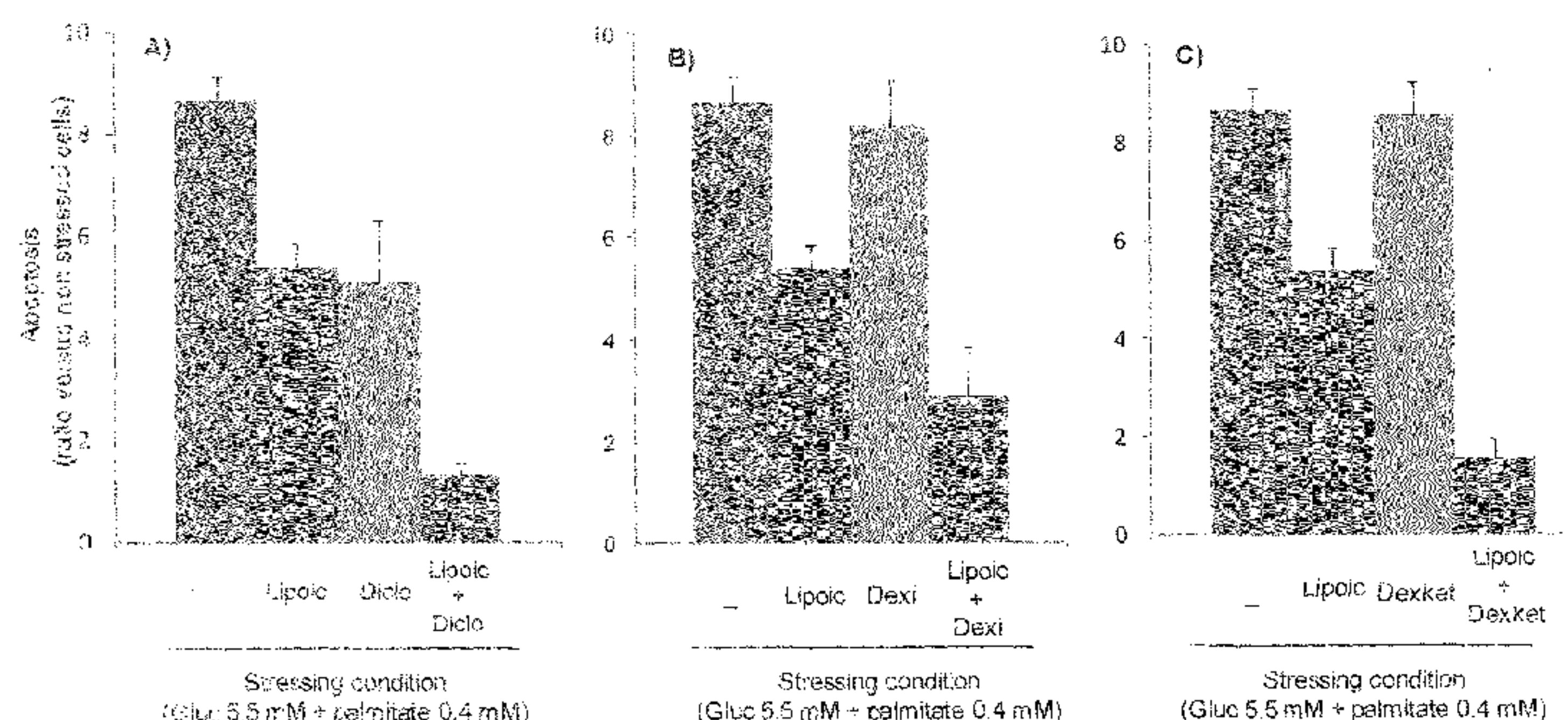
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(54) Title: COMBINATION THERAPIES FOR TREATING METABOLIC DISORDERS

The combination of (R) Lipoic Acid and diclofenac, dexibuprofen, or dexketoprofen protects beta-cells from cellular stress implicated in diabetes related pancreas dysfunction



INS-1E β-cells were pretreated overnight with lipoic acid 100 μM, diclofenac 100 μM (Diclo), dexibuprofen 500 μM (Dexi) and Dexketoprofen 500 μM (Dexket) alone or in combination as indicated in graphics A, B and C.

Figure 1

(57) **Abstract:** This invention is directed to pharmaceutical combinations comprising an antioxidant agent, an anti-inflammatory agent, and optionally at least one other anti-diabetic agent useful for treating metabolic disorders. This invention also encompasses pharmaceutically acceptable compositions comprising an antioxidant agent, an anti-inflammatory agent, optionally at least one other anti-diabetic agent, and at least one pharmaceutically acceptable carrier. The combinations and compositions of this invention are useful as methods for treating metabolic disorders including diabetes, particularly Type I and Type II diabetes, as well as diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular disease, inflammatory disorders, nephropathy, neuropathy, retinopathy, β-cell dysfunction, dyslipidemia, LADA, metabolic syndrome, hyperglycemia, insulin resistance, and/or chronic obstructive pulmonary disease in a mammal, particularly a diabetic mammal, and specifically a human patient. This invention is particularly directed to pharmaceutical compositions comprising a lipoic acid, one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, and optionally one or more pharmaceutically acceptable carriers. The compositions of this invention are useful as methods for treating metabolic disorders including type II diabetes, insulin resistance, beta-cell dysfunction, and hyperglycemia in a patient, particularly a diabetic patient.

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COMBINATION THERAPIES FOR TREATING METABOLIC DISORDERS

BACKGROUND

Type II diabetes and its underlying obesity, also called diabetes, is rapidly becoming a worldwide epidemic. There are currently more than 194 million people with diabetes worldwide, and Type II diabetes accounts for up to 90% of diabetics in overall patient populations. It is a well known in the art that diabetes is a risk factor for cardiovascular diseases associated also with dyslipidemia and hypertension. With such long-term complications, diabetes is already the fifth leading cause of morbidity and mortality, imposing a high financial burden on health care costs for society. With a projected doubling of the number of global cases of diabetes by 2030, the development of effective diabetes prevention and treatment strategies is of paramount importance.

Type II diabetes mellitus (T2DM) is a metabolic disorder in which carbohydrate and lipid metabolism are improperly regulated by insulin (insulin resistance) resulting in elevated fasting and postprandial serum glucose levels (hyperglycemia) and increased levels of circulating free fatty acids (FFA) and triglycerides (TG). T2DM is preceded by a long period of insulin resistance during which blood glucose is maintained near normal levels by compensatory hyperinsulinemia. When pancreatic β -cells are no longer able to compensate for insulin resistance by adequately increasing insulin production, impaired glucose tolerance appears. This condition is characterised by an excessive blood glucose concentration in the postprandial phase whereas fasting glucose remains in the normal range. The combination of persistent overfeeding with a sedentary lifestyle leads to overt diabetes characterised by hyperglycemia.

Recently, it has been suggested that oxidative stress and inflammation are key features of obesity and type II diabetes, exacerbating its progression and cardiovascular complications. For example, the antioxidant enzymes responsible for scavenging free radicals have been reported to be diminished in diabetic patients. Glutathione pools become depleted in diabetic patients following frequent and severe hyperglycemic episodes. In particular, pancreatic β -cells that are sensitive to oxidative free radicals become damaged. It is well recognized that pancreatic β -cell dysfunction resulting from prolonged exposure to high glucose and/or elevated free fatty acid (FFA) levels

contributes to glucose intolerance and subsequent occurrence of type II diabetes in patients.

Lifestyle modifications, in terms of reduced caloric intake and increased physical activity, can reduce the incidence of type II diabetes up to 58% in the insulin resistant patient population. However, failure of long-term adherence to these modifications limits the potential of this approach. Pharmacological therapies to prevent type II diabetes are an important therapeutic strategy for patients unable to maintain these necessary lifestyle modifications. However, no single anti-diabetic agent can currently be recommended for preventing diabetes. An important distinction to be made here is whether known anti-diabetic agents prevent or delay the onset of diabetes, since the average time period between the onset of β -cell dysfunction and development of diabetes is ten years. This point is illustrated by the fact that several drugs from different classes are on the market today and yet the diabetes population is still growing.

Anti-inflammatory and antioxidant agents may possess potential anti-diabetic properties. Salicylates and aspirin lower glucose levels in patients with diabetes, inducing sometimes hypoglycemic episodes in patients already under anti-diabetic treatments. However, such effects are only reported to be observed when the salicylate dosage is high and associated with undesirable side-effects. Recently, researchers at the Joslin Diabetes Center (Boston USA) reported that treatment of type II diabetes patients with 4 grams/day of salsalate, a non-steroidal anti-inflammatory drug (NSAID) similar to aspirin, lowered fasting glucose and reduced inflammation. Such high doses of NSAID required for chronic treatment of diabetes are known to cause stomach ulceration, bleeding and to have other deleterious effects. These drawbacks effectively preclude the use of anti-inflammatories such as NSAIDs for use as antidiabetic agents.

With regard to antioxidants, research has shown that antioxidant drugs can be used to protect against oxidative stress in experimental models of Type I and Type II diabetes. For instance, nicotinamide, desferrioxamine and N-acetylcysteine have been reported to partially protect islets from immune destruction during low-dose streptozotocin-induced insulinitis, a process in which hydroxyl radicals play an important role. However, there has been no demonstration that antioxidant therapy is sufficient as a treatment for T2DM, nor is there any evidence that antioxidants have any specific

effects in protecting islet cells other than in experimentally-induced diabetes models that are known to use oxidative stress to produce hyperglycemia.

The need for new drugs able to prevent β -cell failure and disease progression remains especially high in pre-diabetic and type II diabetic patients to slow down or stop the ongoing epidemic. Thus, there remains a need in the art for pharmaceutical compositions that are useful for treating metabolic disorders, particularly including type II diabetes.

SUMMARY OF THE INVENTION

This invention relates to pharmaceutical combinations comprising certain combinations of an anti-inflammatory agent and an antioxidant agent. Pharmaceutical combinations of this invention are useful for treating diabetes, particularly Type I and Type II diabetes, as well as diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular disease, inflammatory disorders, nephropathy, neuropathy, retinopathy, β -cell dysfunction, dyslipidemia, LADA, metabolic syndrome, hyperglycemia, insulin resistance, and/or chronic obstructive pulmonary disease in a mammal, particularly a diabetic mammal, and specifically a human patient. Such pharmaceutical combinations are also useful for reducing advanced glycated end products (AGEs), reactive oxygen species (ROS), lipid peroxidation, tissue and/or plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a diabetic mammal, particularly a diabetic mammal, and specifically a human patient. Also, pharmaceutical combinations of this invention are useful for protecting pancreatic β -cells, preventing their impairment or failure and subsequent lower insulin secretion in a mammal, particularly a diabetic mammal and specifically a human patient.

As provided herein, this invention is exemplified by the use of pharmaceutical combinations comprising an antioxidant selected from resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, curcumin, alpha-tocopherol and idebenone in combination with an anti-inflammatory selected from sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac,

ibuprofen, dexibuprofen and dexketoprofen for treating the disorders disclosed herein in a mammal, particularly a diabetic mammal, and specifically a human patient. Particularly-advantageous embodiments of the combinations of this invention are combinations of the antioxidants N-acetylcysteine, alpha-lipoic acid (particularly (R)- alpha-lipoic acid) or
5 taurine with the anti-inflammatories sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), naproxen, paracetamol, diclofenac, dexibuprofen or dexketoprofen. In particular, this invention is exemplified by the use of the pharmaceutical combination comprising N-acetylcysteine (NAC), alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt
10 thereof and an anti-inflammatory for treating the disorders disclosed herein in a mammal, particularly a diabetic mammal and specifically a human patient. Particular examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations
15 of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically
20 acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC,
25 alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal.

Pharmaceutical combinations of this invention, comprising an antioxidant and an anti-inflammatory agent, advantageously show additive or synergistic effects relative to treatment with an antioxidant agent alone or an anti-inflammatory agent alone. Such additive or synergistic effects permit lower dosages of antioxidant and anti-inflammatory
30 agents to be administered while improving the anti-diabetic effect and reducing side effects associated with monotherapy. As provided herein, this invention is exemplified

by the use of pharmaceutical combinations comprising an antioxidant selected from resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, curcumin, alpha-tocopherol and idebenone in combination with an anti-inflammatory selected from sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen and dexketoprofen for treating the disorders disclosed herein in a mammal, particularly a diabetic mammal and specifically a human patient. Particularly-advantageous embodiments of the combinations of this invention are combinations of the antioxidants N-acetylcysteine, alpha-lipoic acid (particularly (R)- alpha-lipoic acid) or taurine with anti-inflammatories sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), naproxen, paracetamol, diclofenac, dexibuprofen or dexketoprofen. In particular, treatment with the pharmaceutical combination of N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and anti-inflammatory compounds including sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen and dexketoprofen, improves anti-diabetic effects while lowering the risk of gastric bleeding, tinnitus or other deleterious side effects associated with anti-inflammatory administration. Particular examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac;

and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal.

This invention thus provides methods for treating diabetes, particularly Type I and Type II diabetes, as well as diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular disease, inflammatory disorders, nephropathy, neuropathy, retinopathy, β -cell dysfunction, dyslipidemia, LADA, metabolic syndrome, hyperglycemia, insulin resistance, and/or chronic obstructive pulmonary disease, in a mammal, particularly a diabetic mammal, and specifically a human patient that includes the step of administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising an anti-inflammatory agent, an antioxidant agent. In accordance with this invention, methods are also provided for reducing AGEs, ROS, lipid peroxidation, tissue and/or plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a mammal, particularly a diabetic mammal, and specifically a human patient that comprise administering to the for treating the disorders disclosed herein in a mammal, particularly a diabetic mammal and specifically a human patient, a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising an anti-inflammatory agent, an antioxidant agent. As provided herein, the methods of this invention for treating diabetes comprise the step of administering a therapeutically-effective amount of a combination of an antioxidant selected from resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, curcumin, alpha-tocopherol and idebenone in combination with an anti-inflammatory selected from sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen and dexketoprofen for treating the disorders disclosed herein in a mammal, particularly a diabetic mammal and specifically a human patient. Particularly-advantageous embodiments of the combinations of this invention are combinations of the antioxidants N-acetylcysteine, alpha-lipoic acid (particularly (R)- alpha-lipoic acid) or

taurine with anti-inflammatories sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), naproxen, paracetamol, diclofenac, dexibuprofen or dexketoprofen. Particular examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal.

The invention also provides pharmaceutically acceptable compositions comprising an anti-inflammatory agent, an antioxidant agent, and at least one pharmaceutically acceptable carrier. The pharmaceutically acceptable compositions of this invention are useful for treating diabetes, particularly Type I and Type II diabetes, as well as diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular disease, inflammatory disorders, nephropathy, neuropathy, retinopathy, β -cell dysfunction, dyslipidemia, LADA, metabolic syndrome, hyperglycemia, insulin resistance, and/or chronic obstructive pulmonary disease, in a for treating the disorders disclosed herein in a mammal, particularly a diabetic mammal and specifically a human patient. The pharmaceutically acceptable compositions are also useful for reducing AGEs, ROS, lipid peroxidation, tissue and plasma $\text{TNF}\alpha$ and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a for treating the disorders disclosed herein in a mammal, particularly a diabetic mammal and specifically a human patient. As provided herein, the

pharmaceutical compositions for treating diabetes comprise a combination of an antioxidant selected from resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, idebenone, probucol and curcumin in combination with an anti-inflammatory selected from sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen and dexketoprofen in amounts that are therapeutically-effective for treating the disorders disclosed herein in a mammal, particularly a diabetic mammal and specifically a human patient. Particularly-advantageous embodiments of the combinations of this invention are combinations of the antioxidants N-acetylcysteine, alpha-lipoic acid (particularly (R)-alpha-lipoic acid) or taurine with anti-inflammatories sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), naproxen, paracetamol, diclofenac, dexibuprofen or dexketoprofen. Particular examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal.

