(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
14 January 2010 (14.01.2010)

PCT

(10) International Publication Number
WO 2010/005965 A1

(51) International Patent Classification:
A01N 59/26 (2006.01)

(21) International Application Number:
PCT/US2009/049807

(22) International Filing Date:
7 July 2009 (07.07.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

61/078,926	8 July 2008 (08.07.2008)	US
61/143,123	7 January 2009 (07.01.2009)	US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

WO 2010/005965 A1

(54) **Title**: COLONIC PURGATIVE FORMULATIONS AND METHODS OF USING THE SAME

(57) **Abstract**: This invention relates to colonic purgative compositions in a liquid or solid dosage form, comprising at least a first and second purgative, wherein the first purgative is sodium phosphate and the second purgative is magnesium citrate. Oral administration of the colonic formulations may be used for effecting partial or complete purgation of the colon in a mammal. The formulations and methods of this invention are particularly useful to cleanse the bowel prior to diagnostic and surgical procedures and can also be employed in lower dosages as a laxative to promote elimination and/or to relieve constipation.

COLONIC PURGATIVE FORMULATIONS AND METHODS OF USING THE SAME

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application Serial No. 61/078,926 filed July 8, 2008 and U.S. Provisional Application Serial No. 61/143,123 filed January 7, 2009, which are incorporated herein by reference in there entirety.

TECHNOLOGY FIELD

[0002] The invention relates generally to oral dosage formulations comprising sodium phosphate and magnesium citrate. More specifically, the invention features compositions and methods for the oral administration of colonic purgative formulations comprising sodium phosphate and magnesium citrate.

BACKGROUND

[0003] It is desirable to identify compounds that sufficiently cleanse the colon but do not cause adverse side effects. It is also desirable to identify compounds that are used to treat constipation and promote fecal elimination, for instance, but that do not produce uncomfortable or embarrassing side effects such as gas.

[0004] In order to carry out a number of medical procedures, such as colonoscopy, radiographic examination, and in preparation for patients undergoing bowel surgery, it is often critical that the colon be emptied as completely as possible. For example, one of the most essential conditions for obtaining satisfactory radiographs is that the intestines be cleansed sufficiently, particularly with regard to the elimination of gas from the colon. The same condition also applies when the colon is preoperatively prepared for surgery, or for diagnostic procedures such as colonoscopies, in which case it is also necessary to remove fecal waste materials.

[0005] Water enemas have been previously employed to empty the colon wherein large quantities of water are introduced into the colon to induce emptying. The contents of the colon are expelled in the form of a suspension. It has been recognized that the introduction of too large a quantity of water in enemas or too frequently administered enemas may be injurious to the patient. In view of the hazard and disadvantages associated with large volume water enemas, enemas of a hypertonic aqueous solution substituted the large water enema. The advantage of these salt formulations is that they require significantly less water volume

in their administration. The effect of these hypertonic enemas is based on the increase of the osmotic pressure in the colon which, in turn, may have undesirable side effects, particularly, if the hypertonic solution diffuses through the wall of the colon and disturbs the fluid balance of the body. While an improvement over simple water enemas, this potential side effect limits the utility of these compositions.

[0006] Many enema compositions in aqueous solutions include a contact laxative agent causing peristalsis in the colon with sufficient concentration of laxation without the need for excessive amounts of water. Such compositions often include salt mixtures and may also include chemical agents such as propylene glycol and non-ionic wetting agents such as polyether alcohols. The problems with these formulations, aside from the often problematic methods of enema administration, are incomplete evacuation of the bowels often requiring repeated administrations and the inclusion of certain chemicals which may have an irritating effect on the colonic walls. Furthermore, because it is often necessary to employ repeated washout enemas to clear the colon effectively, the potential for such chemical irritation is greatly increased.

[0007] Recently, it has been noted that oral sodium phosphate drug products administered to patients before colonoscopy are associated with a series of potential negative side effects including, but not necessarily limited to, a risk for acute renal failure, nephropathy, chronic renal dysfunction, and/or nephrocalcinosis. High phosphate concentrations likely cause an impairment of normal renal function. Patients with existing renal or cardiac conditions or patients predisposed to renal or cardiac problems that are prescribed formulations comprising phosphate or sulfate anions, can experience side effects associated with abnormal renal function. Physicians have questioned the safety of oral sodium phosphate solutions and oral sodium phosphate tablets.

[0008] Current formulations for partial and complete purgation of the colon may have significant side effects including, but not necessarily limited to, volume-related discomfort, nausea, cramping, and vomiting.

[0009] There is a need for colonic purgative formulations in liquid and solid dosage forms of that provide low toxicity and few harmful side effects. New sodium phosphate formulations are disclosed that provide a lower phosphate concentration and that produce the same or greater purgative effect, as compared to existing liquid or solid formulations, with a concomitant reduction in the risk of adverse renal side-effects. The present invention addresses these and other needs associated with improved patient tolerance.

SUMMARY

[0010] In some embodiments, the invention relates to compositions comprising a sodium phosphate salt and a magnesium citrate salt. In some embodiments, the formulation may contain one or more osmotic purgatives in addition to the sodium phosphate salt and a magnesium citrate salt.

[0011] The formulations of the present invention may be in a liquid or solid dosage form. In some embodiments of the invention, the formulation is a liquid dosage form. In some embodiments of the invention, the formulation is solid dosage form. In some embodiments of the invention, the formulation comprises a sodium phosphate salt chosen from monobasic sodium phosphate, dibasic sodium phosphate, tribasic sodium phosphate, or combination thereof. In some embodiments of the invention, the formulation comprises a magnesium citrate salt chosen from monobasic magnesium citrate, dibasic magnesium citrate, tribasic magnesium citrate, or combination thereof.

[0012] In some embodiments of the invention, the formulation comprises from about 1% to about 99% sodium phosphate salt by weight; and from about 0.1% to about 1 % of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 80% to about 90% sodium phosphate salt by weight; and from about 0.1% to about 10% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 70% to about 80% sodium phosphate salt by weight; and from about 0.1% to about 20% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 60% to about 70% sodium phosphate salt by weight; and from about 20% to about 30% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 50% to about 60% sodium phosphate salt by weight; and from about 30% to about 40% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 40% to about 50% sodium phosphate salt by weight; and from about 40% to about 50% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 30% to about 40% sodium phosphate salt by weight; and from about 50% to about 60% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 20% to about 30% sodium phosphate salt by weight; and from about 60% to about 70% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 10% to about 20% sodium phosphate salt by weight; and from about 70% to about 80% of

magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 5% to about 10% sodium phosphate salt by weight; and from about 85% to about 90% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 10% sodium phosphate salt by weight; and up to about 90% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 5% sodium phosphate salt by weight; and up to about 95% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 1% sodium phosphate salt by weight; and up to about 99% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation further comprises at least one inert diluent. In some embodiments of the invention, the formulation further comprises at least one inert dispersal agent. In some embodiments of the invention, the formulation further comprises at least one buffering agent.

[0013] In another embodiment of the invention, the formulation comprises less than about 20% sodium phosphate salt by weight; and up to about 80% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 30% sodium phosphate salt by weight; and up to about 70% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 40% sodium phosphate salt by weight; and up to about 60% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 50% sodium phosphate salt by weight; and up to about 50% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 60% sodium phosphate salt by weight; and up to about 40% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 70% sodium phosphate salt by weight; and up to about 30% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 80% sodium phosphate salt by weight; and up to about 20% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 90% sodium phosphate salt by weight; and up to about 10% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 95% sodium phosphate salt by weight; and up to about 5% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 99% sodium phosphate salt by weight; and up to about 1% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about

99.5% sodium phosphate salt by weight; and up to about 0.5% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 1% to about 99% sodium phosphate salt by weight; and from about 0.1% to about 1 % of magnesium citrate salt by weight. In another embodiment the formulation comprises from about 80% to about 90% sodium phosphate salt by weight; and from about 0.1% to about 10% of magnesium citrate salt by weight.

[0014] The invention further relates to use of a sodium phosphate salt and a magnesium citrate salt in the preparation of a medicament for treating constipation.

[0015] In some embodiments of the invention, the invention relates to a method of purging the colon of a mammal comprising administering a formulation comprising a sodium phosphate salt and a magnesium citrate salt. In some embodiments of the invention, the method comprises preparing a mixture a sodium phosphate salt and a magnesium citrate salt. In some embodiments of the invention, the method comprises forming an orally administrable dosage form of the mixture. In another embodiment of the invention, the method relates to method of purging the colon using a liquid or solid dosage form. In some embodiments of the invention, the method comprises: orally administering a purgative effective dosage of the formulation; and allowing said administered formulation to induce purgation. In some embodiments of the invention, the method or purging the colon of a subject comprises: administering any formulation described herein above. In some embodiments of the invention, the invention relates to a method of purging the colon of a mammal comprising preparing the formulation comprising a sodium phosphate salt and a magnesium citrate salt, administering a formulation comprising a sodium phosphate salt and a magnesium citrate salt, allowing said administered formulation to induce purgation.

[0016] The invention relates to a method of treating a mammal having constipation comprising administering a formulation comprising a sodium phosphate salt and a magnesium citrate salt. Some embodiments of the invention relates to a method of treating a patient having constipation comprising preparing a formulation comprising a sodium phosphate salt and a magnesium citrate salt; and administering the formulation comprising a sodium phosphate salt and a magnesium citrate salt to the subject. In some embodiments of the invention, the method comprises: forming an orally administrable dosage form of the mixture prior to administration to a mammal. In some embodiments, the orally administrable dosage form may be in an anhydrous powder which is dissolved in a solvent prior to administration to a mammal. In some embodiments, of the invention the orally administrable

dosage form is packaged in a sachet. Such sachets may be part of a kit. In some embodiments of the invention, the method of treating a mammal having constipation comprises administering a formulation comprising a sodium phosphate salt and a magnesium citrate salt wherein the mammal is orally administered a purgative effective dosage of said formulation. In some embodiments of the invention, the method of treating a subject having constipation comprises allowing said administered formulation to induce purgation. In some embodiments of the invention, the method of treating a subject having constipation comprises administering a formulation comprising a sodium phosphate salt and a magnesium citrate salt wherein the subject is orally administered a purgative effective dosage of said formulation.

[0017] The present invention also relates to a method of making a formulation comprising a sodium phosphate salt and a magnesium citrate salt. In some embodiments of the invention, the method comprises administering the formulation comprising any of the percentages of a sodium phosphate salt and a magnesium citrate salt described above. In some embodiments of the invention, the method of making the formulation comprising a sodium phosphate salt and a magnesium citrate salt for use in inducing purgation of the colon in a subject comprises preparing a liquid formulation. In some embodiments of the invention, the method of making the formulation comprising a sodium phosphate salt and a magnesium citrate salt for use in inducing purgation of the colon in a subject comprises preparing a liquid formulation. In some embodiments of the invention, the method of making the formulation comprising a sodium phosphate salt and a magnesium citrate salt for use in inducing purgation of the colon in a subject comprises preparing a solid formulation. In some embodiments of the invention, the method of making the formulation comprising a sodium phosphate salt and a magnesium citrate salt for use in inducing purgation of the colon in a subject comprises preparing an oral solid or liquid formulation. In some embodiments of the invention, the method of making a formulation comprising a sodium phosphate salt and a magnesium citrate salt for use in inducing purgation of the colon in a subject comprising preparing a solid dosage form in a tablet or capsule. In some embodiments of the invention, the method of making the formulation comprising a sodium phosphate salt and a magnesium citrate salt for use in inducing purgation of the colon in a subject comprises preparing a formulation comprising at least one inert diluent. In some embodiments of the invention, the method of making the formulation comprising a sodium phosphate salt and a magnesium citrate salt for use in inducing purgation of the colon in a subject comprises preparing a formulation comprising at least one inert dispersal agent. In some embodiments of the

invention, the method of making the formulation comprising a sodium phosphate salt and a magnesium citrate salt for use in inducing purgation of the colon in a subject comprises mixing the magnesium citrate salt and the sodium phosphate salt prior to administration. In some embodiments of the invention, the method of making the formulation comprising a sodium phosphate salt and a magnesium citrate salt for use in inducing purgation of the colon in a subject comprises packaging the the magnesium citrate salt and the sodium phosphate salt as anhydrous salts in a sachet.

