



- (51) **International Patent Classification:**
A61K 31/40 (2006.01) *A61P 3/10* (2006.01)
- (21) **International Application Number:**
PCT/IB2016/057089
- (22) **International Filing Date:**
24 November 2016 (24.11.2016)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
4430/MUM/2015 26 November 2015 (26.11.2015) IN
- (71) **Applicant:** **CADILA HEALTHCARE LIMITED** [IN/IN]; Zydus Tower, Satellite Cross Roads, Ahmedabad, Gujarat 380015 (IN).
- (72) **Inventors:** **JAIN, Mukul**; CADILA HEALTHCARE LIMITED, Zydus Tower, Satellite Cross Roads, Ahmedabad, Gujarat 380015 (IN). **JOHARAPURKAR, Amit Arvind**; CADILA HEALTHCARE LIMITED, Zydus Tower, Satellite Cross Roads, Ahmedabad, Gujarat 380015 (IN). **KSHIRSAGAR, Samadhan Govind**; CADILA HEALTHCARE LIMITED, Zydus Tower, Satellite Cross Roads, Ahmedabad, Gujarat 380015 (IN).
- (74) **Agents:** **VENKITACHALAM, Manoj** et al.; Subramaniam & Associates, Central Square, Suite-328, Plaza

III, 20 Manoharlal Khurana Marg, Bara Hindu Rao (off Rani Jhansi Road), Delhi 110006 (IN).

- (81) **Designated States** (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
- (84) **Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

[Continued on next page]

- (54) **Title:** DUAL PPAR MODULATORS FOR THE TREATMENT OF DIABETIC NEPHROPATHY AND RELATED DISEASES

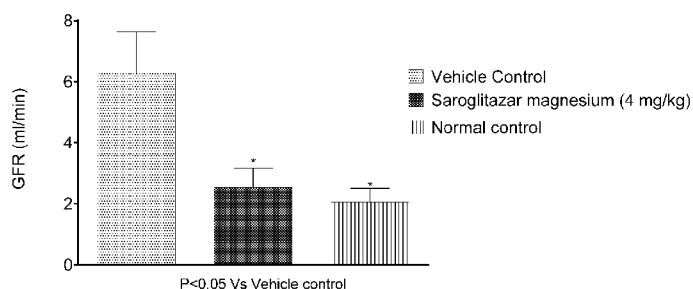
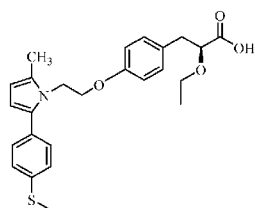


Figure-1



Formula (1)

(57) **Abstract:** The present invention relates to the use of Saroglitzar or a pharmaceutically acceptable salt thereof, for the treatment of, or the prevention, delay of progression, or treatment of a disease or condition associated with abnormalities of the diabetic Kidney. Which is selected from diabetic nephropathy, diabetic kidney disease, renal hypertrophy, hyperfiltration, nephrotic syndrome, early stage diabetic kidney disease, chronic kidney disease and associated disorders. The present invention further relates to the use of a pharmaceutical composition comprising Saroglitzar, or a pharmaceutically acceptable salt thereof, for the prevention, delay of progression, or treatment of a disease or condition which is selected from diabetic nephropathy, diabetic kidney disease, renal hypertrophy, hyperfiltration, nephrotic syndrome, early stage diabetic kidney disease, chronic kidney disease and associated disorders. Formula (1)



Declarations under Rule 4.17:

Published:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))* — *with international search report (Art. 21(3))*

DUAL PPAR MODULATORS FOR THE TREATMENT OF DIABETIC NEPHROPATHY AND RELATED DISEASES

FIELD OF INVENTION

5 The present invention relates to the use of Saroglitazar or a pharmaceutically acceptable salt thereof, for the treatment of, or the prevention, delay of progression, or treatment of a disease or condition associated with abnormalities of the diabetic kidney. Such abnormalities may include one or more of diabetic nephropathy, diabetic kidney disease, renal hypertrophy, hyperfiltration, nephrotic syndrome, early stage diabetic
10 kidney disease, chronic kidney disease and associated disorders. The present invention further relates to the use of a pharmaceutical composition comprising Saroglitazar, or a pharmaceutically acceptable salt thereof, for the prevention, delay of progression, or treatment of a disease or condition which is selected from diabetic nephropathy, diabetic kidney disease, renal hypertrophy, hyperfiltration, nephrotic syndrome, early stage
15 diabetic kidney disease, chronic kidney disease and associated disorders.

BACKGROUND OF INVENTION

Diabetes is a major cause of morbidity and mortality in the world. The incidence of diabetes mellitus has reached epidemic proportions. The number of people afflicted with this disease will only continue to increase. By 2040 more than 600 million people
20 worldwide will have developed this disease (<http://www.diabetesatlas.org/>; accessed 20-Nov-2015). Specifically, diabetes mellitus is the leading cause of end stage renal disease and therefore, any newly diagnosed patient with diabetes mellitus would be considered at risk for the development of diabetic nephropathy. Several years prior to the development of renal insufficiency, diabetic patients also exhibit renal disease manifested by renal
25 hypertrophy and hyperfiltration. Elevated blood glucose levels are responsible for the plethora of systemic complications, the most serious of which are diabetic nephropathy. Diabetic nephropathy presents as proteinuria then progresses to renal inflammation and the associated decline in glomerular filtration barrier, which all ultimately lead to end stage kidney disease (Rossing P., *Kidney Int Suppl*, 120 (2011), pp. S28–S32).
30 Individuals with end stage kidney disease are left with no other options but permanent

dialysis or kidney transplant to maintain renal function. Therefore, therapies aimed at maintaining the integrity of the glomerular filtration barrier will be beneficial for prevention of end stage kidney disease (Kanwar Y.S., *Exp Biol Med* (Maywood), 233 (2008), pp. 4–11). The glomerular filtration barrier is composed of podocytes and glomerular endothelial cells. Podocytes are key cells for maintaining the integrity of the glomerular filtration barrier in humans. Insulin resistance is a central and pathogenic feature of type II diabetes contributing to the development of obesity, dyslipidemia, hypertension, and cardiovascular disease (Maric C., *Contrib Nephrol*, 170 (2011), pp. 28–35). Hyperglycemia has also recently been demonstrated to be a principal causative factor in the development of micro- and macrovascular complications in diabetic patients. Furthermore, dyslipidemia associated with increased plasma triglycerides and decreased plasma high-density lipoprotein cholesterol together with hypertension represent two additional important risk factors associated with cardiorenal complications. In the ‘UK Prospective Diabetic Study (UKPDS)’, over a median of 15 years from diagnosis of type 2 diabetes mellitus (T2DM), it was reported that 38% of 4031 individuals with diabetes mellitus developed albuminuria and 29% of 5032 individuals developed renal impairment [Ratnakaran R., *Diabetes*, 55 (2006), pp. 1832–1839]. Thus, nephropathy is one of major complications of uncontrolled diabetes mellitus.

Diabetic nephropathy is structurally associated with mesangial cell expansion, thickening of glomerular and tubular basement membrane, glomerular hypertrophy, glomerulosclerosis, tubulointerstitial inflammation and fibrosis, tubular dilation and atrophy [Balakumar P., *J Cardiovasc Pharmacol*, 54 (2009), pp. 129–138]. It results in albuminuria, increased serum creatinine and urea nitrogen levels and decreased glomerular filtration rate. It remains unclear to determine potential risk factors involved in the disease progression of diabetic nephropathy, though hyperglycemia and hypertension play key roles in this circumstance. Numerous studies revealed that chronic hyperlipidemia is an additional risk factor for the initiation and progression of diabetic nephropathy [Kang A.Y., *Diabetes Metab J*, 35 (2011), pp. 264–272].

