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(74) Agents: **LANG, Hilary, Dorr** et al.; Foley Hoag, LLP, 155  
Seaport Boulevard, Boston, MA 02210-2600 (US).

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(71) Applicant (*for all designated States except US*): **GELE-  
SIS, INC.** [US/US]; 222 Berkeley Street, Suite 1040,  
Boston, MA 02116 (US).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **ELENKO, Eric**  
[US/US]; 4 Longfellow Place, Apt. #502, Boston, MA  
02114 (US). **RON, Eyal, S.** [US/US]; 7 Coach Road,  
Lexington, MA 02420 (US). **ZOHAR, Yishai** [US/US];  
134 Vine Street, Newton, MA 02467 (US).

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(57) Abstract: One aspect of the present invention relates to methods for inducing satiation to prevent or treat obesity and manage weight/body composition by decreasing food intake both during a meal and to increasing the duration of time between meals. Specifically methods to increase the size of a food bolus without increasing the corresponding energy density are disclosed. In addition, methods of inducing satiation through small intestine volume displacement and placement of pressure on the walls of the small intestine in a manner which is non-invasive and does not result in significant pain or discomfort are disclosed.



WO 2009/049105 A2

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## ***Methods for Inducing Satiation***

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### **RELATED APPLICATION**

This application claims the benefit of priority of United States Provisional Patent Application No. 60/978,576 filed on October 9, 2007, which is hereby incorporated by reference in its entirety.

### **FIELD OF THE INVENTION**

The present invention is in the field of methods for inducing satiation to prevent or treat obesity and manage weight by decreasing food intake both during a meal and to increase the duration of time between meals.

### **BACKGROUND OF THE INVENTION**

Public health efforts and current antiobesity agents have not controlled the increasing epidemic of obesity. This disorder is increasingly prevalent in industrialized nations because of the abundance of food and the reduced activity levels that accompany the movement of populations from rural to urban settings. Obesity is loosely defined as an excess of body fat over that needed to maintain health.

Obesity is a condition in which excess body fat has accumulated to such an extent that health may be negatively affected.[ World Health Organization (2000). Technical report series 894: Obesity: Preventing and managing the global epidemic] It is commonly defined as a body mass index (BMI = weight divided by height squared) of 30 kg/m<sup>2</sup> or higher. This distinguishes it from being overweight as defined by a BMI of between 25–29.9 kg/m<sup>2</sup>.

Excessive body weight is associated with various diseases, particularly cardiovascular diseases, diabetes mellitus type 2, obstructive sleep apnea, certain types of cancer, and osteoarthritis (National Heart, Lung, and Blood Institute. Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults NIH Publication No. 98-4083 September 1998 National Institutes of Health). As a result, obesity has been found to reduce life expectancy. The primary treatment for obesity is dieting and physical exercise. If this fails, anti-obesity drugs and (in severe cases) bariatric surgery can be tried (National Institute for Health and Clinical Excellence. Clinical

Guideline 43: Obesity: The prevention, identification, assessment and management of overweight and obesity in adults and children. London, 2006).

Obesity arises from too much energy intake compared with a person's basal metabolic rate and level of physical exercise. Excessive caloric intake and a lack of physical activity in genetically susceptible individuals is thought to explain most cases of obesity, with purely genetic, medical, or psychiatric illness contributing to only a limited number of cases. With rates of adult and childhood obesity increasing, authorities view it as a serious public health problem.

Obesity is associated with increased morbidity and mortality. Detrimental effects of obesity on health include an increased risk of cardiovascular disease and the associated conditions of hypertension, diabetes, and hyperlipidemia. Millions of people are clinically obese and, in view of the deleterious effects of obesity on health, would benefit from treatment. Additionally, many people, although not clinically obese, can improve their health and well-being by losing weight.

The pathogenesis of obesity is multifactorial and includes the control of feeding behavior, mechanisms of fat storage, the components of energy intake and expenditure, and genetic and psychological influences. Likewise, the treatment of obesity is generally multifactorial. Unfortunately, the mechanisms of fat storage and genetic influences are not, generally speaking, amenable to treatment. Moreover, the control of feeding behavior and psychological influences require prolonged treatment. In addition, although the components of energy intake and expenditure are treatable, many obese individuals are resistant to or incapable of engaging in activities which significantly increase their energy expenditure. Therefore, controlling energy intake is an attractive approach for the treatment or prevention of obesity.

Various drugs and drug classes are known to be weight loss and antiobesity agents. These drugs consist of biological path way affecting agents such as 1) central nervous system agents that affect neurotransmitters or neural ion channels; 2) leptin/insulin/central nervous system pathway agents; 3) gastrointestinal-neural pathway agents; 4) agents that may increase resting metabolic rate ("selective"  $\beta$ -3 stimulators/agonist, uncoupling protein homologues, and thyroid receptor agonists); and 5) other more diverse agents. These suppressants, however, typically do not create a true feeling of satiation, such as that

brought on by a "full" stomach and/or they cause undesirable side-effects, such as anxiety, and hyperactivity and may have adverse side effects.

Amphetamines (dextroamphetamine) have been used as weight loss and anti-obesity drugs, but can cause unacceptable tachycardia and hypertension. They also have a high rate of abuse potential. Other sympathomimetic adrenergic agents, including phentermine, benzphetamine, phendimetrazine, mazindol, and diethylpropion, may have adverse cardiovascular side effects, and their indicated use is only short-term (12 weeks). In 2000, the appetite suppressant phenylpropanolamine was removed from United States market because of unacceptable risks of stroke, especially in adult women. Other weight loss agents, such as orlistat and sibutramine, also can have adverse side effects. For example, orlistat use frequently results in adverse events including flatus, oily stools, fecal urgency or fecal incontinence, and abdominal pain, particularly among patients who do not follow the recommended low-fat diet. Further, daily multivitamin supplementation is recommended to prevent the potential of impaired absorption of fat-soluble vitamins (A, D, E, and K) that may theoretically occur with long-term use. The use of sibutramine may increase blood pressure and heart rate, and its use is contraindicated in patients with uncontrolled hypertension, CHD, cardiac dysrhythmias, congestive heart failure, or stroke.

The sensation of satiety as a means of suppressing of appetite is well known in the art and is linked to both obesity treatment and effecting weight loss. For example, U.S. Patent No. 5,336,486 to Acharya *et al.* describes the false sensation of satiety induced by filling the stomach with heavy digestible vegetable fibers. Consuming large amounts of fiber, however, requires the patient to expel large quantities of fiber which can cause gastrointestinal discomfort. Others are unable to tolerate such high volumes of fiber for other reasons. To diminish the discomfort caused by a full stomach which retains vegetable fibers for a period of time higher than is normal, diet recipes based on vegetable fibers have been refined by the addition of easily digestible products with a low number of calories. See U.S. Patent Nos. 5,063,073 to Kratochvil; 5,654,028 to Christensen *et al.*; and 6,426,077 to Grace *et al.*

U.S. Patent Nos. 5,405,616 and 6,103,269 to Wounderlich *et al.* describe a material composed of gelatin or collagen hydrolysate, one or more active agents and one or more excipients (i.e., plasticizers, odorants, etc.). The material is prepared as a solution or suspension and then freeze-dried to obtain a solid material. The solid material can be administered as a powder, tablet or capsule. When the dried polymeric material comes in

contact with the aqueous medium of the stomach, it first becomes swollen in a few minutes and then is dissolved, resulting in a solution that will not interfere with the emptying of the gastrointestinal tract.

Likewise, inclusion of low energy density foods with significant volume results in reduction of overall caloric intake in a single meal (Bell *et al.* Am J Clin Nutr, 67:412–20, 1998; Rolls *et. al.* Am J Clin Nutr, 70: 448-455, 1999). Given the success in reducing caloric intake in one meal, the finding that a longer term approach of including low energy density foods as a staple of the diet reduces weight loss over the long term is understandable and has been demonstrated (Ello-Martin *et. al* Am J Clin Nutr ,85:1465–7, 2007; Greene *et. al.* Obesity, 14: 1795-1801,2006). The concept of eating low energy foods to induce satiety by taking up stomach volume has sometimes been called the "volumetrics diet" for which non-technical books have been written for those who wish to follow this approach (see Barbara Rolls, "Volumetrics Eating Plan" Harper Collins, 2007). The drawback of the volumetrics diet is limited food choice which in turn can result in poor compliance.

Intragastric balloons which are surgically inserted into a patient's stomach and then inflated have been used to take up stomach volume (for examples see U.S. Patents Nos. 4,416,267; 5,259,399; 6,733,512; 5,234,454; and 7,214,233). Devices other than balloons have also been suggested as semi-permanent implants to take up stomach volume (for example U.S. Patent Nos. 7,066,945 and 7,033,384; US Patent Application Publication Nos. 2005/0245957 and 2006/0217757A1; and PCT Application Publication No. WO 2007/017842). Nevertheless, the continual stimulation produced by these devices results in habituation and adaptation by the patient negating their efficacy over an extended period of time.

A study was conducted to determine the effects of various levels of gastric distension on spontaneous meal intake (Gastric distention by balloon and test-meal intake in obese and lean subjects by Allan Geliebter, PhD; Sandra Westreich, BS; and Dennis Gage, MD, Am J Clin Nutr 1988;48:592-4). A balloon was inserted into the stomach of four lean and four obese subjects before consumption of a lunch meal. On different days the balloon was filled with 0, 200, 400, 600, and 800 mL water in a random sequence. As balloon volume increased, food intake decreased, with a balloon volume of 400 mL significantly reducing intake ( $p < 0.01$ ).

An approach for displacement of stomach volume is use of polymeric materials. Low caloric products for controlling body weight can be obtained by using collagenic biopolymers, such as: soluble collagen, gelatin or collagen hydrolysate. See U.S. Patent Nos. 5,100,688; 5,211,976; 5,219,599; 5,665,234; and 5,665,419. Commercial products, such as "Dietary Supplement -CALORAD®," produced by EYI-Essentially Yours Industries, Inc.-USA, have been used for weight loss control and also as a muscular stimulant, as well as an aid for osteoporosis and for arthritis treatment.

Absorbent materials for water and aqueous media, including fluids secreted by the human body, are well known in the literature. These materials are typically polymer-based and are produced in the form of powders, granules, microparticles or fibers. Upon contact with an aqueous medium, polymeric materials swell by absorbing the liquid phase into their structure without dissolving. A "hydrogel" is a polymeric material which has the ability to absorb water and swell. If the water absorbency is more than 20 g water per 1 g of dried polymer, the material is referred to as a "superabsorbent polymer" (SAP).

Chen Jun et al. in "Gastric retention properties of superporous hydrogel composite" J. Controlled Release, 64, 39-51, 2000, and in U.S. Pat. No. 6,018,033 and Park K. et al. in U.S. Pat. No. 5,750,585 and U.S. Pat. No. 6,271,278 disclose that hydrogels obtained by grafting and cross-linking a mixture of acrylic acid, acrylamide, potassium salt of 3-sulfopropyl acrylate and N,N'-methylenebisacrylamide in the presence of AcDi-Sol® (small cross-linked polysaccharide), swell in the stomach after oral administration and can be used as an auxiliary in diet control. Burnett D.R. et al. in W0 2004/056343 A1 discloses an ingestible formulation for transient, noninvasive reduction of gastric volume comprising polymeric formulations capable of being retained in the stomach for a certain period of time followed by rapid degradation upon entering an intestine. The concept of using polymers for taking up stomach volume to induce satiation is also disclosed by others (see, for example, US Patent Application Publication Nos. 20050245957 and 20060142794; and PCT Application Nos. WO 2006/047882 and WO 2006/070337).

Other polymers, which are non bio-degradable polymers, may swell in the stomach and act as stomach-filler and yet these polymers by virtue of their non-degradability will increase the risk for impaction (syndrome of moderate toxemia, an absence of fecal movements and straining in some cases. There is a collection of putty-like or hardened feces in the rectum or sigmoid) and / or act as laxatives – an undesirable affect. Laxatives (or purgatives) are foods, compounds, or drugs taken to induce bowel movements or to

loosen the stool, most often taken to treat constipation. Certain types of laxatives are bulking agents that cause stool to be bulkier and retain more water. Additionally, these laxatives may form an emollient gel, making it easier for peristaltic action to move stool along. These bulking agents include dietary fiber and synthetic hydrogels, such as polyacrylic acids, including calcium polycarbophyl (such as Noveon AA-1 CA-1 or CA-2, Lubrizol, OH). (Some products containing this type of polymers are: Equalactin, FiberCon, Fiber-Lax, FiberNorm, Konsyl, Mitrolan all recommend a dose of about 1-1.5. g per administration, other products containing similar non-degradable polymers, such as cross-linked polyacrylic acid hydrogel homopolymers (such as Carbopol 971P, 71G, 974P, Lubrizol., OH)

Both the natural non-digested fibers and the synthetic hydrogels absorb water and may act as stomach fillers because of the bulking effect, and yet they do not degrade in the GI track.