[0018] The present invention is directed toward a kit comprising a composition or formulation comprising a sodium phosphate salt and a magnesium citrate salt. In some embodiments of the invention, the kit further comprises an oral rehydration mixture. In some embodiments, kits of the present invention comprise a first container and a second container wherein the first container comprises a sodium phosphate salt and a magnesium citrate salt and the second container comprises oral rehydration mixture or solution. In some embodiments, kits of the present invention can be used by a subject in need of medical evaluation of gastrointestinal health. In some embodiments, kits of the present invention can be used by a subject having constipation, preparing to undergo a colonoscopy, or preparing to undergo a diagnostic test, surgical procedure, or other medical evaluation that requires purgation of the colon.

[0019] Additional features and advantages of the invention will be made apparent from the following detailed description of illustrative embodiments.

DETAILED DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

[0020] Various terms relating to the methods and other aspects of the present invention are used throughout the specification and claims. Such terms are to be given their ordinary meaning in the art unless otherwise indicated. Other specifically defined terms are to be construed in a manner consistent with the definition provided herein.

[0021] As used in this specification and the appended claims, the singular forms "a," "an," and "the" include plural referents unless the content clearly dictates otherwise.

[0022] The term "about" as used herein when referring to a measurable value such as an amount, a temporal duration, and the like, is meant to encompass variations of ±20%, ±10%, ±5%, ±1%, or ±0.1% from the specified value, as such variations are appropriate to perform the disclosed methods.

[0023] The term "anhydrous" is used throughout the specification to describe a form in which the purgative salts according to the present invention can be administered.

Anhydrous formulations are those which essentially have excluded water from the formulations, except, in such instances where the salt is hydrated or otherwise complexed with small amounts of water.

[0024] The term "salt" refers to acidic salts formed with inorganic and/or organic acids, as well as basic salts formed with inorganic and/or organic bases. Examples of these acids and bases are well known to those of ordinary skill in the art. Salts according to the present invention may be used in a variety of forms, for example anhydrous or a hydrated crystalline form. In some embodiments, the salts may be those that are physiologically tolerated by a patient. In some embodiments of the invention, the term "purgative salt" refers to one or more of the anhydrous compounds which find use in purgative products according to the present invention. Salts according to the present invention may be found in their anhydrous form or as in hydrated crystalline form (i.e., complexed or crystallized with one or more molecules of water). Suitable purgative salts for use in the present invention include, for example, monobasic, dibasic, and tribasic magnesium citrate or a mixture of monobasic, dibasic, and tribasic citrate and phosphate salts.

[0025] The term "subject" is used throughout the specification to describe an animal to whom treatment with the compositions according to the present invention is provided or administered. For treatment of those conditions which are specific for a specific subject, such as a human being or such as a mammal, the term “patient” may be interchangeably used. In some instances in the description of the present invention, the term "patient" will refer to human patients. In some embodiments, the subject may be a mammal to whom the present invention is provided or administered.

[0026] The term "purgative" refers to any substance that promotes defecation. The term

purgative encompasses a range of cathartic effects. For instance, the term purgative encompasses mild catharsis, producing laxation ("partial purgation"), as well as stronger catharsis, providing complete or near-complete emptying of the large bowel ("complete purgation"). In some embodiments of the invention, the term refers to diarrhea. In another embodiment of the invention, the term refers to a softening or loosening of the feces or laxation. Unless modified by "partial" or "complete," purgative or purgation encompasses the full range of purgative processes, including both complete purgation and laxation ("partial purgation"). The term “active agent” may be used to describe the total amount of purgative in the formulation of the invention. One skilled in the art would recognize that formulations

of the invention may comprise active agents that comprise a sodium phosphate salt and a magnesium citrate salt. One skilled in the art would recognize that formulations of the invention may comprise active agents that comprise a sodium phosphate salt, a magnesium citrate salt, and at least one other purgative.

[0027] The term "osmotic" refers to any substance that promotes the passage of a solvent from a solution of lesser to one of greater solute concentration when the two solutions are separated by a membrane that selectively prevents the passage of solute molecules, but is permeable to the solvent. In the present invention, the term "osmotic" may refer to the ability of a substance to draw water into the intestines.

[0028] The term "fermentable" refers to any substance that can be anaerobically catabolized to simpler compounds, usually by bacteria and/or yeast. There are many types of fermentation, differing in the waste products formed and the fermentable substance. Fermentable substances include, but are not limited to, sugars, sugar-alcohols, polysaccharides, lactose, sorbitol, and mannitol. A fermentable substance releases explosive gases upon fermentation. The compound mannitol, for instance, can be fermented by bacteria that are typically resident in the colon of most humans and other mammals, during which hydrogen gas is released. The term "nonfermentable" refers to a substance that is not fermentable.

[0029] The term "soluble" or "water soluble" refers to an aqueous solubility that is higher than 1/10,000 (mg/ml). The solubility of a substance, or solute, is the maximum mass of that substance that can be dissolved completely in a specified mass of the solvent, such as water. "Practically insoluble" or "insoluble," on the other hand, refers to an aqueous solubility that is 1/10,000 (mg/ml) or less. Water soluble or soluble substances include, for example, polyethylene glycol.

[0030] The term "binder" refers to any substance that exerts a physicochemical attractive force between molecules, and hence may be used in formulation of a dosage form. In some embodiments of the invention, the binder may be mixed with other components of the composition, so that it is distributed uniformly throughout the dosage form. The binder may also provide a matrix upon which any additional components can associate. In some embodiments of the invention, the binder is soluble and non-fermentable. Non-limiting examples of tablet binders include starches, gelatin and sugars such as lactose, fructose, glucose and the like. Natural and synthetic gums are also convenient, including acacia, alginates, methylcellulose, and polyvinylpyrrolidone. Polyethylene glycol, ethylcellulose and

waxes can also serve as binders. In some embodiments of the invention, the formulation does not comprise polyethylene glycol. In some embodiments of the invention, the formulation does not comprise a binder.

[0031] "Effective amount" refers to an amount of a compound, material, or composition, as described herein effective to achieve a particular biological result such as, but not limited to, biological results disclosed, described, or exemplified herein. Such results may include, but are not limited to, purgation, the enhancement or promotion of purgation, as determined by any means suitable in the art. The effective amount of the composition may be dependent on any number of variables, including without limitation, the species, breed, size, height, weight, age, overall health of the subject, the type of formulation, the mode or manner of administration, the type and/or severity of the particular condition being treated, or the need to enhance laxation. The appropriate effective amount can be routinely determined by those of skill in the art using routine optimization techniques and the skilled and informed judgment of the practitioner and other factors evident to those skilled in the art. Preferably, a therapeutically effective dose of the compounds described herein will provide partial or complete purgative power with an increased safety margin relative to existing liquid or solid purgative formulations.

[0032] The terms "medical evaluation of the colon" refers to any procedure during which the condition of the colon is observed or evaluated by a health care provider. In some embodiments of the invention, the procedure may be a sedated colonscopy. In some embodiments of the invention, the procedure may be an unsedated colonscopy. In some embodiments of the invention, the procedure may be a capsule endoscopy. In some embodiments of the invention, the procedure may be a vertical colonscopy. In some embodiments of the invention, the procedure may be a sigmoidoscopy.

[0033] The physiology of intestinal secretion and absorption is generally well known as reflected in the reported literature. Intestinal absorption of sodium and water occurs largely in the small intestine. Approximately nine liters of gastrointestinal fluid is produced per day from the saliva, stomach, liver, pancreas and proximal small intestine and all but one to one and one half liters is reabsorbed by the small intestine before this passes the ileo-cecal valve into the colon. The colon then efficiently reabsorbs approximately 80% of the residual fluids culminating into a normal stool output of approximately 200 milliliters per day. The majority of sodium and water reabsorbed by the jejunum is due to the high permeability of the membranes of the cells of the small intestine along with active sodium pumping from the

cell into the interstitial fluid, culminating eventually into absorption into the capillary system. The net flux of sodium and water from the lumen into the blood is dependent upon many different factors. For example, changes in the intra-luminal osmolality of the proximal intestinal contents will promote a decrease in reabsorption of sodium and water and a net secretion of water into the lumen, ultimately producing diarrhea. As the osmolality of intra-luminal fluid increases, this produces a transmucosal flux of water from the capillary and interstitial fluid into the lumen in an effort to produce isotonicity. This tremendous flux of water that occurs with highly osmolar intra-luminal substances brings along with it sodium via a solvent drag phenomenon, thusly, which increases intra-luminal water to tremendous degrees. The amount of intra-luminal water increases directly proportional to the osmolality of the intra-luminal fluid. The formulations create, among other things, an increase in intra-luminal fluid of the small bowel to a significant degree allowing for a net secretion of sodium and water into the lumen, and thus allowing for tremendous fluxes of water to be present within the gastrointestinal lumen, producing a purgative effect.

[0034] The sodium phosphate and magnesium citrate salts of the instant invention may be in a liquid or solid dosage form in an effective amount for purgation while maintaining or increasing the safety margin after administration to a subject as compared to existing formulations containing sodium phosphate. The purgative effect of the phosphate salts appears to be proportionately related to the increase in the anionic state of the phosphate salt and may be differentiated in their mode of action from other salt formulations which are capable of producing a limited cathartic effect. One such salt, magnesium citrate, for example, exerts its effect via the magnesium cation which causes hypermotility of the gut and osmosis in the gut. The citrate anion is well-tolerated by patients and also does not have the unpalatable and excessively salty taste of the phosphate or sulfate anions of other purgatives.

[0035] An increased safety margin may result from magnesium cations and phosphate anions precipitating to form a salt. In some embodiments, the magnesium ions may create a phosphate trap so that excess phosphate is not absorbed by the bowel. In some embodiments, magensium ions create a decrease in the amount of phosphate absorbed by the subject potentially resulting in a further decrease serum phosphate levels. The concomitant use of compositions and or formulations comprising a magnesium citrate salt and a sodium phosphate salt could further protect against significant hyperphophatemia. In some embodiments, the formulations could be considered intraluminal phosphate traps.

[0036] In some embodiments, the invention relates to a method of purgation prior to medical evaluation of the colon. In some embodiments, dosing regimens have been designed that do not result in the formation of an intraluminal precipitant that obstructs visibility of the colon during medical evaluation of the colon. In some embodiments, an increased safety margin may result from dosing regimens that do not result in the formation of a magnesium phosphate precipitant that obstructs visibility of the colon upon medical evaluation. In some embodiments, methods of inducing purgation comprise administering the combination of magnesium citrate and sodium phosphate no sooner than about 10 hours prior to medical evaluation of the colon. In some embodiments, methods of inducing purgation comprise administering the combination of magnesium citrate and sodium phosphate no sooner than about 11 hours prior to medical evaluation of the colon. In some embodiments, methods of inducing purgation comprise administering the combination of magnesium citrate and sodium phosphate no sooner than about 12 hours prior to medical evaluation of the colon. In some embodiments, methods of inducing purgation comprise administering the combination of magnesium citrate and sodium phosphate no sooner than about 13 hours prior to medical evaluation of the colon. In some embodiments, methods of inducing purgation comprise administering the combination of magnesium citrate and sodium phosphate no sooner than about 14 hours prior to medical evaluation of the colon. In some embodiments, methods of inducing purgation comprise administering the combination of magnesium citrate and sodium phosphate no sooner than about 15 hours prior to medical evaluation of the colon. In some embodiments, methods of inducing purgation comprise administering the combination of magnesium citrate and sodium phosphate no sooner than about 16 hours prior to medical evaluation of the colon. In some embodiments, methods of inducing purgation comprise administering the combination of magnesium citrate and sodium phosphate no sooner than about 17 hours prior to medical evaluation of the colon. In some embodiments, methods of inducing purgation comprise administering the combination of magnesium citrate and sodium phosphate no sooner than about 18 hours prior to medical evaluation of the colon. In some embodiments, methods of inducing purgation comprise administering the combination of magnesium citrate and sodium phosphate no sooner than about 19 hours prior to medical evaluation of the colon. In some embodiments, methods of inducing purgation comprise administering the combination of magnesium citrate and sodium phosphate no sooner than about 20 hours prior to medical evaluation of the colon.

[0037] The formation of a precipitant may be due to the formation of magnesium phosphate salt due to the greater dissolution coefficient of magnesium phosphate as compared to sodium phosphate.