Dyslipidemia is a condition associated with hypertriglyceridemia, elevated LDL levels and decreased HDL levels. Dyslipidemia affects around 50% of patients with

T2DM [K. Vijayaraghavan *Lipids Health Dis*, 9 (2010), p. 144]. Diabetic dyslipidemia is linked with hyperglycemia, followed by elevated levels of triglycerides and LDL cholesterol, and reduced levels of HDL cholesterol [Solano M.P., *Cardiol Rev*, 14 (2006), pp. 125–135]. Though the precise mechanism involved in diabetes-associated
5 dyslipidemia is not clear, the insulin resistance in T2DM could play a key role in elevating lipid levels. Importantly, both insulin resistance and T2DM synergistically influence the progression of dyslipidemia [Adiels M., *Arterioscler Thromb Vasc Biol*, 28 (2008), pp. 1225–1236]. The reduced insulin action accelerates intracellular hydrolysis of triglycerides with enhanced release of non-esterified fatty acids (NEFA), which provides
10 substrate to the liver, resulting in alterations of plasma lipids. It has been suggested that the overproduction of very low-density lipoprotein (VLDL) levels is the hallmark of the dyslipidemia in T2DM. Moreover, hyperglycemia causes glucotoxicity by inducing apoptosis of insulin secreting β -cells of islets of Langerhans, and also determines the degree of accumulation of oxidized LDL. Taken together, diabetes mellitus is strongly
15 associated with rise in VLDL, LDL and triglyceride levels and consequent decrease in HDL levels. On the other hand, the association between lipid accumulation and insulin resistance is a major hallmark of T2DM [N.A. van Herpen, *Physiol Behav*, 94 (2008), pp. 231–241]. Hyperlipidemia has been suggested to be an independent risk factor for development and progression of diabetic nephropathy. Antihyperlipidemic therapy,
20 therefore, be beneficial in preventing the induction and progression of diabetic nephropathy.

The peroxisome proliferator-activated receptor (PPAR) family of nuclear receptors is composed of three family members. The main classes of PPAR agonists are: PPAR-alpha agonists, PPAR-gamma agonists and PPAR-beta/delta (β/δ) agonists;
25 PPAR-alpha is the main target of fibrate drugs, such as gemfibrozil, ciprofibrate, bezafibrate, and fenofibrate; Number of study describes the PPAR-alpha agonist fenofibrate for the treatment of diabetic nephropathy (Kidney International (2006) 69, 1511–1517); However the high doses of fenofibrate are associated with renal toxicity. At present the mechanisms by which PPAR-alpha agonists
30 improve diabetic nephropathy remain unclear. Other fibrates have been tested for the

diabetic nephropathy, but they have more problems when they are prescribed along with statins and generally not shown the effect as like fenofibrate.

PPAR- γ is the main target of the drug class of thiazolidinedione's (TZDs), such as Pioglitazone and Rosiglitazone. There are some limitations of TZDs in treatment of diabetic nephropathy. Though there is evidence from clinical trials and basic studies pronounced the protective role of TZDs in diabetic nephropathy (DN), the severe side effects greatly restricted their use in patients. Troglitazone had to quit the market owing to the severe hepatotoxicity. Rosiglitazone has been found to be significantly associated with the increased risk of cardiovascular complications including heart failure and myocardial infarction leading to the restriction or withdrawal from the markets. As for the pioglitazone, it has been thought to have a different safety profile with no increase of cardiovascular disease as compared with other TZDs. But, it still conserves the effects of bodyweight gain, bone loss, edema, and fluid retention which may increase the incidence of congestive heart failure [P. Shah and S. Mudaliar, "Pioglitazone: side effect and safety profile," *Expert Opinion on Drug Safety*, vol. 9, no. 2, pp. 347– 354, 2010]. Role of PPAR γ agonists in the treatment of diabetic nephropathy is not well established. In a pilot study, Pioglitazone was found not to reduce proteinuria over four months (Agarwal R et.al., A pilot randomized controlled trial of protection of renal protection with pioglitazone in diabetic nephropathy, *Kidney International*, 68, 2005, 285-292.)

Only a few therapeutic candidate has been developed as PPAR-(δ) agonists. GW610742 is known as PPAR-(δ) agonists and it's used in Diabetic nephropathy.

A fourth class, which is dual PPAR agonist, is represented by the so-called *glitazars*, which bind to both the alpha and gamma PPAR isoforms. These include the compounds Aloglitazar, Muraglitazar, Tesaglitazar and Saroglitazar.

Dual PPAR agonists such as Tesaglitazar and Aloglitazar have been shown to cause a significant increase in creatinine or blood urea nitrogen (Diabetes, Vol. 56, and August 2007). While, surprisingly we found that Saroglitazar does not show or cause significant increase in creatinine or blood urea nitrogen. Rather it decreases creatinine in the long term which odes good for the treatment of patients with diabetic nephropathy.

No promising therapeutic options are available in the present clinical scenario to manage efficiently the diabetic nephropathy. Currently the only treatment suggested to prevent or reverse the renal hypertrophy of diabetic nephropathy is rigorous insulin therapy, although in practical application, insulin therapy has yielded disappointing results.

5 Nevertheless, angiotensin converting enzyme inhibitors and angiotensin-II-AT1 receptor blockers are currently employed to improve structural and functional status of the diabetic kidney. These interventions, however, also, are not optimal in improving overall outcomes of diabetic nephropathy. Hence, there is a continuing need of developing promising therapeutic interventions to manage this insidious condition adequately.

10 The present invention describes the use of a PPAR modulator of formula (1) or its pharmaceutically acceptable salts, preferably the Magnesium salt, for the prevention and treatment of diabetic nephropathy, diabetic kidney disease, renal hypertrophy, hyperfiltration, nephrotic syndrome, early stage diabetic kidney disease, chronic kidney disease and associated disorders.

15 SUMMARY OF THE INVENTION

The compound of formula (1) (Saroglitazar) is approved as its Magnesium salt for the treatment of diabetic dyslipidemia or hypertriglyceridemia in type 2 diabetes, not controlled by statins alone.

20 Surprisingly, it has been found that Saroglitazar or a pharmaceutically acceptable salt thereof, preferably the Magnesium salt, is suitable for use in the treatment or the prevention, delay of progression, or treatment of a disease or condition associated with abnormalities of the diabetic kidney. . Such abnormalities may include one or more of diabetic nephropathy, diabetic kidney disease, renal hypertrophy, hyperfiltration, nephrotic syndrome, early stage diabetic kidney disease, chronic kidney disease and
25 associated disorders. Therefore, according to one embodiment of the present invention is provided the use of Saroglitazar, or a pharmaceutically acceptable salt thereof for the treatment and/or amelioration of the conditions associated with diabetic nephropathy.

In another embodiment is provided a pharmaceutical composition containing Saroglitazar or its pharmaceutically acceptable salts, preferably the Magnesium salt for
30 the treatment of one or more of the diseases described hereinbefore.

In another embodiment is provided a method of treating the diseases described hereinbefore, by providing a therapeutically effective amount of Saroglitazar or its pharmaceutically acceptable salts, preferably the Magnesium salt to a patient in need of treatments of diseases associated with diabetic nephropathy. The above and other
5 embodiments of the present invention are described in further details hereinafter.