While polymers and related material have been suggested as a means to take up stomach volume, the method of using such materials to increase the size of a food bolus without increasing the corresponding caloric density of the food density has not been disclosed. The advantages of forming a mixture between food and such polymers or related materials include both greater efficacy in inducing satiation and increased safety (e.g., a decreased chance of impaction). Formation of a mixture with food would ideally be done with a polymer that, when swollen, has the same rheological properties as ground food and/or digested food, and would thus form a homogenous mixture.

The principal of taking up volume in the small intestine and putting pressure on the intestinal wall by a swollen polymeric material to reduce food intake has not been reported. The small intestine produces a number of hormones in response to food which induce satiation such as CCK (April *et. al.* Gastroenterology, 128: 175-191, 2005; Huda *et. al.* Obesity Reviews, 7: 163-182, 2006; Cuppies *et. al.* American Journal of Physiology, 288:1438-1443, 2005). For instance it has been shown that directly infusing food into the small intestine, particularly lipids results in a sense of satiety in humans (Catiglione *et. al.* Physiol Behav. 64:141-145, 1998) and in animals (Reidelberger *et. al.* Am J Physiol. 244:R872-881, 1983). Partial bypass of the small intestine as part of bariatric surgical procedures have been done (Matarasso *et. al.* Plast Reconstr Surg., 119: 1357-62, 2007). Gastric sleeves that result in partial bypass of the small intestine have also been suggested (for example US Patent Application Publication No. 20050169341). Binmoeller has

disclosed use of a device which can be inserted into the small intestine to reduce flow of nutrients and aid in creation of a satiation signal (see US Patent Application Publications No. 20060178691 and US20070293885A1). But, gastric bypass, gastric sleeves and the device disclosed by Binmoeller are highly invasive and carry a great risk of complications, including mortality. The nutrient deprivation produced by bypass and gastric sleeves are also problematic and not appropriate for patient populations other than the morbidly obese. Nutrient deprivation does not work by taking up intestinal volume or creating pressure on the intestinal wall, but rather works by the opposite means of restricting flow and absorption of nutrients to the small intestine.

Insertion of and inflation of balloons into the small intestine of rats results in decreased fluid intake, but also appears to also evoke a painful reaction when the balloons are inflated passed a certain point (Bardos, Behav Neurosci., 111:834-844, 1997). Likewise, balloon insertion into the intestine was perceived negatively by rats as shown in a taste aversion paradigm (Bardos, Physiol Behav., 74:407-413, 2001). Actual use of a balloon in people would be highly invasive and difficult to insert and maintain. In addition, as is the case with balloons inserted into the stomach, continual stimulation of the small intestine could result in habituation and adaptation, as well as pain, which does not occur with the episodic stimulation produced naturally by food.

Therefore, there is a need for methods that: would allow for intestinal volume to be displaced in a manner that is non-invasive and/or creates pressure on the small intestine walls. Such a method should be achieved without causing impaction and / or over-pressurizing the intestine, and therefore, not result in the painful sensations caused by balloons described by Bardos, or similar devices. To date, no such method exists.

### **SUMMARY OF THE INVENTION**

One aspect of the present invention relates to methods for inducing satiation to treat obesity, reduce fat, weight loss, and/or prevent weight gain.

One approach involves the creation of a food bolus that has an increase in volume, without the corresponding increase in energy density, by administering to a subject a composition comprising a material that has substantially similar rheological properties as ground food (so that the bolus thereby enlarged maintains its basic rheological properties). In other words, one aspect of the present invention relates to methods of increasing the

volume of a food bolus in a subject, without increasing the corresponding energy density of the food bolus, through the creation of a mixture of orally ingested food and subsequently administered material, thereby inducing a feeling of satiation in a subject.

In another aspect of the present invention relates to methods of prolonging gastric emptying time by maintaining the swollen polymer mixed with digested food in the stomach for extended time period of time that are substantially longer than without the polymer. In another aspect of the present invention relates to methods of prolonging gastric emptying time by maintaining the swollen polymer mixed with digested food in the gastrointestinal track as long as possible for extended time period of time that are substantially longer than without the polymer..

Another approach involves displacing volume and/or creating pressure on the walls of the intestine of a subject in a non-invasive manner, without creating significant pain or unreasonable discomfort in the subject, by administering a composition comprising a material which swells in the intestine and increases the volume of the intestinal contents. In other words, the present invention relates to methods of using compositions comprising materials which have the ability to displace volume and/or induce pressure on the walls of the intestine in order to induce a feeling of satiation directly or through prolonging gastric emptying time.

Furthermore, the present invention understands that if the physical characteristics of the reduction of flow rate of food breakdown products through the small intestine increases the contact time between the small intestine and the partially digested food cause the ileum break, thus releasing hormones and neurotransmitters such as cholecystokinins (CCK), leptin, obestatin, nesfatin-1 and other neural signals that may induce satiety. Furthermore, slower flow in the upper GI cause slower stomach emptying, thereby enhancing the satiety.

Accordingly, one aspect of the invention relates to a method of inducing satiation in a subject comprising the step of: administering a composition to the subject; wherein the composition swells in the subject's intestine or both the subject's stomach and the small intestine. In some embodiments, the composition swells in the subject's stomach and subsequently collapses and/or partially degrades after a first period of time, and swells in the small intestine and subsequently collapses and/or degrades after a second period of time. In other embodiments, the composition swells only in the subject's small intestine.

In other embodiments, the composition swells only in the subject's small intestine and subsequently collapses and/or degrades after a period of time.

In some embodiments, wherein the composition creates pressure on the wall of the small intestine, increases the volume of intestine's content, or both.

In some embodiments, the composition has substantially similar rheological properties as ground food. In other embodiments, the composition combines with an existing food bolus in the subject without increasing the energy density of the food bolus.

In other embodiments, the composition is coated with a coating that dissolves in a third period of time. In some embodiments, the coating is selected from the group consisting of cellulose ethers, Instacoat Aqua, mixtures of acrylic resin, and mixtures thereof. In other embodiments, the coating is selected from the group consisting of ETHOCEL, METHOCEL, HPMC and PVA based systems, ethyl acrylate/methyl methacrylate copolymers and mixtures thereof. In other embodiments, the coating dissolves at a pH of greater than 3.5. In some embodiments, the coating dissolves at a pH of about 5, while in other embodiments, the coating dissolves at a pH of about 6.5.

In still further embodiments, the coating is an enteric coating. In some embodiments, the enteric coating is selected from the group consisting of cellulose derivatives, acrylic derivatives, hydroxypropyl methylcellulose derivatives, maleic acid-vinyl compound copolymers, and copolymers of methyl methacrylate and ethyl acrylate. In other embodiments, the enteric coating is selected from the group consisting of cellulose acetate phthalate, polyvinyl acetate phthalate, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate succinate, carboxymethylethylcellulose, cellulose acetate succinate, methylcellulose phthalate, hydroxymethylethylcellulose phthalate, hydroxypropylmethylcellulose phthalate, hydroxypropylmethylcellulose acetate succinate, polyvinyl alcohol phthalate, polyvinyl butylate phthalate, polyvinyl acetoacetal phthalate, poly(vinyl acetate, maleic acid anhydride), poly(vinyl butyl ether, maleic acid anhydride), poly(styrene, maleic acid monoester), poly(ethyl acrylate, methacrylic acid), poly(styrene, acrylic acid), poly(methyl acrylate, methacrylic acid, octyl acrylate), and poly(methacrylic acid, methylmethacrylate).

In other embodiments, the composition further comprises an excipient, such as plasticizers, diluents, binders, lubricants, glidants, colorants, stabilizers, surfactants, flavorants, preservatives, anti-oxidants, buffering agents and combinations thereof.

In some embodiments, the composition swells by absorbing water, gastric fluid, intestinal-fluid, or a mixture thereof, and degrades in the gastrointestinal tract. In other embodiments, the composition degrades in the gastrointestinal tract and releases water before excretion. In some embodiments, the composition resides in the stomach for a first period of time, passes into the intestinal tract, and degrades substantially in the intestinal tract after a second period of time, wherein the second period of time is longer than the first period of time. In some embodiments, the first period of time is 0.5 to 8 hours, such as about 0.5, 1, 2, 3, 4, 5, 6, 7, or 8 hours. In some embodiments, the second period of time is 1 to 72 hours, such as 6 to 48 hours, or about 1, 2, 4, 8, 16, 24, 36, 48 or 72 hours.

In other embodiments, the present invention relates to a method of inducing satiation in a subject comprising the step of: administering a composition to the subject; wherein the composition degrades preferentially in the colon. In some embodiments, the composition swells in the subject's stomach, the subject's small intestine, or both, and then degrades preferentially in the colon. In some embodiments, the composition degrades in the colon at a faster rate than in the stomach or the intestine. In other embodiments, the composition degrades exclusively in the colon. In some embodiments, the composition that degrades in the colon comprises oligosaccharides, polysaccharides, or a mixture thereof.

In some embodiments of any of the aforementioned methods, the composition comprises an amount of a polymer that swells in the stomach to a volume of 200 mL to 1000 mL. In other embodiments, the polymer swells to a volume of about 200, 400, 600, or 800 mL in the stomach, or 300 mL to 800 mL.

In some embodiments, the amount of the composition administered comprises 2 to 8 grams of a polymer. In other embodiments, the polymer swells in a gastrointestinal environment to at least 50 times its original volume, such as 50 to 400 times its original volume. In other embodiments, the polymer swells in a gastrointestinal environment to about 50, 100, 150, 200, 300 or 400 times its original volume.

In some embodiments, the composition comprises one or more polymeric materials selected from the group consisting of homopolymers, copolymers, cross-linked polymers, polysaccharides, oligosaccharides, polymer blends, super porous polymers, superabsorbent polymers, interpenetrating polymers or polymer composites. In other embodiments, the composition comprises a superabsorbent polymer.

In some embodiments, the superabsorbant polymer comprises a synthetic polymer crosslinked with a natural polymer. In some embodiments, the synthetic polymer comprises a poly(styrene-co-maleic anhydride/acid) polymer. In some embodiments, the natural polymer is selected from the group consisting of collagen, hyaluronic acid, gelatin, albumin, a polysaccharide, and mixtures thereof. In other embodiments, the superabsorbent polymer comprises SMAc and gelatin. In a further embodiment, the composition comprises SMAc and gelatin, and NaOH in a ratio of 90:10:80 (by dry weight). In another embodiment, the SMAc and the gelatin are cross-linked. In another embodiment, the SMAc has a molecular weight of between about 650,000 Da to about 3,000,000 Da, about 850,000 Da to about 1,500,000 Da, or about 1,000,000 Da.

In some embodiments, the any of the aforementioned methods, the composition is administered orally. In some embodiments, the composition is administered in a tablet, capsule, caplet, powder, syrup, solution, suspension, sachet or shake.

In some embodiments, the composition further comprises an appetite suppressant, an antiobesity nutraceutical or an antiobesity agent. In other embodiments, the aforementioned methods further comprise administering an appetite suppressant, antiobesity nutraceutical or an antiobesity agent to the subject. For example, the appetite suppressant, antiobesity nutraceutical or antiobesity agent can be selected from the group consisting of sibutramine hydrochloride, orlistat, rimonabant, benzphetamine, diethylpropion, mazindol phendimetrazine, phentermine, amphetamine, fenfluramine, nalmetrene, Phentermine (Fastin, Adipex, Ionamin and others); Diethylpropion (Tenuate); Sibutramine (Meridia, Reductil); Rimonabant (Acomplia); benfluorex; butenolide; diethylpropion; FG 7142 (N-methyl-9H-pyrido[5,4-b]indole-3-carboxamide); norpseudoephedrine; phenmetrazine; phentermine; phenylpropanolamine; pyroglutamyl-histidyl-glycine; sibutramine; Phendimetrazine (Prelu-2, Bontril); Benzphetamine (Didrex); Oxyntomodulin; Methylphenidate; (Concerta) (Ritalin); Phenylethylamine (Trimspa), pyruvate, DHEA, B-hydroxy-B-methylbutyrate, chitosan, conjugated linoleic acid (CLA), hoodia gordonii, bitter orange (citrus naringin), kava, usnic acid, ephedra, and combinations thereof.

In another embodiment, any of the aforementioned methods further comprises performing a surgical intervention for obesity on the subject, such as gastric banding, gastric bypass surgery, intragastric balloon, implantable gastric stimulator and gastric electrical stimulation.

In some embodiments, the present invention relates to a methods of inducing satiety in a subject comprising using a mechanical device, such as a non-polymeric mechanical device, to apply pressure to the intestinal wall in the subject. In some embodiments, the mechanical device creates pressure on the wall of the small intestine in a non-invasive manner. In some embodiments, the device that creates pressure on the wall of the small intestine or reduces the follow of food in the intestine in a non-invasive manner.