[0038] Some embodiments of the invention include a formulation comprising sodium phosphate, magnesium citrate, and at least one other purgative. Various purgatives are available commercially, and any available form of the material can be used in the practice of this invention. Purgatives, in addition to sodium phosphate and magnesium citrate that may be used in the invention include, but are not limited to, non-osmotic, osmotic, and bulk-forming purgatives. The invention may contain one additional purgative, more than one additional purgative from the same category, or more than one additional purgative from different categories may be used. Many purgatives may have more than one role or function, or may be classified in more than one group. Such classifications are descriptive only, and not intended to limit any use of a particular purgative. One skilled in the art would readily appreciate that the percentages used in the embodiments disclosed below may be relative to the total percentage of active ingredients in the formulation. One skilled in the art would readily appreciate that, if at least one other purgative is used in the formulation, the percentages of the embodiments disclosed below may represent and be relative to the total percentage of sodium phosphate and magnesium citrate in the formulation. For example, if a formulation comprises a sodium phosphate salt, a magnesium citrate salt , and an additional purgative X, an embodiment that comprises about 40% sodium phosphate and about 60% magnesium citrate salt, the percentages can be relative to the total amount of sodium phosphate salt and magnesium citrate salt in the formulation. If a sodium phosphate salt and a magnesium citrate salt are the only active purgative agents or ingredients in the formulation comprises, the percentages disclosed below can be relative to the total percentage of active purgative ingredients in the formulation.

[0039] In some embodiments of the invention, at least one osmotic purgative is used in the formulation of the invention. Osmotic purgatives act by increasing intestinal osmotic pressure thereby promoting retention of fluid within the bowel. Osmotic purgatives that may be included in the composition include salts, for example, magnesium chloride, magnesium hydroxide, magnesium phosphate, magnesium sulfate, magnesium tartrate, sodium phosphate, sodium tartrate, sodium sulfate, potassium tartrate, magnesium oxide, sodium sulfate, or salts thereof. Other examples of osmotic purgatives include glycerin, sorbitol, mannitol, lactitol, alcohol sugars, L-sugars, polyethylene glycol, and lactulose. However,

purgatives that are fermentable should only be used in embodiments where a spark would not be produced in the colon. In some embodiments of the invention, the formulation does not comprise purgatives with sulfate anions. In some embodiments of the invention, the formulation does not comprise purgatives with phosphate anions other than the sodium phosphate salt.

[0040] An embodiment of the invention may be formed into an easily administered dosage form. Dosage forms of the invention include solid or liquid dosage forms. If in a solid dosage form, an embodiment of the invention includes dosage form such as tablets or into capsules by methods well known in the art. When forming tablets containing the purgative formulation, it will be appreciated that the salts can be compressed into a uniform mixture and can optionally include inert diluents such as a tablet binder. The tablet binder may be a pharmaceutically acceptable binder and is one which produces no appreciable osmotic effects. Examples of useful binders include non-ionic detergents from the Pluronic™ series, such as Pluronic F-68™(a trademark of BASF-Wyandotte Chemicals, defined as a condensate of ethylene oxide with a condensate of propylene oxide and propylene glycol), related non-ionic surfactants, and mechanical adhesives such as polyvinyl alcohol and sodium carboxymethylcellulose, among numerous others. Microcrystalline cellulose (MCC) may also be used to enhance the compactability of the purgative salts into the tablet or capsule form. A soluble, nonfermentable binder that may be used in the formulations of the invention includes polyethylene glycol (PEG). PEG is represented by the structural formula:

$$HOCH_2(CH_2OCH_2)_mCH_2OH,$$

wherein m represents the average number of oxyethylene groups. Any PEG polymer may be employed in the compositions contemplated herein. In some embodiments, the PEG polymers are solid at room temperature (i.e., 25 degree C.) and/or soluble in (or miscible with) water at room temperature. In some embodiments of the invention, the average molecular weight of the PEG polymer is at least 200, at least 400, at least 600, at least 1,000, at least 1540, at least 3000, at least 4,000, or at least 8,000. In some embodiments of the invention, the average molecular weight of the PEG polymer is from about 7,000 to about 9,000.

[0041] The amount of binder may vary depending on the desired characteristics of the solid dosage form and can be determined by one of ordinary skill in the art. In some embodiments of the invention, a PEG binder comprises from about 5 to about 20%, in another embodiment from about 7.5 to about 15%, and in an additional embodiment about

10% by weight. In some embodiments of the invention, the formulation does not comprise a PEG binder.

[0042] In some embodiments of the invention, the composition of the invention is free of insoluble binder or only contains levels of insoluble binder that do not impede or obstruct the visualization of the colon. One of ordinary skill may readily modify the additives combined with the purgative salts according to the present invention in order to optimize the formulations for oral delivery.

[0043] Solid dosage forms are well known in the art. Solid dosage forms are easier for a patient or caregiver to identify, handle and administer. They are also non-invasive and have high patient compliance. Solid dosage forms can be divided into several groups, based upon the route by which the drug is delivered, including, for example, gastrointestinal (GI) tract delivery, suppository (rectal, vaginal and urethral) delivery, and transdermal delivery. The majority of solid dosage forms on the market are designed for gastro-intestinal delivery. GI delivery is often referred to simply as "oral delivery," because a tablet or capsule is initially introduced orally, and swallowed. However, this type of solid delivery form is designed to dissolve in the GI tract.

[0044] In addition to the purgative salts in either solid or liquid form, the formulations and compositions of the present invention may also contain optional ingredients to enhance the characteristics of the solid dosage form, maintain the integrity of particles of the active ingredient during the formulation process, and/or enhance the safety of the formulation. Any additional components may be compatible with the other ingredients in the formulations of the invention, in particular the active ingredients, and may be inert. If inert, the additional component does not adversely affect the osmolarity, osmolality, or isotoncity of the formulations or interfere, to a measureable degree, with the biological function of the purgative. Additional optional ingredients that may be used in the formulations of the invention include, for example, coatings, diluents, binders, glidants, lubricants, colors, disintegrants, flavors, sweeteners, polymers or waxes.

[0045] Non-limiting examples of diluents include various types of starch, cellulose, crystalline cellulose, microcrystalline cellulose, lactose, fructose, sucrose, mannitol or other sugar alcohols, kaolin, calcium phosphate or sulfate, inorganic salts such as sodium chloride and powdered sugar. Powdered cellulose derivatives are also useful. In some embodiments of the invention, the formulation does not include a diluent.

[0046] Lubricants, for example, may be included in the formulations of the invention. Such lubricants include, but are not limited to, magnesium stearate, potassium stearate, talc, stearic acid, sodium lauryl sulphate, and paraffin. In some embodiments of the invention, the colonic purgative formulation further comprises magnesium stearate. Lubricants serve to facilitate the manufacturing of a solid dosage form. In some embodiments of the invention, the formulation does not comprise a lubricant.

[0047] Additional suitable ingredients also include, but are not limited to, carriers, such as sodium citrate and dicalcium phosphate; fillers or extenders, such as stearates, silicas, gypsum, starches, lactose, sucrose, glucose, mannitol, talc, and silicic acid; binders, such as hydroxypropyl methylcellulose, hydroxymethyl-cellulose, alginates, gelatin, polyvinyl pyrrolidone, sucrose, and acacia; humectants, such as glycerol; disintegrating agents, such as agar, calcium carbonate, potato and tapioca starch, alginic acid, certain silicates, colloidal silicon dioxide, sodium starch glycolate, crospovidone, and sodium carbonate; solution retarding agents, such as paraffin; absorption accelerators, such as quaternary ammonium compounds; wetting agents, such as cetyl alcohol and glycerol monostearate; absorbents, such as kaolin and bentonite clay; stabilizers, such as fumaric acid; coloring agents; buffering agents; dispersing agents; preservatives; organic acids; and organic bases.

[0048] In some embodiments of the instant invention, the tablet or capsules may also

include inert dispersal agents which will facilitate dissolution of the tablet or capsule contents in the stomach of the patient. Preferably, the dispersal agent is a pharmaceutically acceptable dispersant and is one which also produces no appreciable osmotic effects. Examples of acceptable dispersants include microcrystalline cellulose (which is also useful as a compacting agent) and anhydrous lactose. In some embodiments, the dispersal agent is AC-DI-SOL, a cross-linked starch.

[0049] In some embodiments of the present invention, the formulation or composition

may also include a buffering agent to minimize any acid imbalance which may accompany ingestion of the purgative formulation. Suitable buffering agents include magnesium hydroxide, aluminum hydroxide, calcium carbonate and magnesium carbonate. In some embodiments, the formulation does not include a buffering agent.

[0050] In some embodiments of the invention, an additional component in the formulations of the invention may function to maintain the electrolyte balance in a patient.

For example, formulations of the invention may further comprise calcium, phosphate, potassium, magnesium, other anions, or salts thereof, which may normally be lost in diarrhea fluid.

[0051] In some embodiments of the invention, the formulation or composition comprises an additional component that causes stimulation of the motility of the gut, such as a stimulant laxative. A stimulant laxative of the invention may include, but are not necessarily limited to, Dulcolax®, or bisacodyl sodium containing product. In some embodiments of the invention, the composition comprises up to 15 grams of bisacodyl sodium salt. In some embodiments of the invention, the composition comprises up to 10 grams of bisacodyl sodium salt. In some embodiments of the invention, the composition comprises up to 5 grams of bisacodyl sodium salt. In some embodiments of the invention, the composition comprises up to 4 grams of bisacodyl sodium salt. In some embodiments of the invention, the composition comprises up to 3 grams of bisacodyl sodium salt. In some embodiments of the invention, the composition comprises up to 2 grams of bisacodyl sodium salt. In some embodiments of the invention, the composition comprises up to 1 grams of bisacodyl sodium salt.

[0052] Acidic or basic compounds may also be optionally added to the formulation to adjust the pH of the compound or to alter the disintegration characteristics of a tablet or capsule. Acidic or basic compounds that may be included in the formulations of the invention include, but are not limited to, sodium carbonate, sodium bicarbonate, sodium phosphate, calcium carbonate, magnesium hydroxide, potassium hydroxide, magnesium carbonate, and aluminum hydroxide. It will be appreciated that a change of the pH may also change the taste characteristics of the formulation. Formulations very high in pH typically are very bitter in taste. As the pH drops, the taste becomes less bitter, then salty, and may eventually become sour.

[0053] In some embodiments of the invention, the orally administered purgative formulation may be easily and conveniently administered and avoids the problems and objectionable tastes of known formulations. It can also be seen that it is desirable to have such a purgative formulation which may be administered without large volumes of water necessary in conventional formulations and which avoids other potentially irritant chemicals or chemicals which could effect osmolality. Nonetheless, it may be desirable to add a flavoring agent to the compositions of the present invention. A wide range of flavors are available for preparing good tasting and desirable medications within the scope of the present

invention. These may be required in order to mask the taste of the amount of purgative or purgatives. Flavorings may be combined, as desired, to produce a particular flavor mix which is compatible with a particular medication. Some of the confectioner's flavorings which may be used in the context of the present invention include artificial vanilla, vanilla cream, mint, berry, cherry, spearmint, grape, coconut, chocolate, menthol, licorice, lemon, lemon-lime, and butterscotch. Each of these flavorings is obtainable in a concentrated powder form. Some embodiments of the invention include flavoring agents prepared by spray drying. Other flavorings known in the confectionary arts may also be acceptable because of the ease of combining the ingredients of the present invention. Any number of flavorings may be combined in any desired ratio in order to produce the specific desired taste characteristics required for any particular application. For example, flavor combinations may be varied in order to be compatible with the flavor characteristics of any specific drug.

[0054] Flavoring agents may be varied in order to identify an optimal visual field during medical evaluation of the colon. In some embodiments, the formulation does not comprise certain flavoring agents. In some embodiments, the formulation does not comprise a flavoring agent that impairs visualization of the intestines during medical evaluation. In some embodiments, the formulation does not comprise an orange flavoring agent, which may impair the visualization of the colon during medical evaluation of the colon.

[0055] In order to produce a desirable color for the end product, artificial colorings may also be added to the composition. The flavorings described above are generally a white powder, as are the other major components. Therefore, additional coloring is necessary if a colored end product is desired. Coloring may also be important as a code to indicate the type of formulation. Any type of color known to be "generally regarded as safe" ("GRAS"), and thus generally used in the confectionary trade, or otherwise approved by the appropriate regulatory authority for use in formulations administered to subjects, may be used to provide coloring to the product.

