Colon Cleansing Compositions~~COLONOSCOPY PREPARATION~~

The present invention relates to a method of cleansing the colon using colon cleansing solutions, and compositions and kits associated therewith. Colon cleansing compositions are also known as lavage solutions, bowel cleansers, purgatives or colonic evacuants.

Colon or bowel cleansing is important before numerous surgical or diagnostic procedures, including colonoscopy, barium enema examination, sigmoidoscopy and colon surgery. Such procedures are often carried out on an outpatient basis and thus it is desirable that the colon cleansing be carried out by the patient at home, prior to arrival at the hospital or surgery where the procedure is to take place. It is therefore important that patient compliance is good without medical supervision if satisfactory colon cleansing is to be achieved prior to the procedure.

Intestinal lavage, in which a large volume of an electrolyte solution containing sodium sulphate and polyethylene glycol is ingested, is one of the most common methods for colon cleansing. These osmotically active agents are non-absorbable or only poorly absorbable and thus retain water in the bowel, resulting in copious diarrhoea and cleansing of the colon.

For effective cleansing, many of these compositions must be ingested in quantities of between 2 to 4 litres. The unpleasant taste of these compositions combined with the large volumes required to be ingested often contributes to nausea or vomiting, resulting in poor patient compliance and failure to consume the full volume of solution. Poor patient compliance can lead to inadequate preparation of the colon which can, in turn, lead to cancellation or repetition of the colonoscopy becoming necessary or, worse, non-detection of lesions or polyps indicative of cancer risk.

A number of improved colon cleansing compositions are described in WO 2004/037292. A colon cleansing composition according to WO 2004/037292 that comprises polyethylene glycol 3350, sodium sulphate, an ascorbate component, electrolytes, sweetener and flavouring is commercialised as a powder for oral solution under the tradename MOVIPREP® (registered trademark of Velinor AG, a member of the Norgine group of companies). The MOVIPREP solution is effective despite being taken in a substantially lower volume than other colon cleansing solutions. Typically, only 2 litres of the solution need to be taken by an adult patient, a significant benefit when compared to taking 4 litres of previous solutions.

Various regimens for the timing of ingestion of colon cleansing solutions are mentioned in the literature and in patient information leaflets that accompany colon cleansing products. For example, the MOVIPREP solution mentioned above may be taken (optionally with additional clear liquids also optionally being taken) in the evening before the examination or procedure, or the MOVIPREP solution may be taken in a "split-dose" regimen, with approximately half of the cleansing solution

being taken the evening before the examination or procedure ("first dose"), and the remainder being taken the following morning ("second dose").

Despite the advances that have been made, all colon cleansing products on the market continue to require a subject to ingest a large volume of solution (2 litres in the case of the MOVIPREP solution). Many subjects find the ingestion of a large volume unpleasant or difficult and poor patient compliance thus remains a problem. There remains a need for alternative colon cleansing solutions that are effective when ingested in small volumes.

When comparing the pharmacokinetic profiles of the components of the MOVIPREP solution (ascorbate component, sodium sulphate, PEG 3350 and electrolytes) in subjects who had taken the solution in the "evening before" regimen with the pharmacokinetic profiles in subjects who had taken the solution in the "split-dose" regimen in a clinical study, the present inventors found that a surprisingly high proportion of the ascorbate component of the first dose of the "split-dose" regimen was absorbed into the subjects' circulations. The proportion of the ascorbate component that was found to be absorbed into the circulation was then excreted in the subjects' urine over time, rather than being expelled in faeces. Whilst this absorption into the circulation is not harmful to the subject, it does reduce the osmotic strength of the solution, and hence it reduces the solution's ability to cleanse the colon. It is also wasteful of the component. The finding was surprising in view of the commonly accepted view in the literature that a maximum of 3g of ascorbic acid can be absorbed in the intestines per day (Hornig, D. *et al.*, Int. J. Vit. Nutr. Res., 1980, **50**, 309). Ascorbate-containing colon cleansing solutions have to date been formulated on that basis.

Summary

In one aspect, the present invention refers to a colon cleansing solution comprising:
a) 60 to 150 g/ litre of an ascorbate component, the ascorbate component being ascorbic acid, one or more salts of ascorbic acid, or a mixture of ascorbic acid and one or more salts of ascorbic acid; and
b) 10 to 200 g per litre polyethylene glycol.

In another aspect, the present invention refers to a composition, optionally presented in two or more parts, for admixture with water to provide a solution of the present invention.

In another aspect, the present invention refers to a composition for admixture with water for the preparation of a colon cleansing solution of the present invention, comprising the following components in the following weight ratios:
a) ascorbate anion provided by ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof:

0.82 to 10.0 parts

b) polyethylene glycol: 1.0 part.

In another aspect, the present invention refers to a kit comprising:

- a first colon cleansing solution, and

- a second colon cleansing solution,

the second colon cleansing solution being the solution of the present invention in water.

In another aspect, the present invention refers to a kit comprising:

A) a first component, being a composition for the preparation of a first colon cleansing solution by admixture with water; and

B) a second component, being a composition for the preparation of a second colon cleansing solution by admixture with water;

and optional instructions for use,

the second colon cleansing solution being the solution of the present invention in water,

the first solution being different from the second.

In another aspect, the present invention refers to a solution of the present invention for use in cleansing the colon of a subject in combination with a colon cleansing solution comprising:

(i) 130 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da; and

(ii) 8.0 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof.

In another aspect, the present invention refers to a solution of the present invention for use in cleansing the colon of a subject in combination with a colon cleansing solution consisting essentially of water and:

(i) 130 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da;

(ii) 8.0 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof;

(iii 1) 1.0 to 3.0 g/L sodium chloride;

(iii 2) 0.5 to 1.5 g/L potassium chloride;

(iv) one or more flavouring agents;

(v) one or more sweeteners.

In another aspect, the present invention refers to a solution that is hyper-osmotic and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, for use in a method of cleansing the colon of a subject comprising:

- administering to the subject an effective amount of a first cleansing solution; and then after a time interval

- administering to the subject an effective amount of a second cleansing solution,

wherein the second cleansing solution is a solution of the present invention, is hyper-osmotic and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and wherein the first cleansing solution is either substantially free from ascorbic acid and salts thereof, or contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, in an amount providing a lower concentration of ascorbate anion than is present in the second cleansing solution.

In another aspect, the present invention refers to a kit comprising:

- a first colon cleansing solution; and

- a second colon cleansing solution,

wherein the second colon cleansing solution is a solution of the present invention, is hyper-osmotic and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and wherein the first colon cleansing solution is either substantially free from ascorbic acid and salts thereof, or contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, in an amount providing a lower concentration of ascorbate anion in the first colon solution than is present in the second colon cleansing solution.

In another aspect, the present invention refers to a kit comprising:

a) a first component, being a composition for the preparation of a first colon cleansing solution by admixture with water; and

b) a second component, being a composition for the preparation of a second colon cleansing solution by admixture with water,

and instructions for use that specify the volume to which each component is to be made up with water,

wherein the second colon cleansing solution, when made up to the instructed specified volume with water, is a solution of the present invention, is hyper-osmotic and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and wherein the first colon cleansing solution is either substantially free from ascorbic acid and salts thereof, or contains, when made up to the instructed specified volume with water, ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, in an amount providing, a lower concentration of ascorbate anion in the first colon solution than in the second colon cleansing solution.

Detailed Description

The invention thus provides, in a first aspect, a colon cleansing solution comprising:

a) 60 to 150g/~~300 to 2000 mmol per~~ litre of an ascorbate component, the ascorbate component being~~ascorbate anion provided by~~ ascorbic acid, one or more salts of ascorbic acid, or a mixture of ascorbic acid and one or more salts of ascorbic acid~~thereof~~; and

b) 10 to 200 g per litre polyethylene glycol.

The solution of the invention is a surprisingly effective colon cleansing solution as measured by stool output, providing satisfactory clearance of stools from the colon with ingestion of a smaller total volume of solution than with the standard 2 or 4 litre solutions of the prior art.

The ascorbate component is~~anion may be provided by~~ ascorbic acid, ~~by~~ one or more salts of ascorbic acid, or ~~by~~ a mixture of ascorbic acid and one or more salts of ascorbic acid. ~~For convenience, they will be referred to herein as the "ascorbate component".~~ Suitable salts include alkali metal salts and alkaline earth metal salts. For example a salt may be selected from sodium, potassium, magnesium and calcium salts. For example, preferred salts of ascorbic acid include sodium ascorbate, potassium

ascorbate, magnesium ascorbate and calcium ascorbate. In an ~~embodiment~~example, the ascorbate component~~anion~~ is ~~provided by~~ ascorbic acid, one or more salts of ascorbic acid selected from sodium ascorbate, potassium ascorbate, magnesium ascorbate and calcium ascorbate, or a mixture thereof. Particularly preferred salts of ascorbic acid are magnesium ascorbate and sodium ascorbate, for example sodium ascorbate. In one ~~embodiment~~example, the solution comprises ascorbic acid and one or more salts of ascorbic acid (and preferably no further ascorbate), for example ascorbic acid and sodium ascorbate (and preferably no further ascorbate), or ascorbic acid and magnesium ascorbate (and preferably no further ascorbate).

~~The solution of the invention preferably comprises ascorbate anion in a concentration of: 300-1500mmol per litre, for example 300-1200mmol per litre, for example 300-1000mmol per litre, for example 300-850mmol per litre, for example 350-800mmol per litre, for example 400-700 mmol per litre.~~

~~Ascorbic acid has a molecular weight of 176g/mol. Accordingly, the 300 to 2000mmol ascorbate anion per litre can be provided by 52.8 to 352g/litre ascorbic acid.~~

~~Sodium ascorbate has a molecular weight of 198g/mol. Accordingly, the 300 to 2000mmol ascorbate anion per litre can be provided by 59.4 to 396g/litre sodium ascorbate.~~

~~Potassium ascorbate has a molecular weight of 214g/mol. Accordingly, the 300 to 2000mmol ascorbate anion per litre can be provided by 64.2 to 428g/litre potassium ascorbate.~~

~~Magnesium ascorbate has a molecular weight of 374.5g/mol and each mole of magnesium ascorbate provides two moles of ascorbate. Accordingly, the 300 to 2000mmol ascorbate anion per litre can be provided by 56.2 to 374.5g/litre magnesium ascorbate.~~

~~Depending on the pH of the solution, some ascorbate anion may be protonated and thus exist as free ascorbic acid. At the pH of solutions that would typically be administered, only a very minor proportion of ascorbate is protonated. In calculations of concentrations of "ascorbate anion" herein, the concentration of "ascorbate anion" is taken as the total concentration of all ascorbate anion present, including the proportion that is protonated.~~

A solution of the invention comprises ~~50 to 450g/litre of an ascorbate component, the ascorbate component being ascorbic acid, one or more salts of ascorbic acid or a mixture of ascorbic acid and one or more salts of ascorbic acid. For example, a solution of the invention comprises 50 to 300g/litre of ascorbate component, for example 50 to 200g/litre, for example~~ 60 to 150g/litre of the ascorbate component, for example 60 to 120g/litre, for example 80 to 120g/litre, for example 100 to 120g/litre.

(Firmenich UK Ltd., Hayes Road, Southall, Middlesex UB2 5NN). More preferred flavourings are lemon, kiwi, strawberry and grapefruit.