In some embodiments, the present invention relates to a composition comprising one or more polymeric materials selected from the group consisting of homopolymers, copolymers, cross-linked polymers, polymer blends, super porous polymers, superabsorbant polymers, interpenetrating polymers and polymer composites, oligosaccharides, and at least one pharmaceutically acceptable carrier or excipient. In some embodiments, the composition comprises an enteric substance. In some embodiments, the enteric substance coats or encapsulates the polymeric material. In other embodiments, the enteric substance is blended with the polymeric material. In other embodiments, a portion of the polymeric material is coated with or blended with the enteric substance, and a portion of the polymeric material is not coated with or blended with the enteric substance. Thus, the composition will swell in part in the stomach, and in part in the small intestine and/or the colon.

Yet another approach involves administering a composition to a subject which comprises a material which will swell in the stomach, and provide rheological properties similar to digested food, prolong stomach emptying, collapse and/or degrade after a first period of time, pass into the intestine, swell again in the intestine, and then collapse/degrade after a second period of time.

Yet another approach involves administering a composition to a subject which comprises a material which will swell in the stomach and slow gastric emptying time to extend the satiety effect of limited calorie meal.

Yet another approach involves administering a composition to a subject which comprises a material which will swell in the small intestine and increase the resistance to peristaltic flow while maintaining a rheology similar to digested food to enhance satiety feeling for prolonged time.

These embodiments of the present invention, as well as other embodiments, along with their features and characteristics, will be apparent from the description and claims that follow.

## BRIEF DESCRIPTION OF THE FIGURES

**Figure 1** depicts a photograph of an excised rat stomach with tied off ends containing food and poly(styrene-co-maleic anhydride/acid) cross-linked with gelatin (SAP).

**Figure 2** depicts a photograph of an excised rat's stomach contents. The rat was administered poly(styrene-co-maleic anhydride/acid) cross-linked with gelatin (SAP) and then allowed access to food. The photograph shows food mixed with SAP to form a homogeneous mixture.

**Figure 3** depicts a graph showing the decrease in food intake of rats administered poly(styrene-co-maleic anhydride/acid) cross-linked with gelatin (SAP).

**Figure 4** depicts a graph showing that the poly(styrene-co-maleic anhydride/acid) cross-linked with gelatin (SAP) produced a significant decrease in food intake compared to the water control in a within-subject design.

**Figure 5** depicts the reduction of food intake in rats upon administration of poly(styrene-co-maleic anhydride/acid) cross-linked with gelatin (SAP).

**Figure 6** depicts a decrease in food intake in rats upon administration of 8 mL of poly(styrene-co-maleic anhydride/acid) cross-linked with gelatin (SAP).

**Figure 7** depicts a graph which shows that sub-chronic administration of poly(styrene-co-maleic anhydride/acid) cross-linked with gelatin (SAP) for four days did not influence the production of feces.

**Figure 8** depicts a graph which shows that sub-chronic administration of poly(styrene-co-maleic anhydride/acid) cross-linked with gelatin (SAP) for four days did not influence the percentage of fecal water content.

**Figure 9** depicts a graph which shows that sub-chronic administration of poly(styrene-co-maleic anhydride/acid) cross-linked with gelatin (SAP) for four days did not influence the production of urine.

**Figures 10-11** depict graphs which show that while rats which were administered poly(styrene-co-maleic anhydride/acid) cross-linked with gelatin (SAP) consumed less food, an increase in waste production was not observed.

**Figure 12** depicts a graph which shows the swell--collapse--re-swell--degrade cycle that was observed for poly(styrene-co-maleic anhydride/acid) cross-linked with gelatin (SAP) in laboratory experiments *in vitro*.

**Figure 13** depicts a possible swell--collapse--re-swell--degrade cycle for hydrogel with a colonic degrading bond.

## DETAILED DESCRIPTION OF THE INVENTION

One aspect of the present invention relates to a method of oral administration of a composition to a subject that will cause the volume of a food bolus in the subject's stomach and/or intestine to increase without increasing the energy density of the bolus. In certain embodiments, the subject is a primate, bovine, ovine, equine, porcine, avian, rodent, feline, or canine. In certain embodiments, the subject is a human.

In certain embodiments, the composition administered comprises one or more polymeric materials selected from the group consisting of homopolymers, copolymers, polymer blends, cross-linked polymers, polymer blends, superporous polymers, interpenetrating polymers, superabsorbent polymers and polymer composites. In certain embodiments, the polymeric material is a superabsorbent polymer. In certain embodiments, the polymeric materials are biocompatible for human use. In certain embodiments, the polymeric material has rheological properties to similar to those of ground food. In certain embodiments, the polymeric material is hydrogel. A more detailed discussion of the materials which may be used is provided below.

In certain embodiments, after administration, the polymeric material will swell in the stomach. For example, the polymeric material, upon absorption of water or gastric fluids and/or upon mixing with food in the stomach, will cause the volume of a food bolus to increase without increasing the energy density of the bolus. In such embodiments, the increased size of the food bolus will result in satiation and decreased caloric intake. In certain embodiments, the polymeric material will only remain swollen in the stomach for a period of time, after which it will shrink, degrade and/or collapse.

In certain embodiments, after administration, the polymeric material will swell in the intestine. In certain embodiments, the polymeric material will swell in the small intestine. In certain embodiments, the polymeric material will swell in the intestine and thereby take up volume and/or exert pressure on the walls of the small intestine. In certain

embodiments, the polymeric material will displace volume in the small intestine and thereby result in satiation and decreased caloric intake. In certain embodiments, the polymeric material will exert pressure on the small intestine walls and thereby result in satiation and decreased caloric intake. In certain embodiments, the polymeric materials will only remain swollen in the intestine for a period of time, after which it will shrink, degrade and/or collapse.

In certain embodiments, the method involves administering to a subject a composition comprises a polymeric material which will swell in the stomach, shrink after a first period of time, pass into the intestine, swell again in the intestine, and then shrink after a second period of time. In another embodiment, the polymeric material will swell in the stomach and then pass into the small intestine, where it will collapse, shrink and/or degrade. In yet another embodiment of the invention, the polymeric material will swell in the stomach, pass through the small intestine and not shrink in either the stomach or the small intestine.

In certain embodiments, the method involves administering to a subject a composition comprises a polymeric material which will swell in the stomach, shrink after a first period of time, pass into the intestine, swell again in the intestine, pass to the colon and then shrink, collapse and/or degrade. In a different embodiment, the polymeric material will swell in the stomach and then pass into the small intestine, and then to the colon where it will collapse, shrink and/or degrade. In yet another embodiment of the invention, the polymeric material will swell in the stomach, pass through the small intestine and not shrink in either the stomach or the small intestine but will degrade, shrink and or collapse in the colon

Yet another approach involves administering a composition to a subject which comprises a material which will swell in the stomach and thereby slow gastric emptying time to extend the satiety effect of a limited calorie meal.

Data from the use of gastric balloons that occupy stomach volume, a procedure which is a common practice for weight loss in some parts of the world, indicates that at least 200 mL of volume, but preferably over 400 mL, is needed for efficacy. Our animal models have demonstrated that the amount of reduction of food intake caused by swollen hydrogel in the stomach is correlated directly with the amount of material that was administered. Based on the in vivo data, it was also demonstrated that the amount of the

reduction of food intake is also affected by the amount of swollen polymer in the intestine, which is also “volume driven.”

The data illustrates that the amount of swollen polymer volume in the stomach and/or intestine are important for efficacy. Yet, the need for a material with rheological properties similar to the digested food and yet degradable before exertion is important for efficacy. Yet, the need for degradable polymer is important, as non-degradable polymer at the amounts needed to initiate satiety (at least 200 mL when swollen) will cause adverse and /or undesired side effects like diarrhea and dehydration. Therefore, having materials that degrade in the gastrointestinal track are important for safety and compliance.

Accordingly, in a further embodiment, the polymeric material increases its volume in the stomach, for example, the polymeric material induces satiation following absorbing water and/or physiological fluids and swells to at least 200, 300, 400, 600 and 800 mL, while in other embodiments, the material swells to about 400 mL..

Yet another approach involves administering a composition to a subject which comprises a material which will swell in the small intestine and increases the resistance to peristaltic flow (i.e., viscosity) while maintaining a rheology (e.g., elastic modulus) similar to digested food to enhance satiety for prolonged time.

In a further embodiment, the polymeric material induces satiation following absorbing water and/or physiological fluids such as chyme (or Chymus). In another embodiment, the feeling of satiation lasts for not less than 10 minutes and not more than 48 hours.

In certain embodiments, the composition will comprise a polymeric material which will only swell in the small intestine (i.e., it will not swell in any other part of the gastrointestinal (GI) track). In some of such embodiments, the polymeric material will be packaged so that it will only be released in the pH environment of the small intestine (i.e. at a pH of about 5.5). In other such embodiments, the polymeric material will be packaged so that it will only be released by enzymes found the small intestine.

In certain embodiments, the composition will comprise a polymeric material which will only swell in the small intestine and resulting in slower gastric emptying and prolong satiety. For example, gastric emptying can be 2 to 6 times longer than without the material.

### **Polymeric Materials**

The compositions of the present invention may comprise polymeric materials, for example, homopolymers, copolymers, cross-linked polymers, polymer blends, super porous polymers, interpenetrating polymers or polymer composites. In one embodiment, the polymeric material is a superabsorbent polymer such as a hydrogel. Suitable polymers which form can form a hydrogel include both synthetic and natural polymers.

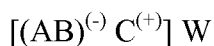
Examples of synthetic polymers which can form hydrogels include polyacrylic and polymethacrylic acid polymers, cellulose derivatives such as hydroxypropyl cellulose, polyethyleneglycol polymers, copolymers and block copolymers, azo containing polymers, and other water swellable, biocompatible polymers. Examples of natural polymers which can form hydrogels include collagen, hyaluronic acid, gelatin, albumin, polysaccharide, and derivatives thereof. Natural polymers can also be of the type isolated from various plant materials such as psyllium.

Structurally, such water-absorbent polymeric materials are three dimensional macromolecular configurations. They are produced through several methods: a) synthesis from monomers (cross-linking polymerization); b) synthesis from polymers and polymerization auxiliary (grafting and cross-linking polymerization); c) synthesis from polymers and non-polymerization auxiliary (cross-linking polymers); d) synthesis from polymers with energy sources (cross-linking polymers without auxiliaries) and e) synthesis from polymers (cross-linking by reactive polymer-polymer intercoupling). The raw materials and technology used in synthesis are main factors in the creation of hydrogels' key properties and their range of applications.

There are a known number of methods for obtaining high purity absorbent materials for aqueous media with three-dimensional polymeric configurations and with potential applications in pharmaceutical and/or medical field: a) chemical methods: ionic and/or coordinative intercomplexing (i.e., U.S. Patent No. 4,570,629 to Widra and U.S. Patent No. 5,153,174 to Band *et al.*); cross-linking with oligomers or reactive polymers that have reactive groups with double bonds or rings (i.e., U.S. Patent No. 5,489,261 Franzblau *et al* and U.S. Patent No. 5,863,984 to Doillon *et al.*); cross-linking with radiation (i.e., U.S. Patent No. RE33,997 to Kuamz *et al.*; U.S. Patent No. 4,264,155 to Miyata; and U.S. Patent No. 5,948,429 to Bell *et al.*); and b) physical methods: cross-linking with microwaves (i.e., U.S. Patent Nos. 5,859,077 and 6,168,762 to Reichman *et al.*); freeze-drying (i.e., U.S. Patent Nos. 5,676,967 to Williams *et al.* and 5,869,080 to McGregor *et al.*); and

dehydrothermo-crosslinking (i.e., U.S. Patent No. 4,837,285 to Berg *et al.*; U.S. Patent No. 4,950,485 to Akhtar *et al.*; and U.S. Patent No. 4,971,954 to Brodsky *et al.*).

In certain embodiments, the polymeric material is represented by the formula:



wherein, A represents a carboxylic containing copolymer; B represents a biopolymer; C represents a counterion; and W represents one or more waters bound to the polymer. See, for example, PCT Application Publication No. WO 07/115169, which is hereby incorporated by reference in its entirety.

In certain embodiments, A comprises co-monomers M1 and M2 in ratio of 20:80 to 80:20. In another embodiment, A comprises co-monomers M1 and M2 in a ratio of 40:60 to 60:40.

In another embodiment, M1 comprises co-monomers maleic anhydride and maleic acid. In another embodiment, M1 comprises co-monomers itaconic anhydride and itaconic acid. In another embodiment, M1 comprises co-monomers citraconic anhydride and citraconic acid. In another embodiment, M1 comprises co-monomers 2-octenylsuccinic anhydride and 2-octenylsuccinic acid.