[0056] In some embodiments it may be necessary to add sugars, sugar alcohols, or other sweeteners to the composition for flavor enhancement. Suitable artificial sweeteners include aspartame, acesulfame K, saccharin, sucralose, altitame, cyclamic acid and its salts, glycerrhizinate, dihydrochalcones, thaumatin, monellin, or any other non-cariogenic, sugar-free sweetener, alone or in combination. For compositions which contain a sugar alcohol, additional sweeteners may not be necessary, due to the naturally sweet taste of these polyhydric alcohols. It is desired that a sweetener or combination of sweeteners be obtained

which is compatible with the purgative agent and the other components such that a good tasting solid dosage form is produced.

[0057] As mentioned previously, the compositions may also include a disintegrating agent. Tablet disintegrators are substances which swell when wetted to break up the tablet and release the purgative, and include starches such as corn and potato starches, clays, celluloses, aligns, gums, methylcellulose, agar, bentonite, wood cellulose, powdered natural sponge, cation-exchange resins, alginic acid, guar gum, citrus pulp, carboxymethyl cellulose, and sodium lauryl sulfate.

[0058] Solid form dosages in a formulation can be prepared according to any means suitable in the art. The solid dosage form of the invention may be a tablet or capsules. Capsules are prepared by mixing the purgative mixture with a suitable diluent and filling the proper amount of the mixture in capsules. Tablets are prepared by direct compression, by wet granulation, or by dry granulation. Their formulations usually incorporate diluents, binders, lubricants and disintegrators as well as the compound.

[0059] A lubricant can be used in a tablet formulation to prevent the tablet and punches from sticking in the die. The lubricant can be chosen from such slippery solids as talc, magnesium and calcium stearate, stearic acid and hydrogenated vegetable oils.

[0060] Tablets can be coated with sugar as a flavor and sealant, or with film-forming protecting agents to modify the dissolution properties of the tablet. The compounds may also be formulated as chewable tablets, by using large amounts of pleasant-tasting substances such as mannitol in the formulation, as is now well-established in the art.

[0061] Liquid dosage forms are well known in the art. Suitable liquid formulations include, for example, the list of liquid formulations included in *Remington: The Science and Practice of Pharmacy*, 20th Edition. Baltimore, MD: Lippincott Williams & Wilkins, 2000. Concentrated aqueous phosphate and sulfate solutions are, at times, extremely unpalatable, so much so that the recommended dosage form is administered ice cold so as to minimize the objectionable saline taste. Often patients complain of severe nausea and vomiting, possible secondary to the extremely salty taste of the preparation. Frequently, patients cannot even tolerate the ingestion of this preparation at the initial dose and often the second dose becomes even more problematic due to the unpalatable extremely salty taste, even when the taste is partially masked by the use of flavoring agents. An embodiment of the invention includes liquid dosage forms that have the same or increased purgative power as compared to existing

liquid formulations but have an improved safety margin, fewer side effects, and/or better taste.

[0062] Also contemplated are liquid formulations and solid form preparations which are intended to be converted, shortly before use, to liquid form preparations. Such liquid forms include solutions, suspensions, syrups, slurries, and emulsions. One embodiment of the invention involves solid form preparations which are intended to be converted, shortly before use, to liquid form preparations wherein the solid form preparation, or formulation, comprises magnesium citrate and sodium phosphate as anhydrous powders. Shortly before use, the anhydrous powders of the embodiment may be dissolved in a fluid such as water to produce a liquid preparation. In one embodiment of the invention, the composition that comprises magnesium citrate and sodium phosphate as anhydrous powders is in a sachet. Liquid preparations may be prepared by conventional means with pharmaceutically acceptable additives such as suspending agents (*e.g.*, sorbitol syrup, cellulose derivatives or hydrogenated edible fats or oils); emulsifying agents (*e.g.*, lecithin or acacia); non-aqueous vehicles (*e.g.*, almond oil, oily esters, or fractionated vegetable oils); and preservatives (*e.g.*, methyl or propyl-p-hydroxybenzoates or sorbic acid). These preparations may contain, in addition to the active agent, colorants, flavors, stabilizers, buffers, artificial and natural sweeteners, dispersants, thickeners, solubilizing agents, and the like. Certain embodiments of the invention may not contain colorants, flavors, stabilizers, buffers, artificial and natural sweeteners, dispersants, thickeners, solubilizing agents, and the like, if such inactive agent impairs or obstructs visibility of the colon during medical evaluation. The compositions may be in powder form, anhydrous or otherwise, for constitution with a suitable vehicle such as sterile water, saline solution, or alcohol, before use. In some embodiments of the invention sachets containing the composition may be produced for dissolution in a suitable vehicle such as sterile water, saline solution, or alcohol, before use. Some embodiments of the invention relate to liquid formulations comprising magnesium citrate salt and sodium phosphate salt of certain weight percentages, that, when administered to a subject, reduce or eliminate the formation of a precipitant when administered prior to medical evaluation of the colon that requires purgative treatment. In some embodiments of the invention, the liquid formulations comprising magnesium citrate salt and sodium phosphate salt of certain weight percentages, that, when administered to a subject, reduce or eliminate the formation of a magnesium phosphate precipitant which impairs visibility of the colon during medical evaluation of the colon. Some embodiments of the invention relate to liquid formulations comprising

magnesium citrate salt and sodium phosphate salt of certain weight percentages, that, when administered to a subject, do not cause formation of magnesium phosphate salt precipitant visible to physician using a camera in the colon during medical evaluation of the colon.

[0063] Some embodiments of the invention relate to liquid formulations and compositions that comprise additional additives such as potassium chloride. Subjects administered oral purgative agents may have a dramatic drop in electrolytes and or potassium levels due to an imbalanced flow of fluid into the bowel. The resulting drop in potassium can cause potassium hypokalemia. One of skilled in the art would realize that some embodiments of the invention can comprise electrolytes such as potassium chloride. In some embodiments of the invention, the liquid formulation comprises potassium chloride. In some embodiments. the liquid formulation does not comprise potassium chloride.

[0064] The present invention also encompasses methods of using the colonic purgative formulations. The colonic purgative formulations of the invention produce a broad range of activities, depending on the dosage administered. The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal or human being with a purgative formulation and allowing said formulation to purge the colon. The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal or human being in need of a purgative formulation and allowing said formulation to purge the colon. The formulations of the invention may also be used at lower doses in order to regulate, soften or loosen the stool. Thus, the present invention also encompasses methods of maintaining the elimination or increasing the elimination of feces in the bowel, comprising administering to at least one patient a purgative formulation and promoting the elimination of feces in the bowel. The colonic purgative formulations of the invention may also be used to treat a patient with constipation.

[0065] The colonic purgative formulations of the invention may be used to treat a patient with constipation. The colonic purgative formulations of the invention may also be used to treat a patient in need thereof. Patients may need treatment with the purgative formulation because of a previously diagnosed condition that causes constipation. The constipation may be caused by a variety of factors including, but not limited to, at least one of travel; change in daily routine; lack of exercise; immobility caused by injury, illness, or aging; dehydration; irritable bowel syndrome; pregnancy; diabetes; hypothyroidism; hypercalcemia; cancer of the colon or rectum; uterine prolapse; vaginal vault prolapse; rectal

prolapse; scarring from surgery; injury of the colon or rectum; Parkinson's disease; multiple sclerosis; stroke; hemorrhoid or anal fissures; delaying bowel movements; anxiety; depression; eating disorders; and obsessive-compulsive disorder. The constipation may also be idiopathic, i.e. of unknown causation.

[0066] In another embodiment of the invention the composition of the invention is used to treat a patient suffering from, or susceptible to, constipation due to administration of a medication that causes constipation. A medication that may cause constipation includes, but is not limited to antacids that contain aluminum; antidepressants; blood pressure medications; calcium channel blockers; calcium supplements; chemotherapy medications; cold medicines; antihistamines; diuretics; iron supplements; medications for Parkinson's disease; lipid-lowering agents; pain medications; opiates; codeine; and tranquilizers.

[0067] One of skill in the art will recognize that the appropriate dosage of the colonic purgative compositions may vary depending on the individual being treated and the purpose. For example, the age, body weight, and medical history of the individual patient may affect the therapeutic efficacy of the therapy. Further, a lower dosage of the composition may be needed to produce a mild catharsis, while complete purgation may require a higher dose. A competent physician can consider these factors and adjust the dosing regimen to ensure the dose is achieving the desired therapeutic outcome without undue experimentation. It is also noted that the clinician and/or treating physician will know how and when to interrupt, adjust, and/or terminate therapy in conjunction with individual patient response. Dosages may also depend on the strength of the particular purgative(s) chosen for the formulation. Dosages may also depend on whether the patient in need thereof has been previously diagnosed with a medical condition that causes irregular bowel evacuation.

[0068] Multiple doses may be administered to the subject per day. Multiple doses may be administered in a dosing regimen within about 24 hours. In some embodiments of the invention methods of purging the colon comprise administering to at least one patient, mammal, or human being a purgative formulation and allowing said formulation to purge the colon. In some embodiments of the invention, the total dosage is administered in at least two application periods. In an additional embodiment of the invention, the total dosage is administered in two or more separate application periods. In some embodiments, a dosing regimen may include one, two, three, four or more administration steps wherein the formulation of the present invention is administered in only one of the administration steps.

[0069] In some embodiments of the invention, methods of purging the colon comprise administering to at least one patient, mammal, or human being with a purgative formulation comprising magnesium citrate and sodium phosphate between about 20 hours to about 10 hours prior to medical evaluation, and allowing said formulation to purge the colon. In some embodiments of the invention, the methods of purging the colon comprise: (i) administering a purgative formulation comprising magnesium citrate and sodium phosphate to at least one patient, mammal, or human being between about 20 hours to about 14 hours prior to medical evaluation of the colon; (ii) administering a second purgative formulation to at least one patient, mammal, or human being between about 6 hours to about 3 hours prior to medical evaluation of the colon; and allowing said formulation to purge the colon. In some embodiments, the purgative formulation may be administered about 18 hours prior to an invasive procedure involving the colon. In some embodiments the formulation may be administered about 17 hours prior to the invasive procedure involving the colon. In some embodiments the formulation may be administered about 16 hours prior to the invasive procedure involving the colon. In some embodiments the formulation may be administered about 3 hours prior to the invasive procedure involving the colon.

[0070] The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal, or human a series of two or more purgative formulations wherein at least one purgative formulation comprises magnesium citrate and sodium phosphate; and allowing said formulation to purge the colon. The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal, or human a series of three formulations within 24 hours wherein at least one formulation comprises a purgative formulation comprising magnesium citrate and sodium phosphate; and allowing said formulation to purge the colon. The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal, or human a series of two or more compositions wherein at least one composition is a purgative formulation comprising magnesium citrate and sodium phosphate; and allowing said formulation to purge the colon. The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal, or human a series of two or more compositions in an 18 hour time period wherein at least one composition is a purgative formulation comprising magnesium citrate and sodium phosphate; and allowing said formulation to purge the colon. The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal, or human a series of

three or more compositions in a 21 hour time period wherein: (i) a first composition comprises Ducolax® which is administered from about 21-18 hours prior to medical evaluation of the colon; (ii) a second composition comprises an oral formulation comprising magnesium citrate salt and sodium phosphate salt which is administered between about 18-14 hours prior to medical evaluation of the colon; (iii) a third composition comprises an oral formulation comprising a purgative agent salt which is administered at about 3 hours prior to medical evaluation of the colon. The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal, or human a series of three or more compositions in a 21 hour time period wherein: (i) a first composition comprises Ducolax® which is administered from about 21 to about14 hours prior to medical evaluation of the colon; (ii) a second composition comprises an oral formulation comprising magnesium citrate salt and sodium phosphate salt which is administered between about 21 to about 14 hours prior to medical evaluation of the colon; (iii) a third composition comprises an oral formulation comprising a purgative agent which is administered at about 3 hours prior to medical evaluation of the colon. The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal, or human a series of three or more compositions between about 21-14 hours prior to medical evaluation of the colon wherein: (i) a first composition comprises Ducolax® which is administered at about 18 hours prior to medical evaluation of the colon; (ii) a second composition comprising an oral formulation comprising magnesium citrate salt and sodium phosphate salt is administered at about 17 hours prior to medical evaluation of the colon; (iii) a third composition comprising an oral formulation comprising magnesium citrate salt is administered at about 3 hours prior to medical evaluation of the colon. The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal, or human a series of two or more compositions in an 18 hour time period wherein: (i) a first composition comprises Ducolax® which is administered at about 18 hours prior to medical evaluation of the colon; (ii) a second composition comprises an oral formulation comprising magnesium citrate salt and sodium phosphate salt which is administered at about 17 hours prior to medical evaluation of the colon; (iii) a third composition comprising an oral formulation comprises magnesium citrate salt and sodium phosphate salt which is administered at about 3 hours prior to medical evaluation of the colon. The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal, or human a series of two or more compositions in an 18 hour time period wherein: (i) a first composition

comprises Ducolax® which is administered between about 20 hours to about 18 hours prior to medical evaluation of the colon; (ii) a second composition comprises an oral formulation comprising magnesium citrate salt and sodium phosphate salt which is administered between about 18 to about 17 hours prior to medical evaluation of the colon; (iii) a third composition comprises an oral formulation comprising magnesium citrate salt which is administered between about 6 to about 3 hours prior to medical evaluation of the colon.