List of abbreviations:

GFR- glomerular filtration rate

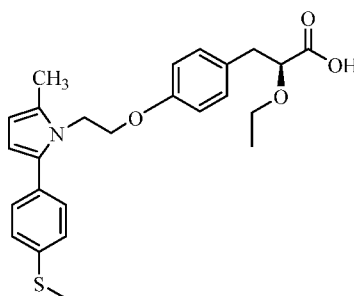
BUN-blood urea nitrogen

BRIEF DESCRIPTION OF DRAWING

- 10 Figure-1: Effect of the Saroglitazar Magnesium on GFR
Figure-2: Effect of the Saroglitazar Magnesium on microalbuminurea
Figure-3: Effect of the Saroglitazar Magnesium on serum creatinine
Figure-4: Effect of the Saroglitazar Magnesium on serum BUN
Figure-5: Effect of the Saroglitazar Magnesium on serum urea
15 Figure-6: Effect of the Saroglitazar Magnesium on serum glucose

DETAILED DESCRIPTION

The present invention thus provides the use of Saroglitazar of formula (1), or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the prevention, delay of progression, or treatment of a disease or condition associated with
20 abnormalities of the diabetic kidney. Such abnormalities may include one or more of diabetic nephropathy, diabetic kidney disease, renal hypertrophy, hyperfiltration, nephrotic syndrome, early stage diabetic kidney disease, chronic kidney disease and associated disorders.



25

(1)

The pharmaceutically acceptable salt of compound of formula (1) is selected from organic or inorganic salts. Inorganic salt is selected from Calcium, Magnesium, Sodium, Potassium, Zinc, Ammonium and Lithium. Organic salt is selected from L-Arginine, Tromethamine, L-Lysine, Meglumine, Benethamine, Piperazine, Benzylamine, 5 Dibenzylamine, Dicyclohexylamine, Diethylamine, Diphenylamine, α -naphthylamine, O-phenylenediamine, 1,3-Diaminopropane, (S)- α -naphthyl ethylamine, (S)-3-methoxyphenylethylamine, (S)-4-methoxyphenylethylamine, (S)-4-chlorophenyl ethylamine, (S)-4-methylphenylethylamine, Cinchonine, Cinchonidine, (-)-Quinine, Benzathine, Ethanolamine, Diethanol amine, Triethanolamine, imidazole, Diethylamine, 10 Ethylenediamine, Choline, Epamine, Morpholine 4-(2-hydroxyethyl), N-N-diethylethanolamine, Deanol, Hydrabamine, Betaine, Adamantanamine, L-Adamantanmethylethylamine and Tritylamine.

In one of the preferred embodiment the pharmaceutically acceptable salt of compound of formula (1) is Magnesium.

15 In another preferred embodiment, the pharmaceutically acceptable salt of compound of formula (1) is selected from calcium, sodium and potassium.

In one of the preferred embodiment is described the use of the Magnesium salt of compound of formula (1) for the manufacture of a medicament for the prevention, delay of progression, or treatment of a diabetic nephropathy.

20 In another of the preferred embodiment is described the use of the calcium, sodium and potassium salt of compound of formula (1) for the manufacture of a medicament for the prevention, delay of progression, or treatment of a diabetic nephropathy.

The invention also provides a pharmaceutical composition containing 25 Saroglitzar or its pharmaceutically acceptable salts, preferably the Magnesium salt for the treatment of one or more of the diseases described hereinbefore.

The invention also provides a pharmaceutical composition containing Saroglitzar or its pharmaceutically acceptable salts, preferably the calcium, sodium and potassium salt for the treatment of one or more of the diseases described hereinbefore.

Further the invention provides a method of treating the diseases described hereinbefore, by providing a therapeutically effective amount of Saroglitzar or its pharmaceutically acceptable salts, preferably the Magnesium salt to a patient in need thereof.

5 Further the invention provides a method of treating the diseases described hereinbefore, by providing a therapeutically effective amount of Saroglitzar or its pharmaceutically acceptable salts, preferably the calcium, sodium and potassium salt to a patient in need thereof.

The pharmaceutically acceptable salt of compound of formula (1) is selected
10 form organic or inorganic salts. Inorganic salt is selected from Calcium, Magnesium, Sodium, Potassium, Zinc, Ammonium and Lithium. Organic salt is selected from L-Arginine, Tromethamine, L-Lysine, Meglumine, Benethamine, Piperazine, Benzylamine, Dibenzylamine, Dicyclohexylamine, Diethylamine, Diphenylamine, α -naphthylamine, O-phenylenediamine, 1,3-Diaminopropane, (S)- α -naphthyl ethylamine, (S)-3-
15 methoxyphenylethylamine, (S)-4-methoxyphenylethylamine, (S)-4-chlorophenylethylamine, (S)-4-methylphenylethylamine, Cinchonine, Cinchonidine, (-)-Quinine, Benzathine, Ethanolamine, Diethanol amine, Triethanolamine, imidazole, Diethylamine, Ethylenediamine, Choline, Epolamine, Morpholine 4-(2-hydroxyethyl), N-N-diethylethanolamine, Deanol, Hydrabamine, Betaine, Adamantanamine, L-
20 Adamantanmethylethylamine and Tritylamine.

In one of the preferred embodiment the pharmaceutically acceptable salt of compound of formula (1) is Magnesium.

In another preferred embodiment, the pharmaceutically acceptable salt of compound of formula (1) is selected from calcium, sodium or potassium..

25 In one of the preferred embodiment use of the Magnesium salt of compound of formula (1) for the manufacture of a medicament for the prevention, delay of progression, or treatment of one or more diseases selected from diabetic nephropathy, diabetic kidney disease, renal hypertrophy, hyperfiltration, nephrotic syndrome, early stage diabetic kidney disease, chronic kidney disease and associated disorders.

The present invention also provides suitable pharmaceutical composition of compounds of formula (1) or their pharmaceutically acceptable salts. The pharmaceutical composition of the present invention essentially comprises of:

- 5 - the pharmaceutically active substance of formula (1) or its pharmaceutically acceptable salt;
- a suitable buffering agent;
- a suitable stabilizer;
- optionally with one or more pharmaceutically acceptable excipients.

10 The pharmaceutically acceptable salt of compound of formula (1) is as described earlier.

 The suitable stabilizers used in pharmaceutical composition are selected from Polacrillin potassium, Potassium chloride, Sodium stearyl fumarate and preferably selected from Sodium stearyl fumarate. The suitable buffering agent are selected from sodium acetate, ammonia solution, ammonium carbonate, sodium borate, adipic Acid, 15 glycine, monosodium glutamate and preferably selected from ammonia solution.

 The pharmaceutically acceptable excipients are selected at least one from carriers, binders, antioxidant agents, disintegrating agents, wetting agents, lubricating agents, chelating agents, surface active agents, and the like.

20 Diluents include, but are not limited to lactose monohydrate, lactose, polymethacrylates selected from Eudragit, potassium chloride, sulfobutyl ether b-cyclodextrin, sodium chloride, spray dried lactose, and preferably sulfobutyl ether b-cyclodextrin. Carriers include, but are not limited to lactose, white sugar, sodium chloride, glucose, urea, starch, calcium carbonate and kaolin, crystalline cellulose, and silicic acid. Binders include, but are not limited to carbomers selected from carbopol, 25 gellan, gum Arabic, hydrogenated vegetable oil, polymethacrylates selected from Eudragit, xanthan, lactose and Zein. Antioxidant agents include, but are not limited to, Hypophosphorous acid, Sodium formaldehyde, sodium formaldehyde sulfoxylate, sulfur dioxide, tartaric acid, thymol and methionine. Disintegrating agents include, but are not limited to, bicarbonate salt, chitin, gellan gum, polacrillin potassium and Docusate 30 Sodium. Wetting agents include, but are not limited to, Glycerin, lactose, Docusate

Sodium and Glycine, Lubricating agents used include, but are not limited to, Glycerin behenate, hydrogenated vegetable oil, sodium stearyl fumarate and Myristic Acid. Chelating agents include, but are not limited to, Maltol and Pentetic Acid. Surface active agents include but are not limited to, Nonionic surfactant selected from alkyl
5 polyglucosides, cocamide DEA, cocamide MBA, cocamide TEA, decyl maltoside and octyl glucoside; Anionic surfactant selected from arachidic acid and arachidonic acid; Cationic surfactant selected from cetyl trimethylammonium bromide and cetylpyridinium chloride.