The amount of flavouring required depends on the nature and strength of the flavouring in question. Typically, it is 0.05 to 2.0 g per litre.

The cleansing solution preferably includes a sweetener. Sugar-based sweeteners are generally not suited for colon cleansing compositions because the delivery of unabsorbed sugars to the colon provides a substrate for bacteria. Such sugars may be metabolised by the bacteria to form explosive gases such as hydrogen and methane. The presence of explosive gases in the colon can be highly dangerous when electrical apparatus is to be used during colonoscopy or other procedures. Preferred sweeteners include aspartame, acesulfame potassium (acesulfame K), sucralose and saccharine, and/or combinations thereof. For example, compositions of the invention may comprise one or both of aspartame and acesulfame potassium (acesulfame K). For example, compositions of the invention may comprise one or both of sucralose and acesulfame potassium (acesulfame K). Alternatively, compositions of the invention can be substantially free from added sweeteners, for example to minimize the number of different components in the compositions. Citric acid may also be present as a taste enhancer. Citric acid and/or salts thereof may replace some or all of the ascorbate in solutions of the invention.

The amount of sweetener required depends on the nature and strength of the sweetener being considered. Typically, it is 0.10 to 1.0 g per litre.

The invention thus provides a colon cleansing solution comprising:

a) 60 to 150 g/~~300 to 2000 mmol per~~ litre ascorbate componen~~tanion~~;

b) 10 to 200 g per litre PEG.

c) one or more electrolytes;

d) optionally one or more alkali metal or alkaline earth metal sulphates;

e) optionally one or more flavouring agents; and

f) optionally one or more sweeteners.

In particular, the invention provides a colon cleansing solution comprising ~~(or consisting essentially of water and)~~:

a) 60 to 150 g/~~300 to 2000 mmol per~~ litre ascorbate componen~~tanion~~;

b) 10 to 200 g per litre PEG having an average molecular weight of 3000 to 4000 Da; and

c) sodium chloride and potassium chloride~~.~~;

Optional additional ingredients in such a solution include

d) ~~optionally~~ sodium sulphate;

e) ~~optionally~~ one or more flavouring agents; and

f) ~~optionally~~ one or more sweeteners.

For example, the solution may consist essentially of water, and:

a) 60 to 150 g/litre ascorbate component;
b) 10 to 200 g per litre PEG having an average molecular weight of 3000 to 4000 Da;
c) sodium chloride and potassium chloride;
d) sodium sulphate;
e) one or more flavouring agents; and
f) one or more sweeteners.

Each of c) and d) may be present in the concentrations described above. Each of e) and f) may be as described above and/or be in the concentrations described above.

In particular, the invention provides a colon cleansing solution ~~comprising (or~~ consisting essentially of water and):

a) 60 to 150 g/~~300 to 2000 mmol per~~ litre ascorbate componentanion;
b) 10 to 200 g per litre PEG having an average molecular weight of 3000 to 4000 Da;
c) sodium chloride and potassium chloride;
e) one or more flavouring agents; and
f) one or more sweeteners.

In one embodiment, the one or more components of c), d) e) and f) are present in the solution. In an alternative presentation, some or all of components c), d) e) and f) may be provided separately from the solution, for example in a tablet or capsule. In an embodiment, the solution may comprise a) the ascorbate component and b) PEG, and optional flavouring and sweetener (e) and f)), and a tablet or capsule may comprise c) the one or more electrolytes and/or d) the one or more alkali metal or alkaline earth metal sulphates, again with optional flavouring and sweetener (e) and f)). The flavouring and sweeteners need not be the same in the tablet or capsule as in the solution.

In general it is not necessary for the solutions to include preservatives or anti-oxidants. Nevertheless, low levels of anti-oxidants or preservatives may be used if required.

Preferably, the colon cleansing solution is hyper-osmotic. That is to say that it has a higher osmotic strength than blood in the human body. It may, for example have a measured osmolality in the range 500 to 2000 mOsmol/kg. For example, the osmolality may be in the range 700 to 1800 mOsmol/kg, for example 800 to 1700 mOsmol/kg, for example 900 to 1600 mOsmol/kg, for example 900 to 1300 mOsmol/kg, for example 1000 to 1300 mOsmol/kg.

Osmolality can be measured in various ways. In general, either freezing point depression or vapour-pressure alteration is used. For example, an Advanced Instruments, Inc Model 3250 osmometer (a freezing point depression device) can be used. Vapour pressure measurement can also be used, for example using an ELITech Group Vapro 5600 device. Osmolality values cited herein are preferably taken to be values measured using a freezing point depression osmometer, for example using an Advanced Instruments, Inc Model 3250 osmometer following standard operating procedure.

When carrying out a bowel cleansing treatment, a subject typically takes a single dose or a split dose of cleansing solution. In a split-dose treatment, typically two doses are taken separated by a time interval, for example an overnight interval. Each dose in a split dose treatment is smaller than the

impede inspection of the colon during the colonoscopy. Typically the clear fluid is a water-based beverage, including, for example, water, lemonade, cola drinks, cordial drinks, clear fruit juices and even clear alcohol-containing beverages, for example beer. It is desirable that the clear fluid does not contain substantial amounts of or essentially any dietary fibre, as such fibre interferes with the cleansing of the colon according to the present invention. Accordingly, fruit juices, for example orange juice and kiwi juice, and fruit "squashes" should be strained before use. Clear fruit cordials, for example, lime cordial, are generally suitable. In view of the desirability of avoiding drinks containing glucose, so as to reduce the risk of explosive concentrations of hydrogen or methane building up in the gut, "diet" drinks containing no or low sugar are especially suitable, for example liquid drinks for diabetics, diet Coke (RTM), diet lemonade, dietary carbonated drinks or dietary cordials.

The invention further provides a composition (for example a dry composition, for example a powder) for the preparation of a solution of the invention. A composition can be provided in a quantity for the preparation of a dose of the solution, for example a 500ml dose. The invention provides a composition for admixture with water for the preparation of a colon cleansing solution of the invention, wherein the composition is optionally presented in two or more parts and comprises the following components in the following weight ratios:

a) 0.82 to 10.0 parts~~150 to 1000 mmol~~ ascorbate anion provided by ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and

b) 1.0 part~~5 to 100 g~~ polyethylene glycol.

For example, the components may be in dry powder, granular or other dry form. They may alternatively be in the form of concentrates or slurries. Components may be in the same or different physical forms. For example, the composition is a dry composition, for example a dry powder composition. For example, one or both of components a) and b) are dry powders.

As set out above, the ascorbate anion may be provided by ascorbic acid, by one or more salts of ascorbic acid, or by a mixture of ascorbic acid and one or more salts of ascorbic acid. Preferred forms of the ascorbate component are as set out above in relation to solutions of the invention.

~~The composition of the invention preferably comprises ascorbate anion in an amount of: 150 to 750mmol, for example 150 to 600mmol, for example 150 to 500mmol, for example 150 to 425mmol, for example 175-400mmol, for example 200-350 mmol.~~

~~Ascorbic acid has a molecular weight of 176g/mol. Accordingly, the 150 to 1000 mmol ascorbate anion can be provided by 26.4 to 176g ascorbic acid.~~

~~Sodium ascorbate has a molecular weight of 198g/mol. Accordingly, the 150 to 1000 mmol ascorbate anion can be provided by 29.7 to 198g sodium ascorbate.~~

~~Potassium ascorbate has a molecular weight of 214g/mol. Accordingly, the 150 to 1000 mmol ascorbate anion can be provided by 32.1 to 214g potassium ascorbate.~~

~~Magnesium ascorbate has a molecular weight of 374.5g/mol and each mole of magnesium ascorbate provides two moles of ascorbate. Accordingly, the 150 to 1000 mmol ascorbate anion can be provided by 28.1 to 187.25g magnesium ascorbate.~~

In solid form, ascorbic acid is typically made up of protonated free ascorbic acid. In calculations of concentrations of "ascorbate anion" herein, the number of moles of "ascorbate anion" is taken as the total concentration of all ascorbate anion present, including the proportion that is protonated.

The weight of the ascorbate component may be 20 to 220g, for example 20 to 150g, for example 20 to 100g, for example 25 to 220g, for example 25 to 150g, for example 25 to 100g, for example 25 to 75g, for example 20 to 60g, for example 50 to 60g.

In an embodiment, the ascorbate component consists essentially of sodium ascorbate alone. For example, it may be present in an amount as mentioned immediately above.

In an alternative embodiment, the ascorbate component comprises (or consists essentially of) sodium ascorbate and ascorbic acid. For example, they may be present in a total amount as mentioned immediately above. They may be in a weight ratio of sodium ascorbate : ascorbic acid from 1:10 to 10:1, for example 2:8 to 8:2, for example 3:7 to 7:3, for example 1.4:1 to 1.8:1.

In an alternative embodiment, the ascorbate component comprises (or consists essentially of) sodium ascorbate and magnesium ascorbate. For example, they may be present in a total amount as mentioned immediately above. They may be in a weight ratio of sodium ascorbate : magnesium ascorbate from 1:10 to 10:1, for example 2:8 to 8:2, for example 3:7 to 7:3, for example 1.8:1 to 1.4:1.

Preferred forms of the PEG are as set out above in relation to solutions of the invention. The composition may comprises 5 to 100 g of PEG. Preferably, the composition comprises 5 to 80g of PEG, more preferably 5 to 60g, for example 10 to 50g, for example 15 to 45g, for example 20 g or 40 g of PEG.

The composition may additionally comprise one or more of:

c) one or more electrolytes;

d) one or more alkali metal or alkaline earth metal sulphates;

e) one or more flavouring agents; and

f) one or more sweeteners.

Preferred electrolytes are as set out above in relation to solutions of the invention. For example, the composition may comprise sodium chloride in an amount of 0.5 to 5g, for example 1 to 4 g, for

example 1.5 to 3.5g. For example, the composition may comprise potassium chloride in an amount of 0.5 to 5g, for example 0.5 to 4 g, for example 0.75 to 3g, for example 1.0 to 2.5g.

Preferred alkali metal or alkaline earth metal sulphates are as set out above in relation to solutions of the invention. For example, the composition may comprise a sulphate component in an amount of 1 to 10g, for example 2.5 to 7.5g, for example 4 to 7.5g, for example 5 to 7g, for example 6g. The one or more sulphate salts may be provided in any pharmaceutically acceptable form: they may each be anhydrous, or be in a hydrated form. The weights mentioned herein refer to the weight of the sulphate salt excluding any water of hydration.

Preferred flavouring agents are as set out above in relation to solutions of the invention. For example the amount of flavouring agent may be 0.025 to 1.0 g.

Preferred sweeteners are as set out above in relation to solutions of the invention. For example the amount of sweetener may be 0.05 to 0.5 g.

In particular, the invention provides a composition comprising the following components in the following weight ratios ~~(or consisting essentially of)~~:

a) 0.82 to 10.0 parts ~~150 to 1000 nmol~~ ascorbate anion;

b) 1.0 part ~~5 to 100 g~~ PEG having an average molecular weight of 3000 to 4000 Da; and ~~.~~

c) sodium chloride and potassium chloride ~~;~~

Optional components in such a composition include:

d) ~~optionally~~ sodium sulphate;

e) ~~optionally~~ one or more flavouring agents; and

f) ~~optionally~~ one or more sweeteners.