The present invention encompasses methods of purging the colon comprising: (i) administering a first composition comprising bicosadyl sodium to at least one patient, mammal, or human from about 21 hours to about 11 hours prior to medical evaluation of the colon; and (ii) administering a second composition comprising magnesium citrate salt and sodium phosphate salt to the patient, mammal, or human between about 20 to about 10 hours prior to medical evaluation of the colon. The present invention encompasses methods of purging the colon comprising: (i) administering a first composition comprising bicosadyl sodium to at least one patient, mammal, or human from about 21 hours to about 11 hours prior to medical evaluation of the colon; (ii) administering a second composition comprising magnesium citrate salt and sodium phosphate salt to the patient, mammal, or human between about 20 to about 10 hours prior to medical evaluation of the colon; and (iii) administering a third composition comprising an oral formulation comprising a purgative agent which is administered between about 6 to about 3 hours prior to medical evaluation of the colon. The present invention encompasses methods of purging the colon comprising: (i) administering a first composition comprising bicosadyl sodium to at least one patient, mammal, or human from about 21 hours to about 11 hours prior to medical evaluation of the colon; (ii) administering a second composition comprising magnesium citrate salt and sodium phosphate salt to the patient, mammal, or human between about 20 to about 10 hours prior to medical evaluation of the colon; and (iii) administering a third composition comprising an oral formulation comprising magnesium citrate salt which is administered between about 6 to about 3 hours prior to medical evaluation of the colon. In some embodiments, the first composition comprises a stimulant laxative. In some embodiments, the first composition comprises 20 milligrams of Ducolax®. In some embodiments, the first composition comprises four 5-gram Ducolax® tablets. In some embodiments of the invention, the second composition comprises a liquid formulation or a solid formulation comprising magnesium citrate and sodium phosphate.

[0071] The present invention encompasses methods of treating constipation comprising administering to at least one patient, mammal, or human at least one formulation wherein the formulation comprises a purgative formulation comprising magnesium citrate and sodium phosphate; and allowing said composition to purge the colon. The present invention encompasses methods of treating constipation comprising administering at least one formulation wherein the formulation comprises a purgative formulation comprising magnesium citrate and sodium phosphate to at least one patient, mammal, or human in need thereof; and allowing said composition to purge the colon. The present invention encompasses methods of treating constipation comprising administering to at least one patient, mammal, or human a series of two or more purgative formulations wherein at least one purgative formulation comprises magnesium citrate and sodium phosphate; and allowing said formulation to purge the colon. The present invention encompasses methods of treating constipation comprising administering a series of two or more purgative formulations wherein at least one purgative formulation comprises magnesium citrate and sodium phosphate to at least one patient, mammal, or human in need thereof; and allowing said formulation to purge the colon. The present invention encompasses methods of treating constipation comprising administering to at least one patient, mammal, or human a series of two or more purgative formulations wherein at least one purgative formulation comprises magnesium citrate and sodium phosphate; and allowing said formulation to purge the colon. The present invention encompasses methods of treating constipation comprising: (i) administering to at least one patient, mammal, or human a series of two or more compositions; wherein at least one composition is a purgative formulation comprising magnesium citrate and sodium phosphate; and wherein at least one composition comprises a stimulant laxative; and (ii) allowing said compositions to purge the colon.

[0072] The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal, or human a series of two or more purgative formulations wherein at least one purgative formulation comprises magnesium citrate and sodium phosphate; and allowing said formulation to purge the colon. The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal, or human a series of three formulations within 24 hours wherein at least one formulation comprises a purgative formulation comprising magnesium citrate and sodium phosphate; and allowing said formulation to purge the colon. The present invention encompasses methods of purging the colon comprising administering to at least one patient,

mammal, or human a series of two or more compositions wherein at least one composition is a purgative formulation comprising magnesium citrate and sodium phosphate; and allowing said formulation to purge the colon. The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal, or human a series of two or more compositions in an 18 hour time period wherein at least one composition is a purgative formulation comprising magnesium citrate and sodium phosphate; and allowing said formulation to purge the colon. The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal, or human a series of three or more compositions in an 18 hour time period wherein: (i) a first composition comprises Ducolax® which is administered at about 18 hours prior to medical evaluation of the colon; (ii) a second composition comprises an oral formulation comprising magnesium citrate salt and sodium phosphate salt which is administered at about 17 hours prior to medical evaluation of the colon; (iii) a third composition comprises an oral formulation comprising magnesium citrate salt and sodium phosphate salt which is administered at about 3 hours prior to medical evaluation of the colon. The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal, or human a series of three or more compositions in an approximate 18 hour time period wherein: (i) a first composition comprises Ducolax® which is administered at about 18 hours prior to medical evaluation of the colon; (ii) a second composition comprising an oral formulation comprising magnesium citrate salt and sodium phosphate salt is administered at about 17 hours prior to medical evaluation of the colon; (iii) a third composition comprising an oral formulation comprising magnesium citrate salt is administered at about 3 hours prior to medical evaluation of the colon. The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal, or human a series of two or more compositions in an 18 hour time period wherein: (i) a first composition comprises Ducolax® which is administered at about 18 hours prior to medical evaluation of the colon; (ii) a second composition comprises an oral formulation comprising magnesium citrate salt and sodium phosphate salt which is administered at about 17 hours prior to medical evaluation of the colon; (iii) a third composition comprising an oral formulation comprises magnesium citrate salt and sodium phosphate salt which is administered at about 3 hours prior to medical evaluation of the colon. The present invention encompasses methods of purging the colon comprising administering to at least one patient, mammal, or human a series of two or more compositions in an 18 hour time period wherein: (i) a first composition

comprises Ducolax® which is administered between about 20 hours to about 18 hours prior to medical evaluation of the colon; (ii) a second composition comprises an oral formulation comprising magnesium citrate salt and sodium phosphate salt which is administered between about 18 to about 17 hours prior to medical evaluation of the colon; (iii) a third composition comprises an oral formulation comprising magnesium citrate salt which is administered between about 6 to about 3 hours prior to medical evaluation of the colon.

[0073] The present invention encompasses methods of treating constipation comprising administering to at least one patient, mammal, or human a series of two or more purgative formulations wherein at least one purgative formulation comprises magnesium citrate and sodium phosphate; and allowing said formulation to purge the colon. The present invention encompasses methods of treating constipation comprising administering to at least one patient, mammal, or human a series of three formulations within 24 hours wherein at least one formulation comprises a purgative formulation comprising magnesium citrate and sodium phosphate; and allowing said formulation to purge the colon. The present invention encompasses methods of treating constipation comprising administering to at least one patient, mammal, or human a series of two or more compositions wherein at least one composition is a purgative formulation comprising magnesium citrate and sodium phosphate; and allowing said formulation to purge the colon. The present invention encompasses methods of treating constipation comprising administering to at least one patient, mammal, or human a series of two or more compositions in an 18 hour time period wherein at least one composition is a purgative formulation comprising magnesium citrate and sodium phosphate; and allowing said formulation to purge the colon. The present invention encompasses methods of treating constipation comprising administering to at least one patient, mammal, or human in need thereof a series of three or more compositions in an 18 hour time period wherein: (i) a first composition comprises Ducolax® which is administered at about 18 hours prior to medical evaluation of the colon; (ii) a second composition comprises an oral formulation comprising magnesium citrate salt and sodium phosphate salt which is administered at about 17 hours prior to medical evaluation of the colon; (iii) a third composition comprises an oral formulation comprising magnesium citrate salt and sodium phosphate salt which is administered at about 3 hours prior to medical evaluation of the colon. The present invention encompasses methods of treating constipation comprising administering to at least one patient, mammal, or human in need thereof a series of three or more compositions in an approximate 18 hour time period wherein: (i) a first composition

comprises Ducolax® which is administered at about 18 hours prior to medical evaluation of the colon; (ii) a second composition comprising an oral formulation comprising magnesium citrate salt and sodium phosphate salt is administered at about 17 hours prior to medical evaluation of the colon; (iii) a third composition comprising an oral formulation comprising magnesium citrate salt is administered at about 3 hours prior to medical evaluation of the colon. The present invention encompasses methods of treating constipation comprising administering to at least one patient, mammal, or human in need thereof a series of two or more compositions in an 18 hour time period wherein: (i) a first composition comprises Ducolax® which is administered at about 18 hours prior to medical evaluation of the colon; (ii) a second composition comprises an oral formulation comprising magnesium citrate salt and sodium phosphate salt which is administered at about 17 hours prior to medical evaluation of the colon; (iii) a third composition comprising an oral formulation comprises magnesium citrate salt and sodium phosphate salt which is administered at about 3 hours prior to medical evaluation of the colon. The present invention encompasses methods of treating constipation comprising administering to at least one patient, mammal, or human in need thereof a series of two or more compositions in an 18 hour time period wherein: (i) a first composition comprises Ducolax® which is administered between about 20 hours to about 18 hours prior to medical evaluation of the colon; (ii) a second composition comprises an oral formulation comprising magnesium citrate salt and sodium phosphate salt which is administered between about 18 to about 17 hours prior to medical evaluation of the colon; (iii) a third composition comprises an oral formulation comprising magnesium citrate salt which is administered between about 6 to about 3 hours prior to medical evaluation of the colon.

[0074] The dose of the purgative formulations may vary. In some aspects of the invention, the compositions comprise a percentage of sodium phosphate salt and a percentage of magnesium citrate salt relative to the total weight of active ingredients used in the formulation. In some embodiments the range of percentage of sodium phosphate salt and a percentage of magnesium citrate salt relative to the total weight of active ingredients used in the formulation can be from about 0.01% to about 90% by weight. In some embodiments of the invention, the formulation comprises from about 1% to about 99% sodium phosphate salt by weight; and from about 0.1% to about 1 % of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 80% to about 90% sodium phosphate salt by weight; and from about 0.1% to about 10% of magnesium citrate

salt by weight. In some embodiments of the invention, formulation comprises from about 70% to about 80% sodium phosphate salt by weight; and from about 10% to about 20% of magnesium citrate salt by weight. In some embodiments of the invention, the liquid or solid dosage form comprises from about 60% to about 70% sodium phosphate salt by weight; and from about 20% to about 30% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 50% to about 60% sodium phosphate salt by weight; and from about 30% to about 40% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 40% to about 50% sodium phosphate salt by weight; and from about 40% to about 50% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 30% to about 40% sodium phosphate salt by weight; and from about 50% to about 60% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 20% to about 30% sodium phosphate salt by weight; and from about 60% to about 70% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 10% to about 20% sodium phosphate salt by weight; and from about 70% to about 80% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 5% to about 10% sodium phosphate salt by weight; and from about 85% to about 90% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 10% sodium phosphate salt by weight; and up to about 90% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 5% sodium phosphate salt by weight; and up to about 95% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 1% sodium phosphate salt by weight; and up to about 99% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation further comprises at least one inert diluent. In some embodiments of the invention, the formulation further comprises at least one inert dispersal agent. In some embodiments of the invention, the formulation further comprises at least one buffering agent. In some embodiments of the invention, the formulation further comprises at least one additional purgative. In some embodiments of the invention, the formulation further comprises at least one additional purgative wherein said additional purgative is not an osmotic sulfate or phosphate salt.