Usually the compositions used in the invention are adapted for oral
10 administration. However, they may be adapted for other modes of administration, for example parenteral administration, sublingual or transdermal administration. The dose range is from 0.1 mg to 10 mg per kilogram of body weight.

The compositions may be in the form of tablets, capsules, powders, granules, lozenges, suppositories, reconstitutable powders, or liquid preparations, such as oral or
15 sterile parenteral solutions or suspensions.

In order to obtain consistency of administration it is preferred that a composition of the invention is in the form of a unit dose.

Unit dosage presentation forms for oral administration may be in tablet or capsule form and may as necessary contain conventional excipients such as binding agents, fillers, lubricants, glidants, disintegrates and wetting agents.
20

The solid oral compositions may be prepared by conventional methods of blending, filling or tableting. Repeated blending operations may be used to distribute the active agent throughout those compositions employing large quantities of fillers. Such operations are of course conventional in the art. The tablets may be coated according to
25 methods well known in normal pharmaceutical practice, in particular with an enteric coating.

Oral liquid preparations may be in the form of, for example, emulsions, syrups, or elixirs, or may be presented as a dry product for reconstitution with water or other suitable vehicle before use. Such liquid preparations may contain conventional additives
30 such as suspending agents, for example sorbitol, syrup, methyl cellulose, gelatin,

hydroxyethylcellulose, carboxymethyl cellulose, aluminium stearate gel, hydrogenated edible fats; emulsifying agents, for example lecithin, sorbitan monooleate, or acacia; non-aqueous vehicles (which may include edible oils), for example almond oil, fractionated coconut oil, oily esters such as esters of glycerine, propylene glycol, or ethyl alcohol; 5 preservatives, for example methyl or propyl p-hydroxybenzoate or sorbic acid; and if desired conventional flavouring or colouring agents.

For parenteral administration, liquid dosage forms are prepared utilizing the compound and a sterile vehicle, and, depending on the concentration used, can be either suspended or dissolved in the vehicle. In preparing solutions the compound can be 10 dissolved in water for injection and filter sterilized before filling into a suitable vial or ampoule and sealing. Advantageously, adjuvants such as a local anesthetic, a preservative and buffering agent can be dissolved in the vehicle. To enhance the stability, the composition can be frozen after filling into the vial and the water removed under vacuum. Parenteral suspensions are prepared in substantially the same manner, except that the 15 active compound is suspended in the vehicle instead of being dissolved, and sterilization cannot be accomplished by filtration. The compound can be sterilized by exposure to ethylene oxide before suspending in the sterile vehicle. Advantageously, a surfactant or wetting agent is included in the composition to facilitate uniform distribution of the compound.

20 Compositions may contain from 0.1% to 99% by weight, preferably from 10-60% by weight, of the active material, depending upon the method of administration.

Examples of binding agents include acacia, alginic acid, carboxymethylcellulose calcium, carboxymethylcellulose sodium, dextrates, dextrin, dextrose, ethylcellulose, gelatin, liquid glucose, guar gum, hydroxyethyl cellulose, hydroxypropyl cellulose, 25 hydroxypropyl methylcellulose, magnesium aluminium silicate, maltodextrin, methyl cellulose, polymethacrylates, polyvinylpyrrolidone, pregelatinised starch, sodium alginate, sorbitol, starch, syrup, tragacanth.

Examples of fillers include calcium carbonate, calcium phosphate, calcium sulphate, carboxymethylcellulose calcium, carboxymethylcellulose sodium, compressible 30 sugar, confectioner's sugar, dextrates, dextrin, dextrose, dibasic calcium phosphate

dihydrate, dibasic calcium phosphate, fructose, glyceryl palmitostearate, glycine, hydrogenated vegetable oil-type 1, kaolin, lactose, maize starch, magnesium carbonate, magnesium oxide, maltodextrin, mannitol, microcrystalline cellulose, polymethacrylates, potassium chloride, powdered cellulose, pregelatinised starch, sodium chloride, sorbitol, starch, sucrose, sugar spheres, talc, tribasic calcium phosphate, xylitol.

Examples of lubricants include calcium stearate, glyceryl monostearate, glyceryl palmitostearate, magnesium stearate, microcrystalline cellulose, sodium benzoate, sodium chloride, sodium lauryl sulphate, stearic acid, sodium stearyl fumarate, talc, zinc stearate.

Examples of glidants include colloidal silicon dioxide, powdered cellulose, magnesium trisilicate, silicon dioxide, talc.

Examples of disintegrants include alginic acid, carboxymethylcellulose calcium, carboxymethylcellulose sodium, colloidal silicon dioxide, croscarmellose sodium, crospovidone, guar gum, magnesium aluminium silicate, microcrystalline cellulose, methyl cellulose, polyvinylpyrrolidone, polacrillin potassium, pregelatinised starch, sodium alginate, sodium lauryl sulphate, sodium starch glycollate.

An example of a pharmaceutically acceptable wetting agent is sodium lauryl sulphate. The compositions are prepared and formulated according to conventional methods, such as those disclosed in standard reference texts and are well within the scope of a skilled person. For example, the solid oral compositions may be prepared by conventional methods of blending, filling or tableting. Repeated blending operations may be used to distribute the active agent throughout those compositions employing large quantities of fillers. Such operations are of course conventional in the art. The tablets may be coated according to methods well known in normal pharmaceutical practice.

Compositions may, if desired, be in the form of a pack accompanied by written or printed instructions for use.

No adverse toxicological effects are expected for the compositions or methods of the invention in the above mentioned dosage ranges.

In some embodiments of the methods described above, the method can further include administration of a second therapeutic agent as provided hereinabove to the

patient. The second therapeutic agent includes insulin and insulin analogs; GLP-1 (7-37) (insulinotropin) and GLP-1 (7-36)-NH₂; biguanides; glycogen phosphorylase inhibitors; aldose reductase inhibitors; α 2-antagonists; imidazolines; glitazones (thiazolidinediones); PPAR-gamma agonists; fatty acid oxidation inhibitors; α -glucosidase inhibitors; β -agonists; lipid-lowering agents; antiobesity agents; vanadate, vanadium complexes and peroxovanadium complexes; amylin antagonists; glucagon antagonists; gluconeogenesis inhibitors; somatostatin agonists and antagonists; antilipolytic agents; statins; antihypertensives; neprilysin inhibitor; angiotensin converting enzyme inhibitors; calcium channel blockers; diuretics; and renin inhibitors.

10 The Saroglitazar of formula (1), or a pharmaceutically acceptable salt thereof can be prepared by the general processes and examples disclosed in WO2003009841 and its Mg salt can be prepared by the process and example disclosed in WO2012104869.

 The following studies were conducted in suitable animal models as described hereinafter.

15 **Biological Studies**

Effect of Saroglitazar Magnesium on streptozotocin induced diabetic nephropathy in wistar rats.