For example, the composition may consist essentially of the following components in the following weight ratios:

a) 0.82 to 10.0 parts ascorbate anion;

b) 1.0 part PEG having an average molecular weight of 3000 to 4000 Da;

c) sodium chloride and potassium chloride;

e) one or more flavouring agents; and

f) one or more sweeteners.

Each of c) and d) may be present in the amounts described above. Each of e) and f) may be as described above and/or be in the amounts described above.

In one embodiment, the one or more components of c), d) e) and f) are present in the composition for making up a solution. In an alternative presentation, some or all of components c), d) e) and f) may be provided separately from the composition for making up the solution, for example in a tablet or capsule. In an embodiment, there may be provided the ascorbate component and PEG, and optional flavouring and sweetener, in a form for admixture with water, and a tablet or capsule comprising the one or more electrolytes and/or the one or more alkali metal or alkaline earth metal sulphates, again with optional flavouring and sweetener. The flavouring and sweeteners need not be the same in the tablet or capsule as in the composition for admixture with water.

In some embodiments, it is desirable to package the ascorbate and the PEG components separately from each other.

In an embodiment, the composition can be provided to the subject with a plurality of flavouring agents (each optionally with one or more sweeteners), each separately packaged. The subject can then select a preferred flavouring (or flavouring and sweetener combination) according to his or her taste. The subject also has the choice of not using any flavouring or sweetener at all.

~~In a further aspect, the invention provides a composition comprising the following components in the following weight ratios:~~

~~a) ascorbate 0.82 to 10.0 parts; and~~
~~b) polyethylene glycol 1.0 part.~~

As mentioned above, for example, the components may be in dry powder, granular or other dry form. They may alternatively be in the form of concentrates or slurries. Components may be in the same or different physical forms. For example, the composition is a dry composition, for example a dry powder composition. For example, one or both of components a) and b) are dry powders.

As set out above, the ascorbate anion may be provided by ascorbic acid, by one or more salts of ascorbic acid, or by a mixture of ascorbic acid and one or more salts of ascorbic acid. Preferred forms of the ascorbate component are as set out above in relation to solutions of the invention.

Preferred forms of the PEG are as set out above in relation to solutions of the invention. The composition of the invention preferably comprises ascorbate anion in a weight ratio to PEG of 0.82 to 5.0 :1. More preferably, the weight ratio is 0.9 to 5.0 : 1, for example 1.0 to 4.0 : 1, for example 1.0 to 3.0 : 1, for example 1 to 2 : 1, or 2 to 3 :1.

The composition may additionally comprise one or more of:
c) one or more electrolytes;
d) one or more alkali metal or alkaline earth metal sulphates;
e) one or more flavouring agents;
f) one or more sweeteners.

Preferred electrolytes are as set out above in relation to solutions of the invention. For example, the composition may comprise sodium chloride in a weight ratio to PEG of 0.005 to 1.0 :1, for example 0.01 to 0.6 : 1, for example 0.03 to 0.5 : 1, for example 0.04 to 0.4 : 1, for example 0.05 to 0.3 : 1, for example 0.06 to 0.2 : 1. For example, the composition may comprise potassium chloride in a weight ratio to PEG of 0.005 to 1.0 :1, for example 0.005 to 0.50 : 1, for example 0.01 to 0.50 : 1, for example 0.01 to 0.10 : 1, for example 0.02 to 0.08 : 1, for example 0.03 to 0.07 : 1.

For example, the invention provides a composition comprising the following components in the following weight ratios:

a) ascorbate anion: 0.82 to 10.0 parts;
b) polyethylene glycol: 1.0 part;
c1) sodium chloride: 0.005 to 1.0 parts; and
c2) potassium chloride: 0.005 to 1.0 parts.

The composition is preferably substantially free from sodium bicarbonate. For example, it is substantially free from any bicarbonate.

Preferred alkali metal or alkaline earth metal sulphates are as set out above in relation to solutions of the invention. For example, the composition may comprise a sulphate component (for example sodium sulphate) in a weight ratio to PEG of 0.01 to 0.50 :1, For example, the composition may comprise a sulphate component (for example sodium sulphate) in a weight ratio to PEG of 0.02 to 0.25 : 1, for example 0.03 to 0.22 : 1, for example 0.05 to 0.20 : 1, for example 0.10 to 0.20 : 1.

Preferred flavouring agents are as set out above in relation to solutions of the invention. For example the composition may comprise a flavouring agent in a weight ratio to PEG of 0.0005 to 0.025 : 1, for example 0.001 to 0.025 : 1, for example 0.003 to 0.010 : 1.

Preferred sweeteners are as set out above in relation to solutions of the invention. For example the composition may comprise a sweetener in a weight ratio to PEG of 0.0005 to 0.025 : 1, for example 0.001 to 0.025 : 1, for example 0.002 to 0.010 : 1.

In particular, the invention provides a composition comprising ~~(or consisting essentially of)~~ the following components in the following weight ratios:

a) ascorbate anion: 0.82 to 10.0 parts
b) polyethylene glycol having an average molecular weight of 3000 to 4000 Da: 1.0 part; and
c) sodium chloride and potassium chloride.

Optional additional components in such a composition include:
d) ~~optionally~~ sodium sulphate;
e) ~~optionally~~ one or more flavouring agents; and
f) ~~optionally~~ one or more sweeteners.

Such a composition may consist essentially of the following components in the following weight ratios:

a) ascorbate anion: 0.82 to 10.0 parts

b) polyethylene glycol having an average molecular weight of 3000 to 4000 Da: 1.0 part;

c) sodium chloride and potassium chloride;

e) one or more flavouring agents: and

f) one or more sweeteners.

Each of c) and d) may be present in the weight ratios to PEG described above. Each of e) and f) may be as described above and/or be in the weight ratios to PEG described above.

Preferred compositions of the invention are dry compositions, for example dry powder compositions.

As mentioned above, the solutions of the invention find use in cleansing the colon. The invention thus provides, in a second aspect a solution according to the invention ~~in water of:~~

~~a) 300 to 2000 mmol per litre ascorbate anion provided by ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and~~

~~b) optionally 10 to 200 g per litre polyethylene glycol;~~

for use in cleansing the colon of a mammal.

~~The solution for use in cleansing the colon of a mammal preferably comprises ascorbate anion in a concentration of: 300-1500mmol per litre, for example 300-1200mmol per litre, for example 300-1000mmol per litre, for example 300-850mmol per litre, for example 350-800mmol per litre, for example 400-700 mmol per litre. As set out above, the ascorbate anion may be provided by ascorbic acid, by one or more salts of ascorbic acid, or by a mixture of ascorbic acid and one or more salts of ascorbic acid. Preferred forms of the ascorbate component are as set out above in relation to solutions of the invention.~~

~~In a preferred embodiment, PEG is present. Preferred forms of the PEG and preferred amounts thereof are as set out above in relation to solutions of the invention.~~

~~The solution for use in cleansing the colon of a mammal may additionally comprise one or more of:~~

~~c) one or more electrolytes;~~

~~d) one or more alkali metal or alkaline earth metal sulphates;~~

~~e) one or more flavouring agents;~~

~~f) one or more sweeteners.~~

~~Preferred electrolytes and preferred amounts thereof are as set out above in relation to solutions of the invention.~~

~~Preferred alkali metal or alkaline earth metal sulphates and preferred amounts thereof are as set out above in relation to solutions of the invention.~~

~~Preferred flavouring agents and preferred amounts thereof are as set out above in relation to solutions of the invention.~~

~~Preferred sweeteners and preferred amounts thereof are as set out above in relation to solutions of the invention.~~

~~For example, the solution in water comprises:~~

~~a) 150 to 1000 mmol ascorbate anion; and~~

~~b) optionally 5 to 100 g PEG.~~

~~In particular, the invention provides a solution comprising (or consisting essentially of water and):~~

~~a) 150 to 1000 mmol ascorbate anion;~~

~~b) 5 to 100 g PEG having an average molecular weight of 3000 to 4000 Da;~~

~~c) sodium chloride and potassium chloride;~~

~~d) optionally sodium sulphate;~~

~~e) optionally one or more flavouring agents; and~~

~~f) optionally one or more sweeteners~~

~~for use in cleansing the colon of a mammal.~~

~~Each of c) and d) may be as described above and/or be present in the amounts described above in relation to solutions of the invention. Each of e) and f) may be as described above and/or be in the amounts described above.~~

As mentioned above, a bowel cleansing treatment typically involves a subject taking a single dose or a split dose of cleansing solution. The volume of solution that a subject takes in a single dose treatment is described hereinabove. The subject may take some additional clear fluid after taking the solution as described hereinabove.

The volume of solution that a subject takes in a split dose treatment is described hereinabove. The subject may take some additional clear fluid after each or either dose the solution as described hereinabove.

The solutions and compositions of the invention find particular use in split dose colon cleansing treatments in which the subject takes two different solutions: a first colon cleansing solution, followed by a second colon cleansing solution. Preferably, the solution of the invention is the second colon cleansing solution. Alternatively, it may be the first solution. The invention thus finds utility in ~~provides~~ a method of cleansing the colon of a mammal comprising:

- the subject taking an effective amount of a first colon cleansing solution;

- the subject taking an effective amount of a second colon cleansing solution,

the second colon cleansing solution being a solution comprising

a) 60 to 150 g/~~300 to 2000 mmol per~~ litre ascorbate; and

b) optionally 10 to 200 g per litre polyethylene glycol.

The method ~~of the invention~~ may be used to cleanse the colon prior to carrying out a diagnostic, therapeutic or surgical procedure on the colon, rectum or anus or elsewhere in the abdomen. The diagnostic or surgical procedure may, for example, be colonoscopy, barium enema examination,

sigmoidoscopy or colon surgery. Preferably, the first solution is of different composition from the second.

The invention further finds utility in ~~provides~~ a method of conducting a diagnostic or surgical procedure, for example, a colonoscopy, barium enema examination, sigmoidoscopy or colon surgery, comprising the steps of:

a) cleansing the colon by use of a solution ~~a method~~ of the invention, and then

b) carrying out the diagnostic or surgical procedure.

The invention provides a kit comprising:
- a first colon cleansing solution, and
- a second colon cleansing solution,
the second colon ~~cleansing solution~~ being a solution according to the invention ~~in water of:~~
~~a) 300 to 2000 mmol per litre ascorbate anion provided by ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and~~
~~b) optionally 10 to 200 g per litre polyethylene glycol.~~

In an embodiment, the first solution is different from the second. The kit may comprise instructions for use.

The invention further provides a first colon solution, and a second colon solution, for use in a method of cleansing the colon comprising:
- the subject taking an effective amount of a first colon cleansing solution;
- the subject taking an effective amount of a second colon cleansing solution,
the second colon cleansing solution being a solution ~~in~~ according to the invention ~~water of:~~
~~a) 300 to 2000 mmol per litre ascorbate anion provided by ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and~~
~~b) optionally 10 to 200 g per litre polyethylene glycol.~~

In an embodiment, the first solution is different from the second.

The second colon cleansing solution is ~~preferably~~ as described hereinabove in relation to solutions and uses of the first aspect of the invention. It is preferably used in a volume as described hereinabove in relation to solutions and uses of the invention.

per litre, for example 0.1 to 3.0g per litre, for example 0.2 to 2.0 g per litre, for example 0.5 to 1.5 g per litre, for example 0.5 to 1.1 g per litre.