In another embodiment, M2 comprises an olefin. In another embodiment, M2 comprises a monoolefin. In another embodiment, M2 comprises ethylene, propene, isobutylene, styrene, alpha-methylstyrene, alkylated styrenes, ethylstyrene, tertbutylstyrene, vinyl-toluene, vinyl esters of saturated C<sub>1</sub>-C<sub>4</sub>-carboxylic acids, vinyl formate, vinyl acetate, vinyl propionate, alkyl vinyl ethers, ethyl vinyl ether, butyl vinyl ether, acrylate, methacrylate esters, 2-ethylhexyl acrylate, n-butyl acrylate, isobutyl acrylate, t-butyl acrylate, hexyl acrylate, n-butyl methacrylate, lauryl methacrylate, isodecyl methacrylate, conjugated diolefins, butadiene, isoprene, piperylene, allenes, allene, methyl allene, chloroallene, olefin halides, vinyl chloride, vinyl fluoride, polyfluoro-olefins, esters of monoethylenically unsaturated C<sub>3</sub>-C<sub>6</sub>-carboxylic acids, esters of monohydric C<sub>1</sub>-C<sub>8</sub>-alcohols and acrylic acid, esters of monohydric C<sub>1</sub>-C<sub>8</sub>-alcohols and methacrylic acid, esters of monohydric C<sub>1</sub>-C<sub>8</sub>-alcohols and maleic acid, monoesters of maleic acid, monomethyl maleate, 2-hydroxyethyl acrylate, hydroxypropyl acrylate, hydroxybutyl acrylate, hydroxyethyl methacrylate, hydroxypropyl methacrylate, hydroxybutyl methacrylate, N-vinyl lactams, N-vinylpyrrolidone, N-vinylcaprolactam, acrylic and methacrylic esters of alkoxylated monohydric saturated alcohols, vinyl pyridine, vinyl

morpholine, N-vinylformamide, dialkyldiallylammonium halides, dimethyldiallylammonium chloride, diethyldiallylammonium chloride, allylpiperidinium bromide, N-vinylimidazoles, N-vinylimidazole, 1-vinyl-2-methylimidazole, N-vinylimidazolines, N-vinylimidazoline, 1-vinyl-2-methylimidazoline, 1-vinyl-2-ethylimidazoline, 1-vinyl-2-propylimidazoline, acrylic acid, methacrylic acid, acrylamide, methacrylamide or acrylonitrile. In another embodiment, M2 comprises styrene.

In another embodiment, the ratio of M1:M2 is not less than 20: 80 and not greater than 80:20. In another embodiment, the ratio of M1:M2 is not less than 40:60 and not greater than 60:40.

In another embodiment, M1 comprises co-monomers maleic anhydride and maleic acid, and M2 comprises styrene.

In another embodiment, B comprises a carbohydrate, protein, soybean protein, collagen, collagenic biopolymers, gelatin, collagen hydrolysates, or albumin casein. In another embodiment, B is a gelatin or a carbohydrate. In another embodiment, the gelatin is derived from either terrestrial or marine animals. In another embodiment, the carbohydrate is derived from vegetable sources. In another embodiment, B has a Bloom Index not less than 20 and not higher than 500 bloom. In another embodiment, B has a Bloom Index between 100 and 300 bloom. In another embodiment, B has an isoelectric point (IP) not less than 3.5 and not greater than 9.5. In another embodiment, B has an IP not less than 4.5 and not greater than 8.5.

In another embodiment, the ratio of A:B is from 95:5 to 50:50 by weight. In another embodiment, the ratio of A:B is from 90:10 to 70:30 by weight. In another embodiment, the ratio of A:B is 90:10, 85:15, 80:20, or 75:25 by weight.

In another embodiment, C is an inorganic cation. In another embodiment, C is  $\text{Li}^{(+)}$ ,  $\text{Na}^{(+)}$ ,  $\text{K}^{(+)}$ , or  $\text{NH}_4^{(+)}$ . In another embodiment, C is  $\text{Na}^{(+)}$  or  $\text{NH}_4^{(+)}$ . In another embodiment, C is  $\text{Ca}^{(+2)}$  or  $\text{Mg}^{(+2)}$ .

In another embodiment, the molar content of  $\text{C}^{(+)}$ , expressed in mol/gram of (A+B), is not less than 0.002 mol/g and not greater than 0.004 mol/g. In another embodiment, the molar content of  $\text{C}^{(+)}$ , expressed in mol/gram of (A+B), is not less than 0.0025 mol/g and not greater than 0.0035 mol/g.

In another embodiment, M1 comprises co-monomers maleic anhydride and maleic acid, M2 comprises styrene, B is a gelatin, C is Na<sup>(+)</sup>, K<sup>(+)</sup>, or NH<sub>4</sub><sup>(+)</sup>.

In another embodiment, the ratio of A:B is from 95:5 to 55:45 by weight. In another embodiment, the ratio of A:B is from 90:10 to 70:30 by weight. In another embodiment, the ratio of A:B is 90:10, 85:15, 80:20, or 75:25 by weight.

In another embodiment, the polymeric material has humidity content not less than 1% and not greater than 15% by weight. In another embodiment, the polymeric material has a humidity content between 5 % and 10% by weight.

Viscosimetric average molecular weight,  $M_v$ , was estimated using the evaluation of intrinsic viscosity  $[\eta_{rel}]$  based on relative viscosity  $[\eta]$  of one solution of polymer with concentration  $c = 0.5$  g/100 ml in tetrahydrofuran at 25°C, using the calculus formulae (Raju K.V.S.N., Yaseen M. *J. Appl. Polym. Sci.*, 45, 677-681, 1992; Chee K. K. J., *Appl. Polym. Sci.*, 34, 891-899, 1987 and Spiridon D. et al. *Polymer International*, 43, 175-181, 1997).

$$[\eta] = \frac{\sqrt{2(\eta_{rel} - \ln(\eta_{rel}) - 1)}}{c}$$

$$[\eta] = 0.77 * 10^{-4} * M_v^{0.725}$$

In certain embodiments, the viscosimetric average molecular mass of the polymeric material,  $M_v$ , is not less than 100,000 and not greater than 2,500,000 evaluated from intrinsic viscosity,  $[\eta]$ , in tetrahydrofuran at 25°C. In other embodiments,  $M_v$  of the polymeric material is not less than 500,000 and not greater than 2,000,000 evaluated from intrinsic viscosity,  $[\eta]$ , in tetrahydrofuran at 25°C.

In another embodiment, the free absorbency of the polymeric material for distilled water, FADW, at 37 °C after 24 hours of contact with water is not less than 200 g /g. In another embodiment, FADW for the polymeric material at 37 °C after 24 hours of contact with water is higher than 250 g/g.

In another embodiment, B is digested by enzymes in the small intestine. In a further embodiment, the enzymes include pancreatin enzymes. In another embodiment, the digestion of B results in shrinkage of the polymer and release of absorbed water.

As used herein, the term “polymeric materials” include fibers and/or a gums. The gums which may be used include, for example, guar gum, tamarind seed gum, xanthum gum, locust bean (carob seed) gum and konjac gum. Fibers which may be used include both soluble and non-soluble fibers. In one embodiment, the fibers are natural fibers such as plant derived fibers. In another embodiment, the fibers are synthetic fibers.

### **Enzymatic Degradation**

In certain embodiments, the polymer (e.g., A and/or B, as described above) is digested by enzymes in the stomach. In certain embodiments, the polymer (e.g., A and/or B, as described above) is digested by enzymes in the intestine. In certain embodiments, the polymer (e.g., A and/or B, as described above) is digested by enzymes in the colon. In certain such embodiment, the enzymes include pectinase and other enzymes produced by colonic microflora. In certain embodiment, the digestion of the polymer results in shrinkage of the polymer and release of absorbed water.

For example, one aspect of the invention relates to a composition which may be administered orally, which is a useful for creating, enhancing or prolonging satiation feeling, comprising a polymer (A and/or B, as described above) that (a) has the ability to absorb water from gastric fluids when mixed with water or foods and therefore to swell in the stomach, (b) swells by at least 50 times its original weight both in the stomach and in the small intestine, (c) when swollen can be mixed homogeneously with the digested food and has similar rheological properties, therefore cannot cause to impaction, and (d) is degradable by the colon enzymes causing the release of at least 50% of the absorbed water allowing their absorption by the human body.

In addition, another aspect of the invention relates to a composition which may be administered orally, which is useful for creating, enhancing or prolonging satiation feeling, comprising a polymer (A and/or B, as described above) that (a) has the ability to absorb water from gastric fluids when mixed with water or foods and therefore to swell in the stomach, (b) swells by at least 50 times its original weight both in the stomach and in the small intestine, (c) when swollen can be mixed homogeneously with the digested food and has similar rheological properties, therefore cannot cause to impaction, and (d) is degradable by the stomach or by the small intestine enzymes the degradation is slow enough to allow its ability to swell in the small intestine by at least 25 times its originally weight for more than 2 hours.

## Coatings

In certain embodiments, the composition will comprise polymeric particles coated individually. In other embodiments, the composition will contain polymeric particles which are encapsulated with coating. In certain embodiments, the coating will prevent swelling in the stomach.

In certain embodiments, the composition will comprise polymeric material with an enteric coating. The term “enteric coating” is used to mean a barrier applied to oral medication that controls the location in the digestive system where it is absorbed. Enteric refers to the small intestine; therefore enteric coatings prevent release of medication before it reaches the small intestine. Most enteric coatings work by presenting a surface that is stable at the highly acidic pH found in the stomach, but breaks down rapidly at a less acidic (relatively more basic) pH. For example, they will not dissolve in the acidic juices of the stomach (pH at about 3), but they will in the higher pH (pH above about 5.5) environment present in the small intestine. Materials used for enteric coatings include fatty acids, waxes, and shellac as well as plastics. In one embodiment, the enteric coating is not digestible by the stomach of the subject, thereby preventing release of the polymeric material in the stomach of the subject. In one embodiment, the enteric coating is designed to dissolve under digestive conditions after a time period; and the time period is not less than about 50 minutes, thereby preventing release of the polymeric material in the subject until after the material has been emptied from the stomach.

Examples of such enteric coatings include cellulose, vinyl, and acrylic derivatives, cellulose acetate phthalate, polyvinyl acetate phthalate, derivatives of hydroxypropyl methylcellulose such as hydroxypropyl methylcellulose phthalate or hydroxypropyl methylcellulose acetate succinate, copolymers of methyl methacrylate and ethyl acrylate and combinations thereof. More specifically suitable coatings include cellulose derivative include carboxymethylethylcellulose, cellulose acetate phthalate, cellulose acetate succinate, methylcellulose phthalate, hydroxymethylethylcellulose phthalate, hydroxypropylmethylcellulose phthalate, hydroxypropylmethylcellulose acetate succinate and the like; polyvinyl derivative include polyvinyl alcohol phthalate, polyvinyl butylate phthalate, polyvinyl acetoacetal phthalate and the like; maleic acid-vinyl compound copolymer include poly(vinyl acetate, maleic acid anhydride), poly(vinyl butyl ether, maleic acid anhydride), poly(styrene, maleic acid monoester), and the like; acrylic copolymer include poly(ethyl acrylate, methacrylic acid), poly(styrene, acrylic acid),

poly(methyl acrylate, methacrylic acid, octyl acrylate), poly(methacrylic acid, methylmethacrylate) (e.g. Eudragit L and Eudragit S, each being trade name, available from Rohm Pharma, Germany), and combinations thereof as well as similar enteric coatings known to one in the art.

In certain embodiments, the composition will comprise a coating that will dissolve at a predetermined rate based on the thickness of the coating and the composition of the coating. Such coatings could include cellulose ethers (such as ETHOCEL and METHOCEL and their mixtures) Instacoat Aqua (which includes HPMC and PVA based systems) and mixtures of acrylic resin (such as ethyl acrylate/methyl methacrylate copolymers).

### **Methods of Formulation and Administration**

In certain embodiments, the composition is administered orally. Suitable oral dosage forms include tablets, capsules, caplets, powders, syrups, solutions, suspension and shakes. In one embodiment, the composition is compressed with one or more excipients, and optionally with one or more pH modifying agents and/or one or more active agents, to form a tablet. Suitable excipients used to prepare tablets include binding agents, preservatives, lubricants, antioxidants, glidants, flavorants, colorants, and combinations thereof.

In one embodiment, the polymeric material is encapsulated in a hard or soft gelatin capsule. The capsule fill material contains the material, and optionally one or more pH modifying agents and/or active agents. The fill material may also contain one or more excipients. As described above, suitable excipients include, but are not limited to, plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, aggregation prevention agents, solubilizers, glidants, bioavailability enhancers, solvents, and combinations thereof.

In certain embodiments, the composition will further comprise one or more pharmaceutically acceptable excipients selected from the group consisting of plasticizers, diluents, binders, lubricants, glidants, colorants, stabilizers, surfactants, flavorants, preservatives, anti-oxidants, buffering agents and combinations thereof. In certain embodiments, the buffering agent is selected from the group consisting of ammonium bicarbonate, ammonium carbonate, ammonium hydroxide, sodium bicarbonate, calcium carbonate, calcium hydroxide, magnesium carbonate, potassium bicarbonate, potassium carbonate, potassium hydroxide, sodium carbonate, sodium hydroxide, or combinations thereof.