[0075] In other embodiments of the invention, the formulation comprises less than about 20% sodium phosphate salt by weight; and up to about 80% of magnesium citrate salt

by weight of active ingredients in the formulation. In some embodiments of the invention, the formulation comprises less than about 30% sodium phosphate salt by weight; and up to about 70% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 40% sodium phosphate salt by weight; and up to about 60% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 50% sodium phosphate salt by weight; and up to about 50% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 60% sodium phosphate salt by weight; and up to about 40% of magnesium citrate salt by weight. In some embodiments of the invention, formulation comprises less than about 70% sodium phosphate salt by weight; and up to about 30% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 80% sodium phosphate salt by weight; and up to about 20% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 90% sodium phosphate salt by weight; and up to about 10% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 95% sodium phosphate salt by weight; and up to about 5% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 99% sodium phosphate salt by weight; and up to about 1% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises less than about 99.5% sodium phosphate salt by weight; and up to about 0.5% of magnesium citrate salt by weight. In some embodiments of the invention, the formulation comprises from about 1% to about 99% sodium phosphate salt by weight; and from about 0.1% to about 1 % of magnesium citrate salt by weight. In another embodiment the formulation comprises from about 80% to about 90% sodium phosphate salt by weight; and from about 0.1% to about 10% of magnesium citrate salt by weight.

[0076] In some embodiments, subjects can be administered formulations in which the formulation is provided in a daily dose range of about 0.01 mg/kg to about 500 mg/kg of the weight of the subject. The dose administered to the subject can also be measured in terms of total amount of sodium phosphate administered per day. In some embodiments, a subject is administered between about 1 mg to about 40 grams of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 40 grams of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 35 grams of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 30 grams

of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 25 grams of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 20 grams of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 15 grams of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 10 grams of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 5 grams of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 4 grams of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 3 grams of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 2 grams of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 1800 milligrams of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 1600 milligrams of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 1400 milligrams of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 1200 milligrams of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 1000 milligrams of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 800 milligrams of sodium phosphate salt per day. In some embodiments, a subject is administered up to about 700 milligrams of sodium phosphate salt per dose. In some embodiments, a subject is administered up to about 600 milligrams of sodium phosphate salt per dose. In some embodiments, a subject is administered up to about 500 milligrams of sodium phosphate salt per dose. In some embodiments, a subject is administered up to about 400 milligrams of sodium phosphate salt per dose. In some embodiments, a subject is administered up to about 300 milligrams of sodium phosphate salt per dose. In some embodiments, a subject is administered up to about 200 milligrams of sodium phosphate salt per dose. In some embodiments, a subject is administered up to about 100 milligrams of sodium phosphate salt per dose. In some embodiments, a subject is administered up to about 50 milligrams of sodium phosphate salt per dose. The dose administered to the subject can also be measured in terms of total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 60 grams. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up

to about 55 grams. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 50 grams. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 45 grams. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 40 grams. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 35 grams. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 30 grams. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 25 grams. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 20 grams. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 15 grams. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 10 grams. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 5 grams. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 4 grams. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 3 grams. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 2 grams. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 1 gram. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 0.5 grams. In some embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 0.25 grams. In some

embodiments the total amount of sodium phosphate salt and magnesium citrate salt administered to the subject, mammal, or human patient is up to about 0.1 grams.

[0077] The dose administered to the subject can also be measured in terms of total amount of sodium phosphate salt and magnesium citrate salt administered per ounce of liquid prepared. In some embodiments, the magnesium citrate is at a concentration of about 2.5 grams per ounce of solution. In some embodiments, the magnesium citrate is at a concentration of about 2.25 grams per ounce of solution prepared. In some embodiments, the magnesium citrate salt is at a concentration of about 2.25 grams per ounce of solution prepared. In some embodiments, the magnesium citrate is at a concentration of about 2.0 grams per ounce of solution prepared. In some embodiments, the magnesium citrate is at a concentration of about 1.9 grams per ounce of solution. In some embodiments, the magnesium citrate is at a concentration of about 1.8 grams per ounce of solution. In some embodiments, the magnesium citrate is at a concentration of about 1.7 grams per ounce of solution. In some embodiments, the magnesium citrate is at a concentration of about 1.6 grams per ounce of solution. In some embodiments, the magnesium citrate is at a concentration of about 1.5 grams per ounce of solution. In some embodiments, the magnesium citrate is at a concentration of about 1.4 grams per ounce of solution. In some embodiments, the magnesium citrate is at a concentration of about 1.3 grams per ounce of solution. In some embodiments, the magnesium citrate is at a concentration of about 1.2 grams per ounce of solution. In some embodiments, the magnesium citrate is at a concentration of about 1.1 grams per ounce of solution. In some embodiments, the magnesium citrate is at a concentration of about 1.0 grams per ounce of solution. In some embodiments, the magnesium citrate is at a concentration of about 0.9 grams per ounce of solution. In some embodiments, the magnesium citrate is at a concentration of about 0.8 grams per ounce of solution. In some embodiments, the magnesium citrate is at a concentration of about 0.7 grams per ounce of solution. In some embodiments, the magnesium citrate is at a concentration of about 0.6 grams per ounce of solution. In some embodiments, the magnesium citrate is at a concentration of about 0.5 grams per ounce of solution. In some embodiments, the magnesium citrate is at a concentration of about 0.4 grams per ounce of solution. In some embodiments, the magnesium citrate is at a concentration of about 0.3 grams per ounce of solution prepared. In some embodiments, the magnesium citrate is at a concentration of about 0.2 grams per ounce of solution prepared. In

some embodiments, the magnesium citrate is at a concentration of about 0.1 grams per ounce of solution prepared.

[0078] In some embodiments, the sodium phosphate salt is up to a concentration of about 25 grams per ounce of solution. In some embodiments, the sodium phosphate salt is up to a concentration of about 20 grams per ounce of solution. In some embodiments, the sodium phosphate salt is up to a concentration of about 15 grams per ounce of solution. In some embodiments, the sodium phosphate salt is up to a concentration of about 15 grams per ounce of solution. In some embodiments, the sodium phosphate salt is up to a concentration of about 10 grams per ounce of solution. In some embodiments, the sodium phosphate salt is up to at a concentration of about 9 grams per ounce of solution. In some embodiments, the sodium phosphate salt is up to a concentration of about 8 grams per ounce of solution. In some embodiments, the sodium phosphate salt is up to a concentration of about 7 grams per ounce of solution. In some embodiments, the sodium phosphate salt is up to a concentration of about 6 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 5 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 4 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 3 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 2.5 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 2.25 grams per ounce of solution prepared. In some embodiments, the sodium phosphate salt is at a concentration of about 2.1 grams per ounce of solution prepared. In some embodiments, the sodium phosphate salt is at a concentration of about 2.0 grams per ounce of solution prepared. In some embodiments, the sodium phosphate salt is at a concentration of about 1.9 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 1.8 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 1.7 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 1.6 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 1.5 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 1.4 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 1.3 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 1.2 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a

concentration of about 1.1 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 1.0 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 0.9 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 0.8 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 0.7 grams per ounce of solution. In some embodiments, sodium phosphate salt is at a concentration of about 0.6 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 0.5 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 0.4 grams per ounce of solution. In some embodiments, the sodium phosphate salt is at a concentration of about 0.3 grams per ounce of solution prepared. In some embodiments, the sodium phosphate salt is at a concentration of about 0.2 grams per ounce of solution prepared. In some embodiments, the sodium phosphate salt is at a concentration of about 0.1 grams per ounce of solution prepared. One skilled in the art would recognize that embodiments above should not be read in isolation and can be combined so that any unit of sodium phosphate per ounce of solution prepared can applied to embodiment that comprises both sodium phosphate and magnesium citrate. In other words, some embodiments described as comprising 1.0 grams of the sodium phosphate salt per ounce of solution may also comprise 1.0 grams of the magnesium citrate per ounce of solution.

[0079] Dosage may be measured in terms of sodium phosphate salt per liter of liquid formulation prepared. One skilled in the art can increase or decrease the magnesium citrate salt concentration in the dose depending upon the strength of purgative action desired and the risk of developing renal dysfunction. For instance, some embodiments of the invention can include up to 300 grams of sodium phosphate salt per liter of liquid formulation and up to about 100 grams of magnesium citrate salt per liter of liquid formulation. If, after experimentation, that formulation results in unhealthy levels of phosphate in the subject, the magnesium citrate salt concentration can be increased and the sodium phosphate salt concentration can be proportionately decreased. An example of such a increase would be a formulation with a sodium phosphate salt concentration of about 150 grams per liter of formulation and a magnesium citrate salt concentration of about 250 grams per liter of the formulation.

[0080] In some embodiments, the dosage is up to about 500 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 400

grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 300 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 250 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 200 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 150 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 140 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 130 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 120 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 110 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 100 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 90 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 80 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 70 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 60 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 50 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 40 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 30 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 20 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 10 grams of sodium phosphate salt per liter of formulation. In some embodiments, the dosage is up to about 1 gram of sodium phosphate salt per liter of formulation.

[0081] One characteristic of the purgative formulations tested herein is that they may function effectively as purgatives when administered in low volume dosages, as compared to known formulations. Dosages may include 5 to 40 tablets. Dosages may include 7 to 10 tables per dose depending on tablet size and weight, with only fluids necessary to assist in swallowing the tablets, will provide complete purgation. In some embodiments of the invention the dosage includes between 30 to 40 tablets of an oral purgative formulation. In some embodiments of the invention the dosage includes between 20 to 30 tablets of an oral purgative formulation. In some embodiments of the invention the dosage includes between 15 to 20 tablets of an oral purgative formulation. In some embodiments of the invention the

dosage includes between 10 to 15 tablets of an oral purgative formulation. In some embodiments of the invention the dosage includes between 5 to 10 tablets of an oral purgative formulation. In some embodiments of the invention the dosage includes between 1 to 5 tablets of an oral purgative formulation. The dosage may be administered in a single application but can be administered in two applications separated by between approximately 2 to 12 hours. Use of the formulations of this invention in tablet form effectively removes the colonic contents without requiring ingestion of large quantities of water. Conventional purgative products historically and currently available on the market have had to employ much greater liquid volumes in order to obtain the desired result.

[0082] A characteristic of the formulations tested herein is that at lower dosages they will function effectively as laxatives relative to the weight of the mammal being treated. Concentration ranges for laxative effect are from approximately 0.025 to 0.1 grams/kg body wt. and are from 0.05 to 0.07 grams/kg body wt.

[0083] The subject can be any animal, including but not necessarily limited to mammals such as a human, mouse, rat, hamster, guinea pig, rabbit, cat, dog, monkey, cow, horse, pig, and the like. In some embodiments, the subject is a human. In some embodiments, the subject is in need of the formulation for a pre-existing medical condition that disrupts normal bowel evacuation.

[0084] According to some embodiments of the invention, the formulation may be supplied as part of a kit. The kit comprises a sodium phosphate salt and magnesium citrate salt. In another embodiment, the kit comprises sodium phosphate salt and magnesium citrate salt with an oral rehydration mixture. Oral rehydration mixtures are mixtures designed to rehydrate a subject prior to or immediately after a subject takes at least one dose of a purgative. In another embodiment, the kit comprises sodium phosphate salt and magnesium citrate salt with an oral rehydration mixture wherein the sodium phosphate salt and magnesium citrate salt are an anhydrous powder designed to be solubilized prior to administration. In another embodiment, the sodium phosphate salt and magnesium citrate salt are in one container while the oral rehydration mixture is in a second container. In another embodiment, the sodium phosphate salt and magnesium citrate salt are in one container as anhydrous salts while the oral rehydration mixture is in a second container, and a solvent for the anhydrous salts is in a third container. In some embodiments of the invention, the kit comprises anhydrous salts provided as a sachet. The oral rehydration mixture may be

supplied in dry form, to which water may be added to form an oral rehydration solution prior to oral administration.

[0085] Oral rehydration mixtures comprise sugar and salt. Oral rehydration solutions contain sugar, salt and water. In some embodiments of the invention, the salt of the oral rehydration mixture contains sodium, and the sugar may comprise a glucose containing saccharide; the term "glucose containing saccharide" means either glucose, or a saccharide that can be hydrolyzed to form a composition containing glucose. Oral rehydration mixtures or solutions may also contain a variety of excipients and/or additives, for example flavoring agents, coloring agents, carbonation, viscosity modifiers, and/or preservatives.