Diabetic nephropathy was induced in wistar rats with single dose streptozotocin (50 mg/kg, intraperitoneal). One week after streptozotocin administration, animals were
20 dosed orally with Saroglitazar Magnesium (4 mg/kg) or vehicle daily once for 20 weeks. Fluorescein isothiocyanate-labeled inulin (FITC-Inulin) clearance was used to estimate glomerular filtration rate (GFR). Briefly, 5% (w/v) FITC-inulin dissolved in 0.9% (w/v) saline was dialyzed (1000 MWCO) overnight and sterilized by filtration (0.2 μ m). Anesthetized rats received a bolus (25 mg/kg, BW) of FITC-inulin via tail-vein
25 injections. Blood samples (<150 μ L) were collected by the retroorbital puncture into heparinized tubes, and centrifuged for 10 minutes at 10,000 RPM. Blood sampling was carried out at 3, 7, 10, 15, 35, 55 and 75 minutes post injection. Samples were buffered in 500 mM Hepes pH 7.4 and plasma fluorescence was measured (Excitation 485 nm/ Emission 528 nm). Data was analyzed to calculate GFR with appropriate software (e.g.
30 GraphPad Prism) by using a two-phase exponential decay function. At the end of

treatment urine were collected for a day to determine urinary albumin. Serum was used to assay biochemistry.

Result-1 Effect of the Saroglitzazar Magnesium on glomerular filtration rate

FITC inulin clearance were measured for GFR calculation, Creatinine has the substantial drawback that proximal tubular secretion accounts for ~50% of total renal creatinine excretion and therefore creatinine is not a reliable GFR marker. The rate of formation of plasma ultrafiltrate at the glomerulus has become the basis for evaluating renal function (glomerular filtration rate, GFR). The ideal marker to determine GFR should be freely filtered, neither secreted or reabsorbed and not metabolized. Such a behavior was found to be true for inulin, and inulin clearance has become a gold standard for determination of GFR. Results indicate that GFR is significantly increased in untreated diabetic rats when compared with normal control rats. Saroglitzazar Magnesium completely normalizes GFR which is similar to normal animal. Saroglitzazar Magnesium significantly reduced GFR (2.5 ± 0.6 vs 6.3 ± 1.3) compared to STZ-diabetic control showed in figure-1 and Table-1. Data represents mean $\pm$ SEM, n=7 in all except n=6 in Saroglitzazar magnesium, data were analyzed by one way ANOVA followed by Dunnet-t test.

Table-1: Effect of the Saroglitzazar Magnesium on GFR

Treatment group	GFR (ml/min)	% Change Vs Vehicle Control	Statistical analysis
Vehicle Control, PO	6.3 ± 1.3		
Saroglitzazar Magnesium (4 mg/kg,PO)	2.5 ± 0.6	$-59.7 \pm 10^*$	$P<0.05$
Normal Control	2.0 ± 0.5	$-67.5 \pm 7.3^*$	$P<0.05$
Data represents mean $\pm$ SEM, n=7 in all except n=6 in Saroglitzazar Magnesium			

Note: * indicate $P<0.05$ against vehicle control

Result-2: Effect of the Saroglitzazar Magnesium on microalbuminurea

Microalbuminurea rapidly increased with time in the untreated diabetic rats. In the present study, we demonstrate that chronic Saroglitzazar Magnesium treatment prevents the progressive increase in albuminuria (0.7 ± 0.3 vs 1.0 ± 0.3) in diabetic rats showed in

Figure-2 and table-2. Data represents mean $\pm$ SEM, n=7 in vehicle and non-diabetic normal control, n=6 in Saroglitzar Magnesium group, data were analyzed by one way ANOVA followed by Dunnet-t test.

Table-2: Effect of the Saroglitzar Magnesium on microalbuminurea

Treatment group	Urine microalbumin (mg/dL)	% Change Vs Vehicle Control	Statistical analysis
Vehicle Control, PO	1.0 $\pm$ 0.3		
Saroglitzar Magnesium (4 mg/kg,PO)	0.7 $\pm$ 0.3	-32.7 $\pm$ 24.6	NS
Normal Control	0.7 $\pm$ 0.2	-34.4 $\pm$ 15.5	NS
Data represents mean $\pm$ SEM, n=7, 8 and 9 respectively			

5

Result-3 Effect of the Saroglitzar Magnesium on serum creatinine

Serum creatinine increased in the untreated diabetic rats compared to normal control rats. After chronic Saroglitzar Magnesium treatment reduced increase in serum creatinine (0.29 $\pm$ 0.7 vs 0.37 $\pm$ 0.02) when compared to vehicle control, showed in Figure-3 and table-3. Data represents mean $\pm$ SEM, n=7 in vehicle, n=8 in Saroglitzar Magnesium and n=9 in normal control group, data were analyzed by one way ANOVA followed by Dunnet-t test.

10

Table-3: Effect of the Saroglitzar Magnesium on serum creatinine

Treatment group	Serum creatinine (mg/dL)	% Change Vs Vehicle Control	Statistical analysis
Vehicle Control, PO	0.37 $\pm$ 0.02		
Saroglitzar Magnesium (4 mg/kg,PO)	0.29 $\pm$ 0.04	-19.68 $\pm$ 11.02	NS
Normal Control	0.32 $\pm$ 0.02	-13.11 $\pm$ 5.19	NS
Data represents mean $\pm$ SEM, n=7, 8 and 9 respectively			

Result-4 Effect of the Saroglitazar Magnesium on serum BUN

Serum BUN increased in the untreated diabetic rats compared to normal control rats. Chronic Saroglitazar Magnesium treatment reduced increased serum BUN (25.0 ± 3.91 vs 27.4 ± 7.01) when compared to vehicle control, showed in Figure-4 and table-4. Data represents mean $\pm$ SEM, n=7 in vehicle, n=8 in Saroglitazar Magnesium and n=9 in normal control group, data were analyzed by one way ANOVA followed by Dunnet-t test.

Table-4 Effect of the Saroglitazar Magnesium on serum BUN

Treatment group	Serum BUN(mg/dL)	% Change Vs Vehicle Control	Statistical analysis
Vehicle Control, PO	27.4 ± 7.01		
Saroglitazar Magnesium (4 mg/kg,PO)	25.0 ± 3.91	-08.85 ± 14.25	NS
Normal Control	14.8 ± 0.72	-46.12 ± 02.63	NS
Data represents mean $\pm$ SEM, n=7, 8 and 9 respectively			

Result-5 Effect of the Saroglitazar Magnesium on serum urea

Serum urea increased in the untreated diabetic rats compared to normal control rats. Chronic Saroglitazar Magnesium treatment reduced increased serum urea (53.0 ± 8.2 vs 59.0 ± 15.0) when compared to vehicle control, showed in Figure-5 and table-5. Data represents mean $\pm$ SEM, n=7 in vehicle, n=8 in Saroglitazar Magnesium and n=9 in normal control group, data were analyzed by one way ANOVA followed by Dunnet-t test.

Table-5: Effect of the Saroglitazar Magnesium on serum urea

Treatment group	Serum Urea (mg/dL)	% Change Vs Vehicle Control	Statistical analysis
Vehicle Control, PO	59.0 ± 15.0		
Saroglitazar Magnesium (4 mg/kg,PO)	53.6 ± 8.2	-09.1 ± 13.9	Ns
Normal Control	31.9 ± 1.6	-46.0 ± 2.7	Ns
Data represents mean $\pm$ SEM, n=7, 8 and 9 respectively			

Result-6 Effect of the Saroglitazar Magnesium on serum glucose

Serum glucose significantly increased in the untreated diabetic rats compared to normal control rats. Chronic Saroglitazar Magnesium treatment reduced increased serum glucose (566.8 ± 43.8 vs 678.5 ± 26.0) when compared to vehicle control, showed in Figure-4 and table-4. Data represents mean $\pm$ SEM, n=7 in vehicle, n=8 in Saroglitazar Magnesium and n=9 in normal control group, data were analyzed by one way ANOVA followed by Dunnet-t test.