In another aspect, this invention provides uses for pharmaceutical combinations comprising an antioxidant agent, an anti-inflammatory agent, for preparing, or for the manufacture of, a medicament for treating diabetes, particularly Type I and Type II diabetes, as well as diseases and disorders associated with diabetes, including but not

limited to atherosclerosis, cardiovascular disease, inflammatory disorders, nephropathy, neuropathy, retinopathy, β -cell dysfunction, dyslipidemia, LADA, metabolic syndrome, hyperglycemia, insulin resistance, and/or chronic obstructive pulmonary disease in a mammal, particularly a diabetic mammal, and specifically a human patient. This invention also provides uses for pharmaceutical combinations comprising an antioxidant agent, an anti-inflammatory agent, and optionally at least one other anti-diabetic agent, for preparing, or for the manufacture of, a medicament for reducing AGEs, ROS, lipid peroxidation, tissue and/or plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a mammal, particularly a diabetic mammal and specifically a human patient. As provided herein, medicaments for treating diabetes comprise a combination of an antioxidant selected from resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, curcumin, alpha-tocopherol and idebenone in combination with an anti-inflammatory selected from sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen and dexketoprofen in amounts that are therapeutically-effective for treating the disorders disclosed herein in a mammal, particularly a diabetic mammal and specifically a human patient. Particularly-advantageous embodiments of the combinations of this invention are combinations of the antioxidants N-acetylcysteine, alpha-lipoic acid (particularly (R)- alpha-lipoic acid) or taurine with anti-inflammatories sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), naproxen, paracetamol, diclofenac, dexibuprofen or dexketoprofen. Particular examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or

taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal.

. In another aspect, this invention provides uses for pharmaceutically acceptable compositions comprising an anti-inflammatory agent, an antioxidant agent and at least one pharmaceutically acceptable carrier for preparing, or for the manufacture of, a medicament for treating diabetes, particularly Type I and Type II diabetes, as well as diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular disease, inflammatory disorders, nephropathy, neuropathy, retinopathy, β -cell dysfunction, dyslipidemia, LADA, metabolic syndrome, hyperglycemia, insulin resistance, and/or chronic obstructive pulmonary disease in a mammal, particularly a diabetic mammal, and specifically a human patient. This invention also provides uses for pharmaceutically acceptable compositions comprising an anti-inflammatory agent, an antioxidant agent, and at least one pharmaceutically acceptable carrier for the preparation, or manufacture of, a medicament for reducing AGEs, ROS, lipid peroxidation, tissue and/or plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a mammal, particularly a diabetic mammal and specifically a human patient. As provided herein, the pharmaceutical compositions for treating diabetes comprise a combination of an antioxidant selected from resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, curcumin, alpha-tocopherol and idebenone in combination with an anti-inflammatory selected from sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen and dexketoprofen in amounts that are therapeutically-effective for treating the disorders disclosed herein in a mammal, particularly a diabetic mammal and specifically a human patient. Particularly-advantageous embodiments of the combinations of this invention are combinations of the antioxidants N-acetylcysteine, alpha-lipoic acid (particularly (R)- alpha-lipoic acid) or

taurine with anti-inflammatories sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), naproxen, paracetamol, diclofenac, dexibuprofen or dexketoprofen. Particular examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal.

Also provided by the invention are combinations, pharmaceutical compositions, medicaments, and methods of use thereof, comprising advantageous and effecting compositions comprising at least one antioxidant selected from resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, curcumin, alpha-tocopherol and idebenone in combination with one anti-inflammatory selected from sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen and dexketoprofen in amounts that are therapeutically-effective for treating the disorders disclosed herein in a mammal, particularly a diabetic mammal and specifically a human patient. Combinations comprising advantageous pluralities of antioxidants and anti-inflammatory agents fall within the scope of this invention, particularly wherein such combinations show advantages in efficacy, half-life, absorption, solubility, formulation compatability, stability, or synergistic or

complementary effects. The invention also provides embodiments of the combinations as set forth herein optionally comprising an additional antidiabetes drug.

Specific embodiments of this invention will become evident from the following more detailed description of certain preferred embodiments and the claims.

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BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a graphical illustration of the combination of (R) lipoic acid and one of diclofenac, dexibuprofen, or dexketoprofen at protecting pancreatic beta cells. The effect on the combination is shown.

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Figure 2 is a graphical illustration of the combination of salicylate and (R) lipoic acid at protecting pancreatic beta cells.

Figure 3 is a graphical illustration of salicylate alone (0.38, 0.75, and 1.5 mmol/kg) and N-acetylcysteine (NAC) alone (0.38 and 0.75 mmol/kg) at preventing increase of glycemia (hyperglycemia) and reduction of plasma insulin induced by Alloxan-mediated β -cell destruction.

Figure 4 is a graphical illustration of the combination of salicylate (0.38 mmol/kg) and N-acetylcysteine (NAC) (0.19 mmol/kg) at preventing increase of glycemia (hyperglycemia) induced by Alloxan-mediated β -cell destruction.

Figure 5 is a graphical illustration of the combination of salicylate (0.75 mmol/kg) and N-acetylcysteine (NAC) (0.19 mmol/kg) at preventing increase of glycemia (hyperglycemia) induced by Alloxan-mediated β -cell destruction.

Figure 6 is a graphical illustration of the combination of salicylate (0.75 mmol/kg) and N-acetylcysteine (NAC) (0.38 mmol/kg) at preventing increase of glycemia (hyperglycemia) induced by Alloxan-mediated β -cell destruction.

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Figure 7 is a graphical illustration of the combination of salicylate (75 mg/kg/day s.c. infusion) and N-acetylcysteine (0.1% drinking water) at improving fasting glycemia of ob/ob mice after 4 weeks of treatment.

- 5 **Figure 8** is a graphical illustration of salicylate alone (0.75mmol/kg/day i.p.), N-acetylcysteine (NAC) alone (0.75mmols/kg/day i.p.), and the combination of salicylate (0.75mmols/kg/day) and NAC (0.75mmols/kg/day) at reducing Free Fatty Acids and Triglycerides in ob/ob mice after 4 weeks of treatment.
- 10 **Figure 9** is a graphical illustration of the combination of salicylate (75 mg/kg/day s.c. infusion) and (R) lipoic acid (10 mgs/kg/day i.p.) at improving fasting glycemia and glycosylated haemoglobin (HbA1c) of ob/ob mice after 4 weeks of treatment.

- 15 **Figure 10** is a graphical illustration of the combination of salicylate (75 mg/kg/day) and taurine (2.5% drinking water) at improving fasting glycemia of ob/ob mice after 4 weeks of treatment.

DETAILED DESCRIPTION

- This invention provides pharmaceutical combinations comprising an antioxidant agent and an anti-inflammatory agent useful for treating diabetes, particularly Type I and Type II diabetes, as well as diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular disease, inflammatory disorders, nephropathy, neuropathy, retinopathy, β -cell dysfunction, dyslipidemia, LADA, metabolic syndrome, hyperglycemia, insulin resistance, and/or chronic obstructive pulmonary disease in a mammal, particularly a diabetic mammal, and specifically a human patient. The pharmaceutical combinations comprising an antioxidant agent and an anti-inflammatory agent are also useful for reducing AGEs, ROS, lipid peroxidation, tissue and plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a mammal, particularly a diabetic mammal and specifically a human patient. Also, the pharmaceutical combinations comprising an antioxidant agent and an anti-inflammatory agent are useful for protecting
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- 30

pancreatic β -cells, preventing their impairment or failure and subsequent lower insulin secretion in a mammal, particularly a diabetic mammal, and specifically a human patient. Specific, non-limiting examples of pharmaceutical combinations according to the invention are set forth below.

5 As provided herein, the pharmaceutical compositions for treating diabetes comprise a combination of an antioxidant selected from resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, curcumin, alpha-tocopherol and idebenone in combination with an anti-inflammatory selected from sulindac, salicylic acid, diflunisal, 2-hydroxy-4-
10 trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen and dexketoprofen in amounts that are therapeutically-effective for treating the disorders disclosed herein in a mammal, particularly a diabetic mammal and specifically a human patient. Particularly-advantageous embodiments of the combinations of this invention are combinations of the antioxidants N-acetylcysteine,
15 alpha-lipoic acid (particularly (R)- alpha-lipoic acid) or taurine with anti-inflammatories sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), naproxen, paracetamol, diclofenac, dexibuprofen or dexketoprofen. The invention particularly provides pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the
20 group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

 This invention in certain embodiments provides pharmaceutical combinations comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt
25 thereof or taurine, or a pharmaceutically acceptable salt thereof and an anti-inflammatory compound including but not limited to non-steroidal anti-inflammatory drugs (NSAIDs) or a pharmaceutically acceptable salt thereof useful for treating diabetes, particularly Type I and Type II diabetes, as well as diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular disease, inflammatory
30 disorders, nephropathy, neuropathy, retinopathy, β -cell dysfunction, dyslipidemia, LADA, metabolic syndrome, hyperglycemia, insulin resistance, and/or chronic

obstructive pulmonary disease in a mammal, particularly a diabetic mammal, and specifically a human patient. The pharmaceutical combinations comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and an anti-inflammatory compound including but not limited to non-steroidal anti-inflammatory drugs (NSAIDs) or a pharmaceutically acceptable salt thereof are also useful for reducing AGEs, ROS, lipid peroxidation, tissue and plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a mammal, particularly a diabetic mammal, and specifically a human patient. Also, pharmaceutical combinations comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and an anti-inflammatory compound including but not limited to non-steroidal anti-inflammatory drugs (NSAIDs) or a pharmaceutically acceptable salt thereof are useful for protecting pancreatic β -cells, preventing their impairment or failure and subsequent lower insulin secretion in a mammal, particularly a diabetic mammal, and specifically a human patient.

The invention specifically provides such combinations of N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, with an anti-inflammatory compound including sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen and dexketoprofen. Particularly-advantageous embodiments of the combinations of this invention are combinations of the antioxidants N-acetylcysteine, alpha-lipoic acid (particularly (R)- alpha-lipoic acid) or taurine with anti-inflammatories sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), naproxen, paracetamol, diclofenac, dexibuprofen or dexketoprofen. Particular examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable

salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. Each of these combinations can optionally comprise one or more pharmaceutically acceptable carriers, diluents or excipients. The invention particularly provides pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

As set forth herein, certain combinations of antioxidant and anti-inflammatory agents are useful for treating diabetes in a mammal, particularly a diabetic mammal and specifically a human patient. Specific embodiments of such pharmaceutical combinations provided by the invention include pharmaceutical combinations comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-

acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB
5 or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable
10 salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal. Each of these combinations can optionally comprise one or more pharmaceutically acceptable carriers, diluents or excipients. The invention particularly provides pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with
15 one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

Said combinations are useful for treating diabetes, particularly Type I and Type II diabetes, as well as diseases and disorders associated with diabetes, including but not
20 limited to atherosclerosis, cardiovascular disease, inflammatory disorders, nephropathy, neuropathy, retinopathy, β -cell dysfunction, dyslipidemia, LADA, metabolic syndrome, hyperglycemia, insulin resistance, and/or chronic obstructive pulmonary disease in a mammal, particularly a diabetic mammal, and specifically a human patient. The pharmaceutical combinations of the invention are also useful for reducing advanced
25 glycated end products (AGEs), ROS, lipid peroxidation, tissue and plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis. Also, the pharmaceutical combinations of this invention are useful for protecting pancreatic β -cells, preventing their impairment or failure and subsequent lower insulin secretion.

30 It will be understood by the skilled worker that these certain embodiments of the invention are useful for treating a diabetic mammal, preferably a human, whereas other

combinations of antioxidants and anti-inflammatory compounds may not be. The particular combination of antioxidant and anti-inflammatory agent, and the efficacy, half-life, absorption, solubility, formulation compatibility, stability, or synergistic or complementary effects of the combination are determined empirically with each combination of particular agents.

Other aspects of this invention provide methods for treating diabetes, particularly Type I and Type II diabetes, as well as diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular diseases, inflammatory disorders, nephropathy, neuropathy, and retinopathy, in a mammal, particularly a diabetic mammal, and specifically a human patient that includes the step of administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising an antioxidant agent and an anti-inflammatory agent.

In certain embodiments, this invention provides methods for treating metabolic disorders that include pancreatic β -cell dysfunction, dyslipidemia, hyperglycemia, insulin resistance, metabolic syndrome, LADA, type I diabetes, and type II diabetes, in a mammal, particularly a diabetic mammal, and specifically a human patient that includes the step of administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising an antioxidant agent and an anti-inflammatory agent.

In other embodiments, this invention provides methods for reducing advanced glycated end products (AGEs), ROS, lipid peroxidation, tissue and plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a mammal, particularly a diabetic mammal, and specifically a human patient that includes the step of administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising an antioxidant agent and an anti-inflammatory agent.

The invention thus provides methods for treating diabetes, particularly Type I and Type II diabetes, as well as diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular diseases, inflammatory disorders, nephropathy, neuropathy, and retinopathy, in a mammal, particularly a diabetic mammal and particularly a human patient that includes the step of administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising a combination of an antioxidant selected from resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, curcumin, alpha-tocopherol and idebenone in combination with an anti-inflammatory selected from sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen and dexketoprofen in amounts that are therapeutically-effective for treating the disorders disclosed herein in a mammal, particularly a diabetic mammal and specifically a human patient.

In certain embodiments, this invention provides methods for treating metabolic disorders that include pancreatic β -cell dysfunction, dyslipidemia, hyperglycemia, insulin resistance, metabolic syndrome, LADA, type I diabetes, and type II diabetes, in a mammal, particularly a diabetic mammal and particularly a human patient that includes the step of administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising a combination of an antioxidant selected from resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, curcumin, alpha-tocopherol and idebenone in combination with an anti-inflammatory selected from sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen and dexketoprofen in amounts that are therapeutically-effective for treating the disorders disclosed herein in a mammal, particularly a diabetic mammal and specifically a human patient. The invention

particularly provides pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In other embodiments, this invention provides methods for reducing advanced glycated end products (AGEs), ROS, lipid peroxidation, tissue and plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a mammal, particularly a diabetic mammal and specifically a human patient in need of such treatment by administering a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising a combination of an antioxidant selected from resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, curcumin, alpha-tocopherol and idebenone in combination with an anti-inflammatory selected from sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen and dexketoprofen in amounts that are therapeutically-effective for treating the disorders disclosed herein in a mammal, particularly a diabetic mammal and specifically a human patient. The invention particularly provides pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

Specific embodiments of such therapeutic methods provided by the invention include methods for treating diabetes, particularly Type I and Type II diabetes, as well as diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular diseases, inflammatory disorders, nephropathy, neuropathy, insulin resistance and retinopathy, in a mammal, particularly a diabetic mammal, and specifically a human patient that includes the step of administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of

such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. Each of these combinations can optionally comprise one or more pharmaceutically acceptable carriers, diluents or excipients.