Examples of excipients include a saccharide such as sucrose, lactose, mannitol or glucose, starch, partially pregelatinized starch, crystalline cellulose, calcium phosphate, calcium sulfate, precipitated calcium carbonate, hydrated silicon dioxide and the like. Examples of binders include an oligosaccharide or a sugar alcohol such as sucrose, glucose, lactose, maltose, sorbitol or mannitol; a polysaccharide such as dextrin, starch, sodium alginate, carrageenan, guar gum, arabic gum or agar; a natural polymer such as tragacanth, gelatin or gluten; a cellulose derivative such as methylcellulose, ethylcellulose, sodium carboxymethylcellulose or hydroxypropylmethylcellulose; a synthetic polymer such as polyvinylpyrrolidone, polyvinylalcohol, polyvinylacetate, a polyethyleneglycol, polyacrylic acid or polymethacrylic acid; and the like.

In certain embodiments, the dosage form maybe incorporated into a semi-solid base to form a spoonable delivery system. The semi-solid base may be comprised of pectin, guar gum, xanthan gum, gum arabic, gum acacia, locust bean gum, carageenan gum, alginic acid, psyllium hydrocolloid, oat bran gum, rice bran gum, glucomannan, tragacanth gum, karaya gum, tapioca, corn starch, cellulose gums, agar, gelatin, polyacrylates, polysaccharides, polyvinylpyrrolidones, pyrrolidones, polyols, collagen, polyethylene glycols, polyvinylalcohols, polyethers, polyesters, natural or synthetic oils, liquid paraffin, beeswax, silicon waxes, natural or modified fatty acids, or combinations of thereof. Additionally viscous fruit purees such as apple, prune, apricot, pear, pineapple, banana, grape, strawberry, raspberry, blackberry, boysenberry, loganberry, dewberry, gooseberry, cranberry, mulberry, elderberry, blueberry, fig, currant, kiwi may be used.

In certain embodiments, the dosage forms maybe a sachet containing the polymeric powder which could be consumed as a dry powder or added into a semi-solid base to form a spoon-able delivery system. The semi-solid base may be comprised of viscous fruit purees such as apple, prune, apricot, pear, pineapple, banana, grape, strawberry, raspberry, blackberry, boysenberry, loganberry, dewberry, gooseberry, cranberry, mulberry, elderberry, blueberry, fig, currant, kiwi may be used.

In certain embodiments, the composition is administered with an appetite suppressant or antiobesity agent. In certain embodiments, the composition and the appetite suppressant or antiobesity agent are administered sequentially. In certain embodiments, the composition and the appetite suppressant or antiobesity agent are administered simultaneously or sequentially (i.e. in separate formulations). In certain embodiments, the

composition further comprises the appetite suppressant, antiobesity nutraceutical or antiobesity agent (i.e. in the same formulation)

In certain embodiments, the appetite suppressant, antiobesity nutraceutical or antiobesity agent is selected from the group consisting of sibutramine hydrochloride, orlistat, rimonabant, benzphetamine, diethylpropion, mazindol phendimetrazine, phentermine, amphetamine, fenfluramine, nalmetrene, Phentermine (Fastin, Adipex, Ionamin and others); Diethylpropion (Tenuate); Sibutramine (Meridia, Reductil); Rimonabant (Acomplia); benfluorex; butenolide; diethylpropion; FG 7142 (N-methyl-9H-pyrido[5,4-b]indole-3-carboxamide); norpseudoephedrine; phenmetrazine; phentermine; phenylpropanolamine; pyroglutamyl-histidyl-glycine; sibutramine; Phendimetrazine (Prelu-2, Bontril); Benzphetamine (Didrex); Oxynotomodulin; Methylphenidate; (Concerta) (Ritalin); Phenylethylamine (Trimspa), pyruvate, DHEA, B-hydroxy-B-methylbutyrate, chitosan, conjugated linoleic acid (CLA), hoodia gordonii, bitter orange (citrus naringin), kava, usnic acid, ephedra, and combinations thereof.

In certain embodiments, the composition is administered in conjunction with a surgical intervention for obesity. In certain embodiments, the surgical intervention to treat obesity is selected from the group consisting of gastric banding, gastric bypass surgery, intragastric balloon, implantable gastric stimulator and gastric electrical stimulation.

#### **Use of Non-Polymeric Mechanical Devices**

Another aspect of the invention relates to a method of using a non-polymeric mechanical device to displace intestinal volume in a subject. In certain embodiments, the non-polymeric mechanical device includes those previously disclosed to displace stomach volume (see, for example, US Patent No. 7,066,945; US Patent Application Publication No. 20050245957; International Patent Application Publication No. WO 2007/017842; US Patent Application Publication No. 20060217757; and US Patent No. 7,033,384, all of which are hereby incorporated by reference).

### **EXEMPLIFICATION**

The invention now being generally described, it will be more readily understood by reference to the following examples, which are included merely for purposes of illustration of certain aspects and embodiments of the present invention, and are not intended to limit the invention.

All the animal studies in these examples were approved by the respective Institutional Animal Care and Use Committee (IACUC) and the Committee for Animal Protection. Procedures used in the following studies were designed to conform to accepted practices and to minimize or avoid causing pain, distress, or discomfort to the animals. In those circumstances in which required study procedures are likely to cause more than momentary or slight pain or distress, the animals will receive appropriate analgesics or anesthetics unless the withholding of these agents has been justified in writing by the Study Director and approved by the Institutional Animal Care and Use Committee (IACUC).

As described in below, laboratory rats were given a polymeric material of poly(styrene-co-maleic anhydride/acid) cross-linked with gelatin (SAP) by oral gavage under different experimental conditions. The polymer was prepared in accordance with the procedures presented in U.S. Patent No. 6,833,488 and PCT Published Patent Application No. WO2005/084724A1, both of which are hereby incorporated by reference in their entirety. The animals were sacrificed, their stomachs excised and the contents of the stomach were analyzed. The purpose of these experiment was to understand if the polymer would remain separated from the food the animals were allowed to ingest in the case of animals that were allowed to eat or would the polymer increase the size of the food bolus without increasing the corresponding energy density.

## EXAMPLE 1

### *Stomach Content Observation in Rats after the Administration of Polymeric Material*

Wistar rats with the characteristics listed in Table 1 were housed individually in Velaz T4 cages in conventional laboratory conditions. Room temperature was 20-24 °C and the relative humidity was between 30-70%. Fluorescent lighting provided illumination approximately 12 hours per day. Feed and water containers were changed and sanitized at least once weekly. Lignocel (Velaz Ltd., Czech Republic) was used as bedding.

**Table 1.** Wistar rats used in test system.

Species & Strain	Wistar rat
Quality	conventional
Age on delivery	6-9 weeks
Body weight at administration	200-300 g

Number of groups	3
Rats per group	2
Total number of animals	6

The animals were fed *ad libitum* with standard pelletized rodent diet (NOE H4, Racio Breclav, Czech Republic) of monitored quality (analyzed minimally 2 times per year for possible toxic or microbiological contamination) during the acclimation and study periods. Water of monitored quality (analyzed minimally 2 times per year for possible toxic or microbiological contamination) was supplied *ad libitum* during the acclimation and study period. The rats were branded with picric acid solution and acclimated for 5 days. The experimental design and group allocation are presented in Tables 2 and 3, respectively.

**Table 2.** Experimental design.

<b>Procedure</b>	<b>Date</b>
Study initiation	day 1
Acclimation	5 days
Initiation of experimental part	30 days before
Health check	31 days before
Start of the test tem administration	day 1
Dosing	single oral administration by gavage
Necropsy intervals	30, 90 minutes
Body weight	Before administration
Proposed end of the experimental part	day 1

**Table 3.** Group allocation.

<b>Group #</b>	<b>Rats</b>	<b>Test Condition</b>
1	F1, F2	premedicated with H2 blocker
2	F3, F4	no premedication
3	F5, F6	with food consumption

All rats were fasted overnight. The first group of rats were premedicated with the H2 blocker PepcidAC® (10 mg Famotidine, Johnson & Johnson-Merck Consumer Pharmaceuticals, 1 capsule/rat) 4 hours before administration. The second group was not premedicated and was not allowed access to food following oral gavage of SAP. The third group was not premedicated, but was allowed access to food following oral gavage of SAP.

The SAP powder was mixed with tap water at a ratio of 640 mg poly(styrene-co-maleic anhydride/acid) to 50 mL water in order to swell the material. Rats were administered 5 mL of the swollen SAP by oral gavage. Rats in Group 3 (F5, F6) were given food which had been weighed immediately following oral gavage of SAP and were kept in the dark until necropsy. The food consumption of Group 3 was measured and recorded. Necropsy was performed according to Table 4.

**Table 4.** Necropsy intervals and stomach observation.

<b>Animal No.</b>	<b>H2 blocker premedication</b>	<b>Necropsy intervals (min)</b>
F1	Yes	90
F2	Yes	105
F3	No	30
F4	No	90
F5	No	70
F6	No	50

Rats were euthanized using ether, the animals' stomachs were excised and after the stomach outlets were tied off to prevent leakage, the stomachs were weighed (see Figure 1 for an example of an excised stomach with tied off ends). Next, the stomachs were cleaned and the stomach contents were weighed and visually inspected. The rats which were

allowed to eat food and were gavaged orally with SAP, had the food mixed with the polymer to form a homogeneous mixture (see Figure 2). Given that rat F5 received 2.7 g amount of food and the bolus of food that was retrieved from the animals' stomach weighed 6.87 after 70 minutes, it is clear that the polymer increased the total size of the food bolus and extended the emptying time. Similar data was recorded for rat F6. The polymer itself has practically no caloric content and therefore, the effect of oral administration of the polymer was to increase the size of the food bolus without increasing the corresponding energy density and extended the emptying time thus providing an extended satiation feel in the rat.

## EXAMPLE 2

### *Decrease in Food Intake of Rats Administered Poly(styrene-co-maleic anhydride/acid) Cross-linked with Gelatin (SAP)*

SAP which was used in the above example was used in the experimental conditions described herein. The SAP had the ability to: 1) Mix with food to increase the size of the food bolus without increasing the size of the corresponding energy density of the food bolus (as shown in Example 1); 2) Reswell in the intestine after collapsing/shrinking in the stomach. The purpose of this experiment was to show that a polymer with the above properties could decrease food intake which would initiate satiation.

Rats weighing approximately 300 grams were housed in standard caging and fed a standard diet of rat chow. The animals were kept on a 12 hour light and dark cycle. Two hours prior to the lights being shut off, food was removed from the rats. On days in which the rats were subject to an experimental treatment, the animals were orally gavaged with either SAP which was swollen with water prior to gavage or a similar volume of water (e.g., 6 mL of polymer or 6 mL of water were used) prior to the lights being shut off. Three days later, in a classic within subject design, the animals which received water received polymer and visa versa. The amount of food the animals ate was then observed at various time points. The amount of food the animals ate was compared between the two conditions of water and polymer gavage.

As shown in Figure 3, a clear difference could be observed between the animals receiving polymer and the animals receiving water (control rats).

**EXAMPLE 3***Decrease in Food Intake of Rats Administered SAP with Different Groups of Rats*

SAP was prepared and experimental conditions were the same as outlined in example two. However, three different groups of rats were used as compared to example one. The first group of rats was fed a high fat diet (e.g., 20% of chow was fat by weight) in order promote weight gain of the animals. The second group consisted of older animals which also had gained weight over time. The third group consisted of age matched rats to the first group and were younger compared to the second group, but were fed a normal diet.

As was observed in the second example, the SAP produced a significant decrease in food intake compared to the water control in a within-subject design (see Figure 4).

**EXAMPLE 4***Synthesis of a Superabsorbent Polymer (SAP29)*

A superabsorbent polymer (SAP) system was formulated as follows: poly(styrene-co-maleic anhydride/acid) copolymer was mixed with gelatin and NaOH in a dry weight/dry weight ratio of 90:10:80 (copolymer:gelatin:NaOH, respectively). In formulations such as these, the molecular weight of the copolymer can range from about 650,000 Da to about  $3 \times 10^6$  Da, and is preferably in the range of about 850,000 Da to about  $1.5 \times 10^6$  Da. In this particular case, the molecular weight of the copolymer used was about  $1 \times 10^6$  Da. The superabsorbent polymer was made by first making a composite of poly(styrene-co-maleic anhydride/acid) and gelatin. Upon drying of the composite, the material was ground to produce cubical particles between 200 and 900  $\mu\text{m}$ . The particles were exposed to heat (110 °C) for 90 min, thus inducing cross-linking between poly(styrene-co-maleic anhydride/acid) and gelatin. It was theorized that each individual composite particle was cross-linked to form a single molecule of SAP. The theoretical molecular weight of the SAP was over  $1 \times 10^9$ , and the physical dimensions of each SAP molecule was 200-900  $\mu\text{m}$ . This material is referred to as "SAP29" throughout the application.