Table-6 Effect of the Saroglitazar Magnesium on serum urea

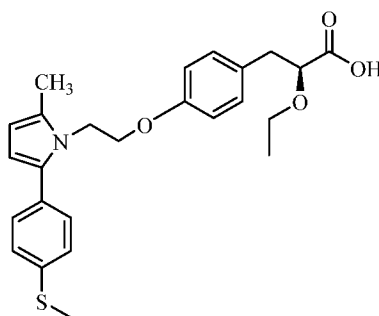
Treatment group	Serum glucose (mg/dL)	% Change Vs Vehicle Control	Statistical analysis
Vehicle Control, PO	678.5 ± 26.0		
Saroglitazar Magnesium (4 mg/kg,PO)	566.8 ± 43.8	$-16.5 \pm 6.5^*$	NS
Normal Control	118.6 ± 5.5	$-82.5 \pm 0.8^*$	P<0.05
Data represents mean $\pm$ SEM, n=7, 8 and 9 respectively			

Note: * indicate P<0.05 against vehicle control

A high percentage of type I and II diabetic patients eventually develop diabetic nephropathy (DN) that may progress to end-stage renal disease (ESRD). This leads to an additional burden on patients and health services. The structural injury in DN develops before the clinical and laboratory abnormalities such as hypertension, albuminuria or reduction of the glomerular filtration rate (Morsy et al. Diabetology & Metabolic Syndrome 2010, 2:29). This animal model is characterized by a 5 to 6 fold increase in blood glucose level and a marked reduction in the BW subsequently subsequent increase serum creatinine and serum urea levels observed in STZ-diabetic rats indicate altered glomerular permeability and increased filtration rate (Pharmacology 2015; 95:229–239) when compared with normal control, mainly due to insulin deficiency and stimulation of excessive lipolysis. On the other hand, treatment with Saroglitazar Magnesium significantly decreased blood glucose and marked reduction in FITC-Inulin clearance (GFR), simultaneously decreasing microalbuminuria, serum creatinine, BUN and Urea. Thus Saroglitazar Magnesium may protect diabetic nephropathy clinically.

We claim:

1. A compound of formula (1) or pharmaceutically acceptable salt thereof,



Formula (1)

for use in the prevention, delay of progression, or treatment of a disease or condition related with disorders of abnormalities of the diabetic kidney.

2. The disorders or the abnormalities of the diabetic kidney according to claim 1 selected from diabetic nephropathy, diabetic kidney disease, renal hypertrophy, hyperfiltration, nephrotic syndrome, diabetic kidney disease, chronic kidney disease.

3. The diabetic kidney disease according to claim 2 which is selected from early stage diabetic kidney disease.

4. The disorders of the abnormalities of the diabetic kidney according to claim 1 is diabetic nephropathy (DN).

5. The pharmaceutically acceptable salt as claimed in claim 1 which are selected from organic or inorganic salts wherein the inorganic salt is selected from Calcium, Magnesium, Sodium, Potassium, Zinc, Ammonium and Lithium And the organic salt is selected from L-Arginine, Tromethamine, L-Lysine, Meglumine, Benethamine, Piperazine, Benzylamine, Dibenzylamine, Dicyclohexylamine, Diethylamine, Diphenylamine, α -naphthylamine, O-phenylenediamine, 1,3-Diaminopropane, (S)- α -naphthylethylamine, (S)-3-methoxyphenylethylamine, (S)-4-methoxyphenyl ethylamine, (S)-4-chlorophenylethylamine, (S)-4-methylphenylethylamine, Cinchonine,

- 5 Cinchonidine, (-)-Quinine, Benzathine, Ethanolamine, Diethanol amine, Triethanolamine, imidazole, Diethylamine, Ethylenediamine, Choline, Epolamine, Morpholine 4-(2-hydroxyethyl), N-N-diethylethanolamine, Deanol, Hydrabamine, Betaine, Adamantanamine, L-Adamantanmethylamine and Tritylamine.
6. The pharmaceutically acceptable salt as claimed in claim 5 which is the magnesium salt.
7. The pharmaceutically acceptable salt as claimed in claim 5 which is selected from calcium, sodium and potassium salt.
- 10 8. A pharmaceutical composition as claimed in claim 1 comprising
- i. the pharmaceutically active substance of Formula (1) or pharmaceutically acceptable salt thereof;
 - ii. suitable additives
 - iii. a suitable stabilizer;
 - 15 iv. optionally with one or more pharmaceutically acceptable excipients for use in the prevention, delay of progression, or treatment of a disease or condition related with disorders of the abnormalities of the diabetic kidney.
9. The pharmaceutical composition as claimed in claim 8, used for the diabetic nephropathy, diabetic kidney disease, renal hypertrophy, hyperfiltration, nephrotic syndrome, diabetic kidney disease, chronic kidney disease.
- 20 10. The pharmaceutical composition of claim 8 wherein the disease condition is diabetic Nephropathy (DN).
11. The pharmaceutical composition as claimed in claim 8 wherein the suitable stabilizer is selected from antioxidants or chelating agents.
- 25 12. The pharmaceutical composition as claimed in claim 8 wherein the suitable antioxidants are selected from citric acid, alpha tocopherol, sodium sulphite, sodium metabisulphite, butylated hydroxy anisole (BHA), BHT (2,6-di-tert-butyl-4-methylphenol), monothioglycerol, Vitamin C (ascorbic acid)

13. The pharmaceutical composition as claimed in claim 8 wherein the suitable chelating agents are selected from Disodium EDTA, citric acid and or its salts, maleic acid, chlorambutol, chlorhexidine.
14. The pharmaceutical composition as claimed in claims 8 to 13 wherein
5 pharmaceutically active substance of Formula (I) is used in the range of 0.5 mg to 5 g.
15. The pharmaceutical composition as claimed in claim 8, wherein the suitable excipients are selected from solubilizers, diluents, fillers, disintegrants, binder, lubricants, glidants, wetting agents and solvents.
- 10 16. The pharmaceutical composition as claimed in claim 8, wherein the suitable additives are selected from sodium benzoate, sodium hydroxide, sodium sulfite and sodium carbonate.
- 15 17. The pharmaceutical composition as claimed in claim 15, wherein the suitable binders are selected from acacia alginic acid, tragacanth, carboxymethylcellulose sodium, poly (vinylpyrrolidone), compressible sugar (e.g., NuTab), ethylcellulose, gelatin, liquid glucose, methyl cellulose, povidone and pregelatinized starch, combinations thereof; poly(ethylene glycol), guar gum, polysaccharide, bentonites, sugars, invert sugars, poloxamers (PLURONIC F68, PLURONIC F127), collagen, albumin, celluloses in nonaqueous solvents, and the
20 like or their suitable combinations; poly(propylene glycol), polyoxyethylene-polypropylene copolymer, polyethylene ester, polyethylene sorbitan ester, poly(ethylene oxide), microcrystalline cellulose, poly(vinylpyrrolidone).
- 25 18. The pharmaceutical composition as claimed in claim 15, wherein the suitable glidants selected from glicoloidal silica, calcium silicate, magnesium silicate, silicon hydrogel, corn starch and talc.
19. The pharmaceutical composition as claimed in claim 15 wherein the suitable glidants selected from calcium stearate, magnesium stearate, mineral oil, stearic acid, zinc stearate.