Additional specific embodiments of such therapeutic methods provided by the invention include methods for treating metabolic disorders that include pancreatic β -cell

dysfunction, dyslipidemia, hyperglycemia, insulin resistance, metabolic syndrome, LADA, type I diabetes, and type II diabetes, in a mammal, particularly a diabetic mammal, and specifically a human patient that includes the step of administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic

acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. Each of these combinations can optionally comprise one or more pharmaceutically acceptable carriers, diluents or excipients

- 5 Additional specific embodiments of such therapeutic methods provided by the invention include methods for reducing advanced glycated end products (AGEs), ROS, lipid peroxidation, tissue and plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a mammal, particularly a diabetic mammal, and specifically a human patient that includes the step of
- 10 administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and a non-
- 15 steroidal anti-inflammatory drug (NSAID) or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a
- 20 pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically
- 25 acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-
- 30 acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically

acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. Each of these combinations can optionally comprise one or more pharmaceutically acceptable carriers, diluents or excipients

Individual disorders can also be treated using methods provided by the invention, such as diabetes, particularly Type I and Type II diabetes, as well as diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular disease, inflammatory disorders, nephropathy, neuropathy, retinopathy, β -cell dysfunction, dyslipidemia, LADA, metabolic syndrome, hyperglycemia, and/or insulin resistance. As will be understood by the skilled worker, particular combinations of an antioxidant compound and an anti-inflammatory compound are administered to a mammal, particularly a diabetic mammal, and specifically a human patient in need thereof, for the treatment of such individual diseases or disorders. As provided herein, the methods of the invention comprise the step of administering to a mammal, particularly a diabetic mammal and specifically a human patient, a pharmaceutical compositions for treating diabetes comprising a combination of an antioxidant selected from resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, curcumin, alpha-tocopherol and idebenone in combination with an anti-inflammatory selected from sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen and dexketoprofen in amounts that are therapeutically-effective for treating the disorders disclosed herein in a mammal, particularly a diabetic mammal and specifically a human patient. Particular examples of such combinations are NAC and salicylic acid or a pharmaceutically acceptable salt

thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC and paracetamol, NAC and ibuprofen, NAC and salsalate, and NAC and diflunisal. Additional particular embodiments include pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

Thus, in certain embodiments, the invention provides methods for treating pancreatic β -cell dysfunction in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically-effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and an anti-inflammatory compound including but not limited to NSAIDs or a pharmaceutically acceptable salt thereof, wherein specific examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt

thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac,

dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In other embodiments, the invention provides methods for treating dyslipidemia in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, wherein specific examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a

pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In other embodiments, the invention provides methods for treating hyperglycemia in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, wherein specific examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic

acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers

In other embodiments, the invention provides methods for treating insulin resistance in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, wherein specific examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate.

Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen,

naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers

In other embodiments, the invention provides methods for treating metabolic syndrome in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, wherein specific examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a

pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers

In other embodiments, the invention provides methods for treating Type I diabetes in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, wherein specific examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic

acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers

In other embodiments, the invention provides methods for treating Type II diabetes in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, wherein specific examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate.

Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen,

naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers

In other embodiments, the invention provides methods for treating Latent Autoimmune Diabetes of Adulthood (LADA) in a patient that includes the step of
5 administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof,
10 wherein specific examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic
15 acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt
20 thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. In additional particular
25 embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers;
30 (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically

acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and
5 optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with
10 one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers

In other embodiments, the invention provides methods for treating atherosclerosis in a patient that includes the step of administering to the patient in need of such treatment
15 a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, wherein specific examples of such combinations
20 are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and
25 ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a
30 pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic

acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC,
alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. In
additional particular embodiments, pharmaceutical compositions comprising (R)
alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a
5 pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically
acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof,
diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more
pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically
acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and
10 optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a
pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable
salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R)
alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a
pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically
15 acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof,
salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more
pharmaceutically acceptable carriers are administered. The invention particularly
provides such methods using pharmaceutical compositions that comprise lipoic acid,
preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected
20 from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen,
naproxen, and salicylate, optionally formulated together with one or more non-toxic
pharmaceutically acceptable carriers

In other embodiments, the invention provides methods for treating cardiovascular
diseases in a patient that includes the step of administering to the patient in need of such
25 treatment a therapeutically effective amount, particularly a synergistically effective
amount of a pharmaceutical composition of a pharmaceutical combination comprising N-
acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine,
and an anti-inflammatory compound including but not limited to an NSAID or a
pharmaceutically acceptable salt thereof, wherein specific examples of such combinations
30 are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and
salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate.

Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen,

naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers

In other embodiments, the invention provides methods for treating inflammatory disorders in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, wherein specific examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a

pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers

In other embodiments, the invention provides methods for treating chronic obstructive pulmonary disease in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, wherein specific examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC,

alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac;
and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and
diflunisal. In additional particular embodiments, pharmaceutical compositions
comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal
5 or a pharmaceutically acceptable salt thereof, and optionally one or more
pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically
acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and
optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a
pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable
10 salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R)
alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a
pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically
acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof,
naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more
15 pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically
acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and
optionally one or more pharmaceutically acceptable carriers are administered. The
invention particularly provides such methods using pharmaceutical compositions that
comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more
20 anti-inflammatories selected from the group consisting of diflunisal, diclofenac,
dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together
with one or more non-toxic pharmaceutically acceptable carriers

In other embodiments, the invention provides methods for treating nephropathy in
a patient that includes the step of administering to the patient in need of such treatment a
25 therapeutically effective amount, particularly a synergistically effective amount of a
pharmaceutical composition of a pharmaceutical combination comprising N-
acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine,
and an anti-inflammatory compound including but not limited to an NSAID or a
pharmaceutically acceptable salt thereof, wherein specific examples of such combinations
30 are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and
salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate.

Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen,

naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers

In other embodiments, the invention provides methods for treating neuropathy in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, wherein specific examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a

pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In other embodiments, the invention provides methods for treating retinopathy in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, wherein specific examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic

acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In other embodiments, the invention provides methods for treating metabolic disorders in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, wherein specific examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate.

Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen,

naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In other embodiments, the invention provides methods for treating insulin resistance in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, wherein specific examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a

pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In other embodiments, the invention provides methods for reducing advanced glycated end products (AGEs), ROS, lipid peroxidation, tissue and plasma $\text{TNF}\alpha$ and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising thereof, wherein specific examples of such combinations are NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate. Alternative embodiments include but are not limited to combinations of NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and paracetamol; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and ibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and salsalate; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexibuprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and dexketoprofen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and HTB, NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and naproxen; NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diclofenac; NAC, alpha-lipoic acid or a pharmaceutically

acceptable salt thereof or taurine and sulindac; and NAC, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and diflunisal. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for treating pancreatic β -cell dysfunction in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combinations comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically

acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more

pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that
5 comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for treating
10 dyslipidemia in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a
15 pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-
20 acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid
25 or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically
30 acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a

pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for treating hyperglycemia in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt

thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically

acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for treating insulin resistance in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-

lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibupofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for treating metabolic syndrome in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal

or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for treating Type I diabetes in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-

acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and
5 dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable
10 salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine,
15 alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more
20 pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R)
25 alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically
30 acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The

invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together
5 with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for treating Type II diabetes in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-
10 acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically
15 acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine,
20 or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-
25 acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a
30 pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof

thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for treating Latent Autoimmune Diabetes of Adulthood (LADA) in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt

thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable

salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for treating atherosclerosis in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically

acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for treating cardiovascular diseases in a patient that includes the step of administering to the patient

in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a

pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers;

5 (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and

10 optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac,

15 dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for treating inflammatory disorders in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a

20 synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine,

25 or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof;

30 N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and

5 sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more

anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for treating chronic obstructive pulmonary disease in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof

thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for treating nephropathy in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically

acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more

pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that
5 comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for treating
10 neuropathy in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a
15 pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-
20 acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid
25 or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB
30 or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a

pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for treating retinopathy in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt

thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically

acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for treating metabolic disorders in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-

lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for reducing advanced glycated end products (AGEs), ROS, lipid peroxidation, tissue and plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a

pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for reducing free fatty acids in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic

acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically

acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more
5 anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for reducing triglycerides in a patient that includes the step of administering to the patient in need of
10 such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine,
15 alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine,
20 or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine,
25 or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB
30 or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof

thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In particular embodiments, the invention provides methods for treating hyperglycemia in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a

pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof. In additional particular embodiments, pharmaceutical compositions comprising (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diflunisal or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, diclofenac or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexibuprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers;

(R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, dexketoprofen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, naproxen or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers; or (R) alpha-lipoic acid or a pharmaceutically acceptable salt thereof, salicylate or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable carriers are administered. The invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

This invention also provides pharmaceutically acceptable compositions comprising an antioxidant agent, an anti-inflammatory agent, and at least one pharmaceutically acceptable carrier useful for treating diabetes, particularly Type I and Type II diabetes, as well as diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular disease, inflammatory disorders, nephropathy, neuropathy, retinopathy, β -cell dysfunction, dyslipidemia, LADA, metabolic syndrome, hyperglycemia, and/or insulin resistance in a mammal, particularly a diabetic mammal, and specifically a human patient. The pharmaceutically acceptable compositions comprising an antioxidant agent, an anti-inflammatory agent, and at least one pharmaceutically acceptable carrier are also useful for reducing AGEs, ROS, lipid peroxidation, tissue and plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis. Also, the pharmaceutically acceptable compositions comprising an antioxidant, an anti-inflammatory agent, and at least one pharmaceutically acceptable carrier are useful for protecting pancreatic β -cells, preventing their impairment or failure and subsequent lower insulin secretion. As provided herein, the pharmaceutically-acceptable compositions comprise a combination of an antioxidant selected from resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, curcumin, alpha-tocopherol and idebenone in combination with an anti-

inflammatory selected from sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen and dexketoprofen in amounts that are therapeutically-effective for treating the disorders disclosed herein in a mammal, particularly a diabetic mammal and specifically a human patient.

In certain embodiments, this invention provides pharmaceutically acceptable compositions comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof, an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier useful for treating diabetes, particularly Type I and Type II diabetes, as well as diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular disease, inflammatory disorders, nephropathy, neuropathy, retinopathy, β -cell dysfunction, dyslipidemia, LADA, metabolic syndrome, hyperglycemia, and/or insulin resistance. The pharmaceutically acceptable compositions comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof, an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier are also useful for reducing advanced glycated end products (AGEs), ROS, lipid peroxidation, tissue and plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis. Also, the pharmaceutically acceptable compositions comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof, an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier are useful for protecting pancreatic β -cells, preventing their impairment or failure and subsequent lower insulin secretion.

The invention particularly provides such pharmaceutically acceptable compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated

together with one or more non-toxic pharmaceutically acceptable carriers. In certain particular embodiments, this invention provides pharmaceutically acceptable compositions comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier useful for treating diabetes, particularly Type I and Type II diabetes, as well as diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular disease,

inflammatory disorders, nephropathy, neuropathy, retinopathy, β -cell dysfunction, dyslipidemia, LADA, metabolic syndrome, hyperglycemia, and/or insulin resistance.

The pharmaceutically acceptable compositions comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically

5 acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically

acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt

thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a

10 pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt

thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a

pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable

15 salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a

pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt

thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine,

20 alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt

thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a

pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a

25 pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine,

alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable

salt thereof, wherein each such combination further comprises at least one

30 pharmaceutically acceptable carrier are useful for reducing advanced glycated end products (AGEs), ROS, lipid peroxidation, tissue and plasma TNF α and IL6 levels, and

for delaying or preventing cardiovascular complications associated with atherosclerosis. Also, the pharmaceutically acceptable compositions comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof
5 such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a
10 pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt
15 thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a
20 pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt
25 thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier are useful for protecting pancreatic β -cells,
30 preventing their impairment or failure and subsequent lower insulin secretion.

In another aspect, this invention provides methods for treating a plurality of diseases and disorders related to dysregulation of glucose homeostasis in a mammal, particularly a diabetic mammal, and specifically a human patient, and specifically diabetes, particularly Type I and Type II diabetes, and diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular disease, inflammatory disorders, nephropathy, neuropathy, retinopathy, β -cell dysfunction, dyslipidemia, LADA, metabolic syndrome, hyperglycemia, and/or insulin resistance. In this aspect, the methods of this invention include the step of administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising an antioxidant agent, an anti-inflammatory agent, and at least one pharmaceutically acceptable carrier.

The invention thus provides methods for treating atherosclerosis, cardiovascular diseases, inflammatory disorders, nephropathy, neuropathy and retinopathy in a mammal, particularly a diabetic mammal, and specifically a human patient, that include the step of administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising an antioxidant agent, an anti-inflammatory agent, and at least one pharmaceutically acceptable carrier.

This invention also provides methods for treating metabolic disorders that include pancreatic β -cell dysfunction, dyslipidemia, hyperglycemia, insulin resistance, metabolic syndrome, LADA, type I diabetes, and type II diabetes, in a mammal, particularly a diabetic mammal, and specifically a human patient that includes the step of administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising an antioxidant agent, an anti-inflammatory agent, and at least one pharmaceutically acceptable carrier.

The invention further provides methods for reducing advanced glycated end products (AGEs), ROS, lipid peroxidation, tissue and plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a mammal, particularly a diabetic mammal, and specifically a human patient that
5 includes the step of administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising an antioxidant agent, an anti-inflammatory agent, and at least one pharmaceutically acceptable carrier.

10 In certain embodiments of this aspect of the invention are provided methods for treating atherosclerosis, cardiovascular diseases, inflammatory disorders, nephropathy, neuropathy, and retinopathy, in a mammal, particularly a diabetic mammal, and specifically a human patient that includes the step of administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such
15 treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof, an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt
20 thereof, and at least one pharmaceutically acceptable carrier.