In an embodiment, the first colon cleansing solution comprises sodium chloride and potassium chloride. They can be present in the amounts mentioned immediately above. For example, sodium chloride may be present at a concentration of 1.5 to 3.0g per litre and potassium chloride may be present at a concentration of 0.2 to 2.0 g per litre.

The first colon cleansing solution preferably includes a flavouring agent. The first colon cleansing solution preferably includes a sweetener. Flavouring agents and sweeteners may be as described hereinabove.

In an embodiment, the first colon cleansing solution may be a solution as commercialised under the tradename MOVIPREP®.

Accordingly, the first colon cleansing solution in a kit of the invention comprises ~~(or consists essentially of water and)~~:

(i) 70 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da; and~~:~~

(ii) 2.0 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof .

Optional components which may be present in such a first colon cleansing solution in a kit of the invention include:

(iii) ~~optionally~~ one or more electrolytes;

(iv) ~~optionally~~ one or more flavouring agents; and

(v) ~~optionally~~ one or more sweeteners.

Such a first colon cleansing solution in a kit of the invention may consist essentially of water and:

(i) 70 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da;

(ii) 2.0 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof ;

(iii) one or more electrolytes;

(iv) one or more flavouring agents; and

(v) one or more sweeteners.

For example, the first colon cleansing solution in a kit of the invention may comprises: ~~(or consists essentially of water and):~~

(i) 90 to 200 g per litre PEG having an average molecular weight of 2500 to 4500 Da.

(ii) 2.0 to 15 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof ; and

(iii) 0.5 to 5.0 g per litre sodium chloride, and 0.05 to 5.0 g per litre potassium chloride.~~;~~

Optional components which may be present in such a first colon cleansing solution in a kit of the invention include:

(iv) ~~optionally~~ one or more flavouring agents; and

(v) ~~optionally~~ one or more sweeteners.

Such a first colon cleansing solution in a kit of the invention may consist essentially of water and:

(i) 90 to 200 g per litre PEG having an average molecular weight of 2500 to 4500 Da.

(ii) 2.0 to 15 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof ;

(iii) 0.5 to 5.0 g per litre sodium chloride, and 0.05 to 5.0 g per litre potassium chloride;

(iv) one or more flavouring agents; and

(v) one or more sweeteners.

The invention further provides, according to a third aspect, a colon cleansing solution comprising: ~~(or consisting essentially of water and):~~

(i) 130 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da; and

(ii) 8.0 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a

mixture thereof.~~;~~

Optional components which may be present in such a first colon cleansing solution include:

(iii 1) ~~optionally~~ 1.0 to 3.0 g per litre sodium chloride;

(iii 2) ~~optionally~~ 0.5 to 1.5 (for example 0.5 to 1.1) g per litre potassium chloride;

(iv) ~~optionally~~ one or more flavouring agents; and

(v) ~~optionally~~ one or more sweeteners.

Such a first colon cleansing solution may consist of water and:

(i) 130 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da;

(ii) 8.0 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof;

(iii 1) 1.0 to 3.0 g per litre sodium chloride;

(iii 2) 0.5 to 1.5 (for example 0.5 to 1.1) g per litre potassium chloride;

(iv) one or more flavouring agents; and

(v) one or more sweeteners.

There is also provided a composition for the preparation of such a solution, for example by admixture with water. Preferred amounts of each of components (i) to (v)in the solutions and compositions of the third aspect of the invention are as set out for the first colon cleansing solutions and first colon cleansing compositions hereinabove and hereinbelow.

In an embodiment, the first colon cleansing solution is provided in a volume of from 300ml up to 1200ml. For example, the first solution may have a volume in a range with a lower limit of 300ml, 400ml, 500ml, 600ml or 700ml. Preferably, the lower limit is 500ml, 600ml or 700ml. The volume may be in a range with an upper limit of 1200ml, 1100ml, 1000ml, 900ml or 800ml. For example the volume may be in the range 400ml to 1100ml, for example 500ml to 1000ml, for example 600ml to 900ml, for example 700ml to 800ml. For example, the first colon cleansing solution is provided in a volume of 750ml. The most appropriate volume will depend on the exact components of the solution and the amounts in which they are present. In general, for a solution of higher osmotic strength, a smaller volume will be required.

The first cleansing solution may, for example, have a measured osmolality in the range 200 to 1500 mOsmol/kg. In a preferred embodiment, it is hyper-osmotic. It may, for example have a measured osmolality in the range 320 to 1500 mOsmol. For example, the measured osmolality of the first cleansing solution is in the range 330 to 1200 mOsmol/kg, for example 340 to 1000 mOsmol/kg, for example 350 to 800 mOsmol/kg, for example 350 to 700 mOsmol/kg.

A colon cleansing solution according to the third aspect of the invention may be used together with a solution of the first aspect of the invention. Alternatively, it may be used in combination with a different other colon cleansing solution, or used in a suitable volume on its own. If used on its own, it may be used in a single dose or in a split dose administration. The invention provides a method of cleansing the colon of a subject comprising administering a solution of the third aspect of the invention. The solution may be administered on its own or in combination with a further, different, solution.

The invention further provides a kit comprising:

A) a first component, being a composition for the preparation of a first colon cleansing solution as described immediately above by admixture with water; and

B) a second component, being a composition for the preparation of a second colon cleansing solution by admixture with water, the second colon cleansing solution being a solution as described hereinabove in relation to solutions and uses of the first aspect of the invention,

Preferably, the kit further comprises instructions for use.

The invention further provides a kit comprising:
A) a first component, being a composition for the preparation of a first colon cleansing solution by admixture with water; and
B) a second component, being a composition for the preparation of a second colon cleansing solution by admixture with water;
and optional instructions for use,
the second colon cleansing solution being the solution of the invention in water,
the first solution being different from the second.

For example, components A) and B) may be in dry powder, granular or other dry form. They may alternatively be in the form of concentrates or slurries. Components A) and B) may be in the same or different physical forms. Components within A) and B) may be in the same or different physical forms. For example, one or both of components A) and B) are dry powders. A portion of either or each of components A) and B) may be in the form of one or more solid tablets or capsules.

For example, a kit of the invention may comprise

A) a first component, being a composition for the preparation of a first colon cleansing solution comprising ~~(or consisting essentially of water and)~~:

(i) 70 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da; and~~,~~

(ii) 2 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof;

~~(iii) optionally one or more electrolytes;~~
~~(iv) optionally one or more flavouring agents;~~
~~(v) optionally one or more sweeteners;~~

and

B) a second component, being a composition optionally presented in two or more parts for the preparation of a second colon cleansing solution, according to the invention. ~~comprising~~

~~a) 300 to 2000 mmol per litre ascorbate anion provided by ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and~~

~~b) optionally 10 to 200 g per litre polyethylene glycol.~~

Optional components which may be present in a first colon cleansing solution in a kit as described above include:

(iii) one or more electrolytes;

(iv) one or more flavouring agents;

(v) one or more sweeteners.

The first colon cleansing solution in a kit as described above may consist essentially of water and:

(i) 70 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da;

(ii) 2 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof;

(iii) one or more electrolytes;

(iv) one or more flavouring agents; and

(v) one or more sweeteners.

Preferably, the first solution is of different composition from the second. The concentrations of the components given here are the concentrations attained when the compositions are mixed with water according to the instructions provided with the kit.

The first colon cleansing solution may be used in a volume as described hereinabove, for example 300ml to 1200ml, for example 600ml to 900ml, for example 750ml. The second colon cleansing solution may be used in a volume as described hereinabove, for example 600ml to 900ml, for example 750ml. The second colon cleansing solution may be used in a volume as described hereinabove, for example 250ml up to 1000ml, for example 400ml to 700ml, for example 500ml. Instructions comprised in the kit may instruct the user to prepare a solution by adding water to the required volume, for example a volume as mentioned in this paragraph.

Accordingly, a kit of the invention may comprise:

A) a first component, being a composition for the preparation of a first colon cleansing solution comprising ~~(or consisting essentially of)~~:

(i) 52.5 to 187.5 g PEG having an average molecular weight of 2500 to 4500 Da; and~~.~~

(ii) 1.5 to 15 g of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof.

~~(iii) optionally one or more electrolytes;~~

~~(iv) optionally one or more flavouring agents;~~

~~(v) optionally one or more sweeteners,~~

and

B) a second component, being a composition optionally presented in two or more parts for the preparation of a second colon cleansing solution, according to the invention,~~comprising~~

~~a) 150 to 1000 mmol ascorbate anion; and~~

~~b) optionally 5 to 100 g polyethylene glycol,~~

the first solution being different from the second.

Optional components which may be present in a first component as described above include:

(iii) one or more electrolytes;

(iv) one or more flavourings; and

(v) one or more sweeteners.

For example a kit of the invention may consist essentially of:

A) a first component, being a composition for the preparation of a first colon cleansing solution consisting essentially of:

(i) 52.5 to 187.5 g PEG having an average molecular weight of 2500 to 4500 Da;

(ii) 1.5 to 15 g of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof.;

(iii) one or more electrolytes;

(iv) one or more flavourings; and

(v) one or more sweeteners;

and

B) a second component, being a composition according to the invention optionally presented in two or more parts for the preparation of a second colon cleansing solution,

the first solution being different from the second.

The first component preferably comprises 97.5 to 187.5 g of PEG, for example 67.5 to 150 g of PEG, more preferably 75 to 150 g, for example 90 to 112.5 g, for example 100 g PEG.

Preferably, the first component comprises a sulphate component (for example sodium sulphate) in an amount of 1.5 to 11.25 g, for example 3.75 to 11.25 g, for example 6 to 9 g, for example 6 or 9 g. For example, the first component comprises 6.0 to 15 g of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof.

Preferably, the first component comprises sodium chloride in an amount of 0.375 to 3.75 g. For example, sodium chloride may be present in an amount of 0.75 to 3.0 g, for example 0.75 to 2.25 g, for example 1.125 to 2.25 g, for example 1.5 to 2.25 g.

For example, the first component comprises potassium chloride in an amount of 0.75 to 7.5 g. For example, potassium chloride may be present in an amount of 0.0375 to 3.75 g, for example 0.075 to 2.25 g, for example 0.15 to 1.5 g, for example 0.375 to 1.125 g, for example 0.375 to 0.825 g.

In an embodiment, the first component comprises sodium chloride and potassium chloride. They can be present in the amounts mentioned immediately above. For example, sodium chloride may be present in an amount of 1.125 to 2.25 g and potassium chloride may be present in an amount of 0.15 to 1.5 g.

The second component of the kit of compositions of the invention is ~~preferably~~ a composition for the preparation of a solution of the first aspect of the invention as described herein above.

In an embodiment, a kit of the invention has instructions that instruct the user of the volume to which each component is to be made up with water. For example, the specified volume of water for each solution is less than one litre. For example, the specified volume for the first component may be 300ml to 1200ml, for example 600ml to 900ml, for example 750ml. For example, the specified volume for the second component may be from 250ml to 1000ml, for example 400ml to 700ml, for example 500ml. Further volumes that may be specified in the instructions are the volumes set out hereinabove in relation to the methods of the invention.