20. The pharmaceutical composition as claimed in claim 15, wherein the suitable lubricants are selected from calcium stearate, magnesium stearate, mineral oil, stearic acid and zinc stearate.
21. The pharmaceutical composition as claimed in claim 15, wherein the suitable
5 disintegrant are selected from starches such as corn starch, potato starch, pre-gelatinized and modified starches, sweeteners, clays, microcrystalline cellulose, carsum, alginates, sodium starch glycolate, gums, guar, locust bean, karaya, pectin, tragacanth.
22. The pharmaceutical composition as claimed in claim 15, wherein the suitable
10 wetting agent are selected from poloxamers, gelatin, casein, Glycerol mono-oleate, lecithin (phosphatides), gum acacia, cholesterol, tragacanth, stearic acid, benzalkonium chloride, calcium stearate, glycerol monostearate, cetostearyl alcohol, sodium lauryl sulphate, sodium dodecyl sulfate, salts of bile acids, cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylene alkyl ethers,
15 polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters, polyethylene glycols, polyoxyethylene stearates, colloidal silicon dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulose calcium, carboxy methylcellulose, sodium methyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxy propyl methyl cellulose phthalate,
20 noncrystalline cellulose, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol, and poly vinyl pyrrolidone.
23. The composition as claimed in any claim 8-22 which is formulated in tablet or capsule forms.
24. The composition as claimed in any claim 8-23, wherein the pH is maintained in
25 the range of 6 to 10.