In certain embodiments of this aspect of the invention are provided methods for treating metabolic disorders that include pancreatic β -cell dysfunction, dyslipidemia, hyperglycemia, insulin resistance, metabolic syndrome, LADA, type I diabetes, and type
25 II diabetes, in a mammal, particularly a diabetic mammal, and specifically a human patient that includes the step of administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising an N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine,
30 or a pharmaceutically acceptable salt thereof, an anti-inflammatory compound including

but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

In certain embodiments of this aspect of the invention are provided methods for reducing advanced glycated end products (AGEs), ROS, lipid peroxidation, tissue and plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a mammal, particularly a diabetic mammal, and specifically a human patient that includes the step of administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof, an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating atherosclerosis, cardiovascular diseases, inflammatory disorders, nephropathy, neuropathy, and retinopathy, in a mammal, particularly a diabetic mammal, and specifically a human patient that includes the step of administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically

acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and
sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid
or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable
salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-
5 acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine,
or a pharmaceutically acceptable salt thereof and dexibupofen or a pharmaceutically
acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically
acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB
or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a
10 pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt
thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine,
alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a
pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable
salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt
15 thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a
pharmaceutically acceptable salt thereof, wherein each such combination further
comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating metabolic
disorders that include pancreatic β -cell dysfunction, dyslipidemia, hyperglycemia, insulin
20 resistance, metabolic syndrome, LADA, type I diabetes, and type II diabetes, in a
mammal, particularly a diabetic mammal, and specifically a human patient that includes
the step of administering to the mammal, particularly a diabetic mammal, and specifically
a human patient in need of such treatment a therapeutically effective amount, particularly
a synergistically effective amount of a pharmaceutical composition of a
25 pharmaceutically acceptable composition comprising an N-acetylcysteine, alpha-lipoic
acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically
acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof
such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically
acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and
30 ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt
thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a

pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibupofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable salt thereof and diflunisal, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for reducing advanced glycated end products (AGEs), ROS, lipid peroxidation, tissue and plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a mammal, particularly a diabetic mammal, and specifically a human patient that includes the step of administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a

pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

This invention also provides methods for treating pancreatic β -cell dysfunction in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, an anti-inflammatory compound including but not limited to an NSAID or a

pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

This invention also provides methods for treating dyslipidemia in a patient that includes the step of administering to the patient in need of such treatment a
5 therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable
10 carrier.

This invention also provides methods for treating hyperglycemia in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-
15 acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

This invention also provides methods for treating insulin resistance in a patient
20 that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, an anti-inflammatory compound including but not limited to an NSAID or a
25 pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

This invention also provides methods for treating metabolic syndrome in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a
30 pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine,

an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

5 This invention also provides methods for treating Type I diabetes in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, an anti-inflammatory compound including but not limited to an NSAID or a
10 pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

This invention also provides methods for treating Type II diabetes in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a
15 pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

20 This invention also provides methods for treating Latent Autoimmune Diabetes of Adulthood (LADA) in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically
25 acceptable salt thereof or taurine, an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

This invention also provides methods for treating atherosclerosis in a patient that includes the step of administering to the patient in need of such treatment a
30 therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-

acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

5 This invention also provides methods for treating cardiovascular diseases in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine,
10 an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

 This invention also provides methods for treating inflammatory disorders in a patient that includes the step of administering to the patient in need of such treatment a
15 therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable
20 carrier.

 This invention also provides methods for treating chronic obstructive pulmonary disease in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition
25 comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

 This invention also provides methods for treating nephropathy in a patient that
30 includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a

pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

This invention also provides methods for treating neuropathy in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

This invention also provides methods for treating retinopathy in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

This invention also provides methods for treating metabolic disorders in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

This invention also provides methods for reducing advanced glycated end products (AGEs), ROS, lipid peroxidation, tissue and plasma TNF α and IL6 levels, and

for delaying or preventing cardiovascular complications associated with atherosclerosis in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-
5 acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, an anti-inflammatory compound including but not limited to an NSAID or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating pancreatic
10 β -cell dysfunction in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and
15 salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-
20 acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid
25 or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB
30 or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a

pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating dyslipidemia in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a

pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating hyperglycemia in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a

pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating insulin resistance in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a

pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating metabolic syndrome in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a

pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating Type I diabetes in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a

pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating Type II diabetes in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a

pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating Latent Autoimmune Diabetes of Adulthood (LADA) in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-

acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

10 In particular embodiments, this invention provides methods for treating atherosclerosis in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and 15 salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and 20 sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB 30

or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating cardiovascular diseases in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof

acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating inflammatory disorders in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic

acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating chronic obstructive pulmonary disease in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and

dexibupofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating nephropathy in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine,

or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating neuropathy in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine,

or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating retinopathy in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine,

or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating metabolic disorders in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine,

or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for reducing advanced glycated end products (AGEs), ROS, lipid peroxidation, tissue and plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a

pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibupofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for reducing free fatty acids in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid

or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibupofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for reducing triglycerides in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid

or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In particular embodiments, this invention provides methods for treating hyperglycemia in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid

or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier.

In each of the foregoing methods, the invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In another aspect, this invention provides a use for a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and an anti-inflammatory compound including but not limited to an NSAID for preparing, or for the manufacture of, a medicament for treating diabetes, particularly Type I and Type II diabetes, and diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular disease, inflammatory disorders, nephropathy, neuropathy, retinopathy, β -cell dysfunction, dyslipidemia, LADA, metabolic syndrome, hyperglycemia, insulin resistance, and/or chronic obstructive pulmonary disease, in a mammal, particularly a diabetic mammal,

and specifically a human patient. This invention also provides a use for pharmaceutical combinations comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and an anti-inflammatory compound including but not limited to an NSAID, for preparing, or for the manufacture of, a medicament for reducing
5 AGEs, ROS, lipid peroxidation, tissue and/or plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a mammal, particularly a diabetic mammal, and specifically a human patient.

In particular embodiments, this invention provides a use for a pharmaceutical combination comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically
10 acceptable salt thereof or taurine, and sodium salicylate, for preparing, or for the manufacture of, a medicament for treating diabetes, particularly Type I and Type II diabetes, and diseases and disorders associated with diabetes, including but not limited to atherosclerosis, cardiovascular disease, inflammatory disorders, nephropathy, neuropathy, retinopathy, β -cell dysfunction, dyslipidemia, LADA, metabolic syndrome,
15 hyperglycemia, insulin resistance, and/or chronic obstructive pulmonary disease, in a mammal, particularly a diabetic mammal, and specifically a human patient. This invention also provides a use for a pharmaceutical combinations comprising N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, and sodium salicylate, for preparing, or for the manufacture of, a medicament for
20 reducing AGEs, ROS, lipid peroxidation, tissue and/or plasma TNF α and IL6 levels, and for delaying or preventing cardiovascular complications associated with atherosclerosis in a mammal, particularly a diabetic mammal, and specifically a human patient.

In further particular embodiments, this invention provides a use for a pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid
25 or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine,
30 or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically

acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and
salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid
or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable
salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine,
5 alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a
pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically
acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically
acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and
dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic
10 acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically
acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-
acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine,
or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically
acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically
15 acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and
diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic
acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically
acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof,
wherein each such combination further comprises at least one pharmaceutically
20 acceptable carrier, for preparing, or for the manufacture of, a medicament for treating
diabetes, particularly Type I and Type II diabetes, and diseases and disorders associated
with diabetes, including but not limited to atherosclerosis, cardiovascular disease,
inflammatory disorders, nephropathy, neuropathy, retinopathy, β -cell dysfunction,
dyslipidemia, LADA, metabolic syndrome, hyperglycemia, insulin resistance, and/or
25 chronic obstructive pulmonary disease, in a mammal, particularly a diabetic mammal,
and specifically a human patient. This invention also provides a use for a
pharmaceutically acceptable composition comprising N-acetylcysteine, alpha-lipoic acid
or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable
salt thereof and salicylic acid or a pharmaceutically acceptable salt thereof such as
30 sodium salicylate; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable
salt thereof or taurine, or a pharmaceutically acceptable salt thereof and ibuprofen; N-

acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and paracetamol or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and
5 salsalate or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and sulindac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexketoprofen or a pharmaceutically
10 acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and dexibuprofen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and HTB or a pharmaceutically acceptable salt thereof; N-
15 acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and naproxen or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diclofenac or a pharmaceutically acceptable salt thereof; N-acetylcysteine, alpha-lipoic
20 acid or a pharmaceutically acceptable salt thereof or taurine, or a pharmaceutically acceptable salt thereof and diflunisal or a pharmaceutically acceptable salt thereof, wherein each such combination further comprises at least one pharmaceutically acceptable carrier, for preparing, or for the manufacture of, a medicament for reducing AGEs, ROS, lipid peroxidation, tissue and/or plasma TNF α and IL6 levels, and for
25 delaying or preventing cardiovascular complications associated with atherosclerosis in a mammal, particularly a diabetic mammal, and specifically a human patient.

In each of the foregoing methods, the invention particularly provides such methods using pharmaceutical compositions that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group
30 consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and

salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers.

In another aspect, this invention provides methods for treating any of the
5 aforementioned diseases and disorders: adipocyte dysfunction related diseases,
carbohydrate metabolism related diseases, vascular diseases, neurodegenerative diseases,
cancers, arthritis, osteoarthritis, spondylitis, bone resorption diseases, sepsis, septic
shock, chronic pulmonary inflammatory disease, fever, periodontal diseases, ulcerative
colitis, pyresis, Alzheimer's disease, Parkinson's diseases, cystic fibrosis, dysfunctions of
10 the immune system, stroke, multiple sclerosis, migraine, pain, inflammatory eye
conditions including uveitis, glaucoma and conjunctivitis, degenerative bone or joint
conditions including osteoarthritis, rheumatoid arthritis, rheumatoid spondylitis, gouty
arthritis ankylosing spondylitis, psoriatic arthritis and other arthritic conditions, as well as
inflamed joints, chronic inflammatory skin conditions, including allergic lesions, lichen
15 planus, pityriasis rosea, eczema, psoriasis, and dermatitis, diseases and disorders of the
gastrointestinal tract, including inflammatory bowel disease, Crohn's disease, atrophic
gastritis, gastritis varioliforme, ulcerative colitis, coeliac disease, regional ileitis, peptic
ulceration, particularly irritable bowel syndrome, reflux oesophagitis, and damage to the
gastrointestinal tract resulting from infections, for example, by *Helicobacter pylori*,
20 inflammatory lung disorders such as asthma, bronchitis, particularly chronic obstructive
pulmonary disease, farmer's lung, acute respiratory distress syndrome; bacteraemia,
endotoxaemia (septic shock), aphthous ulcers, gingivitis, pyresis, particularly pain,
including inflammatory pain, neuropathic pain, acute pain or pain of a central origin;
meningitis and pancreatitis, and other conditions associated with inflammation, central
25 nervous system inflammatory conditions and diseases, including ischaemia-reperfusion
injury associated with ischemic stroke; vascular diseases, such as atheromatous and
nonatheromatous, ischemic heart disease, and Raynaud's Disease and Phenomenon in a
mammal, particularly a diabetic mammal, and specifically a human patient comprising
administering to the mammal, particularly a diabetic mammal, and specifically a human
30 patient in need of such treatment a therapeutically effective amount, particularly a
synergistically effective amount of a pharmaceutical composition of a pharmaceutical

combination comprising an antioxidant agent, an anti-inflammatory agent, and optionally at least one other anti-diabetic agent. In certain embodiments, this invention provides uses for pharmaceutical combination for preparing, or for the manufacture of, a medicament for treating the diseases/disorders listed above.

5 In another aspect, this invention provides methods for treating any of the aforementioned diseases and disorders adipocyte dysfunction related diseases, carbohydrate metabolism related diseases, vascular diseases, neurodegenerative diseases, cancers, arthritis, osteoarthritis, spondylitis, bone resorption diseases, sepsis, septic shock, chronic pulmonary inflammatory disease, fever, periodontal diseases, ulcerative
10 colitis, pyresis, Alzheimer's disease, Parkinson's diseases, cystic fibrosis, dysfunctions of the immune system, stroke, multiple sclerosis, migraine, pain, inflammatory eye conditions including uveitis, glaucoma and conjunctivitis, degenerative bone or joint conditions including osteoarthritis, rheumatoid arthritis, rheumatoid spondylitis, gouty arthritis ankylosing spondylitis, psoriatic arthritis and other arthritic conditions, as well as
15 inflamed joints, chronic inflammatory skin conditions, including allergic lesions, lichen planus, pityriasis rosea, eczema, psoriasis, and dermatitis, diseases and disorders of the gastrointestinal tract, including inflammatory bowel disease, Crohn's disease, atrophic gastritis, gastritis varioliforme, ulcerative colitis, coeliac disease, regional ileitis, peptic ulceration, particularly irritable bowel syndrome, reflux oesophagitis, and damage to the
20 gastrointestinal tract resulting from infections, for example, by *Helicobacter pylori*, inflammatory lung disorders such as asthma, bronchitis, particularly chronic obstructive pulmonary disease, farmer's lung, acute respiratory distress syndrome; bacteraemia, endotoxaemia (septic shock), aphthous ulcers, gingivitis, pyresis, particularly pain, including inflammatory pain, neuropathic pain, acute pain or pain of a central origin;
25 meningitis and pancreatitis, and other conditions associated with inflammation, central nervous system inflammatory conditions and diseases, including ischaemia-reperfusion injury associated with ischemic stroke; vascular diseases, such as atheromatous and nonatheromatous, ischemic heart disease, and Raynaud's Disease and Phenomenon in a mammal, particularly a diabetic mammal, and specifically a human patient comprising
30 administering to the mammal, particularly a diabetic mammal, and specifically a human patient in need of such treatment a therapeutically effective amount, particularly a a

synergistically effective amount of a pharmaceutical composition of a pharmaceutically acceptable composition comprising an antioxidant agent, an anti-inflammatory agent, optionally at least one other anti-diabetic agent, and at least one pharmaceutically acceptable carrier. In certain embodiments, this invention provides uses for
5 pharmaceutical combination for preparing, or for the manufacture of, a medicament for treating the diseases/disorders listed above.

The antioxidant agents and anti-inflammatory of this invention may be administered to a mammal, particularly a diabetic mammal, and specifically a human
10 patient combined as a pharmaceutical combination or as a pharmaceutical composition. This invention also includes pharmaceutical combinations wherein the antioxidant and anti-inflammatory agents are administered at the same time, or nearly the same time, as separate agents. Combinations of antioxidants and anti-inflammatory agents according to this invention are provided in ratios of from about 30:1 to about 1:30, alternatively about
15 20:1 to about 1:20 and in further alternatives from about 10:1 to about 1:10.

The term "anti-diabetic agent" as used herein means any one of metformin, glyburide, glimepiride, glipyrider, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, isaglitazone, repaglinide, and nateglinide. In accordance with this invention, the pharmaceutical combinations or
20 pharmaceutically acceptable compositions of this invention optionally include at least one anti-diabetic agent. Preferably, one anti-diabetic agent is optionally combined with the pharmaceutical combinations and pharmaceutically acceptable compositions of this invention.

The term "anti-inflammatory agent" as used herein means any one of sulindac,
25 salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen and dexketoprofen.

The term "antioxidant agent" as used herein means any one of resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, curcumin, alpha-tocopherol and idebenone.

30 The term "N-acetylcysteine, or NAC" as used herein includes esters and amides of N-acetylcysteine. Representative esters and amides of N-acetylcysteine, include, but are

not limited to, methyl N-acetylcysteinate, ethyl N-acetylcysteinate, isopropyl N-acetylcysteinate, propyl N-acetylcysteinate, tert-butyl N-acetylcysteinate, and N²-acetylcysteinamide. Further, the term "N-acetylcysteine" encompasses the (L) form, the (D) form, and mixtures or racemates thereof, wherein the (L) form is the preferred
 5 form of N-acetylcysteine .