In general, the instructions specify that the first and second solutions are to be ingested in succession with a time interval between them. In an embodiment, the instructions specify that the first cleansing solution is ingested first followed, after time interval (for example the time between an evening and the following morning), by ingestion of the second cleansing solution.

It is convenient for the patient for a kit of the invention to be provided in the form of, for example, a box. In a kit of the invention the first and/or second components may each contained in one or more containers. In particular, the second component may be contained in more than one container. For example, if the second component comprises both ascorbic acid and PEG then the ascorbic acid and PEG may be contained in separate containers. The other constituents of the second component (for example one or more of sodium chloride, potassium chloride and sodium sulphate) may be in either of the separate containers. For example, they may be in the container containing the PEG.

If a flavouring component is present in the first or second solution, then in a kit of the invention, the flavouring component for the relevant solution may be provided in a separate container from the other constituents of that solution.

Examples of suitable containers include tubs, bags and sachets. A preferred container is a sachet.

In one embodiment, a kit comprises:

A) a first sachet comprising a first composition for the preparation of the first cleansing solution;

B1) a second sachet;

B2) a third sachet;

wherein the second and third sachets together provide a composition for the preparation of the second cleansing solution.

For example, in a kit of the invention as mentioned immediately above:

A) the first sachet comprises polyethylene glycol and/or sodium sulphate;

B1) the second sachet comprises one or more components selected from polyethylene glycol, one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof, electrolytes and/or one or more salts of ascorbic acid; and

B2) the third sachet comprises ascorbic acid;

the one or more salts of ascorbic acid in the second sachet (B1) and the ascorbic acid in the third sachet (B2) together providing 60 to 150 g/~~300 to 2000 mmol per~~ litre ascorbate component~~anion~~.

For example, in a kit of the invention as mentioned immediately above:

A) the first sachet comprises:

(i) 70 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da.

(ii) 2 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof

(iii) optionally one or more electrolytes;

(iv) optionally one or more flavouring agents; and

(v) optionally one or more sweeteners,

B1) the second sachet comprises:

(i) 10 to 200g per litre polyethylene glycol,

(ii) optionally one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof,

(iii) electrolytes; and

(iv) or one or more salts of ascorbic acid; and

B2) the third sachet comprises ascorbic acid,

the one or more salts of ascorbic acid in the second sachet (B1) and the ascorbic acid in the third sachet (B2) together providing 60 to 150 g/~~300 to 2000 mmol per~~ litre ascorbate component~~anion~~.

A kit of the invention may be for use in a method of cleansing the colon comprising:
- the subject taking an effective amount of a first colon cleansing solution as described herein;
- the subject taking an effective amount of a second colon cleansing solution as described herein.

The invention further finds utility in ~~provides~~ a method of cleansing the colon comprising:
- the subject taking an effective amount of a first colon cleansing solution as described herein;
- the subject taking an effective amount of a second colon cleansing solution as described herein.

In the method, there is typically a time interval between taking the first solution and taking the second solution. Generally, the time interval is at least 4 hours, for example 6 hours or more, for example 8 hours or more. Typically, the time interval is less than 15 hours. The time interval between starting to take the first cleansing solution and starting to take the second cleansing solution may be, for example, the time between an evening and the following morning, for example 12 to 16 hours, for example 14 hours. For example, the subject may sleep (for example overnight) between taking the first and second cleansing solutions.

In a fourth aspect, the invention finds utility in ~~provides~~ a method of cleansing the colon of a subject comprising:

- administering to the subject an effective amount of a first cleansing solution; and then after a time interval

- administering to the subject an effective amount of a second cleansing solution,

wherein the second cleansing solution is hyper-osmotic and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and wherein the first cleansing solution is either substantially free from ascorbic acid and salts thereof, or contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, in an amount providing a lower concentration of ascorbate anion than is present in the second cleansing solution.

For example, the invention finds utility in ~~provides~~ a method of cleansing the colon of a subject comprising:

- the subject taking an effective amount of a first cleansing solution; and then after a time interval

- the subject taking an effective amount of a second cleansing solution,

wherein the second cleansing solution is hyper-osmotic and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and wherein the first cleansing solution is either substantially free from ascorbic acid and salts thereof, or contains ascorbic acid, one or more salts of ascorbic acid,

wherein the second colon cleansing solution, when made up to the instructed specified volume with the clear fluid (for example water), is hyper-osmotic and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and wherein the first colon cleansing solution is either substantially free from ascorbic acid and salts thereof, or contains, when made up to the instructed specified volume with the clear fluid (for example water), ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, in an amount providing a lower concentration of ascorbate anion in the first colon solution than in the second colon cleansing solution.

In an embodiment, the invention finds utility in ~~provides~~ a method of cleansing the colon of a subject comprising:

- administering to the subject an effective amount of a first cleansing solution; and then after a time interval

- administering to the subject an effective amount of a second cleansing solution,

wherein the first cleansing solution contains polyethylene glycol (PEG) and is hyper-osmotic; and wherein the second cleansing solution contains polyethylene glycol (PEG) and is more hyper-osmotic than the first cleansing solution.

For example, the invention finds utility in ~~provides~~ a method of cleansing the colon of a subject comprising:

- the subject taking an effective amount of a first cleansing solution; and then after a time interval

- the subject taking an effective amount of a second cleansing solution,

wherein the first cleansing solution contains polyethylene glycol (PEG) and is hyper-osmotic; and wherein the second cleansing solution contains polyethylene glycol (PEG) and is more hyper-osmotic than the first cleansing solution.

Osmolality can be measured in various ways. In general, either freezing point depression or vapour-pressure alteration is used. For example, an Advanced Instruments, Inc Model 3250 osmometer (a freezing point depression device) can be used. Vapour pressure measurement can also be used, for example using an ELITech Group Vapro 5600 device. Osmolality values cited herein are preferably taken to be values measured using a freezing point depression osmometer, for example using an Advanced Instruments, Inc Model 3250 osmometer following standard operating procedure.

The amount of solution that constitutes an "effective amount" need not be the same for the first and second solutions.

The method of the invention provides satisfactory cleansing of the colon with ingestion of a smaller total volume of the solutions than in the prior art. The reduced volume requirement helps to improve patient compliance.

For example, the second cleansing solution may comprise ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof. In solution, ascorbic acid and salts thereof provide ascorbate anion. Depending on the pH of the solution, some ascorbate anion is protonated and thus exists as free ascorbic acid. At the pH of solutions that would typically be administered, only a very minor proportion of ascorbate is protonated. In calculations of concentrations of "ascorbate anion" herein, the concentration of "ascorbate anion" is taken as the total concentration of all ascorbate anion present, including the proportion that is protonated. Ascorbic acid or salts thereof, contribute to the osmotic load, along with other solutes. In one embodiment, the first cleansing solution does not contain ascorbic acid or a salt thereof. Alternatively, the first solution may contain ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof. Typically, if the first solution contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, it contains them in an amount providing a lower concentration of ascorbate anion than is present in the second cleansing solution.

The invention also provides a kit comprising:

- a first colon cleansing solution; and

- a second colon cleansing solution,

wherein the first cleansing solution contains polyethylene glycol (PEG) and is hyper-osmotic; and wherein the second cleansing solution is a solution according to the invention which contains polyethylene glycol (PEG) and is more hyper-osmotic than the first cleansing solution.

The invention also provides a kit comprising:

a) a first component, being a composition for the preparation of a first colon cleansing solution by admixture with a clear fluid (for example water); and

b) a second component, being a composition for the preparation of a second colon cleansing solution by admixture with a clear fluid (for example water),

and instructions for use that specify the volume to which each component is to be made up with a clear fluid (for example water),

wherein the first cleansing solution contains polyethylene glycol (PEG) and, when made up to the instructed specified volume with the clear fluid (for example water), is hyper-osmotic; and wherein the second cleansing solution contains polyethylene glycol (PEG) and, when made up to the instructed

specified volume with the clear fluid (for example water), is a solution according to the invention which is more hyper-osmotic than the first cleansing solution.

For example, components a) and b) may be in dry powder, granular or other dry form. They may alternatively be in the form of concentrates or slurries. Components a) and b) may be in the same or different physical forms. Components within a) and b) may be in the same or different physical forms. For example, one or both of components a) and b) are dry powders.

In an embodiment, the invention finds utility in ~~provides~~ a method of cleansing the colon of a subject comprising:

- administering to the subject an effective amount of a first cleansing solution; and then after a time interval

- administering to the subject an effective amount of a second cleansing solution,

wherein the first cleansing solution and the second cleansing solution are different, and wherein the first cleansing solution contains an alkali metal sulphate, an alkaline earth metal sulphate or a mixture thereof; and the second cleansing solution is a solution according to the invention~~contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof~~.

The amount of solution that constitutes an "effective amount" need not be the same for the first and second solutions.

The first cleansing solution may contain polyethylene glycol (PEG). When made up to the instructed specified volume with water, it is preferably hyper-osmotic. The second cleansing solution ~~may~~ contains polyethylene glycol (PEG). When made up to the instructed specified volume with water, it may be hyper-osmotic, preferably more hyper-osmotic than the first cleansing solution.

Typically, if the first solution contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, it contains them in an amount providing a lower concentration of ascorbate anion than is present in the second cleansing solution. In an embodiment, the first cleansing solution does not contain ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof. Typically, if the second solution contains an alkali metal sulphate, an alkaline earth metal sulphate or a mixture thereof it contains them in an amount providing a lower concentration of sulphate anion than is present in the first cleansing solution. In an embodiment, the second cleansing solution does not contain an alkali metal sulphate, an alkaline earth metal sulphate or a mixture thereof.

For example, the invention finds utility in ~~provides~~ a method of cleansing the colon of a subject comprising:

- the subject taking an effective amount of a first cleansing solution; and then after a time interval

- the subject taking an effective amount of a second cleansing solution,

wherein the first cleansing solution and the second cleansing solution are different, and wherein the first cleansing solution contains an alkali metal sulphate, an alkaline earth metal sulphate or a mixture thereof; and the second cleansing solution is a solution according to the invention.~~contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof~~.

The amount of solution that constitutes an "effective amount" need not be the same for the first and second solutions.

The method described~~of the invention~~ provides satisfactory cleansing of the colon with ingestion of a smaller total volume of the solutions than in the prior art. The reduced volume requirement helps to improve patient compliance.

~~For example, t~~The second cleansing solution ~~may~~ comprises ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof. In solution, ascorbic acid and salts thereof provide ascorbate anion. Ascorbic acid or salts thereof, contribute to the osmotic load, along with other solutes. In one embodiment, the first cleansing solution does not contain ascorbic acid or a salt thereof. Alternatively, the first solution may contain ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof. Typically, if the first solution contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, it contains them in an amount providing a lower concentration of ascorbate anion than is present in the second solution.

The invention also provides a kit comprising:

- a first colon cleansing solution; and

- a second colon cleansing solution,

wherein the first cleansing solution and the second cleansing solution are different, and wherein the first cleansing solution contains an alkali metal sulphate, an alkaline earth metal sulphate or a mixture thereof; and the second cleansing solution is a solution according to the invention.~~contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof~~.

The first cleansing solution may contain polyethylene glycol (PEG). When made up to the instructed specified volume with water, it is preferably hyper-osmotic. The second cleansing solution ~~may~~ contains polyethylene glycol (PEG). When made up to the instructed specified volume with water, it may be hyper-osmotic, preferably more hyper-osmotic than the first cleansing solution.