[0086] Oral rehydration solutions may comprise from about 0.1-15% (w/v) of sugar, from about 1-10% (w/v) sugar, or from about 5-7% (w/v) sugar. Oral rehydration solutions can contain from about 0.1-200 mmol/L of salt, from about 2-100 mmol/L salt, or from about 10-30 mmol/L salt. Oral rehydration mixtures in solid form may contain salt and sugar in the same proportions as oral rehydration solutions: a ratio of sugar: salt from about 0.1-15 g:0.1-200 mmol, from about 1-10 g:2-100 mmol, or from about 5-7 g:10-30 mmol.

[0087] The kit may contain two or more containers, packs, sachets or dispensers together with instructions for preparation and administration. In some embodiments of the invention, the kit contains at least two doses of an oral purgative. In some embodiments of the invention, the kit contains at least three doses of an oral purgative. In some embodiments of the invention, the kit contains at least four doses of an oral purgative. In some embodiments of the invention, the kit contains at least five doses of an oral purgative. In some embodiments, the oral rehydration mixture or solution can be in one or more additional containers.

[0088] The compositions included in the kit may be supplied in containers of any sort such that the shelf-life of the different components are preserved, and are not adsorbed or altered by the materials of the container. For example, suitable containers include simple bottles that may be fabricated from glass, organic polymers, such as polycarbonate, polystyrene, ceramic, metal or any other material typically employed to hold reagents or food; envelopes, that may consist of foil-lined interiors, such as aluminum or an alloy. Other containers include test tubes, vials, flasks, and syringes. The containers may have two compartments that are separated by a readily removable membrane that upon removal permits the components to mix. Removable membranes may be glass, plastic, rubber, or other inert material.

[0089] Kits may also be supplied with instructional materials. Instructions may be printed on paper or other substrates, and/or may be supplied as an electronic-readable medium, such as a floppy disc, CD-ROM, DVD-ROM, zip disc, videotape, audio tape, or other readable memory storage device. Detailed instructions may not be physically associated with the kit; instead, a user may be directed to an internet web site specified by the manufacturer or distributor of the kit, or supplied as electronic mail.

[0090] The invention relates to the use of a sodium phosphate salt and a magnesium citrate salt in the preparation of a medicament for treating constipation.

[0091] The following examples are provided to describe the invention in greater detail. They are intended to illustrate, not to limit, the invention. Various publications, including patents, published applications, technical articles and scholarly articles are cited throughout the specification. Each of these cited publications is incorporated by reference herein, in its entirety.

EXAMPLE 1

Dosing of Oral Purgative Formulations Comprising Magnesium Citrate

[0092] This example describes four different techniques to target dosing ranges of magnesium citrate and sodium phosphate in oral purgative formulations.

[0093] Ten healthy patients were treated with the following oral purgative regimen 18 hours prior to a colonoscopy procedure:

1. Patients were administered 1 ten ounce bottle of magnesium citrate solution comprising a total of 17.45 grams of magnesium citrate;

2. Patients were then administered four tablets of 1.5 gram sodium phosphate followed by 8 oz of water for proper dissolution of the tablets;

3. Patients were administered three tablets of 1.5 grams of sodium phosphate each followed by 8 oz of water for proper dissolution of the tablets;

[0094] Steps (1) through (3) were repeated 12 hours after the first dosing period. Patients were evaluated through colonoscopy for efficiency of bowel evacuation and questioned after the procedure as to whether they had occurrence of any side effects associated with the treatment. Total evacuation of the bowl was successful in all of the ten patients treated. Mild side effects related to bloating were reported. This example provides a method of identifying a safe amount of a dosing regimen with which healthy patients may be tested for efficacy of oral purgatives comprising sodium phosphate and magnesium citrate.

[0095] Nine patients planning to undergo colonoscopy were given four 5 milligram Ducolax® tablets at approximately 18 hours prior to colonoscopy. Seventeen hours before the procedure, the nine patients were administered 10 oz. of 1.754 g/oz of magnesium citrate solution (with lemon-lime flavoring) and 7 Osmoprep® tablets (Sodium Phosphate Monobasic monohydrate, dibasic anhydrous sodium phosphate). Patients then drank at least six 8 oz. glasses of clear liquid before bedtime. The next morning, 3 hours before the scheduled time of the colonoscopy, patients ingested 10 oz. magnesium citrate solution and 7 Osmoprep® tablets followed by two 8 oz glasses of clear liquid. After ingestion of the clear liquid, oral food and liquid were withheld until the procedure was performed.

[0096] During the procedure, quality of colon cleansing was evaluated and graded as excellent, good, fair, or unsatisfactory in an unblinded fashion based upon visual inspection of the intraluminal space via camera image during the colonoscopy, the amount, if any, of residual fecal matter in the intraluminal space, and the amount of precipitant formed, if any, in the bowel by residual amounts of purgative formulation. Table 1, Line 1 illustrates the quality of the purgative preparations as all 9 patients were scored as "E," or excellent preps. These data suggest that new purgative formulations comprising magnesium citrate and sodium phosphate may be made for efficient bowel evacuation that is equal or improved as compared to the bowel evacuation observed with formulations comprising sodium phosphate as the only purgative agent. Assuming that each tablet had approximately 1.5 grams of sodium phosphate, the total reduction in grams of sodium phosphate load was 27 grams, well over 50% as compared to the total amount of sodium phosphate ordinarily administered prior to medical evaluation of the colon. This difference in total sodium phosphate load equals the total number of grams typically administered to patients for effective purgative action (48 grams) and the amount of sodium phosphate administered to patients in this study (21 grams). The study demonstrates that sodium phosphate load can be reduced from 32 sodium phosphate tablets to 14 sodium phosphate tablets to increase safety and effectuate excellent purgative action.

[0097] A second set of experiments were performed to define the approximate number of grams of magnesium citrate necessary to effectuate a safe bowel cleansing while maintaining a constant volume of sodium phosphate in the total purgative administered to the patients. Table 1, lines 2 and 3, illustrate that the total amount of magnesium citrate was reduced to 15 ounces alternating the 17 hour pre-procedure dose between 5 or 10 ounces of magnesium citrate solution (1.754 grams/oz) as part of the regimen. The amount of sodium

phosphate was held constant at 7 Osmoprep tablets 17 hours prior to procedure and 3 hours prior to procedure. The quality of the colon preparations were scored as excellent or good in 12 of 14 patients and fair in 2 of 14 patients. A visible precipitant was noticed on camera during colonoscopy in all patients taking oral tablet preparations of this experimental arm of the study (data not shown). Table 1, Lines 4-8, illustrate the quality of purgation after administration of various concentrations of liquid sodium phosphate solution in lieu of sodium phosphate tablets. Line 4 describes the results of four patients who took 4 Ducolax® tablets approximately 18 hours prior to procedure, 10 oz. magnesium citrate (1.754 grams/oz) and 0.5 oz Sodium phosphate (20 grams/oz) liquid mixed over ice approximately 17 hours prior to procedure followed by 6-8 eight ounce glasses of any clear liquid. Three hours before the procedure these patients took the same 10 oz. magnesium citrate and 0.5 oz. sodium phosphate liquid combination (Table 1, line 4).The total pre-procedure dose of 20 grams of sodium phosphate. All 4 patients in this experimental arm had an excellent prep but an intraluminal precipitant was present as seen when using Osmoprep® as the source of sodium phosphate. To evaluate if the precipitant issue was a dose dependent phenomenon, total doses of magnesium citrate were varied while maintaining a constant total amount of liquid sodium phosphate over time. Lines 5 through 8 of Table 1 illustrate that the total dose of magnesium citrate was varied between 18 and 12 ounces at a concentration of 1.754 g/oz of fluid. Of the 26 patients in those experimental arms, the quality of the purgative action was scored as excellent in 25 of the cases. One patient of 5 who was administered 12 oz of magnesium citrate prior to colonoscopy scored as having inadequate colon purgation (Table 1, line 8). Despite the excellence of purgation with very low doses of both magnesium citrate and sodium phosphate, intraluminal precipitant became unavoidable in experimental arms of the study that include administration of solid and liquid formulations comprising sodium phosphate 3 hours prior to scheduled procedure.

[0098] Table 2 illustrates another study performed to identify: (i) whether inorganic salt contributed to the precipitant formation; and (ii) whether timing of administration and/or reduction of the amount of sodium phosphate in the cleansing regimen prior to procedure would eliminate the formation of the precipitant. Patients in the study described in Table 2 were administered the following series of purgative agents: four 5 mg tablets of Ducolax® at approximately 17 hours prior to the procedure; 10 ounces Magnesium citrate (1.754 grams/oz) mixed with 1 oz. sodium phosphate liquid (20 rams/oz) over ice at approximately 16 hours prior to the procedure, followed by 6-8 eight ounce glasses of any clear liquid; and

10 ounces of magnesium citrate 3 hours before procedure. As seen in Table 2, line 1, all 5 patients had excellent preps without formation of any precipitant. A change in the timing of administration of the sodium phosphate eliminated the formation of precipitant and yielded extremely clear colonic mucosal visualization. The data suggest that a salt, presumably magnesium phosphate, is responsible for the precipitant and that precipitant complicates or obstructs visualization of the colon during colonoscopy. By eliminating the morning doses of sodium phosphate in the dosing regimen of purgative agents administered to the subject prior to colon procedure, a more adequate colon cleansing regimen was devised as compared to a standard regimen comprising administration steps of the same formulation at approximately 20-14 hours prior to procedure and approximately 5-3 hours prior to procedure.

[0099] The experiments described in Table 2, lines 1-8, demonstrate effective dosing of magnesium citrate in combination with sodium phosphate during a pre-procedure purgation regimen at the same concentrations of solution mentioned above. Table 2, lines 2-4, describes the experiment during which a series of patients were administered decreasing total magnesium citrate doses ranging from about 19 ounces to 18 ounces, and from 18 ounces to 17 ounces, while maintaining a total sodium phosphate dose at 1 ounce. All nine patients scored as excellent preparations and no precipitate was observed.

[0100] As can be seen in Table 2, lines 5 – 6, ten patients were administered a reduced dose of 0.75 oz of sodium phosphate solution given approximately 17 hours prior to scheduled procedure, with either 19 ounces or 16 ounces of magnesium citrate. All formulation and regimens yielded excellent purgative action without formation of precipitant.

[0101] As seen in Table 2, line 7, five patients were evaluated who were administered 16 ounces of magnesium citrate and 0.5 ounces sodium phosphate liquid. All 5 formulations and regimens yielded excellent purgative action without formation of precipitant.

[0102] As seen in Table 2, line 8, seven patients were evaluated with only 9 ounces of magnesium citrate and 1 oz sodium phosphate liquid solution. Five had excellent preps and 2 were fair.

[0103] The studies above demonstrate that effective purgative formulations comprising sodium phosphate and magnesium citrate include embodiments where the formulation comprises about between about 10 grams to about 20 grams (or 0.5 -1.0 oz liquid) sodium phosphate and between about 17.4 – 27.8 grams (or 10 -16 oz liquid)

magnesium citrate. The degree of hyperphosphatemia will be significantly reduced based on two observations: a) a dose reduction of total phosphate by > 60% compared to currently accepted doses and b) the proposed intraluminal phosphate trap. The studies also demonstrate that the quality of purgative formulations remains high or has improved as compared to standard purgative formulations while the safety of electrolyte purgation also improved dramatically.

TABLE 1

Line Schedule of Prep # of PTS Quality of Prep PPTant

Line #	PM	AM	# of PTS	E	G	F	U	PPTant
1	10/7	10/7	9	9				+
2	10/7	5/7	9	6	3			+
3	5/7	10/7	5	3		2		+
4	10/.5	10/.5	4	4				+
5	9/.5	9/.5	4	4				+
6	8/.5	8/.5	10	10				+
7	7/.5	7/.5	7	7				+
8	6/.5	6/.5	5	4			1	+

TABLE 2

Line #	PM	AM	# of PTS	E	G	F	U	PPTant
1	10/1	10/0	5	5				0
2	10/1	9/0	3	3				0
3	10/1	8/0	3	3				0
4	10/1	7/0	3	3				0
5	10/.75	9/0	4	4				0
6	8/.75	8/0	6	6				0
7	7/.5	8/0	5	5				0
8	4/1	5/0	7	5		2		0

Legend
E = Excellent; G = Good; F = Fair; U = Unsatisfactory; PTS = Patients
PPTant = Precipitant, where (+) indicates the presence of precipitant and (0) indicates the absence of precipitant. Numbers under the "PM" and "AM" columns indicate the dosage ratios of magnesium citrate to sodium phosphate in volume that were administered about 17 hours prior to colonoscopy (PM) or about 3 hours prior to colonoscopy (AM).