The term "NSAID" as used herein means non-steroidal anti-inflammatory drug. NSAID agents are a subset of anti-inflammatory agents and include any one of the following sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen and
 10 dexketoprofen.

Combinations according to the invention include at least any anti-oxidant that is N-acetylcysteine, resveratrol, silibinin, α -lipoic acid, particularly (R)- α -lipoic acid, idebenone, taurine, probucol, curcumin, pterostilbene or α -tocopherol, with at least any anti-inflammatory that is sulindac, salicylic acid or salts thereof, diflunisal, HTB,
 15 salsalate, naproxen, paracetamol, dexibuprofen, dexketoprofen, ibuprofen, or diclofenac. Particularly-advantageous embodiments of the combinations of this invention are combinations of the antioxidants N-acetylcysteine, alpha-lipoic acid (particularly (R)-alpha-lipoic acid) or taurine with anti-inflammatories sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), naproxen, paracetamol, diclofenac,
 20 dexibuprofen or dexketoprofen. Particular embodiments of the combinations of the invention include the following:

TABLE I

25 Antioxidants and anti-inflammatories screened at four-five different concentrations in the INS-1E β -cell assay (set forth below) showing concentrations that reduced apoptosis promoted by high (11 mM) glucose and high (0.4 mM) palmitate concentrations

Compound	Concentration range	Combination concentrations
Antioxidants		
N-acetylcysteine	0.1 – 3mM	1mM, 1.5mM
Taurine	0.1 – 3mM	3mM

Compound	Concentration range	Combination concentrations
α -lipoic acid	0.01mM – 1mM	100, 250, 500 μ M
Curcumine	0.001-0.5mM	N.D.
Silibinin	0.001-0.5mM	N.D.
Idebenone	0.01mM – 1mM	50 μ M
Pterostilbene	0.01mM – 1mM	10 μ M
α -tocopherol	0.01mM – 1mM	1mM
Resveratrol	0.01mM – 1mM	10, 50 μ M
Anti-inflammatories		
Salicylate	0.01mM – 1mM	100, 250, 500 μ M
Paracetamol	0.01mM – 1mM	250 μ M
HTB	0.01mM – 1mM	50 μ M
Dexibuprofen	0.01mM – 1mM	100, 250, 500 μ M
Diflunisol	0.01mM – 1mM	50, 100 μ M
Naproxen	0.01mM – 1mM	100, 250, 500 μ M
Dexketoprofen	0.01mM – 1mM	100, 250, 500 μ M
Diclofenac	0.01mM – 1mM	100, 150 μ M
Sulindac	0.01mM – 1mM	250 μ M

Particular combinations providing at least a 30% inhibition of apoptosis in the INS-1E β -cell assay set forth below included:

- α -lipoic acid (0.1 mM) and salicylate (0.5-1mM)
- 5 • α -lipoic acid (0.1 mM) and dexibuprofen (0.5-1mM)
- α -lipoic acid (0.1 mM) and dexketoprofen (0.5-1mM)
- α -lipoic acid (0.1 mM) and diclofenac (0.1mM)

Particular combinations providing protection against insulin resistance in mouse 3T3-L1 adipocytes as described below include:

- 10 • N-acetylcysteine (1.5mM) and diflunisal (25 μ M)
- N-acetylcysteine (1.5mM) and diclofenac (25 μ M)
- N-acetylcysteine (1.5mM) and dexketoprofen (25 μ M)

- N-acetylcysteine (1.5mM) and dexibuprofen (100 μ M)
- N-acetylcysteine (1.5mM) and salicylate (50 μ M)

Pharmaceutical Compositions

5 This invention also provides pharmaceutical compositions that comprise compounds of this invention formulated together with one or more non-toxic pharmaceutically acceptable carriers. The pharmaceutical compositions may be specially formulated for oral administration in solid or liquid form, for parenteral injection, or for rectal administration. The invention particularly provides pharmaceutical compositions
10 that comprise lipoic acid, preferably (R) lipoic acid, in combination with one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate, optionally formulated together with one or more non-toxic pharmaceutically acceptable carriers. The pharmaceutical compositions may be specially formulated for oral administration in solid or liquid form,
15 for parenteral injection, or for rectal administration.

 The term "pharmaceutically acceptable carrier" as used herein means a non-toxic, inert solid, semi-solid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type. Some examples of materials which can serve as pharmaceutically
20 acceptable carriers are sugars such as lactose, glucose and sucrose; starches such as corn starch and potato starch; cellulose and its derivatives such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; powdered tragacanth; malt; gelatin; talc; excipients such as cocoa butter and suppository waxes; oils such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; glycols; such a propylene
25 glycol; esters such as ethyl oleate and ethyl laurate; agar; buffering agents such as magnesium hydroxide and aluminum hydroxide; alginic acid; pyrogen-free water; isotonic saline; Ringer's solution; ethyl alcohol, and phosphate buffer solutions, as well as other non-toxic compatible lubricants such as sodium lauryl sulfate and magnesium stearate, as well as coloring agents, releasing agents, coating agents, sweetening,
30 flavoring and perfuming agents, preservatives and antioxidants can also be present in the composition, according to the judgment of the formulator. This invention provides

pharmaceutical compositions which comprise compounds of the invention formulated together with one or more non-toxic pharmaceutically acceptable carriers. The pharmaceutical compositions can be formulated for oral administration in solid or liquid form, for parenteral injection or for rectal administration.

5 The pharmaceutical compositions of this invention can be administered to humans (patients) and other mammals orally, rectally, parenterally, intracisternally, intraperitoneally, topically (as by powders, ointments or drops), buccally or as an oral or nasal spray. The term "parenterally," as used herein, refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous,
10 intraarticular injection and infusion.

 Pharmaceutical compositions of this invention for parenteral injection comprise pharmaceutically acceptable sterile aqueous or nonaqueous solutions, dispersions, suspensions or emulsions and sterile powders for reconstitution into sterile injectable solutions or dispersions. Examples of suitable aqueous and nonaqueous carriers, diluents,
15 solvents or vehicles include water, ethanol, polyols (propylene glycol, polyethylene glycol, glycerol, and the like), suitable mixtures thereof, vegetable oils (such as olive oil) and injectable organic esters such as ethyl oleate. Proper fluidity may be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersions, and by the use of surfactants.

20 These compositions may also contain adjuvants such as preservative agents, wetting agents, emulsifying agents, and dispersing agents. Prevention of the action of microorganisms may be ensured by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, and the like. It may also be desirable to include isotonic agents, for example, sugars, sodium chloride and the like.
25 Prolonged absorption of the injectable pharmaceutical form may be brought about by the use of agents delaying absorption, for example, aluminum monostearate and gelatin.

 In some cases, in order to prolong the effect of a drug, it is often desirable to slow the absorption of the drug from subcutaneous or intramuscular injection. This may be accomplished by the use of a liquid suspension of crystalline or amorphous material with
30 poor water solubility. The rate of absorption of the drug then depends upon its rate of dissolution which, in turn, may depend upon crystal size and crystalline form.

Alternatively, delayed absorption of a parenterally administered drug form is accomplished by dissolving or suspending the drug in an oil vehicle.

Suspensions, in addition to the active compounds, may contain suspending agents, as, for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan
5 esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar, tragacanth, and mixtures thereof.

If desired, and for more effective distribution, the compounds of this invention can be incorporated into slow-release or targeted-delivery systems such as polymer matrices, liposomes, and microspheres. They may be sterilized, for example, by filtration
10 through a bacteria-retaining filter or by incorporation of sterilizing agents in the form of sterile solid compositions, which may be dissolved in sterile water or some other sterile injectable medium immediately before use.

The active compounds can also be in micro-encapsulated form, if appropriate, with one or more pharmaceutically acceptable carriers as noted above. The solid dosage
15 forms of tablets, dragees, capsules, pills, and granules can be prepared with coatings and shells such as enteric coatings, release controlling coatings and other coatings well known in the pharmaceutical formulating art. In such solid dosage forms the active compound can be admixed with at least one inert diluent such as sucrose, lactose, or starch. Such dosage forms may also comprise, as is normal practice, additional
20 substances other than inert diluents, e.g., tableting lubricants and other tableting aids such as a magnesium stearate and microcrystalline cellulose. In the case of capsules, tablets and pills, the dosage forms may also comprise buffering agents. They may optionally contain opacifying agents and can also be of such composition that they release the active ingredient(s) only, or preferentially, in a certain part of the intestinal tract in a delayed
25 manner. Examples of embedding compositions which can be used include polymeric substances and waxes.

Injectable depot forms are made by forming microencapsulated matrices of the drug in biodegradable polymers such as polylactide-polyglycolide. Depending upon the ratio of drug to polymer and the nature of the particular polymer employed, the rate of
30 drug release can be controlled. Examples of other biodegradable polymers include poly(orthoesters) and poly(anhydrides). Depot injectable formulations are also prepared

by entrapping the drug in liposomes or microemulsions which are compatible with body tissues.

The injectable formulations can be sterilized, for example, by filtration through a bacterial-retaining filter or by incorporating sterilizing agents in the form of sterile solid
5 compositions which can be dissolved or dispersed in sterile water or other sterile injectable medium just prior to use.

Injectable preparations, for example, sterile injectable aqueous or oleaginous suspensions may be formulated according to the known art using suitable dispersing or wetting agents and suspending agents. The sterile injectable preparation may also be a
10 sterile injectable solution, suspension or emulsion in a nontoxic, parenterally acceptable diluent or solvent such as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution, U.S.P. and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil can be employed
15 including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid are used in the preparation of injectables.

Solid dosage forms for oral administration include capsules, tablets, pills, powders, and granules. In such solid dosage forms, the active compound is mixed with at least one inert pharmaceutically acceptable carrier such as sodium citrate or calcium
20 phosphate and/or a) fillers or extenders such as starches, lactose, sucrose, glucose, mannitol, and salicylic acid; b) binders such as carboxymethylcellulose, alginates, gelatin, polyvinylpyrrolidinone, sucrose, and acacia; c) humectants such as glycerol; d) disintegrating agents such as agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates, and sodium carbonate; e) solution retarding agents such as
25 paraffin; f) absorption accelerators such as quaternary ammonium compounds; g) wetting agents such as cetyl alcohol and glycerol monostearate; h) absorbents such as kaolin and bentonite clay; and i) lubricants such as talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, and mixtures thereof. In the case of capsules, tablets and pills, the dosage form may also comprise buffering agents.

DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 2
CONTENANT LES PAGES 1 À 128

NOTE : Pour les tomes additionels, veuillez contacter le Bureau canadien des brevets

JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

THIS IS VOLUME 1 OF 2
CONTAINING PAGES 1 TO 128

NOTE: For additional volumes, please contact the Canadian Patent Office

NOM DU FICHER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

We claim:

1. A pharmaceutical combination comprising a therapeutically-effective amount of an antioxidant agent and an anti-inflammatory agent.

5

2. A pharmaceutical combination of claim 1 further comprising a therapeutically-effective amount of at least one other anti-diabetic agent.

3. The combination according to claim 1 or 2 wherein the antioxidant agent is
10 resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, idebenone or curcumin.

4. The combination according to any one of claims 1 to 3 wherein the anti-inflammatory agent is sulindac, salicylic acid, diflunisal, 2-hydroxy-4-
15 trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen or dexketoprofen.

5. The combination according to claim 1 or 2 wherein the antioxidant is N-acetyl cysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and the
20 anti-inflammatory agent is sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen or dexketoprofen.

6. A pharmaceutically acceptable composition comprising a therapeutically-effective
25 amount of an antioxidant agent, an anti-inflammatory agent, and at least one pharmaceutically acceptable carrier.

7. A pharmaceutically acceptable composition of claim 6 further comprising a therapeutically-effective amount of at least one other anti-diabetic agent.

30

8. The pharmaceutically acceptable composition according to claim 6 or 7 wherein the antioxidant agent is resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, idebenone or curcumin .

5

9. The pharmaceutically acceptable composition according to any one of claims 6 to 8 wherein the anti-inflammatory agent is sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen or dexketoprofen.

10

10. The pharmaceutically acceptable composition according to claim 6 or 7 wherein the antioxidant is N-acetyl cysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and the anti-inflammatory agent is sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen or dexketoprofen.

15

11. A method of treating a metabolic disorder in a patient comprising administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising an antioxidant agent and an anti-inflammatory agent.

20

12. The method according to claim 11 wherein the pharmaceutical composition further comprises at least one other anti-diabetic agent

13. The method according to claim 11 or 12 wherein the pharmaceutical combination comprises an antioxidant agent that is resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, idebenone or curcumin.

25

14. The method according to any one of claims 11 to 13 wherein the pharmaceutical combination comprises an anti-inflammatory agent that is sulindac, salicylic acid,

30

diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen or dexketoprofen.

15. The method according to claim 11 or 12 wherein the pharmaceutical composition
5 comprises an antioxidant agent that is N-acetyl cysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and an anti-inflammatory agent that is sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen or dexketoprofen.

10 16. The method according to any one of claims 11 to 15 wherein the metabolic disorder is Type I diabetes.

17. The method according to any one of claims 11 to 15 wherein the metabolic disorder is Type II diabetes.

15

18. The method according to any one of claims 11 to 15 wherein the metabolic disorder is hyperglycemia.

19. The method according to any one of claims 11 to 15 wherein the metabolic
20 disorder is insulin resistance.

20. The method according to any one of claims 11 to 15 wherein the metabolic disorder is pancreatic β -cell.

25 21. The method according to any one of claims 11 to 15 wherein the metabolic disorder is Latent Autoimmune Diabetes of Adulthood (LADA).

22. The method according to any one of claims 11 to 15 wherein the metabolic disorder is dyslipidemia.

30

23. The method according to any one of claims 11 to 15 wherein the metabolic disorder is metabolic syndrome.

24. A method of treating a metabolic disorder in a patient comprising administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising an antioxidant agent, an anti-inflammatory agent, and at least one pharmaceutically acceptable carrier.

25. The method according to claim 24 wherein the pharmaceutical composition further comprises at least one other anti-diabetic agent

26. The method according to claim 24 or 25 wherein the pharmaceutical combination comprises an antioxidant agent that is resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, idebenone or curcumin.

27. The method according to any one of claims 24 to 26 wherein the pharmaceutical combination comprises an anti-inflammatory agent that is sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen or dexketoprofen.

28. The method according to claim 24 or 25 wherein the pharmaceutical composition comprises an antioxidant agent that is N-acetyl cysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and an anti-inflammatory agent that is sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen or dexketoprofen.

29. The method according to any one of claims 24 to 28 wherein the metabolic disorder is Type I diabetes.

30. The method according to any one of claims 24 to 28 wherein the metabolic disorder is Type II diabetes.

5 31. The method according to any one of claims 24 to 28 wherein the metabolic disorder is hyperglycemia.

32. The method according to any one of claims 24 to 28 wherein the metabolic disorder is insulin resistance.

10 33. The method according to any one of claims 24 to 28 wherein the metabolic disorder is pancreatic β -cell dysfunction.

34. The method according to any one of claims 24 to 28 wherein the metabolic disorder is Latent Autoimmune Diabetes of Adulthood (LADA).

15

35. The method according to any one of claims 24 to 28 wherein the metabolic disorder is dyslipidemia.

20 36. The method according to any one of claims 24 to 28 wherein the metabolic disorder is metabolic syndrome.