The invention also provides a kit comprising:

a) a first component, being a composition for the preparation of a first colon cleansing solution by admixture with a clear fluid (for example water); and

b) a second component, being a composition for the preparation of a second colon cleansing solution by admixture with a clear fluid (for example water),

and instructions for use that specify the volume to which each component is to be made up with a clear fluid (for example water),

wherein the first cleansing solution and the second cleansing solution are different, and wherein the first cleansing solution contains an alkali metal sulphate, an alkaline earth metal sulphate or a mixture thereof; and the second cleansing solution is a solution according to the invention ~~contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof~~.

For example, components a) and b) may be in dry powder, granular or other dry form. They may alternatively be in the form of concentrates or slurries. Components a) and b) may be in the same or different physical forms. Components within a) and b) may be in the same or different physical forms. For example, one or both of components a) and b) are dry powders.

In a further embodiment, the invention finds utility in ~~provides~~ a method of cleansing the colon of a subject comprising:

- administering to the subject an effective amount of a first cleansing solution; and then after a time interval

- administering to the subject an effective amount of a second cleansing solution,

wherein the first cleansing solution and the second cleansing solution are different and, together, comprise the components:

a) 80 to 250g of a polyethylene glycol;
b) 10 to 150g of ascorbic acid, one or more salts of ascorbic acid or a mixture of ascorbic acid and one or more salts of ascorbic acid (the "ascorbate component");
c) 1 to 15g of an alkali metal or alkaline earth metal sulphate or a mixture of alkali metal or alkaline earth metal sulphates (the "sulphate component");
d) 1 to 15g of electrolytes;
e) optionally one or more sweeteners, and
f) optionally one or more flavourings

solution contains a concentration of the ascorbate anion that is greater by at least 100mmol per litre, for example at least 200mmol per litre, at least 300mmol per litre.

For example, the first cleansing solution may be substantially free from an ascorbate component.

For example, the second cleansing solution may comprise:

- 56.6g sodium ascorbate, or
- 33.9g sodium ascorbate and 20.1g ascorbic acid, or
- 33.9g sodium ascorbate, or
- 33.9g sodium ascorbate and 21.4 g magnesium ascorbate.

The second cleansing solution ~~may~~ further comprises polyethylene glycol. The polyethylene glycol (PEG) may, for example, have an average molecular weight of 2500 to 4500 Da, for example 3000 to 4000 Da. For example, the PEG may be PEG 3350 or PEG 4000 as defined in national pharmacopeias. Further examples of suitable PEGs recognized in some national pharmacopeias include Macrogols, for example Macrogol 4000.

For example, the second cleansing solution may comprise 20g or 40g PEG 3350. For example, the second cleansing solution may have a volume of 500ml.

The first cleansing solution may comprise polyethylene glycol and/or an alkali metal sulphate, an alkaline earth metal sulphate, or a mixture thereof.

The polyethylene glycol (PEG) in the first cleansing solution may be as described immediately above for the second cleansing solution. The PEG in the first cleansing solution can be a different PEG from the PEG in the second cleansing solution. For example, one PEG may be PEG3350 and the other PEG may be PEG4000. For example, the first cleansing solution may comprise 100g PEG 3350. For example, the first cleansing solution may have a volume of 750ml.

The first cleansing solution preferably comprises an alkali metal sulphate, an alkaline earth metal sulphate or a mixture thereof. An alkali metal or alkaline earth metal sulphate may, for example, be selected from sodium sulphate, potassium sulphate and magnesium sulphate. The solution may comprise more than one of sodium sulphate, potassium sulphate and magnesium sulphate, for example all three. Preferably, the alkali metal sulphate, an alkaline earth metal sulphate or the mixture thereof is or includes sodium sulphate. Preferably, an alkali metal sulphate or alkaline earth metal sulphate (for example sodium sulphate) is anhydrous.

For example, the first cleansing solution may have a volume of 750ml and comprise 3g, 6g or 9g of sodium sulphate.

example using an ELITech Group Vapro 5600 device. Osmolality values cited herein are preferably taken to be values measured using a freezing point depression osmometer, for example using an Advanced Instruments, Inc Model 3250 osmometer following standard operating procedure.

In general it is not necessary for the solutions to include preservatives or anti-oxidants. Nevertheless, low levels of anti-oxidants or preservatives may be used if required.

The method described~~of the invention~~ may be used to cleanse the colon prior to carrying out a diagnostic, therapeutic or surgical procedure on the colon, rectum or anus or elsewhere in the abdomen in a subject. The subject is most preferably a human. The diagnostic or surgical procedure may, for example, be colonoscopy, barium enema examination, sigmoidoscopy (for example flexible sigmoidoscopy) or colon surgery. The method ~~of the invention~~ may be a method of cleansing the colon prior to a surgical or diagnostic procedure comprising administering the first solution and then after a time interval administering the second solution prior to said procedure.

The solutions, compositions and kits described herein also find use in the treatment of constipation and faecal impaction. The invention thus provides solutions, compositions and kits as described herein for use in the treatment of constipation or faecal impaction. The invention also finds utility in ~~provides~~ methods of treating constipation or faecal impaction comprising administration of solutions as described herein.

The invention further provides a kit comprising:

- a first colon cleansing solution; and

- a second colon cleansing solution,

wherein the second colon cleansing solution is according to the invention and is hyper-osmotic ~~and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof~~; and wherein the first colon cleansing solution is either substantially free from ascorbic acid and salts thereof, or contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, in an amount providing a lower concentration of ascorbate anion in the first colon solution than is present in the second colon cleansing solution.

A kit may further comprise instructions for use. The use may be as described above in relation to methods ~~of the invention~~.

In a kit of the invention, the components of the first and second solutions are as described hereinabove in relation to ~~the~~ methods ~~of the invention~~.

The invention further provides a first solution, and a second solution, for use in a method of cleansing the colon of a subject comprising:

- the subject taking an effective amount of a first cleansing solution; and then after a time interval

- the subject taking an effective amount of a second cleansing solution,

wherein the second cleansing solution is according to the invention and is hyper-osmotic ~~and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof~~; and wherein the first cleansing solution is either substantially free from ascorbic acid and salts thereof, or contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, in an amount providing a lower concentration of ascorbate anion than is present in the second cleansing solution.

The invention further provides a solution that is hyper-osmotic and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, for use in a method of cleansing the colon of a subject comprising:

- the subject taking an effective amount of a first cleansing solution; and then after a time interval

- the subject taking an effective amount of a second cleansing solution,

wherein the second cleansing solution is according to the invention and is hyper-osmotic ~~and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof~~; and wherein the first cleansing solution is either substantially free from ascorbic acid and salts thereof, or contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, in an amount providing a lower concentration of ascorbate anion than is present in the second cleansing solution.

In an embodiment, the first cleansing solution is substantially free from ascorbic acid and salts thereof.

~~The solutions for use in a method of cleansing the colon in accordance with the invention are as described hereinabove in relation to the methods of the invention.~~

In an embodiment, the invention provides a kit comprising:

a) a first component, being a composition for the preparation of a first colon cleansing solution by admixture with a clear fluid (for example water); and

b) a second component, being a composition for the preparation of a second colon cleansing solution by admixture with a clear fluid (for example water),

and instructions for use that specify the volume to which each component is to be made up with water,

wherein the second colon cleansing solution, when made up to the instructed specified volume with the clear fluid (for example water), is a solution according to the invention and is hyper-osmotic ~~and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof~~; and wherein the first colon cleansing solution is either

substantially free from ascorbic acid and salts thereof, or contains, when made up to the instructed specified volume with the clear fluid (for example water), ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, in an amount providing a lower concentration of ascorbate anion in the first colon solution than in the second colon cleansing solution.

The constituent parts of the composition for the preparation of a first cleansing solution by admixture with water are, for example, as described hereinabove in relation to the first solution ~~in the methods of the invention~~. The constituent parts of the composition for the preparation of a second cleansing solution by admixture with water are, for example, as described hereinabove in relation to the second solution ~~in the methods of the invention~~.

For example, components a) and b) may be in dry powder, granular or other dry form. They may alternatively be in the form of concentrates or slurries. Components a) and b) may be in the same or different physical forms. Components within a) and b) may be in the same or different physical forms. For example, one or both of components a) and b) are dry powders.

In an embodiment, a kit of the invention has instructions in which the specified volume of water for each solution is less than one litre. For example, the combination of the specified volumes of the first and second cleansing solutions is preferably less than 2 litres. Preferably, it is 1750ml or less, for example 1500ml or less, for example 1250ml or less. For most adult subjects, a combined volume of more than 500ml is used, for example more than 750ml. For example, a combined volume of from 500ml to 1750ml is used, for example from 750ml to 1500ml, for example from 1000ml to 1500ml, for example 1250ml. For example a volume of 750ml may be specified for the first cleansing solution and a volume of 500ml may be specified for the second cleansing solution. The instructions may specify that a cleansing solution is consumed immediately after it has been prepared. They may specify that the cleansing solution is prepared and then stored in a fridge before consumption at a slightly later time.

In general, the instructions specify that the first and second solutions are to be ingested in succession with a time interval between them. In an embodiment, the instructions specify that the first cleansing solution is ingested first followed, after a time interval (for example the time between an evening and the following morning) by ingestion of the second cleansing solution. The time interval is preferably as described above in relation to the methods of the invention.

It is convenient for the patient for a kit of the invention to be provided in the form of, for example, a box. In a kit of the invention the first and/or second components may each be contained in one or more containers. In particular, the second component may be contained in more than one container. For example, if the second component comprises both ascorbic acid and PEG then the ascorbic acid and PEG may be contained in separate containers. The other constituents of the second component

a) the first sachet comprises 100g PEG 3350, 3g sodium sulphate, 1.4g sodium chloride and 0.3g potassium chloride; or 100g PEG 3350, 6g sodium sulphate, 1.6g sodium chloride and 0.7g potassium chloride; or 100g PEG 3350, 9g sodium sulphate, 2.0g sodium chloride and 1.0g potassium chloride; and optional flavouring and/or optional sweetener;

b) the second sachet comprises (i) 40g PEG 3350, 3.5g sodium chloride and 2.2g potassium chloride; or (ii) 20g PEG 3350 2.7g sodium chloride and 1.3g potassium chloride; or (iii) 40g PEG 3350, 2.8g sodium chloride and 1.3g potassium chloride; or (iv) 40g PEG 3350, 2.8g sodium chloride and 2.0g potassium chloride; or (v) 40g PEG 3350, 3.1g sodium chloride and 1.3g potassium chloride; and optional flavouring and/or optional sweetener; and

c) the third sachet comprises for use with the respectively numbered second sachet (i) 56.6g sodium ascorbate; or (ii) and (iii) 33.9g sodium ascorbate and 20.1g ascorbic acid; or (iv) 33.9g sodium ascorbate; or (v) 33.9g sodium ascorbate and 21.4g magnesium ascorbate.

In such kits, the contents of the sachets may consist essentially of the recited components.

As mentioned above, some or all of the electrolytes may be provided in a tablet or capsule for co-administration with the respective solution. Accordingly, in a kit as described immediately above, some or all of the sodium chloride and potassium chloride in the first or second sachet may instead be provided in a tablet or capsule.