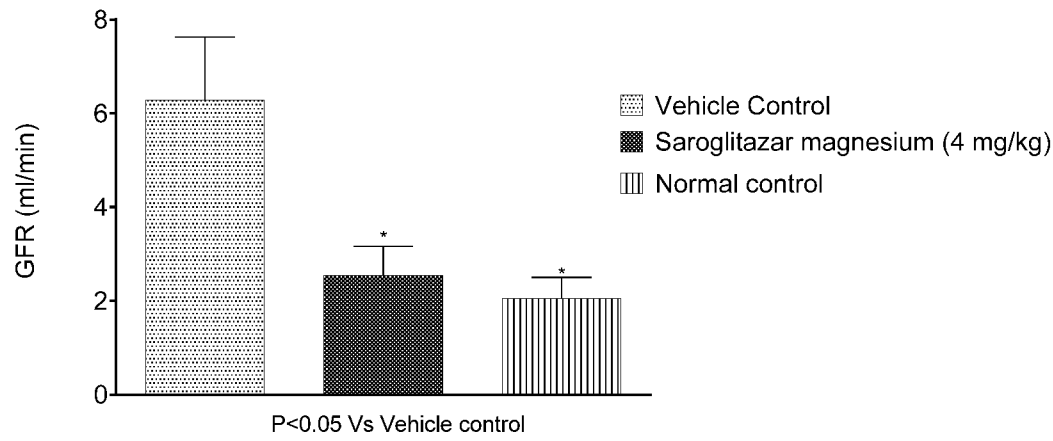


Figure-1

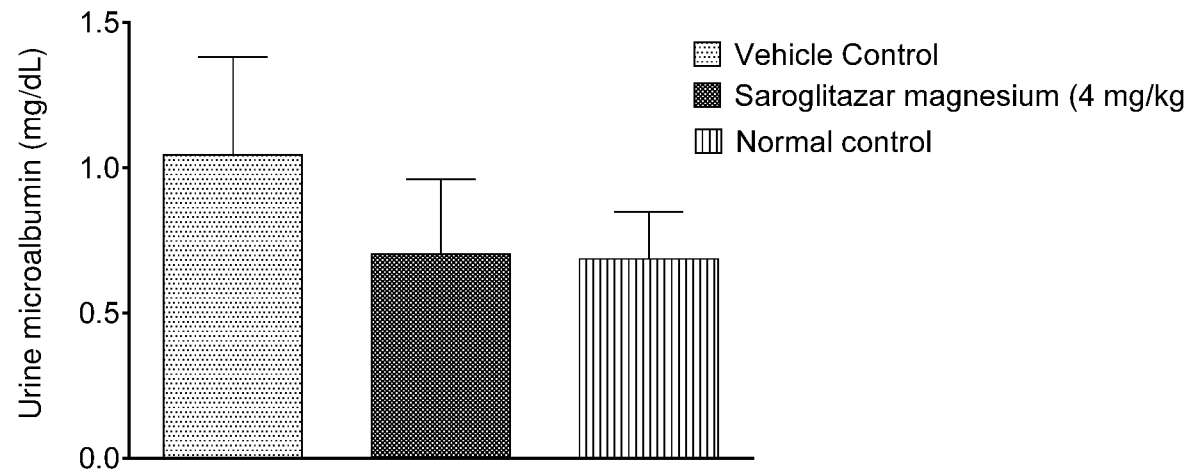


Figure-2

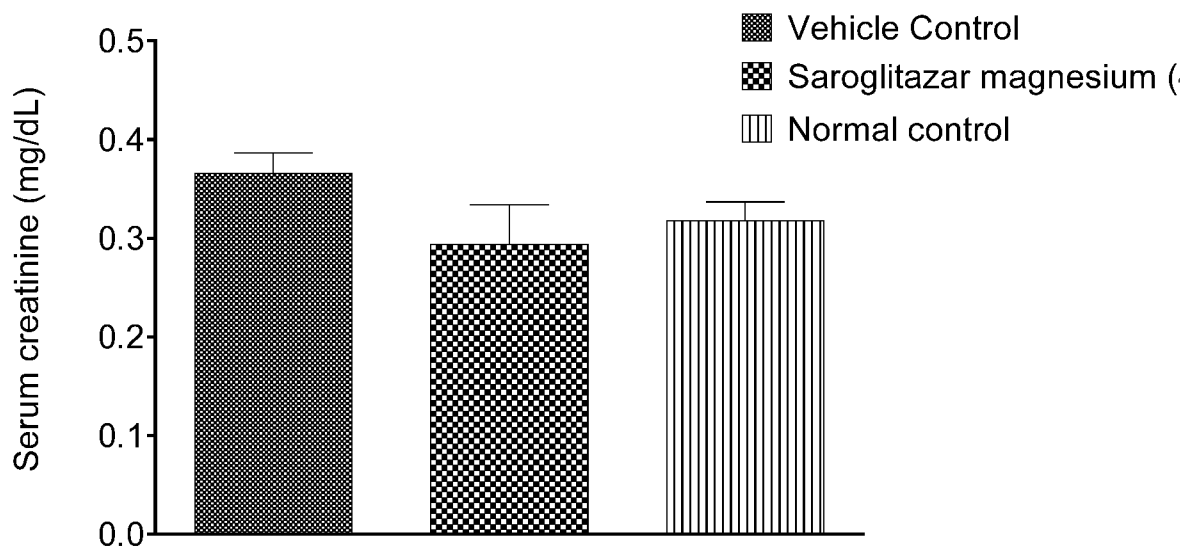


Figure-3

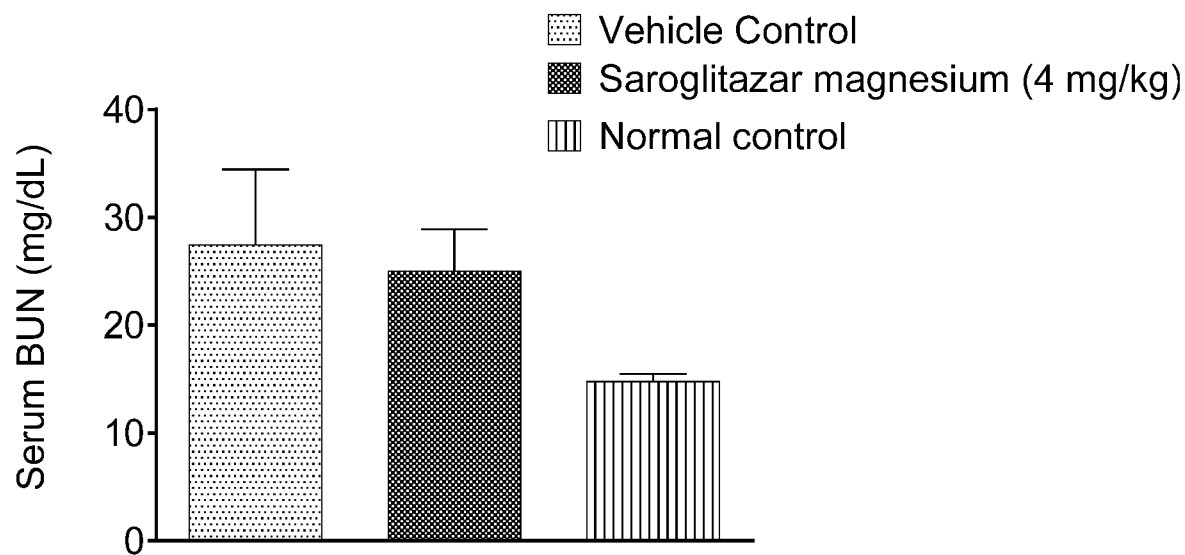


Figure-4

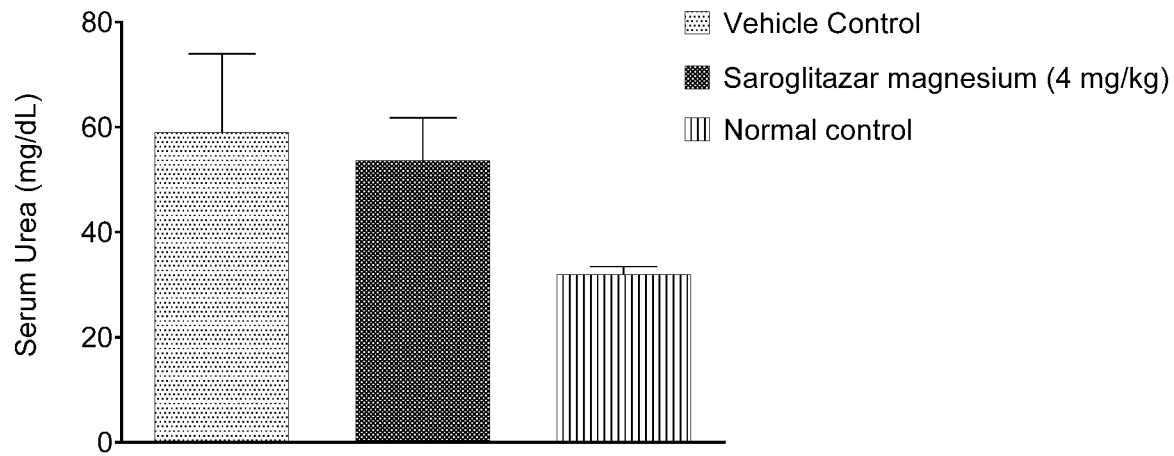


Figure-5

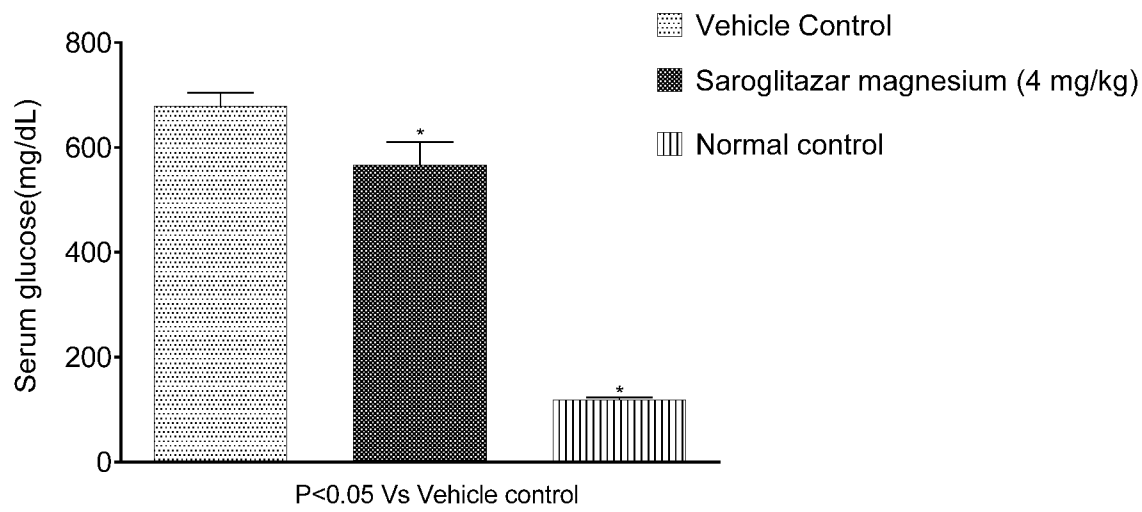


Figure-6

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2016/057089

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/40 A61P3/10
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, BIOSIS, CHEM ABS Data, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2015/001573 A1 (CADILA HEALTHCARE LTD [IN]) 8 January 2015 (2015-01-08) abstract page 12, line 17 - line 24 page 17, line 15 - line 27; claims 1-22 ----- -/--	1-24



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

27 February 2017

Date of mailing of the international search report

03/03/2017

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Ganschow, Silke

INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2016/057089

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	RAJENDRAKUMAR H. JANI ET AL: "A Multicenter, Prospective, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of Saroglitazar 2 and 4?mg Compared with Placebo in Type 2 Diabetes Mellitus Patients Having Hypertriglyceridemia Not Controlled with Atorvastatin Therapy (PRESS VI)", DIABETES TECHNOLOGY & THERAPEUTICS, vol. 16, no. 2, 1 February 2014 (2014-02-01), pages 63-71, XP055155508, ISSN: 1520-9156, DOI: 10.1089/dia.2013.0253 the whole document -----	1-24
X	ARUN SHARMA ET AL: "Saroglitazar, a novel cardiometabolic agent for diabetic dyslipidemia - A Review", JOURNAL OF YOUNG PHARMACISTS, vol. 7, no. 1, 23 December 2014 (2014-12-23), pages 2-6, XP055345058, India ISSN: 0975-1483, DOI: 10.5530/jyp.2015.1.2 the whole document -----	1-24
X	SOSALE ARAVIND SOSALE ET AL: "Saroglitazar for the treatment of hypertriglyceridemia in patients with type 2 diabetes: current evidence", DIABETES, METABOLIC SYNDROME AND OBESITY: TARGETS AND THERAPY, vol. 8, 1 January 2015 (2015-01-01), pages 189-196, XP055293364, DOI: 10.2147/DMSO.S49592 the whole document -----	1-24
A	TING R D ET AL: "MS544 CARDIOVASCULAR AND RENAL SAFETY OF FENOFIBRATE IN THE FIELD STUDY", ATHEROSCLEROSIS SUPPLEMENTS, ELSEVIER, AMSTERDAM, NL, vol. 11, no. 2, 1 June 2010 (2010-06-01), page 219, XP027097905, ISSN: 1567-5688 [retrieved on 2010-06-01] abstract -----	1-24

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2016/057089

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2015001573	A1	08-01-2015	AR 096811 A1 03-02-2016
		AU 2014285704 A1 15-10-2015	
		AU 2016228191 A1 06-10-2016	
		AU 2016250323 A1 10-11-2016	
		AU 2017200507 A1 16-02-2017	
		CA 2904980 A1 08-01-2015	
		CN 105358145 A 24-02-2016	
		EA 201592134 A1 30-06-2016	
		EP 3016650 A1 11-05-2016	
		EP 3120845 A1 25-01-2017	
		HK 1216001 A1 07-10-2016	
		JP 2016523824 A 12-08-2016	
		PH 12015502324 A1 10-02-2016	
		SG 11201507372P A 29-10-2015	
		TW 201513857 A 16-04-2015	
		TW 201636015 A 16-10-2016	
		US 2016068484 A1 10-03-2016	
		WO 2015001573 A1 08-01-2015	