25 37. A method of treating chronic obstructive pulmonary disease in a patient comprising administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising an antioxidant agent, an anti-inflammatory agent.

38. The method according to claim 37 wherein the antioxidant is N-acetylcysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine.

30

39. The method according to claim 37 or 38 wherein the anti-inflammatory is sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen or dexketoprofen.

5 40. A method of treating chronic obstructive pulmonary disease in a patient comprising administering to the patient in need of such treatment a therapeutically effective amount, particularly a synergistically effective amount of a pharmaceutical composition of a pharmaceutical combination comprising an antioxidant agent, an anti-inflammatory agent, optionally at least one other anti-diabetic agent, and at least one
10 pharmaceutically acceptable carrier.

41. The method according to claim 40 wherein the pharmaceutical composition further comprises at least one other anti-diabetic agent

15 42. The method according to claim 40 or 41 wherein the pharmaceutical combination comprises an antioxidant agent that is resveratrol, silibinin, alpha-lipoic acid or a pharmaceutically acceptable salt thereof, pterostilbene, N-acetyl cysteine, taurine, probucol, idebenone or curcumin.

20 43. The method according to any one of claims 40 to 42 wherein the pharmaceutical combination comprises an anti-inflammatory agent that is sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen or dexketoprofen.

25 44. The method according to claims 40 or 41 wherein the pharmaceutical composition comprises an antioxidant agent that is N-acetyl cysteine, alpha-lipoic acid or a pharmaceutically acceptable salt thereof or taurine and an anti-inflammatory agent that is sulindac, salicylic acid, diflunisal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB), salsalate, naproxen, paracetamol, diclofenac, ibuprofen, dexibuprofen or dexketoprofen.

30

45. A method of treating or preventing one or more metabolic disorders in a patient comprising administering to the patient in need of such treatment a therapeutically effective amount of a pharmaceutical composition comprising:

(a) (R) alpha-lipoic acid;

5 (b) one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate; and

(c) optionally one or more pharmaceutically acceptable carriers;

wherein the metabolic disorders are selected from the group consisting of type II diabetes, insulin resistance, pancreatic beta-cell dysfunction, and hyperglycemia.

10

46. The method according to claim 45 wherein the anti-inflammatory is diflunisal.

47. The method according to claim 45 wherein the anti-inflammatory is diclofenac.

15 48. The method according to claim 45 wherein the anti-inflammatory is dexibuprofen.

49. The method according to claim 45 wherein the anti-inflammatory is dexketoprofen.

20 50. The method according to claim 45 wherein the anti-inflammatory is naproxen.

51. The method according to claim 45 wherein the anti-inflammatory is salicylate.

25 52. A method of treating or preventing one or more metabolic disorders in a patient comprising administering to the patient in need of such treatment a synergistically effective amount of a pharmaceutical composition comprising:

(a) (R) alpha-lipoic acid;

(b) one or more anti-inflammatories selected from the group consisting of diflunisal, diclofenac, dexibuprofen, dexketoprofen, naproxen, and salicylate; and

30 (c) optionally one or more pharmaceutically acceptable carriers;

wherein the metabolic disorders are selected from the group consisting of type II diabetes, insulin resistance, pancreatic beta-cell dysfunction, and hyperglycemia.

53. The method according to claim 52 wherein the anti-inflammatory is diflunisal.

5

54. The method according to claim 53 wherein the anti-inflammatory is diclofenac.

55. The method according to claim 53 wherein the anti-inflammatory is dexibuprofen.

10 56. The method according to claim 53 wherein the anti-inflammatory is dexketoprofen.

57. The method according to claim 53 wherein the anti-inflammatory is naproxen.

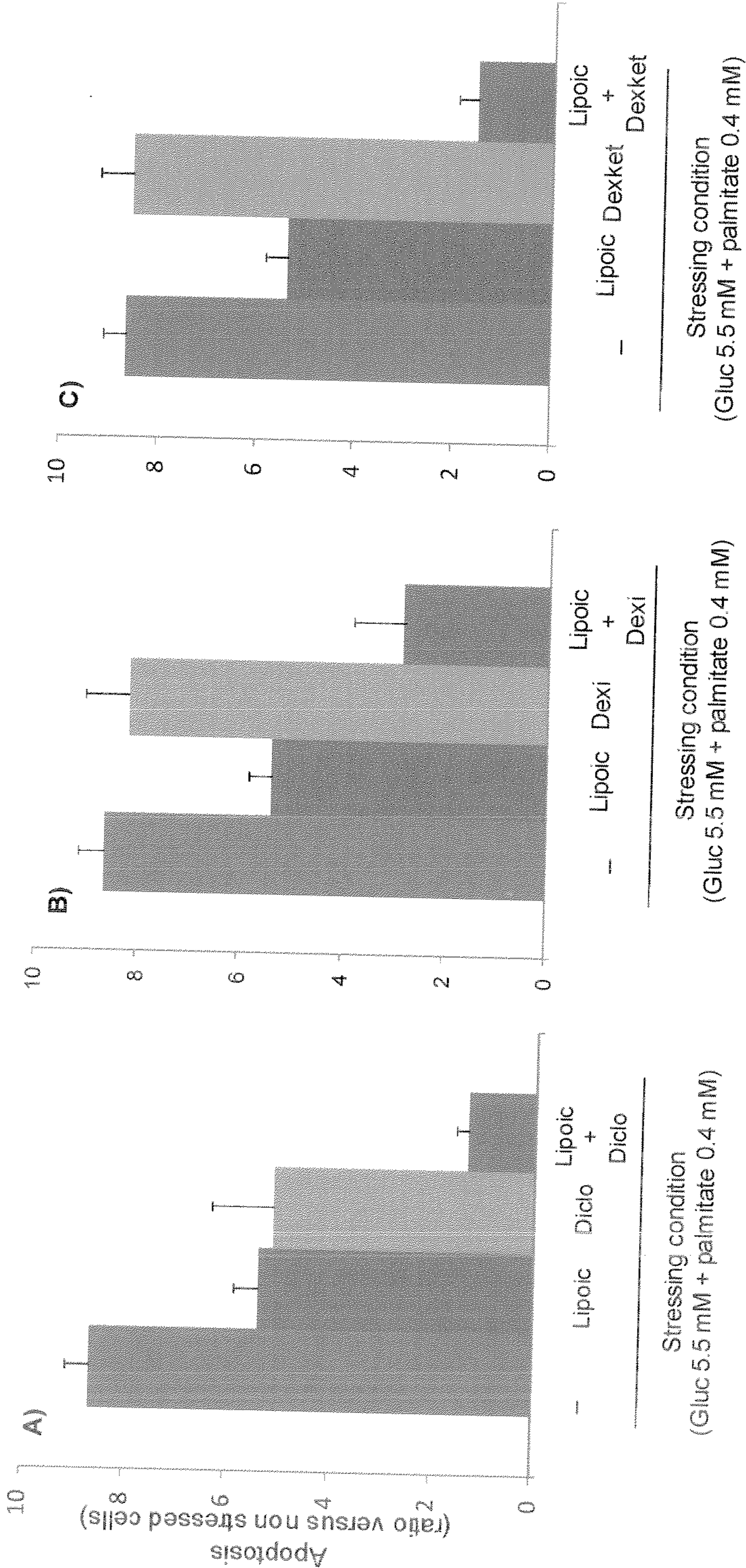
15 58. The method according to claim 53 wherein the anti-inflammatory is salicylate.

59. A pharmaceutical combination according to any one of claims 1 to 5 or a pharmaceutical acceptable composition according to any one of claims 6 to 10 for use in the treatment of a metabolic disorder.

20

60. A pharmaceutical combination or pharmaceutical acceptable composition according to claim 59 wherein the metabolic disorder is Type I diabetes, Type II diabetes, hyperglycemia, insulin resistance, pancreatic β -cell, Latent Autoimmune Diabetes of Adulthood (LADA), dyslipidemia, or metabolic syndrome or for the treatment of chronic
25 obstructive pulmonary disease.

The combination of (R) Lipoic Acid and diclofenac, dexibuprofen, or dexketoprofen protects beta-cells from cellular stress implicated in diabetes related pancreas dysfunction



INS-1E β -cells were pretreated overnight with lipoic acid 100 μ M, diclofenac 100 μ M (Diclo), dexibuprofen 500 μ M (Dexi) and Dexketoprofen 500 μ M (Dexket) alone or in combination as indicated in graphics A, B and C.