In an embodiment, the kit can be provided to the subject with a plurality of flavouring agents (each optionally with one or more sweeteners), each separately packaged. The subject can then select a preferred flavouring (or flavouring and sweetener combination) according to his or her taste. The subject also has the choice of not using any flavouring or sweetener at all.

Unless stated otherwise, a composition that is described herein as comprising a recited set of components is to be taken as comprising the components in admixture. If a composition is said to be presented in two or more parts, then the components need not all be in physical admixture. Typically, they are provided together in the article provided to the subject.

To summarise, the invention provides a colon cleansing solution comprising ~~(or consisting essentially of)~~:

a) 60 to 150 g/~~300 to 2000 mmol per~~ litre ascorbate componen~~tanion~~ (provided by ascorbic acid, one or more salts of ascorbic acid selected from sodium ascorbate, potassium ascorbate, magnesium ascorbate and calcium ascorbate, or a mixture thereof); ~~preferably 350 to 800mmol~~; and

b) 10 to 200 g per litre PEG having an average molecular weight of 3000 to 4000 Da; preferably 20 to 100g per litre.

Optional components in such a solution include:

c) ~~optionally~~ sodium chloride (for example 3 to 7g per litre) and potassium chloride (for example 2 to

5g per litre);

d) ~~optionally~~ sodium sulphate (if present, for example 2 to 20g per litre);

e) ~~optionally~~ one or more flavouring agents; and

f) ~~optionally~~ one or more sweeteners.

Preferably such a solution consists essentially of water and:

a) 60 to 150 g/litre ascorbate component (provided by ascorbic acid, one or more salts of ascorbic acid selected from sodium ascorbate, potassium ascorbate, magnesium ascorbate and calcium ascorbate, or a mixture thereof);

b) 10 to 200 g per litre PEG having an average molecular weight of 3000 to 4000 Da; preferably 20 to 100g per litre;

c) sodium chloride (for example 3 to 7g per litre) and potassium chloride (for example 2 to 5g per litre);

e) one or more flavouring agents; and

f) one or more sweeteners.

The invention also provides a composition (optionally presented in two or more parts) for admixture with water to provide a solution of the invention. The electrolytes may optionally be provided as a tablet or a capsule to be co-administered with the solution.

The invention also finds utility in ~~provides~~ a method of cleansing the colon of a subject comprising:

- administering to the subject an effective amount of a first cleansing solution; and then after a time interval

- administering to the subject an effective amount of a second cleansing solution,

wherein the second cleansing solution is according to the invention and is hyper-osmotic, containing ~~and contains~~ ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof (for example ascorbic acid and sodium ascorbate, for example sodium ascorbate); and wherein the first cleansing solution is either substantially free from ascorbic acid and salts thereof, or contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, in an amount providing a lower concentration of ascorbate anion than is present in the second cleansing solution. The second cleansing solution may comprises PEG and may comprise electrolytes (for example sodium chloride and potassium chloride). The first solution may comprise PEG; it may comprise an alkali metal or alkaline earth metal sulphate (for example sodium sulphate); it may comprise electrolytes (for example sodium chloride and potassium chloride). There are also provided kits comprising a first and a second solution according to the invention, and kits comprising compositions for preparing the first and second solutions.

Claims:

1. A colon cleansing solution comprising:
a) 300 to 2000 mmol per litre ascorbate anion provided by ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and
b) 10 to 200 g per litre polyethylene glycol.

2. A colon cleansing solution as claimed in claim 1 wherein the ascorbate anion is provided by ascorbic acid, one or more salts of ascorbic acid selected from sodium ascorbate, potassium ascorbate, magnesium ascorbate and calcium ascorbate, or a mixture thereof.

3. A colon cleansing solution as claimed in claim 1 or claim 2 comprising (or consisting essentially of):
a) 300 to 2000 mmol per litre ascorbate anion;
b) 10 to 200 g per litre PEG having an average molecular weight of 3000 to 4000 Da;
c) sodium chloride and potassium chloride;
d) optionally sodium sulphate;
e) optionally one or more flavouring agents; and
f) optionally one or more sweeteners.

4. A composition for admixture with water, wherein the composition is optionally presented in two or more parts, and comprises:
a) 150 to 1000 mmol ascorbate anion provided by ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and
b) 5 to 100 g polyethylene glycol.

5. A composition as claimed in claim 4 comprising (or consisting essentially of):
a) 150 to 1000 mmol ascorbate anion;
b) 5 to 100 g PEG having an average molecular weight of 3000 to 4000 Da.
c) sodium chloride and potassium chloride;
d) optionally sodium sulphate;
e) optionally one or more flavouring agents;
f) optionally one or more sweeteners.

6. A composition comprising the following components in the following weight ratios:
a) ascorbate anion provided by ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof: 0.82 to 10.0 parts
b) polyethylene glycol: 1.0 part.

7. A composition as claimed in claim 6 comprising the following components in the following weight ratios:

a) ascorbate anion: 0.82 to 10.0 parts

b) polyethylene glycol: 1.0 part

c1) sodium chloride: 0.005 to 1.0 parts, and

c2) potassium chloride: 0.005 to 1.0 parts.

8. A composition as claimed in claim 6 or claim 7 which is a dry powder composition.

9. A composition as claimed in any one of claims 6 to 8 which is substantially free from any bicarbonate.

10. A composition as claimed in any one of claims 6 to 9 comprising (or consisting essentially of) the following components in the following weight ratios:

a) ascorbate anion: 0.82 to 10.0 parts

b) PEG having an average molecular weight of 3000 to 4000 Da: 1.0 part.

c) sodium chloride and potassium chloride;

d) optionally sodium sulphate;

e) optionally one or more flavouring agents; and

f) optionally one or more sweeteners.

11. A solution in water of:

a) 300 to 2000 mmol per litre ascorbate anion provided by ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and

b) optionally 10 to 200 g per litre polyethylene glycol,

for use in cleansing the colon of a mammal.

12. A solution in water as claimed in claim 11 comprising:

a) 150 to 1000 mmol ascorbate anion; and

b) optionally 5 to 100 g PEG.

13. A solution in water as claimed in claim 11 or claim 12 comprising (or consisting essentially of):

a) 150 to 1000 mmol ascorbate anion;

b) 5 to 100 g PEG having an average molecular weight of 3000 to 4000 Da.

c) sodium chloride and potassium chloride;

d) optionally sodium sulphate;

e) optionally one or more flavouring agents; and

f) optionally one or more sweeteners.

14. A kit comprising:

- a first colon cleansing solution, and

- a second colon cleansing solution,

the second colon cleansing solution being a solution in water of:

a) 300 to 2000 mmol per litre ascorbate anion provided by ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and

b) optionally 10 to 200 g per litre polyethylene glycol.

15. A kit as claimed in claim 14 wherein the first colon cleansing solution comprises (or consists essentially of):

(i) 70 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da;

(ii) 2.0 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof;

(iii) optionally one or more electrolytes;

(iv) optionally one or more flavouring agents; and

(v) optionally one or more sweeteners.

16. A kit comprising:

A) a first component, being a composition for the preparation of a first colon cleansing solution by admixture with water; and

B) a second component, being a composition for the preparation of a second colon cleansing solution by admixture with water;

and optional instructions for use,

the second colon cleansing solution being a solution in water of:

a) 300 to 2000 mmol per litre ascorbate anion provided by ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and

b) optionally 10 to 200 g per litre polyethylene glycol.

the first solution being different from the second.

17. A kit as claimed in claim 16 comprising:

A) a first component, being a composition for the preparation of a first colon cleansing solution comprising:

(i) 70 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da.

(ii) 2 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof

(iii) optionally one or more electrolytes;

(iv) optionally one or more flavouring agents;

(v) optionally one or more sweeteners,

and

B) a second component, being a composition optionally presented in two or more parts for the preparation of a second colon cleansing solution, comprising:
a) 300 to 2000 mmol per litre ascorbate anion; and
b) optionally 10 to 200 g per litre polyethylene glycol,
the first solution being different from the second.

18. A kit as claimed in claim 16 comprising:
A) a first component being a composition for the preparation of a first colon cleansing solution, the first component comprising:
(i) 52.5 to 187.5 g PEG having an average molecular weight of 2500 to 4500 Da.
(ii) 1.5 to 15 g of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof
(iii) optionally one or more electrolytes;
(iv) optionally one or more flavouring agents;
(v) optionally one or more sweeteners,

and

B) a second component being a composition optionally presented in two or more parts for the preparation of a second colon cleansing solution, the second component comprising:
a) 150 to 1000 mmol ascorbate anion; and
b) optionally 5 to 100 g polyethylene glycol.

19. A kit as claimed in any one of claims 16 to 18 which comprises:
A) a first sachet comprising a first composition for the preparation of the first cleansing solution;
B1) a second sachet;
B2) a third sachet;
wherein the second and third sachets together provide a composition for the preparation of the second cleansing solution.

20. A kit as claimed in claim 19 wherein:
A) the first sachet comprises:
(i) 52.5 to 187.5 g PEG having an average molecular weight of 2500 to 4500 Da;
(ii) 1.5 to 15 g of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof;
(iii) optionally one or more electrolytes;

(iv) optionally one or more flavouring agents;

(v) optionally one or more sweeteners,

B1) the second sachet comprises:

(i) 5 to 100g PEG having an average molecular weight of 2500 to 4500 Da;

(ii) optionally one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof;

(iii) electrolytes and/or one or more salts of ascorbic acid; and

B2) the third sachet comprises ascorbic acid,

the one or more salts of ascorbic acid in the second sachet (B1) and the ascorbic acid in the third sachet (B2) together providing 150 to 1000 mmol ascorbate anion.

21. A method of cleansing the colon of a subject comprising:

- administering to the subject an effective amount of a first colon cleansing solution;
- administering to the subject an effective amount of a second colon cleansing solution,

the second colon cleansing solution comprising:

a) 300 to 2000 mmol per litre ascorbate anion provided by ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and

b) optionally 10 to 200 g per litre polyethylene glycol.

22. A kit as claimed in any one of claims 14 to 20, for use in a method of cleansing the colon comprising:

- the subject taking an effective amount of a first colon cleansing solution;
- the subject taking an effective amount of a second colon cleansing solution.

23. A colon cleansing solution comprising (or consisting essentially of):

(i) 130 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da;

(ii) 8.0 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof;

(iii 1) optionally 1.0 to 3.0 g/L sodium chloride;

(iii 2) optionally 0.5 to 1.5 g/L potassium chloride;

(iv) optionally one or more flavouring agents;

(v) optionally one or more sweeteners.

24. A colon cleansing solution as claimsed in claim 23 for use in cleansing the colon of a subject, for example in combination with a solution as claimed in any one of claims 1 to 3.

25. A method of cleansing the colon of a subject comprising:

- administering to the subject an effective amount of a first cleansing solution; and then after a time interval

- administering to the subject an effective amount of a second cleansing solution,

wherein the second cleansing solution is hyper-osmotic and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and wherein the first cleansing solution is either substantially free from ascorbic acid and salts thereof, or contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, in an amount providing a lower concentration of ascorbate anion than is present in the second cleansing solution.