**EXAMPLE 5***Reduction of Food Intake in Rats upon Administration of SAP*

Figure 5 depicts the reduction of food intake in rats upon administration of 8 mL of SAP29 solution (ex-vivo pre-swollen SAP). The rats were compared to a control group that received only water.

It is clear from the data that the time the effect persisted was longer than a typical residence time of food in the stomach (see, for example, Tomlin *et al.* wherein half emptying time was reported as less than 20 min; Tomlin. J. *et al.* Gut. 1993, 34(9): 1177–1181). The extended effect was achieved by slower emptying time and a satiety caused by the polymer re-swelling in the small-intestine.

### EXAMPLE 6

#### *Decrease in Food Intake in Rats upon Administration of SAP*

A total of 21 male Sprague-Dawley rats were randomized into two weight-matched groups (10-11 per group) prior to SAP or vehicle administration (the SAP was pre-swollen in water, 100 mg in 10 mL water). 8 mL of a pre-swollen SAP was administered by oral gavage. Food and water intake (digital balance) as well as locomotor activity (consecutive beam breaks) were monitored online every 5 minutes for 40 hours post-dosing. Food and water intake data were collected using MaNi FeedWin, an online computerized feeding system using digital weighing cells. Two types of baseline food intake (digital balance) and lick counts were monitored. All data were entered into Excel spread-sheets and subsequently subjected to relevant statistical analyses. The results in Figure 6 are presented as mean  $\pm$  SEM unless otherwise stated. Statistical evaluation of the data was carried out using one-way or two-way analysis of variance (ANOVA).

Figure 6 represents a typical study result. Cumulative food intake is graphed over time. There was no difference between the groups at baseline (time = 0). Gavage of 8 mL of SAP led to a significant decrease in food intake. As shown by the gray line (group 1), the SAP induced a marked decrease in food intake that persisted over 18 hours. These data suggest that the administration of SAP leads to a decrease in food intake due to a stomach filling effect, slower gastric emptying time, and a small intestinal effect, all of these effects combined can induce satiety in mammals over a longer period of time than a stomach filler alone will provide.

### EXAMPLE 7

#### *Acute Effects of SAPs on Energy Consumption, Urine Production, and Feces Production*

The behavioral specificity of SAP29 was evaluated by simultaneous examination of energy consumption, urine production, and feces production. The study was conducted in male Sprague-Dawley rats, by sub-chronic per oral administration of SAP29 (10 mL, by gavage, once daily).

Sub-chronic administration of SAP29 for four days did not influence the production of urine (Figure 9) or feces (Figure 7) or the percentage of fecal water content (Figure 8). These data indicates that the adminisitered SAP is being degraded in the GI track and it is not being expelled intact.

The rats consumed less food (Figure 10, and 11,). This result indicates that the administration of these SAP should lead to weight loss over sufficient time periods.

### EXAMPLE 8

#### *In Vitro Modeling of GI Transit of SAP*

Figure 13 depicts the swell--collapse--re-swell--degrade cycle that was observed in laboratory experiments *in vitro*. The polymer used was SAP29.

Simulated gastric fluid (SGF) was prepared by dissolving 2.0 g of sodium chloride, 3.2 g of pepsin and 7.0 ml of concentrated (37%) HCl in distilled water to obtain a solution having a total volume of 1 L. (USP Test Solution Method)

The above SGF solution was mixed with water at a ratio of SGF:water 1:8, respectively, to mimic a person taking the material on an empty stomach (50 mL gastric fluid) with two glasses of water (400 mL).

Simulated intestinal fluid (SIF) was prepared by adding 190 ml of 0.2 N NaOH, 400 ml of distilled water and 10 g of pancreatin to an aqueous potassium hydrogen phosphate solution, adjusting the pH of the resulting solution to 7.5 and adding distilled water to obtain a solution having a total volume of 1 L. (USP Test Solution Method)

Simulated colonic fluid (SCF) is prepared by substituting pectinase for pancreatin in the above simulated intestinal fluid preparation.

### EXAMPLE 9

#### *In Vitro Modeling of GI Transit of SAP Containing Colonic Degradable Bonds*

Figure 14 depicts the swell--collapse--re-swell--degrade in colon cycle that might be observed in laboratory experiments *in vitro*. The solutions that are used in this study are described in Example 8. The polymer could be a polymer containing azo bonds (for example, poly(ethylene oxide) and 5,5-azodisalicylic acid, as described in Macromolecular Rapid Communications 2005, 26(19), 1572 – 1577; or as described in U.S. Patent No. 5,032,572, both of which are hereby incorporated by reference in their entirety). In

addition, other polymers which could be used include oligosaccharides and polysaccharides.

Polysaccharide-based hydrogels are very common since they can be selectively degraded by a colonic enzyme and are natural polymers. These hydrogels are considered safe because they utilize materials that are taken as dietary fiber. Various enzymes that are involved in the degradation of some of these polymers are amylase, chitosanase, pectinase, inulinase, xylanase, dextranase, and galactomannanase. Such polymers are described in: Friend, D. R. "Issues in lower gastrointestinal drug delivery" Pharmaceutical News 1997. 4.12-15; Sintov, A., Rubinstein, A., US Patent No. 5,525,634; Lee, S-S., La, S-B., Lim, C-B., Lee, S., Seo, B-Y., Pai, C-M. US Patent Application Publication No. 20016319518; and Watanabe, S., Kawai, H., Katsuma, M., Fukui, M.: US Patent Application Publication No. 20036506407B2; all of which are hereby incorporated by reference in their entirety.

**EXAMPLE 10***Human experience with non-degradable materials*

The gastric bulking effect of carbomer homopolymer on appetite was investigated in a small human study. These preparations are marketed as hunger management products marketed to reduce the hunger associated with calorie-restricted diets and weight-loss programs. Utilizing a nutraceutical by Wellosophy (Pree™) where each capsule contained 750 mg of the non-degradable polyacrylic acid. .

A single volunteer (gender: male, age: 45 years old, weight: 175 lb) was tested. On the first day of the study the volunteer took 2 capsules (1.5 g, as instructed by the product's insert) with 2 glasses of water 30 minutes before dinner and thereafter ate a normal dinner. No reduction in food intake was noted.

On a second day of study, the volunteer took 6 capsules (9 g, the total daily dose as noted in the product's insert) and drank 2 glasses of water 30 min before dinner and thereafter was served a normal dinner. A meaningful reduction in food intake and a notable satiation feeling was reported. Yet, 3 hours post the 6 capsules administration the volunteer reported on cramps and 48 h post administration the volunteer reported on diarrhea.

The study supported the concept that a certain volume of material is needed to create satiety and yet, if the material does not degrade in the GI track, it will cause adverse events and limit the product's compliance.

**INCORPORATION BY REFERENCE**

All of the U.S. patents and U.S. published patent applications cited herein are hereby incorporated by reference.

**EQUIVALENTS**

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

We claim:

1. A method of inducing satiation in a subject comprising the step of:  
administering a composition to the subject;  
wherein the composition swells in the subject's intestine or both the subject's stomach and the small intestine.
2. The method of claim 1, wherein the composition swells in the subject's stomach and subsequently collapses and/or degrades after a first period of time, and swells in the small intestine and subsequently collapses and/or degrades after a second period of time.
3. The method of claim 1, wherein the composition swells only in the subject's small intestine.
4. The method of claim 3, wherein the composition swells only in the subject's small intestine and subsequently collapses and/or degrades after a period of time.
5. The method of any one of claims 2 to 4, wherein the administration creates pressure on the wall of the small intestine, increases the volume of intestine's content, or both.
6. The method of any one of claims 1-5, wherein the composition has substantially similar rheological properties as ground food.
7. The method of any one of claims 1-6, wherein the composition combines with an existing food bolus in the subject without increasing the energy density of the food bolus.
8. The method of any one of claims 1-7, wherein the composition is coated with a coating that dissolves in a third period of time.
9. The method of claim 8, wherein the coating is selected from the group consisting of cellulose ethers, Instacoat Aqua, mixtures of acrylic resin, and mixtures thereof.
10. The method of claim 8, wherein the coating is selected from the group consisting of ETHOCEL, METHOCEL, HPMC and PVA based systems, ethyl acrylate/methyl methacrylate copolymers and mixtures thereof.
11. The method of claim 8, wherein the coating dissolves at a pH of greater than 3.5.

12. The method of claim 8, wherein the coating dissolves at a pH of about 5.
13. The method of claim 8, wherein the coating dissolves at a pH of about 6.5.
14. The method of claim 8, wherein the coating is an enteric coating.
15. The method of claim 14 wherein the enteric coating is selected from the group consisting of cellulose derivatives, vinyl derivatives, acrylic derivatives, hydroxypropyl methylcellulose derivatives, maleic acid-vinyl compound copolymers, and copolymers of methyl methacrylate and ethyl acrylate.
16. The method of claim 14, wherein the enteric coating is selected from the group consisting of cellulose acetate phthalate, polyvinyl acetate phthalate, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate succinate, carboxymethylethylcellulose, cellulose acetate succinate, methylcellulose phthalate, hydroxymethylethylcellulose phthalate, hydroxypropylmethylcellulose phthalate, hydroxypropylmethylcellulose acetate succinate, polyvinyl alcohol phthalate, polyvinyl butylate phthalate, polyvinyl acetoacetal phthalate, poly(vinyl acetate, maleic acid anhydride), poly(vinyl butyl ether, maleic acid anhydride), poly(styrene, maleic acid monoester), poly(ethyl acrylate, methacrylic acid), poly(styrene, acrylic acid), poly(methyl acrylate, methacrylic acid, octyl acrylate), and poly(methacrylic acid, methylmethacrylate).
17. The method of any one of claims 1-16 wherein the composition further comprises an excipient.
18. The method of claim 17, wherein the excipient is selected from the group consisting of plasticizers, diluents, binders, lubricants, glidants, colorants, stabilizers, surfactants, flavorants, preservatives, anti-oxidants, buffering agents and combinations thereof.
19. The method of any one of claims 1 to 18, wherein the composition swells by absorbing water, gastric fluid, intestinal-fluid, or a mixture thereof, and degrades in the gastrointestinal tract.
20. The method of any one of claims 1 to 19, wherein the composition degrades in the gastrointestinal tract and releases water before excretion.
21. The method of any one of claims 1 to 20, wherein the composition resides in the stomach for a first period of time, passes into the intestinal tract, and degrades

- substantially in the intestinal tract after a second period of time, wherein the second period of time is longer than the first period of time.
- 22.. The method of claim 21, wherein the first period of time is 0.5 to 8 hours.
  23. The method of claim 21 or 22, wherein the second period of time is 1 to 72 hours.
  24. The method of claim 23, wherein the second period of time is 6 to 48 hours.
  25. A method of inducing satiation in a subject comprising the step of:  
administering a composition to the subject;  
wherein the composition degrades preferentially in the colon.
  26. The method of claim 25, wherein the composition swells in the subject's stomach, the subject's small intestine, or both, and then degrades preferentially in the colon.
  27. The method of claim 26, wherein the composition degrades in the colon at a faster rate than in the stomach or the intestine.
  28. The method of claim 27, wherein the composition degrades exclusively in the colon.
  29. The method of claim 28, wherein the composition comprises oligosaccharides, polysaccharides, or a mixture thereof.
  30. The method of claim 1, wherein the composition comprises an amount of a polymer that swells in the stomach to a volume of 200 mL to 1000 mL.
  31. The method of claim 30, wherein the polymer swells to a volume of about 200, 400, 600, or 800 mL in the stomach.
  32. The method of claim 31, wherein the polymer swells in the stomach to a volume of 300 mL to 800 mL.
  33. The method of any one of claims 1 to 32, wherein the amount of the composition administered comprises 2 to 8 grams of a polymer.
  34. The method of claim 33, wherein the polymer swells in a gastrointestinal environment to at least 50 times its original volume.
  35. The method of claim 38, wherein the polymer swells in a gastrointestinal environment to 50 to 400 times its original volume.