EXAMPLE 2

Evaluation of Safety and Efficacy of Oral Purgative Formulations

[0104] This prophetic example describes how the inventive purgative formulations may be manufactured and studied.

[0105] Liquid formulations will be prepared with solutions ranging in sodium phosphate percentage (by weight) as disclosed below:

	Percentage of Magnesium Citrate	Percentage of Sodium Phosphate	Percentage of Other Formulation Components
Liquid Formulation 1	30	60	10
Liquid Formulation 2	40	50	10
Liquid Formulation 3	50	40	10
Liquid Formulation 4	60	30	10
Liquid Formulation 5	70	20	10

Percentages are approximate and may be adjusted to make up for optional formulation components listed as "Other Formulation Components."

[0106] A randomized and multiple dose trial will take place at a chosen clinic. The study will be conducted over a set time period, and will include at least 10-20 healthy subjects, defined as having no known kidney problems or predisposition to renal problems. Subjects can be male or female, 18 years of age or older.

[0107] Over the course of the pre-set time period, formulations will be administered to identify what the effective dose of sodium phosphate is required for purgative action with increasing doses of magnesium citrate relative to sodium phosphate. The formulation will be administered to subjects prior to medical procedures that require colon cleansing. Sodium phosphate concentrations in the oral solution will be titrated down to an effective amount for cleansing in proportion to the amount of magnesium citrate salt be added to the solution. Because it is possible that lower doses of sodium phosphate formulations will cause effective purgative action in cleansing the colon, this study may be performed using single doses. Renal function of patients will be determined by: (i) urine collection of calcium phosphate; or (ii) blood collected over the time period to monitor excretion of calcium phosphate, serum levels of calcium, serum levels of phosphate, serum levels of creatinine, and serum levels of BUN before and after administration of the formulation.

[0108] A purpose of this study will be to demonstrate the reduced risk involving the administration of formulations and compositions comprising a sodium phosphate salt and a magnesium citrate salt. A second purpose will be to demonstrate the minimum percent of sodium phosphate salt required to cleanse the colon effectively in a formulation also containing magnesium citrate salt. The variables to be measured by this study will be a

combination of at least one of the following: (1) excretion of calcium phosphate in urine; (2) serum levels of BUN, creatine and other known metabolic indicators of renal function; (3) serum levels of calcium and phosphate to calculate the calcium phosphate product; and (4) a symptom diary that includes, but is not necessarily limited to, ratings of discomfort associated with gas, taste, and any other observable side effects caused after ingestion of the formulation.

CLAIMS

What is claimed is:

1. A formulation comprising a sodium phosphate salt and a magnesium citrate salt.

2. The formulation of claim 1 wherein the formulation is a liquid dosage form.

3. The formulation of claim 1 wherein the formulation is a solid dosage form.

4. The formulation of claim 2 wherein the sodium phosphate salt is chosen from monobasic sodium phosphate, dibasic sodium phosphate, and tribasic sodium phosphate.

5. The formulation of claim 2 wherein the magnesium citrate salt is chosen from monobasic magnesium citrate, dibasic magnesium citrate, and tribasic magnesium citrate.

6. The formulation of claim 2, 4, or 5 wherein the formulation comprises from about 1% to about 99% sodium phosphate salt by weight; and from about 0.1% to about 1 % of magnesium citrate salt by weight.

7. The formulation of claim 2, 4, or 5 wherein the formulation comprises from about 80% to about 90% sodium phosphate salt by weight; and from about 0.1% to about 10% of magnesium citrate salt by weight.

8. The formulation of claim 2, 4, or 5 wherein the formulation comprises from about 70% to about 80% sodium phosphate salt by weight; and from about 0.1% to about 20% of magnesium citrate salt by weight.

9. The formulation of claim 2, 4, or 5 wherein the formulation comprises from about 60% to about 70% sodium phosphate salt by weight; and from about 20% to about 30% of magnesium citrate salt by weight.

10. The formulation of claim 2, 4, or 5 wherein the formulation comprises from about 50% to about 60% sodium phosphate salt by weight; and from about 30% to about 40% of magnesium citrate salt by weight.

11. The formulation of claim 2, 4, or 5 wherein the formulation comprises from about 40% to about 50% sodium phosphate salt by weight; and from about 40% to about 50% of magnesium citrate salt by weight.

12. The formulation of claim 2, 4, or 5 wherein the formulation comprises from about 30% to about 40% sodium phosphate salt by weight; and from about 50% to about 60% of magnesium citrate salt by weight.

13. The formulation of claim 2, 4, or 5 wherein the formulation comprises from about 20% to about 30% sodium phosphate salt by weight; and from about 60% to about 70% of magnesium citrate salt by weight.

14. The formulation of claim 2, 4, or 5 wherein the formulation comprises from about 10% to about 20% sodium phosphate salt by weight; and from about 70% to about 80% of magnesium citrate salt by weight.

15. The formulation of claim 2, 4, or 5 wherein the formulation comprises from about 5% to about 10% sodium phosphate salt by weight; and from about 85% to about 90% of magnesium citrate salt by weight.

16. The formulation of claim 2, 4, or 5 wherein the formulation comprises less than about 10% sodium phosphate salt by weight; and up to about 90% of magnesium citrate salt by weight.

17. The formulation of claim 2, 4, or 5 wherein the formulation comprises less than about 5% sodium phosphate salt by weight; and up to about 95% of magnesium citrate salt by weight.

18. The formulation of claim 2, 4, or 5 wherein the formulation comprises less than about 1% sodium phosphate salt by weight; and up to about 99% of magnesium citrate salt by weight.

19. The formulation of any of claims 2, or 4 - 18 wherein the formulation comprises at least one inert diluent.

20. The formulation of any of claims 2, or 4 - 18, wherein the formulation comprises at least one inert dispersal agent.

21. The formulation of claim any of claims 2, or 4 - 18, wherein the formulation comprises at least one buffering agent.

22. The formulation of claim 3 wherein the sodium phosphate salt is chosen from monobasic sodium phosphate, dibasic sodium phosphate, tribasic sodium phosphate, and a mixture thereof.

23. The formulation of claim 3 wherein the magnesium citrate salt is chosen from monobasic magnesium citrate, dibasic magnesium citrate, and tribasic magnesium citrate, and a mixture thereof.

24. The formulation of claim 3, 22, or 23 wherein the formulation comprises from about 1% to about 99% sodium phosphate salt by weight; and from about 0.1% to about 1 % of magnesium citrate salt by weight.

25. The formulation of claim 3, 22, or 23 wherein the formulation comprises from about 80% to about 90% sodium phosphate salt by weight; and from about 0.1% to about 10% of magnesium citrate salt by weight.

26. The formulation of claim 3, 22, or 23 wherein the formulation comprises from about 70% to about 80% sodium phosphate salt by weight; and from about 0.1% to about 20% of magnesium citrate salt by weight.

27. The formulation of claim 3, 22, or 23 wherein the formulation comprises from about 60% to about 70% sodium phosphate salt by weight; and from about 20% to about 30% of magnesium citrate salt by weight.

28. The formulation of claim 3, 22, or 23 wherein the formulation comprises from about 50% to about 60% sodium phosphate salt by weight; and from about 30% to about 40% of magnesium citrate salt by weight.

29. The formulation of claim 3, 22, or 23 wherein the formulation comprises from about 40% to about 50% sodium phosphate salt by weight; and from about 40% to about 50% of magnesium citrate salt by weight.

30. The formulation of claim 3, 22, or 23 wherein the formulation comprises from about 30% to about 40% sodium phosphate salt by weight; and from about 50% to about 60% of magnesium citrate salt by weight.

31. The formulation of claim 3, 22, or 23 wherein the formulation comprises from about 20% to about 30% sodium phosphate salt by weight; and from about 60% to about 70% of magnesium citrate salt by weight.

32. The formulation of claim 3, 22, or 23 wherein the formulation comprises from about 10% to about 20% sodium phosphate salt by weight; and from about 70% to about 80% of magnesium citrate salt by weight.

33. The formulation of claim 3, 22, or 23 wherein the formulation comprises from about 5% to about 10% sodium phosphate salt by weight; and from about 85% to about 90% of magnesium citrate salt by weight.

34. The formulation of claim 3, 22, or 23 wherein the formulation comprises less than about 10% sodium phosphate salt by weight; and up to about 90% of magnesium citrate salt by weight.

35. The formulation of claim 3, 22, or 23 wherein the formulation comprises less than about 5% sodium phosphate salt by weight; and up to about 95% of magnesium citrate salt by weight.

36. The formulation of claim 3, 22, or 23 wherein the formulation comprises less than about 1% sodium phosphate salt by weight; and up to about 99% of magnesium citrate salt by weight.

37. The formulation of claim 3, or 22-36 wherein the formulation further comprises at least one inert diluent.

38. The formulation of claim 3, or 22-36 wherein the formulation further comprises at least one inert dispersal agent.

39. The formulation of claim 3, or 22-36 wherein the formulation further comprises at least one buffering agent.

40. The formulation of claim 3, or 22-36 wherein the formulation further comprises at least one non-fermentable binder.

41. The formulation of claim 3, or 22-36 wherein the formulation is a tablet or capsule.

42. The formulation of any of claims 3, or 22-41 wherein the magnesium citrate and sodium phosphate salts are anhydrous powder.

43. The formulation of claim 42 wherein the formulation is packaged in a sachet.

44. A method of purging a colon of a mammal comprising administering at least one formulation of claims 1- 43 to said mammal.

45. A method of treating a mammal having constipation comprising administering at least one formulation of claims 1-43 to said mammal.

46. A method of making a formulation comprising a sodium phosphate salt and a magnesium citrate salt for use in inducing purgation of the colon wherein the method comprises mixing sodium phosphate and magnesium citrate.

47. The method of claim 46 wherein the sodium phosphate salts and magnesium citrate salts are anhydrous powders.

48. The method of claim 47 comprising packaging said anhydrous powders in sachets.

49. A kit comprising a formulation of any of claims 1-43.

50. The kit of claim 49, wherein a first container comprises a formulation of any of claims 1-43 and a second container comprises an oral rehydration mixture.

51. The kit of claim 49, wherein the kit comprises:
(a) a first container comprises a formulation of any of claims 1-43;
(b) a second container comprises an oral rehydration mixture; and
(c) a third container comprises a solvent for the formulation in the first container.

52. Any one kit of claims 49-51, wherein the sodium phosphate salts and magnesium citrate salts are anhydrous salts.

53. Use of a composition comprising a sodium phosphate salt and a magnesium citrate salt in the preparation of a medicament for treating constipation.

54. A formulation according to any one of claims 1- 43 for treating constipation.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 09/49807

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A01N 59/26 (2009.01)
USPC - 424/606
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
USPC- 424/606

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC- 424/601, 681, 682, 703; 514/277, 772.3;
Patents and NPL

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWest (US Patent, PgPub: classification best fit), DialogClassic (Derwent, EPO, JPO, USPTO, WIPO: keyword), GoogleScholar; search terms: colon?, purgat?, sodium phosphat?, magnesium citr?

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US 2005/0271749 A1 (BORODY et al.) 08 December 2005 (08.12.2005), para [0012]-[0017], [0032], [0055], [0056], [0062], [0071], [0075], [0122], [0123]	1, 2, 6-18, 46, 53 ---------- 3-5, 22-36, 47, 48
Y	US 6,162,464 A (JACOB et al.) 19 December 2000 (19.12.2000), col 3, ln 43-65; col 4, ln 21-44; col 5, ln 14-41; col 5, ln 59 to col 6, ln 19	3-5, 22-36, 47, 48
A	US 2005/0129781 A1 (SKIENDZIELEWSKI et al.) 16 June 2005 (16.06.2005), entire document	1-18, 22-36, 46-48, 53
A	US 2004/0192614 A1 (VANNER et al.) 30 September 2004 (30.09.2004), entire document	1-18, 22-36, 46-48, 53

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
05 August 2009 (05.08.2009)	17 AUG 2009
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 09/49807

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 19-21, 37-45, 49-52, and 54
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.