Figure 1

In vitro Beta-cell protection

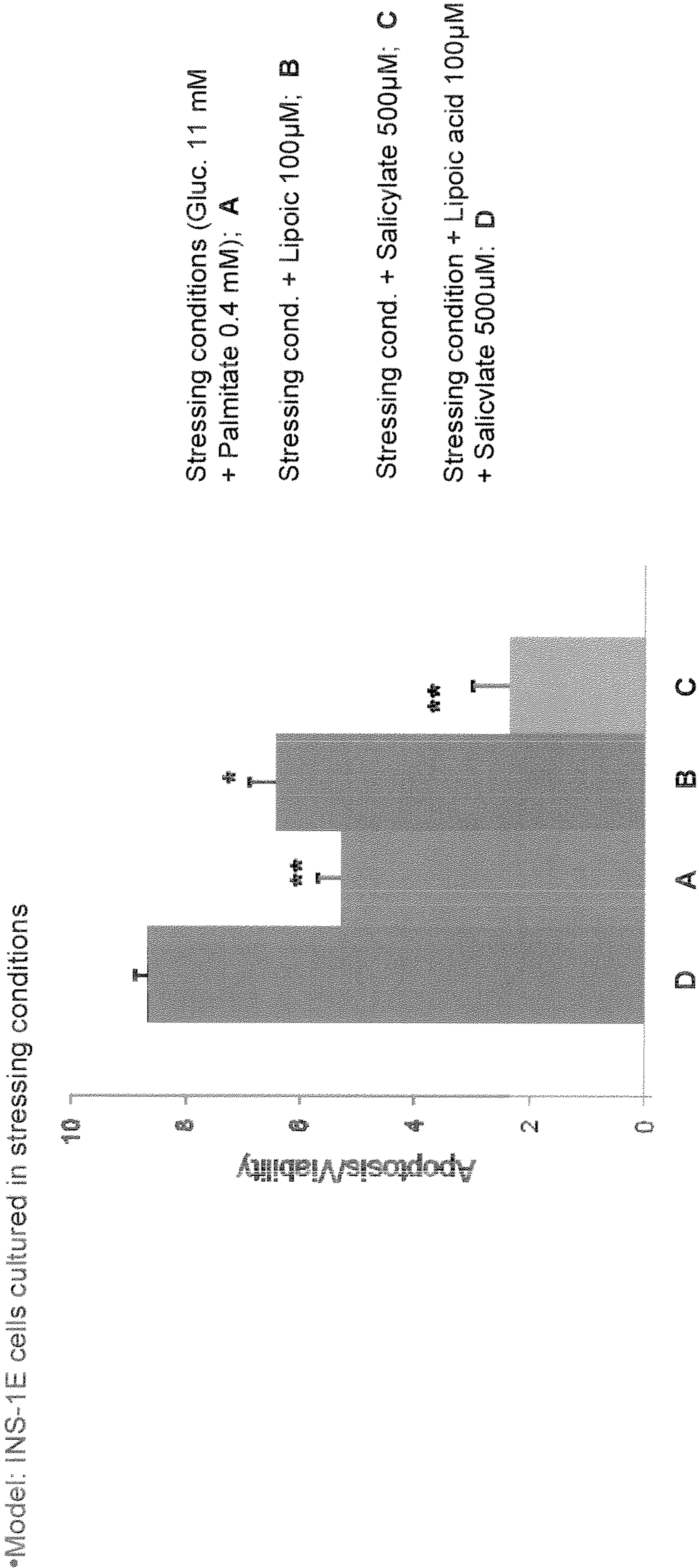


Figure 2

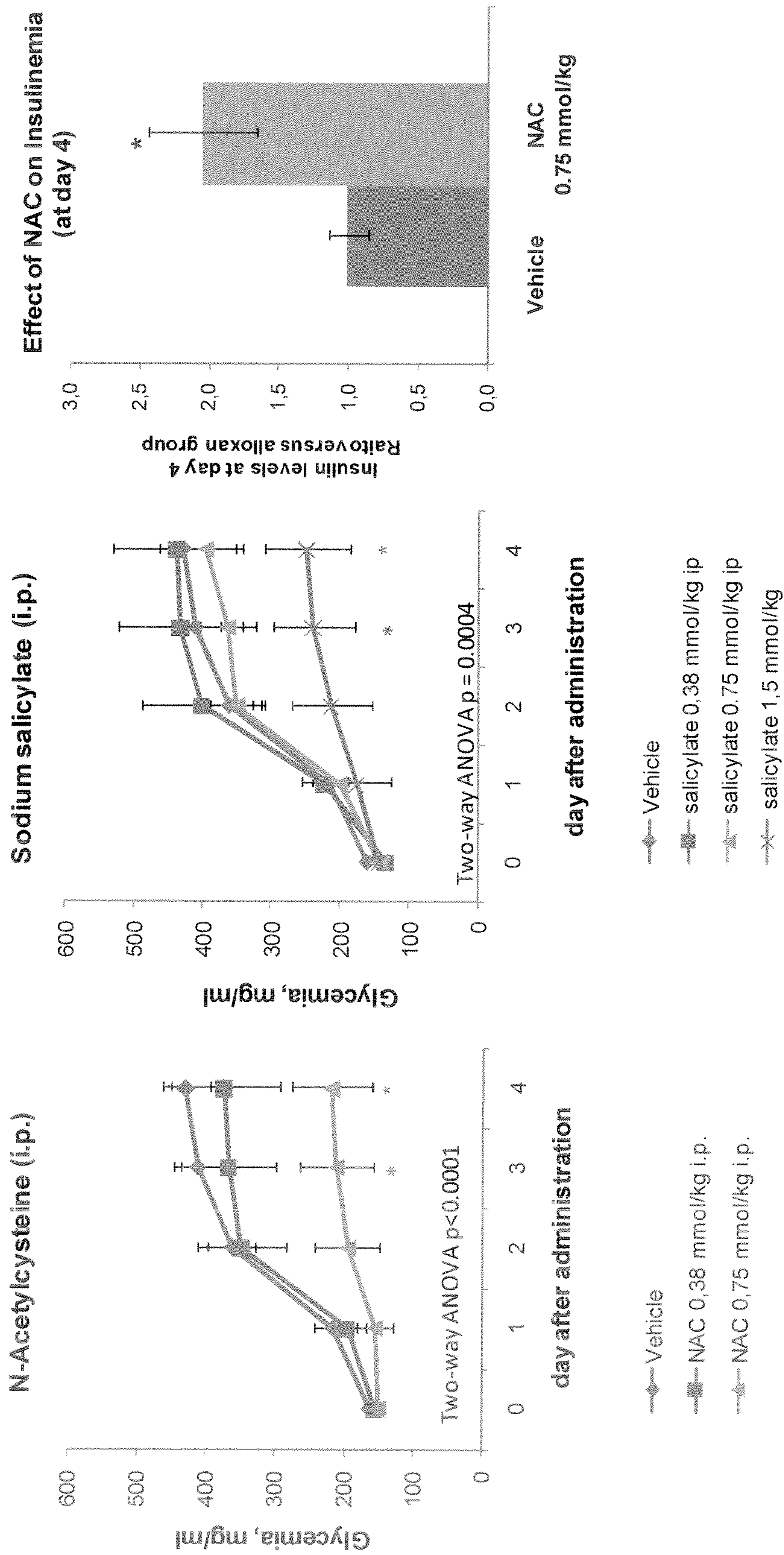
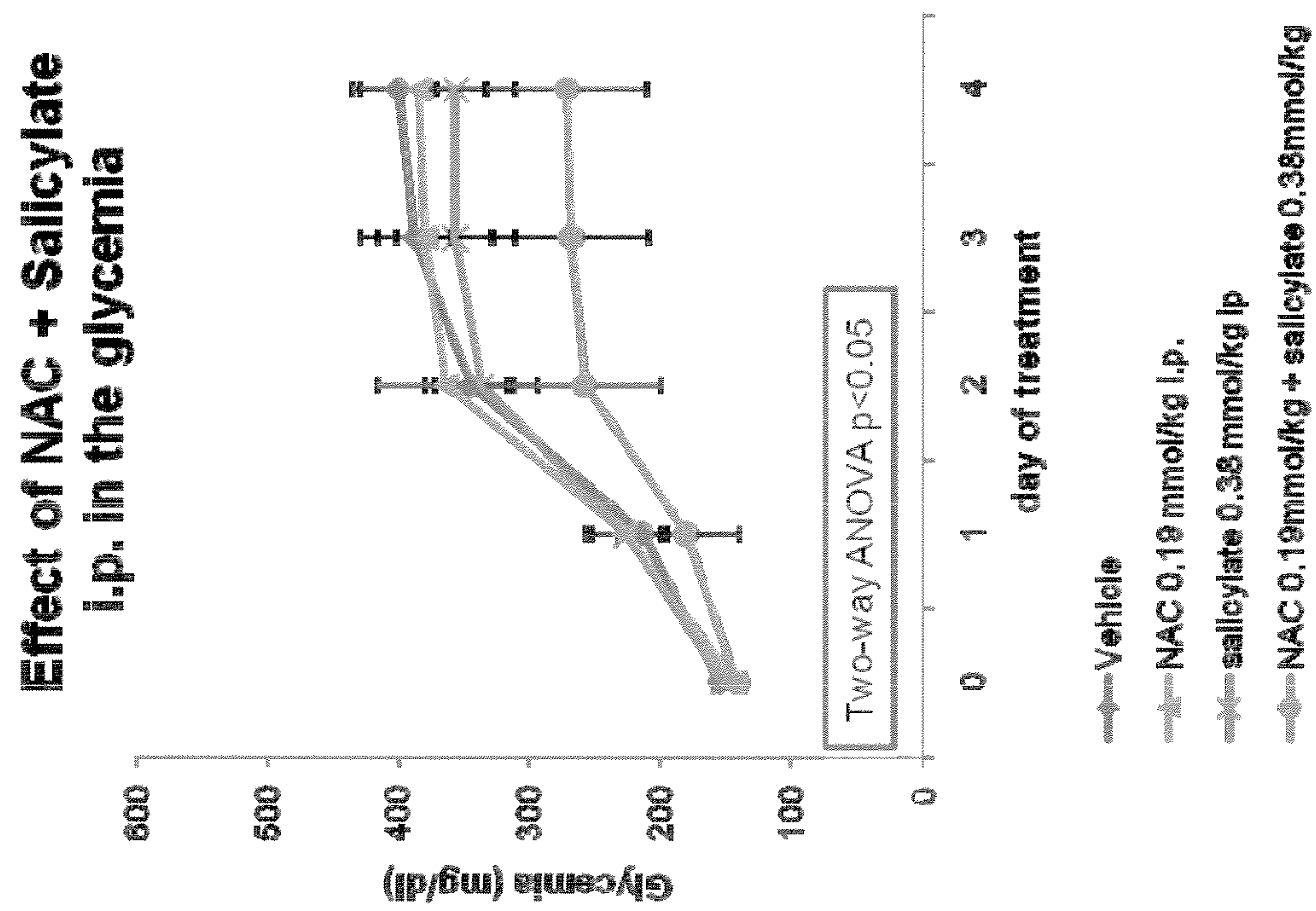


Figure 3

**Figure 4**

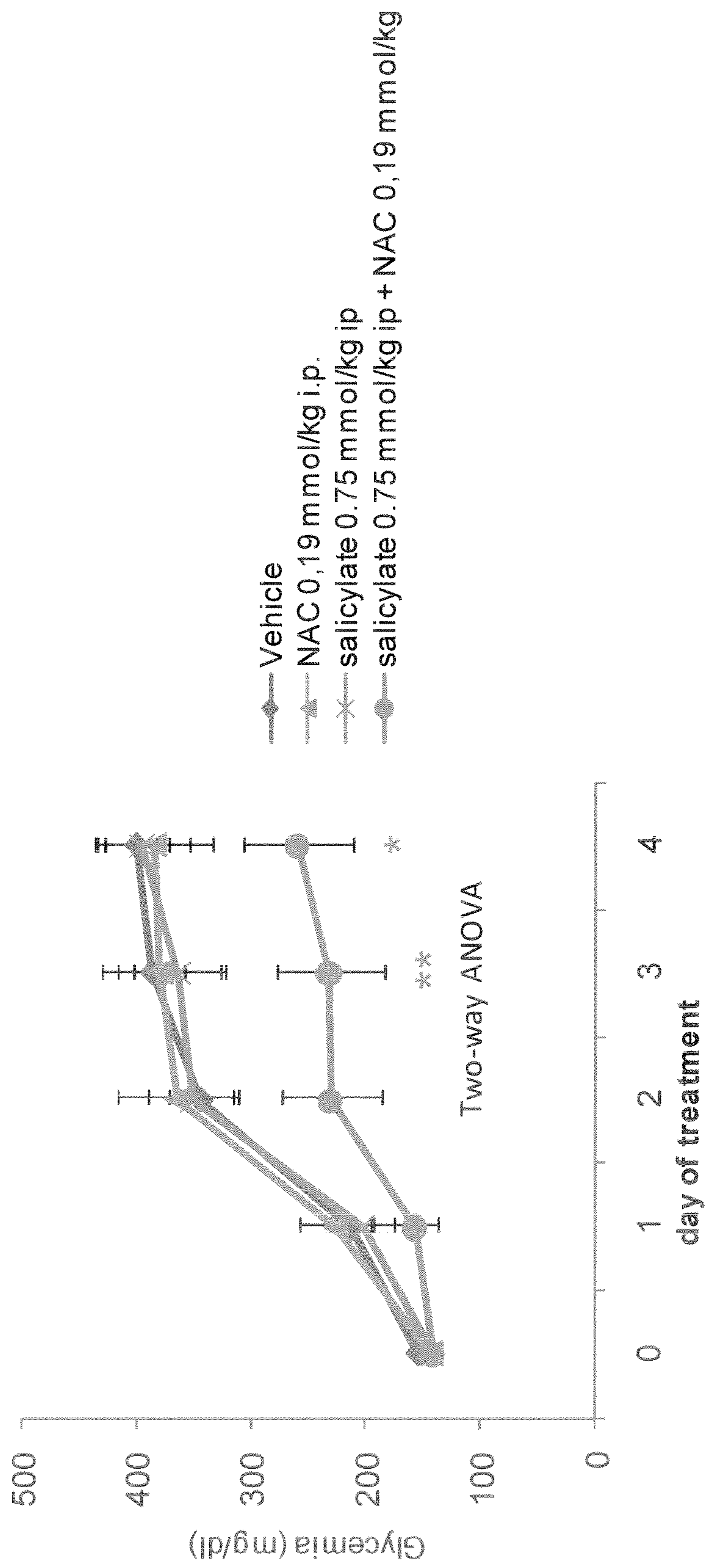
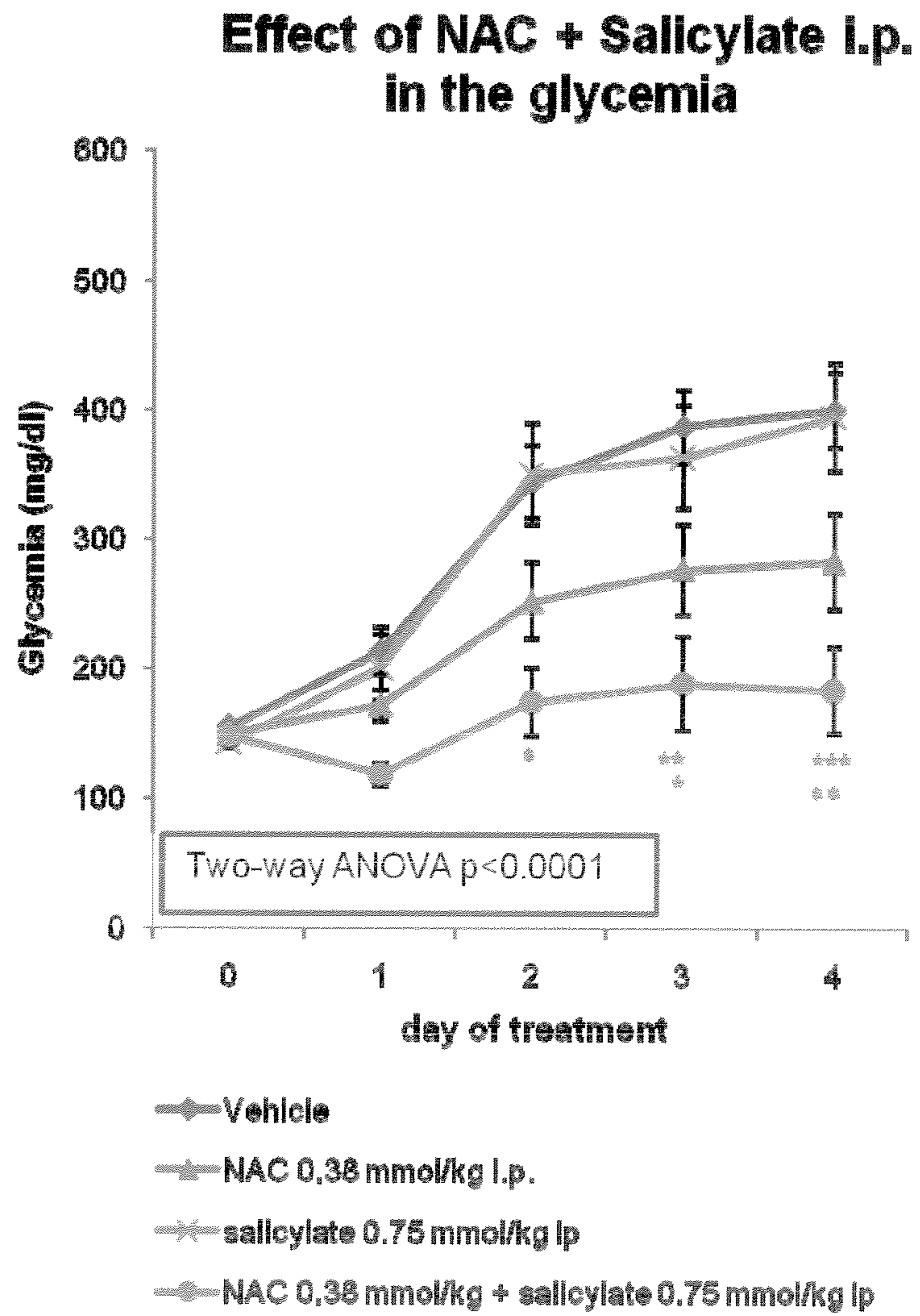
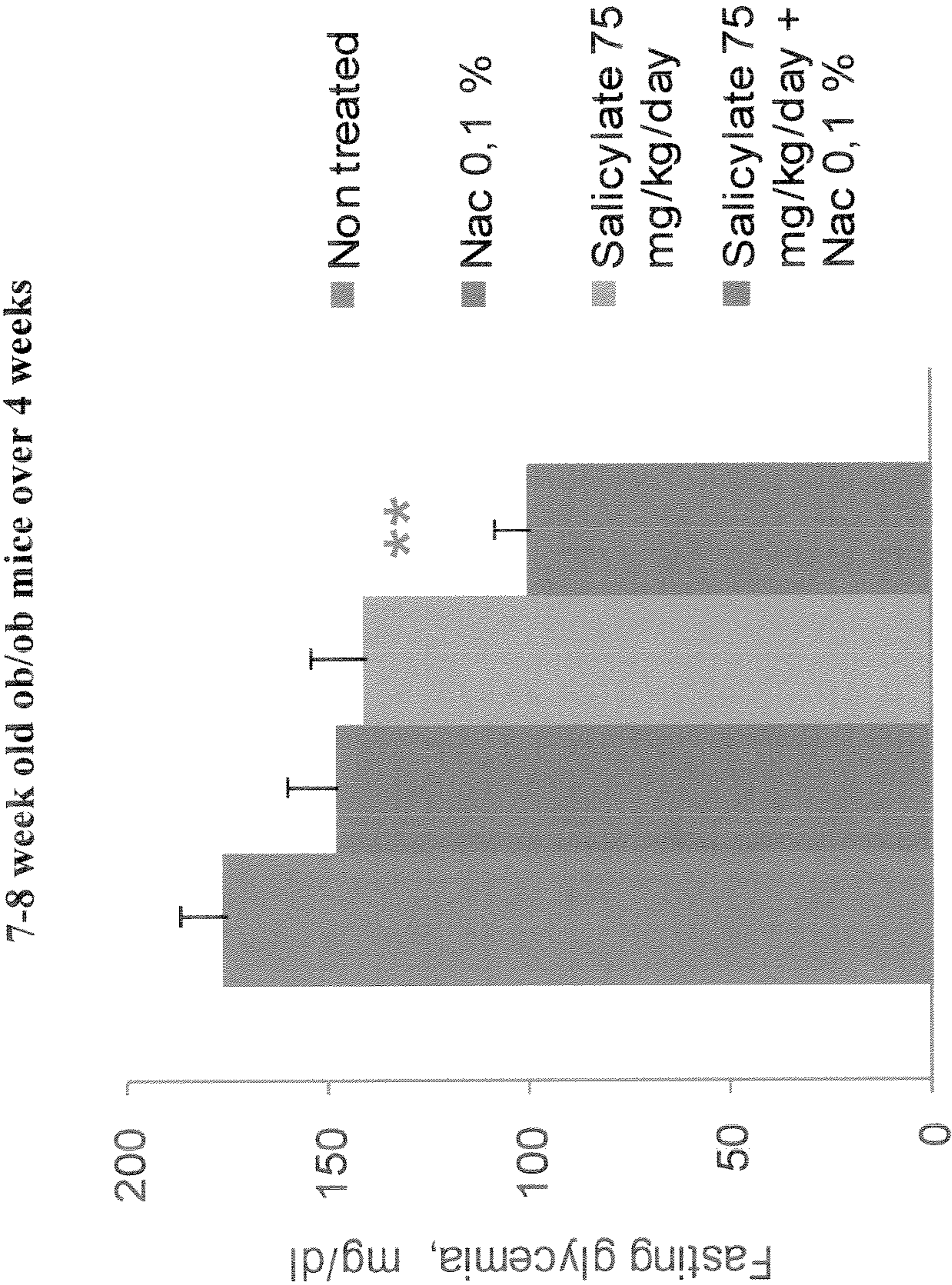