36. The method of claim 35, wherein the polymer swells in a gastrointestinal environment to about 50, 100, 150, 200, 300 or 400 times its original volume.
37. The method of any one of claims 1-36, wherein the composition comprises one or more polymeric materials selected from the group consisting of homopolymers, copolymers, cross-linked polymers, polysaccharides, oligosaccharides, polymer blends, super porous polymers, superabsorbant polymers, interpenetrating polymers or polymer composites.
38. The method of claim 37, wherein the composition comprises a superabsorbent polymer.
39. The method of claim 38, wherein the superabsorbant polymer comprises a synthetic polymer crosslinked with a natural polymer.
40. The method of claim 39, wherein the synthetic polymer comprises a poly(styrene-co-maleic anhydride/acid) polymer.
41. The method of claim 39 or 40, wherein the natural polymer is selected from the group consisting of collagen, hyaluronic acid, gelatin, albumin, a polysaccharide, and mixtures thereof.
42. The method of claim 41, wherein in the superabsorbent polymer comprises SMAc and gelatin.
43. The method of any one of claims 42, wherein the composition comprises SMAc and gelatin, and NaOH in a ratio of 90:10:80 (by dry weight).
44. The method of claim 43, wherein the SMAc and the gelatin are cross-linked.
45. The method of claim 44, wherein the SMAc has a molecular weight of between about 650,000 Da to about 3,000,000 Da.
46. The method of claim 45, wherein the SMAc has a molecular weight of between about 850,000 Da to about 1,500,000 Da.
47. The method of claim 46, wherein the SMAc has a molecular weight of about 1,000,000 Da.
48. The method of any one of claims 1-47 wherein the composition is administered orally.

49. The method of claim 48, the composition is delivered in a tablet, capsule, caplet, powder, syrup, solution, suspension, sachet or shake.
50. The method of any one of claims 1-49, wherein the composition further comprises an appetite suppressant, an antiobesity nutraceutical or an antiobesity agent.
51. The method of any one of claims 50, further comprising the step of:  
administering an appetite suppressant, antiobesity nutraceutical or an antiobesity agent to the subject.
52. The method of claims 50 or 51, wherein the appetite suppressant, antiobesity nutraceutical or antiobesity agent is selected from the group consisting of  
sibutramine hydrochloride, orlistat, rimonabant, benzphetamine, diethylpropion, mazindol phendimetrazine, phentermine, amphetamine, fenfluramine, nalmetrene, Phentermine (Fastin, Adipex, Ionamin and others); Diethylpropion (Tenuate); Sibutramine (Meridia, Reductil); Rimonabant (Acomplia); benfluorex; butenolide; diethylpropion; FG 7142 (N-methyl-9H-pyrido[5,4-b]indole-3-carboxamide); norpseudoephedrine; phenmetrazine; phentermine; phenylpropanolamine; pyroglutamyl-histidyl-glycine; sibutramine; Phendimetrazine (Prelu-2, Bontril); Benzphetamine (Didrex); Oxyntomodulin; Methylphenidate; (Concerta) (Ritalin); Phenylethylamine (Trimspa), pyruvate, DHEA, B-hydroxy-B-methylbutyrate, chitosan, conjugated linoleic acid (CLA), hoodia gordonii, bitter orange (citrus naringin), kava, usnic acid, ephedra, and combinations thereof.
53. The method of any one of claims 1-52, further comprising the step of:  
performing a surgical intervention for obesity on the subject.
54. The method of claim 53, wherein the surgical intervention to treat obesity is selected from the group consisting of gastric banding, gastric bypass surgery, intragastric balloon, implantable gastric stimulator and gastric electrical stimulation.
55. A method of inducing satiation in a subject comprising the step of:  
using a non-polymeric mechanical device to apply pressure to the intestinal wall in the subject.
56. The method claim 55, wherein the non-polymeric mechanical device creates pressure on the wall of the small intestine in a non-invasive manner.

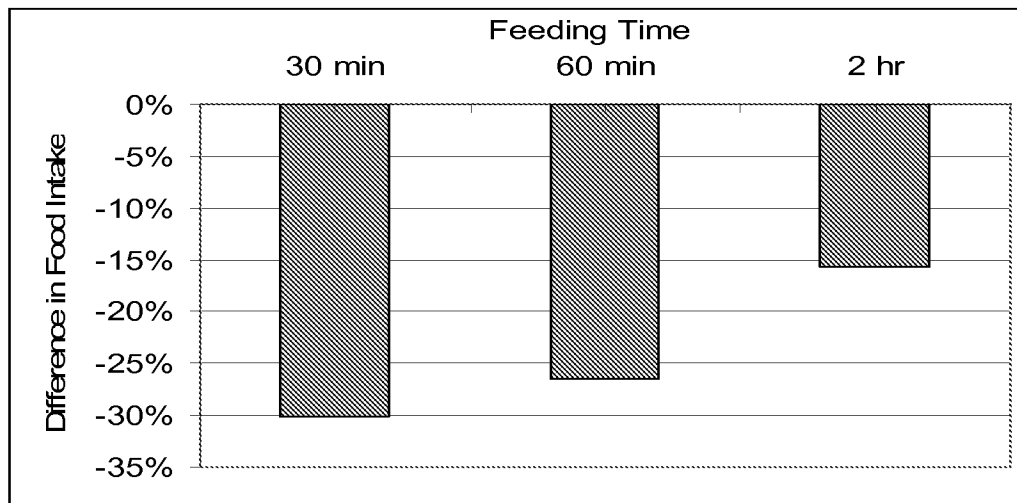
57. The method claim 56, wherein the non-polymeric device that creates pressure on the wall of the small intestine or reduce the follow of food in the intestine in a non-invasive manner.
58. A pharmaceutical composition comprising one or more polymeric materials selected from the group consisting of homopolymers, copolymers, cross-linked polymers, polymer blends, super porous polymers, superabsorbant polymers, interpenetrating polymers and polymer composites, oligosaccharides, and at least one pharmaceutically acceptable carrier or excipient.
59. The composition of claim 58, wherein the composition comprises an enteric substance.
60. The composition of claim 59, wherein the enteric substance coats the polymeric material.
61. The composition of claim 60 wherein the enteric substance is blended with the polymeric material.
62. The composition of claim 63, wherein a portion of the polymeric material is coated with or blended with the enteric substance, and a portion of the polymeric material is not coated with or blended with the enteric substance.

**Figure 1**



**Figure 2**



**Figure 3**

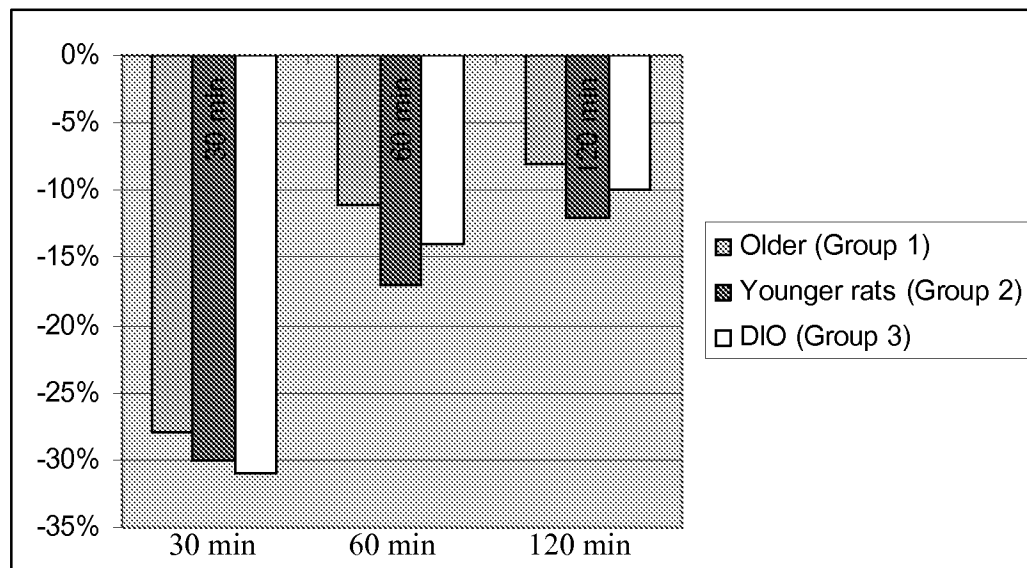
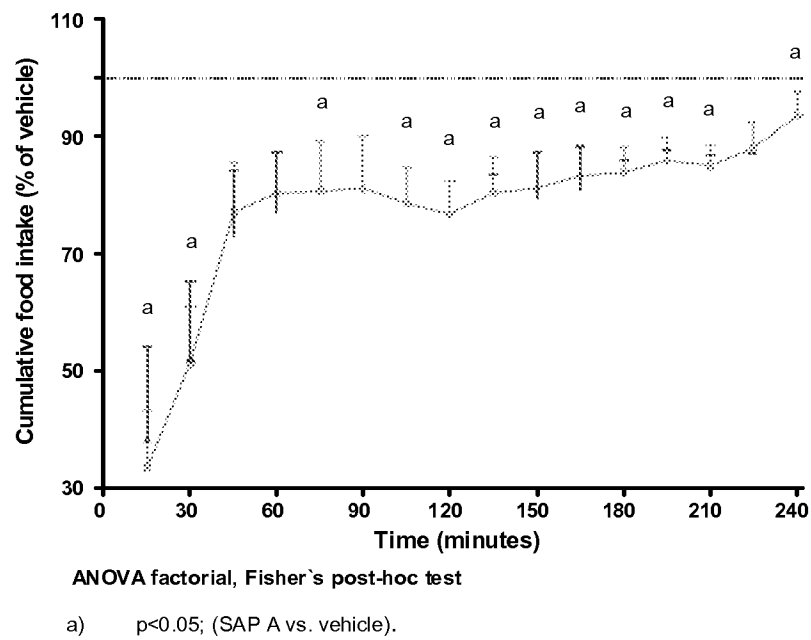
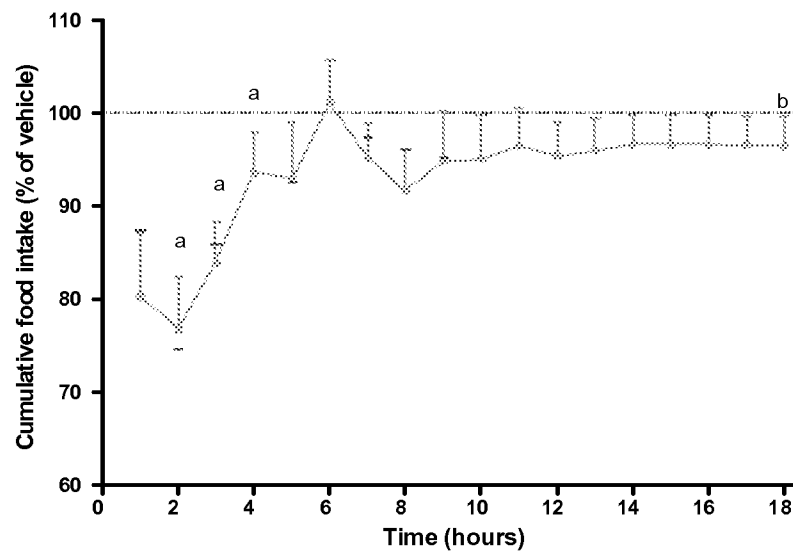
**Figure 4****[B]**

Figure 5



**Figure 6**

ANOVA factorial, Fisher's post-hoc test

a)  $p < 0.05$ ; (SAP A vs. vehicle).

Figure 7

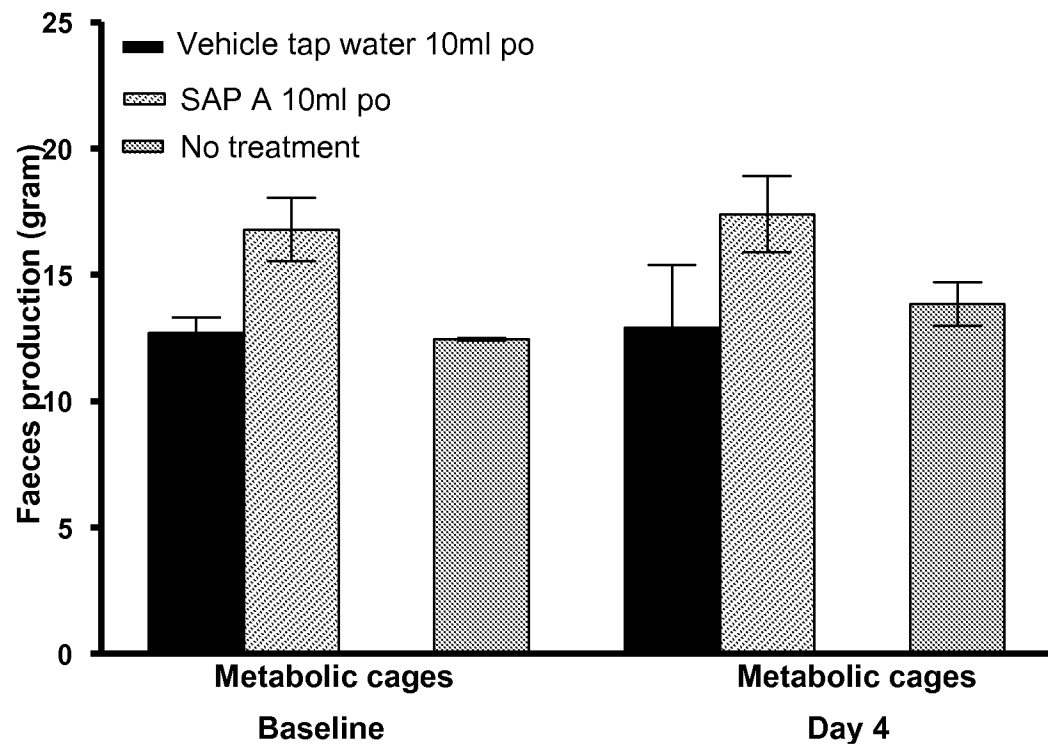


Figure 8

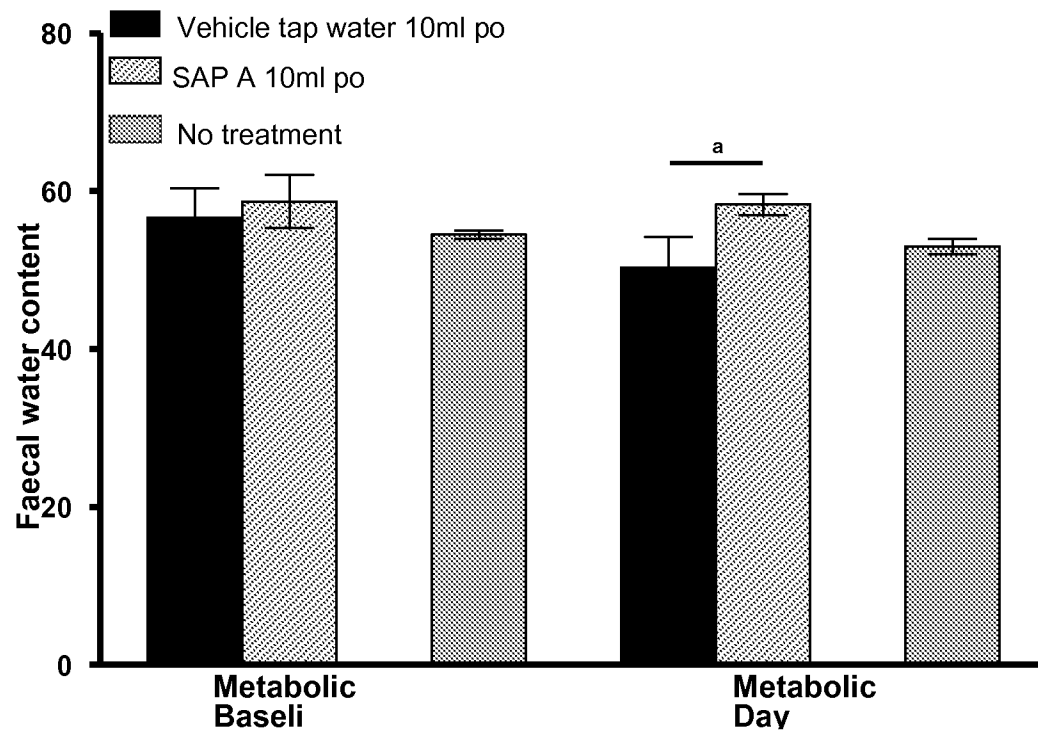


Figure 9

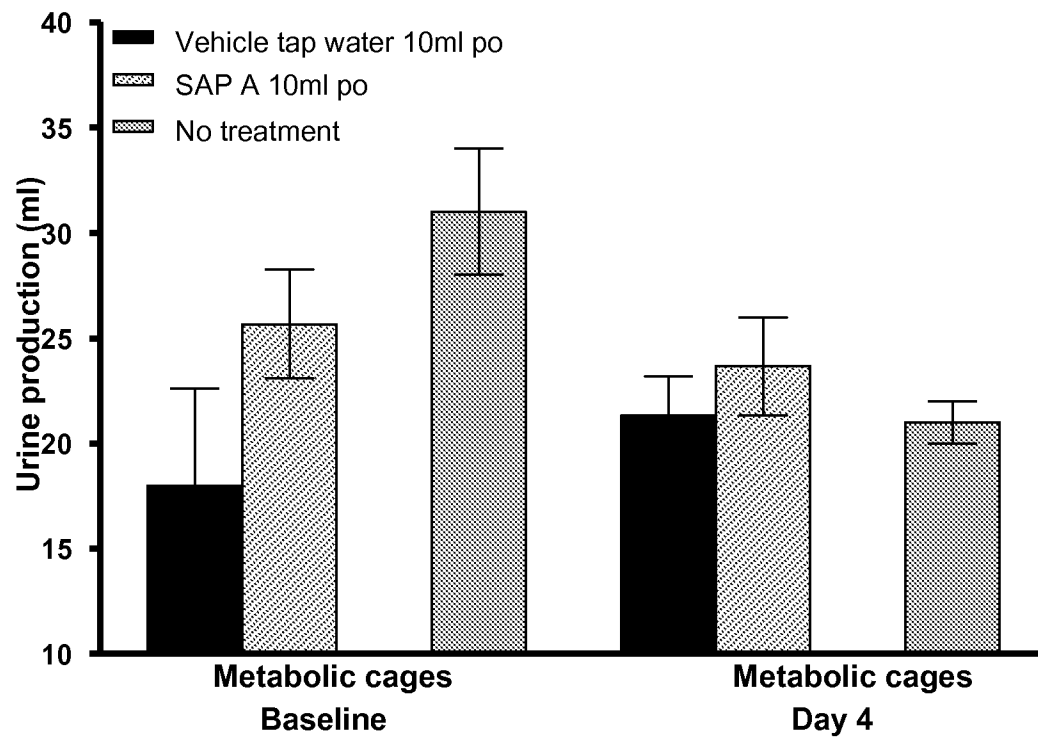


Figure 10

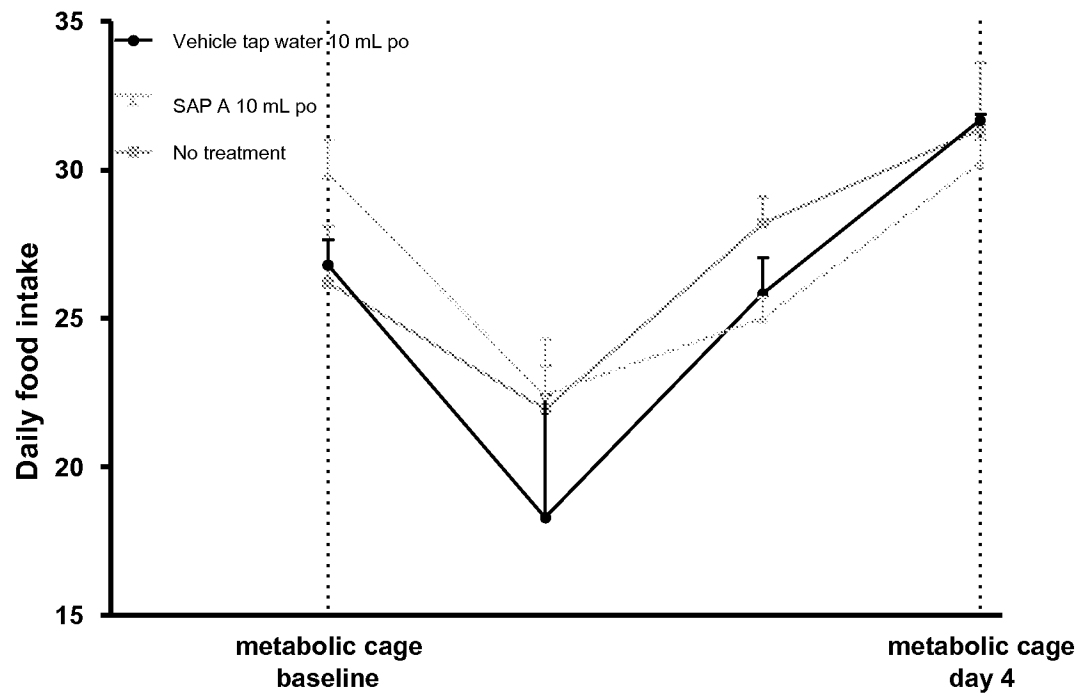


Figure 11

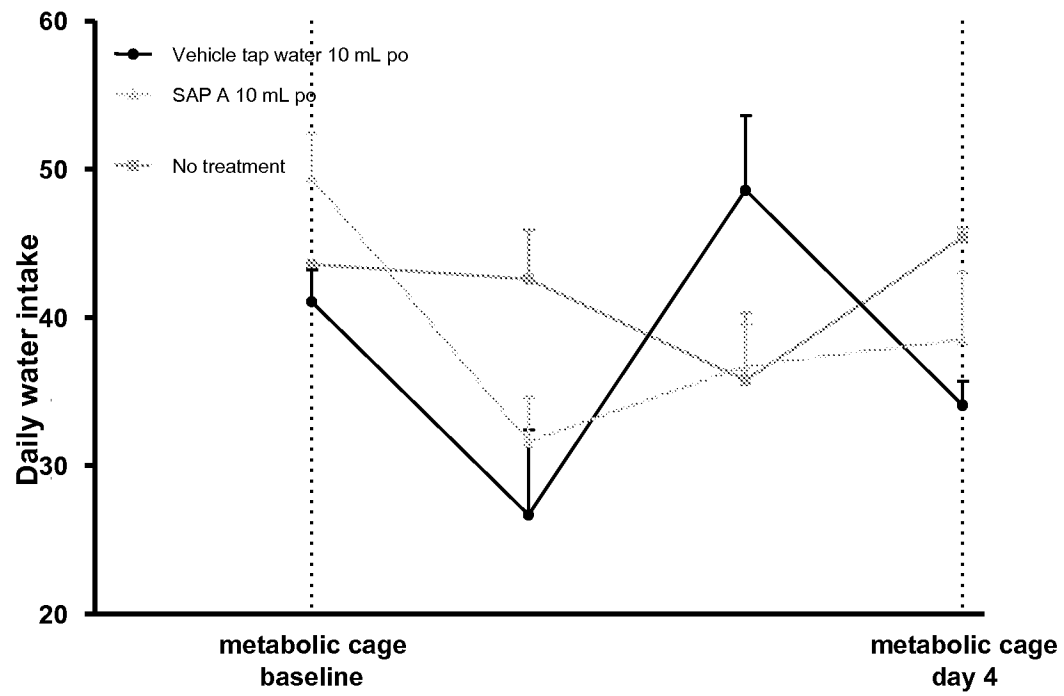


Figure 12

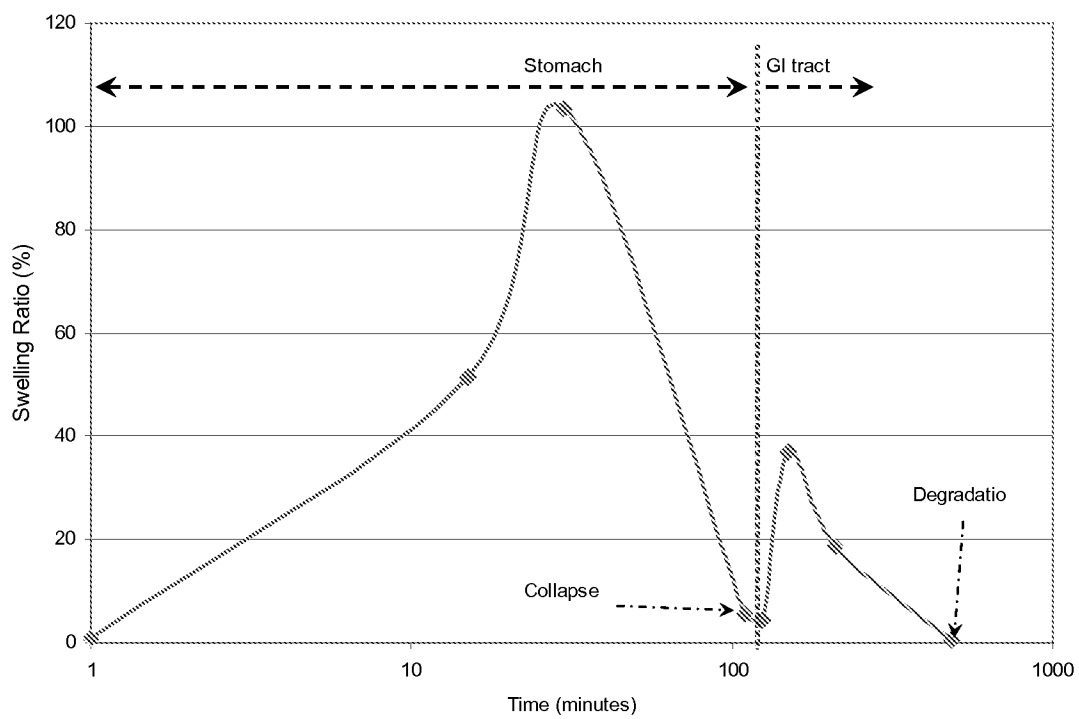


Figure 13