Figure 5

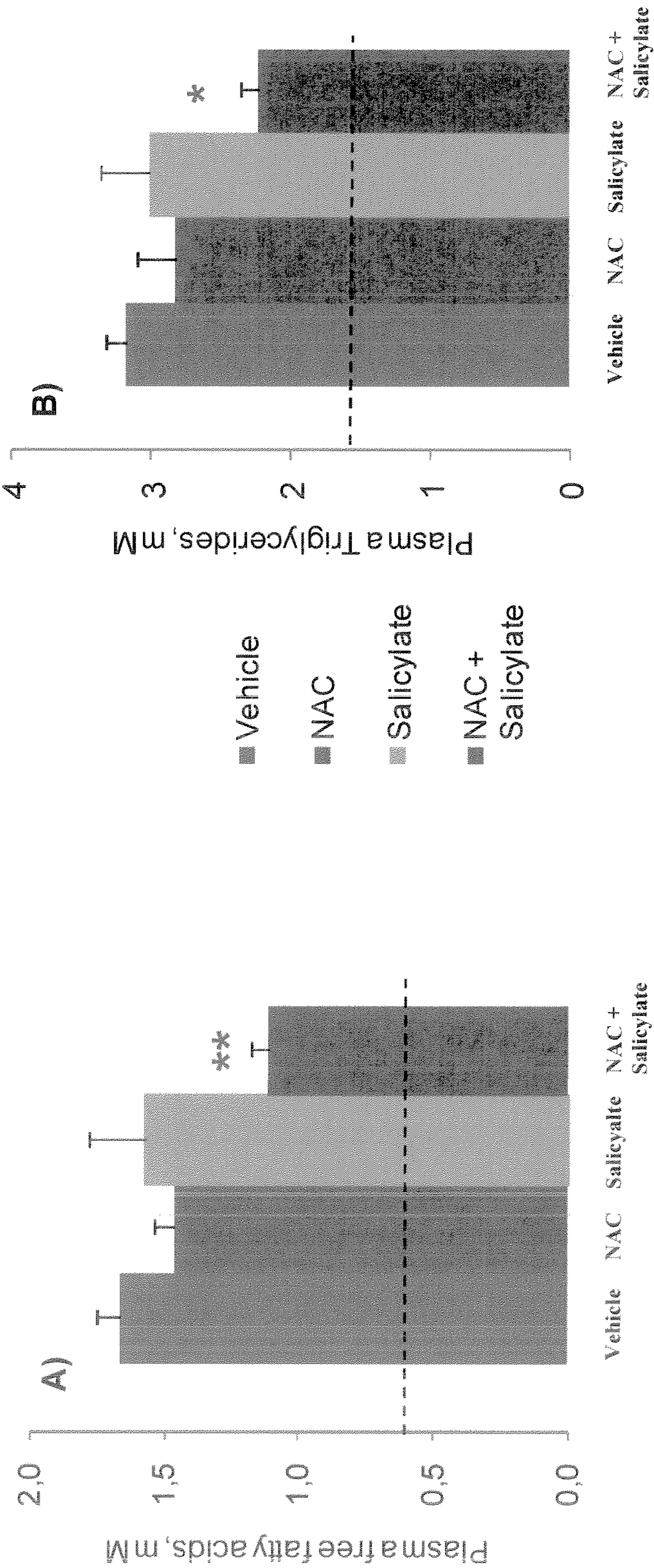
**Figure 6**



Salicylate was delivered to 7-8 week old ob/ob mice over 4 weeks by subcutaneous infusion.
N-Acetylcysteine was administered orally through drinking water.

Figure 7

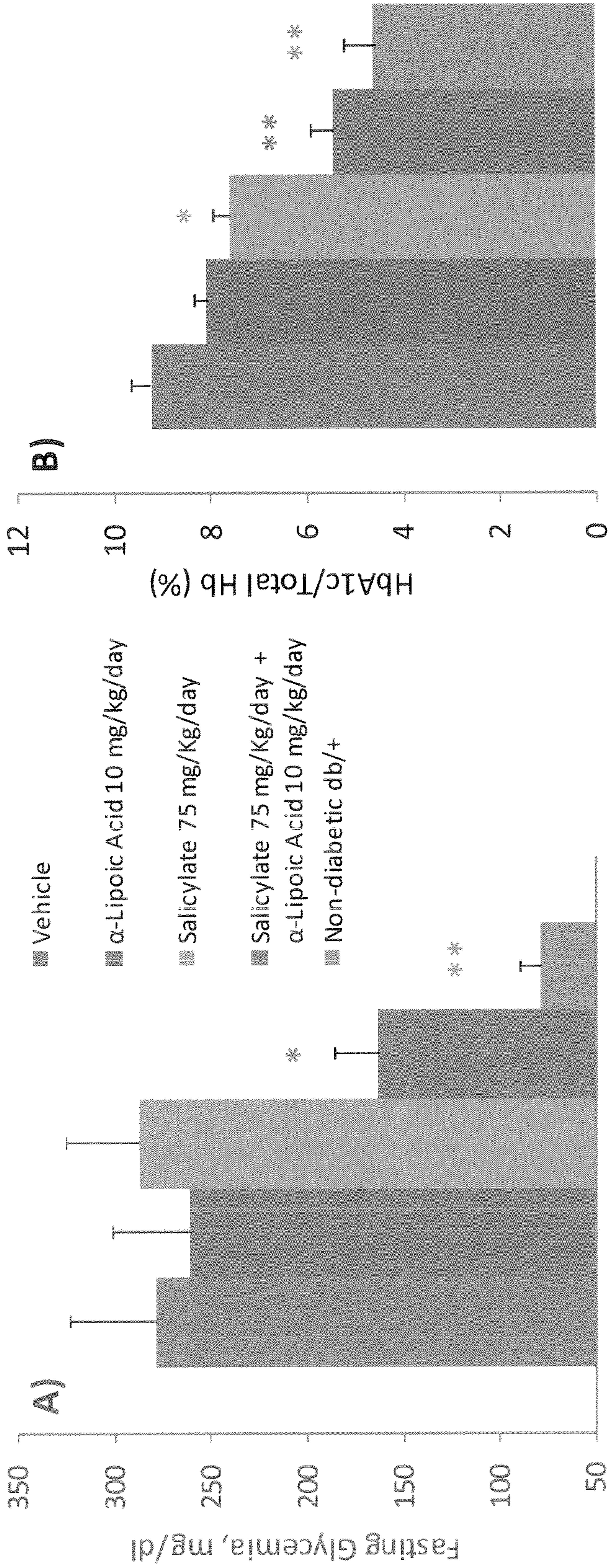
NAC and Salicylate alone or in combination at 0.75 mmol/kg/day i.p. over 4 weeks



Animals (db/db mice) were treated intraperitoneally alone or in combination at 0.75 mmol/kg/day over 4 weeks.

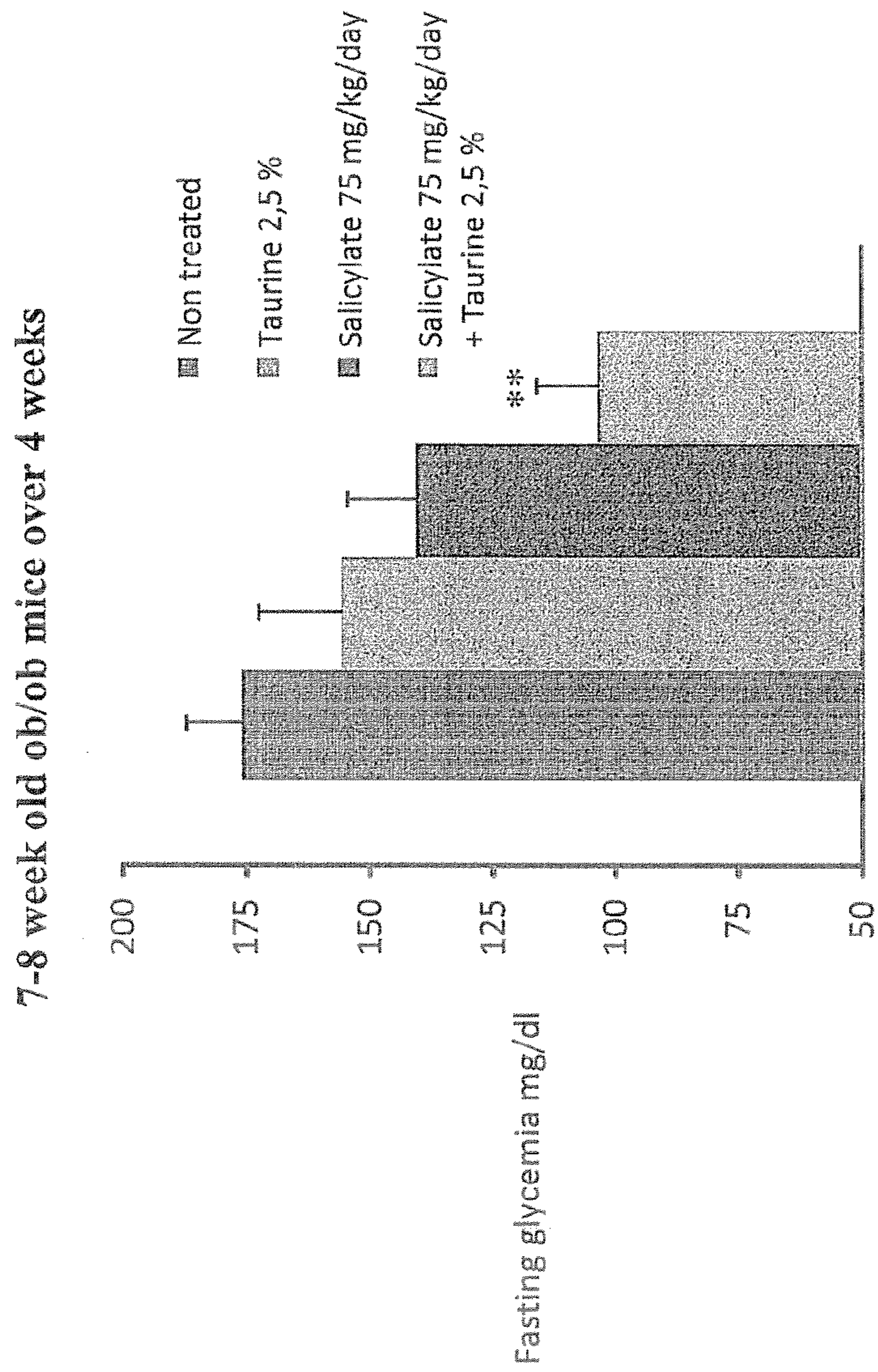
Figure 8

5 week old db/db mice over 4 weeks



Salicylate was delivered to 5 week old db/db mice over 4 weeks by subcutaneous infusion. R- α -Lipoic was administered orally.

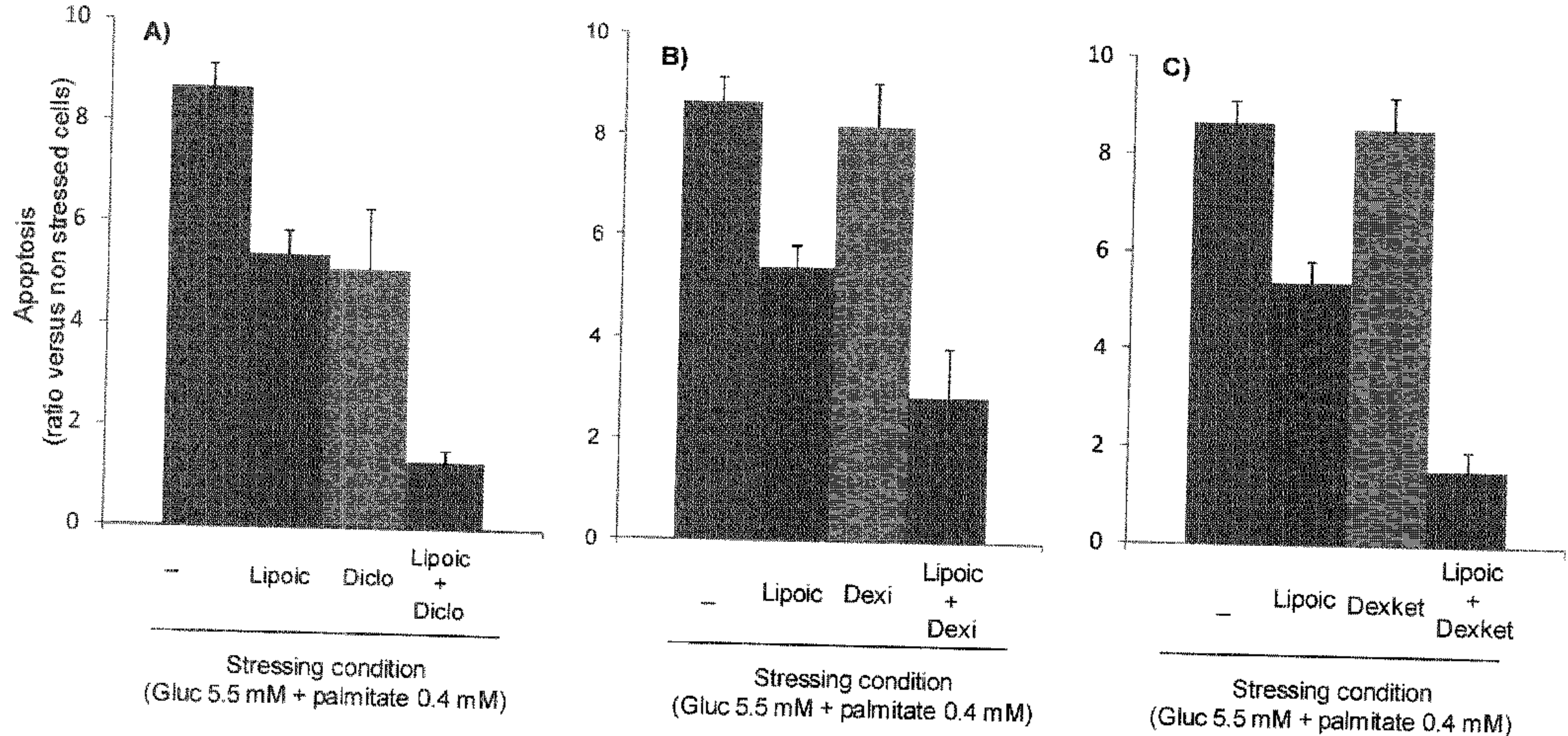
Figure 9



Salicylate was delivered to 7-8 week old ob/ob mice over 4 weeks by subcutaneous infusion. N-Acetylcysteine was administered orally through drinking water.

Figure 10

The combination of (R) Lipoic Acid and diclofenac, dexibuprofen, or dexketoprofen protects beta-cells from cellular stress implicated in diabetes related pancreas dysfunction



INS-1E β -cells were pretreated overnight with lipoic acid 100 μ M, diclofenac 100 μ M (Diclo), dexibuprofen 500 μ M (Dexi) and Dexketoprofen 500 μ M (Dexket) alone or in combination as indicated in graphics A, B and C.

Figure 1