26. A method as claimed in claim 25 wherein the first cleansing solution is a bowel content suspending agent.

27. A method as claimed in claim 25 or claim 26 wherein the second cleansing solution is a bowel motility agent.

28. A method as claimed in any one of claims 25 to 27 wherein the second cleansing solution contains one or more salts of ascorbic acid.

29. A method as claimed in any one of claims 25 to 28 wherein the second cleansing solution comprises polyethylene glycol.

30. A method as claimed in any one of claims 25 to 29 wherein the first cleansing solution comprises polyethylene glycol and/or an alkali metal sulphate, an alkaline earth metal sulphate or a mixture thereof.

31. A method as claimed in any one of claims 25 to 30 wherein the first cleansing solution is substantially free from ascorbic acid and salts thereof.

32. A method as claimed in any one of claims 25 to 31 wherein the first and/or second cleansing solution further comprises one or more of:

a) one or more electrolytes;
b) one or more flavouring agents;
c) one or more sweeteners.

33. A method as claimed in any one of claims 25 to 32 wherein the combined volume of the first and second cleansing solutions is less than 2 litres.

34. A method as claimed in any one of claims 25 to 33 wherein the subject takes from 250ml up to 1000ml of the second cleansing solution.

35. A method as claimed in any one of claims 25 to 34 wherein first cleansing solution has a volume of 750ml and the second cleansing solution has a volume of 500ml.

36. A method as claimed in any one of claims 25 to 35 wherein the measured osmolality of the first cleansing solution is in the range 200 to 1500 mOsmol/kg.

37. A method as claimed in any one of claims 25 to 36 wherein the measured osmolality of the second cleansing solution is in the range 500 to 2000 mOsmol/kg.

38. A kit comprising:

- a first colon cleansing solution; and

- a second colon cleansing solution,

wherein the second colon cleansing solution is hyper-osmotic and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and wherein the first colon cleansing solution is either substantially free from ascorbic acid and salts thereof, or contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, in an amount providing a lower concentration of ascorbate anion in the first colon solution than is present in the second colon cleansing solution.

39. A kit as claimed in claim 38 wherein the first and/or second solution is as described in any one of claims 25 to 37.

40. A kit as claimed in claim 38 or 39, for use in a method of cleansing the colon of a subject, said method comprising:

- the subject taking an effective amount of a first cleansing solution; and then after a time interval

- the subject taking an effective amount of a second cleansing solution.

41. A kit comprising:

a) a first component, being a composition for the preparation of a first colon cleansing solution by admixture with water; and

b) a second component, being a composition for the preparation of a second colon cleansing solution by admixture with water,

and instructions for use that specify the volume to which each component is to be made up with water,

wherein the second colon cleansing solution, when made up to the instructed specified volume with water, is hyper-osmotic and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and wherein the first colon cleansing solution is either substantially free from ascorbic acid and salts thereof, or contains, when made up to the instructed specified volume with water, ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, in an amount providing, a lower concentration of ascorbate anion in the first colon solution than in the second colon cleansing solution.

42. A kit as claimed in claim 41 wherein one or both of components a) and b) are dry powders.

43. A kit as claimed in claim 41 or 42 wherein the specified volume of water for each solution is less than one litre.

44. A kit as claimed in any one of claims 41 to 43 wherein the specified volume for the first component is 750ml.

45. A kit as claimed in any one of claims 41 to 44 wherein the specified volume for the second component from 500ml.

46. A kit as claimed in any one of claims 41 to 45 wherein the instructions specify that the first colon cleansing solution is ingested first followed, after a time interval, by ingestion of the second colon cleansing solution.

47. A kit as claimed in any one of claims 41 to 46 wherein the first and/or second component is each contained in one or more containers.

48. A kit as claimed in claim 47 wherein the second component is contained in more than one container.

49. A kit as claimed in claim 48 wherein the second component comprises both ascorbic acid and PEG and the ascorbic acid and PEG are contained in separate containers.

50. A kit as claimed in any one of claims 47 to 49 wherein each container is a sachet.

51. A kit as claimed in any one of claims 41 to 50 wherein the first component comprises one dose of the first colon cleansing solution, and the second component comprises one dose of the second colon cleansing solution.

52. A kit as claimed in any one of claims 41 to 51 comprising:

a) a first sachet comprising a first composition for the preparation of a first colon cleansing solution;

b) a second sachet;

c) a third sachet;

wherein the second and third sachets together provide a composition for the preparation of a second colon cleansing solution.

53. A kit as claimed in claim 52 wherein:

a) the first sachet comprises polyethylene glycol and/or sodium sulphate, optional flavouring and/or optional sweetener;

b) the second sachet comprises polyethylene glycol, and optionally further components including one or more selected from an alkali metal sulphate, an alkaline earth metal sulphate, or a mixture thereof, electrolytes, one or more salts of ascorbic acid, flavouring and sweetener; and

c) the third sachet comprises ascorbic acid and optionally one or more salts of ascorbic acid.

54. A solution that is hyper-osmotic and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, for use in a method of cleansing the colon of a subject comprising:

- the subject taking an effective amount of a first cleansing solution; and then after a time interval

- the subject taking an effective amount of a second cleansing solution,

wherein the second cleansing solution is hyper-osmotic and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and wherein the first cleansing solution is either substantially free from ascorbic acid and salts thereof, or contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, in an amount providing a lower concentration of ascorbate anion than is present in the second cleansing solution.

Claims:

1. A colon cleansing solution comprising:
a) 60 to 150 g/ litre of an ascorbate component, the ascorbate component being ascorbic acid, one or more salts of ascorbic acid, or a mixture of ascorbic acid and one or more salts of ascorbic acid; and
b) 10 to 200 g per litre polyethylene glycol.

2. A colon cleansing solution as claimed in claim 1 wherein the ascorbate component is ascorbic acid, one or more salts of ascorbic acid selected from sodium ascorbate, potassium ascorbate, magnesium ascorbate and calcium ascorbate, or a mixture thereof.

3. A colon cleansing solution as claimed in claim 1 or claim 2 in which the ascorbate component comprises sodium ascorbate and ascorbic acid.

4. A colon cleansing solution as claimed in claim 3 in which the sodium ascorbate and ascorbic acid are present in a weight ratio of from 1:10 to 10:1.

5. A colon cleansing solution as claimed in claim 1 or claim 2 in which the ascorbate component consists of sodium ascorbate alone.

6. A colon cleansing solution as claimed in any one of claims 1 to 5 comprising:
a) 60 to 150 g/ litre of an ascorbate component;
b) 10 to 200 g per litre PEG having an average molecular weight of 3000 to 4000 Da;
c) sodium chloride and potassium chloride.

7. A colon cleansing solution as claimed in any one of claims 1 to 5 consisting essentially of water and:
a) 60 to 150 g/ litre of an ascorbate component;
b) 10 to 200 g per litre PEG having an average molecular weight of 3000 to 4000 Da;
c) sodium chloride and potassium chloride;
e) one or more flavouring agents; and
f) one or more sweeteners.

8. A colon cleansing solution as claimed in any one of claims 1 to 7 in which the ascorbate component is present at 80 to 120g/litre.

9. A colon cleansing solution as claimed in any one of claims 1 to 8 in which the PEG is present at 30 to 90g/litre.

10. A colon cleansing solution as claimed in any one of claims 1 to 9 which is substantially free from sodium bicarbonate.

11. A composition, optionally presented in two or more parts, for admixture with water to provide a solution as claimed in any one of claims 1 to 10.

12. A dry composition for the preparation of a dose of a solution as claimed in any one of claims 1 to 10 by admixture with water.

13. A dry composition as claimed in claim 12 wherein the dose has a volume of from 400 to 600ml.

14. A composition for admixture with water for the preparation of a colon cleansing solution of claim 1, comprising the following components in the following weight ratios:
a) ascorbate anion provided by ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof: 0.82 to 10.0 parts
b) polyethylene glycol: 1.0 part.

15. A composition as claimed in claim 14 comprising the following components in the following weight ratios:
a) ascorbate anion: 0.82 to 10.0 parts
b) polyethylene glycol: 1.0 part
c1) sodium chloride: 0.005 to 1.0 parts, and
c2) potassium chloride: 0.005 to 1.0 parts.

16. A composition as claimed in claim 14 or claim 15 in which the ascorbate component is present in an amount of 20 to 60g.

17. A composition as claimed in any one of claims 14 to 16 in which the PEG is present in an amount of 15 to 45g.

18. A composition as claimed in any one of claims 14 to 17 which is a dry powder composition.

19. A composition as claimed in any one of claims 14 to 18 which is substantially free from any bicarbonate.

20. A composition as claimed in any one of claims 14 to 19 comprising the following components in the following weight ratios:
a) ascorbate anion: 0.82 to 10.0 parts;
b) PEG having an average molecular weight of 3000 to 4000 Da: 1.0 part; and
c) sodium chloride and potassium chloride;

21. A composition as claimed in any one of claims 14 to 19 consisting essentially of the following components in the following weight ratios:
a) ascorbate anion: 0.82 to 10.0 parts;

b) PEG having an average molecular weight of 3000 to 4000 Da: 1.0 part.

c) sodium chloride and potassium chloride;

e) one or more flavouring agents; and

f) one or more sweeteners.

22. A solution as claimed in any one of claims 1 to 10 for use in cleansing the colon of a mammal.

23. A kit comprising:

- a first colon cleansing solution, and

- a second colon cleansing solution,

the second colon cleansing solution being the solution of any one of claims 1 to 10 in water.

24. A kit as claimed in claim 23 wherein the first colon cleansing solution comprises:

(i) 70 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da;

(ii) 2.0 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof.

25. A kit as claimed in claim 23 wherein the first colon cleansing solution consists essentially of water and:

(i) 70 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da;

(ii) 2.0 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof;

(iii) one or more electrolytes;

(iv) one or more flavouring agents; and

(v) one or more sweeteners.

26. A kit comprising:

A) a first component, being a composition for the preparation of a first colon cleansing solution by admixture with water; and

B) a second component, being a composition for the preparation of a second colon cleansing solution by admixture with water;

and optional instructions for use,

the second colon cleansing solution being the solution of any one of claims 1 to 10 in water,

the first solution being different from the second.

27. A kit as claimed in claim 26 comprising:

A) a first component, being a composition for the preparation of a first colon cleansing solution comprising:

(i) 70 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da; and

(ii) 2 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof ;

and

B) a second component, being a composition optionally presented in two or more parts for the preparation of a second colon cleansing solution, the second colon cleansing solution being a solution as claimed in any one of claims 1 to 10,

the first solution being different from the second.

28. A kit as claimed in claim 26 comprising:

A) a first component, being a composition for the preparation of a first colon cleansing solution consisting essentially of:

(i) 70 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da; and

(ii) 2 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof ;

(iii) one or more electrolytes;

(iv) one or more flavouring agents; and

(v) one or more sweeteners,

and

B) a second component, being a composition optionally presented in two or more parts for the preparation of a second colon cleansing solution, the second colon cleansing solution being a solution as claimed in any one of claims 1 to 10,

the first solution being different from the second.

29. A kit as claimed in claim 26 comprising:

A) a first component being a composition for the preparation of a first colon cleansing solution, the first component comprising:

(i) 52.5 to 187.5 g PEG having an average molecular weight of 2500 to 4500 Da; and

(ii) 1.5 to 15 g of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof

and

B) a second component being a composition optionally presented in two or more parts for the preparation of a second colon cleansing solution, the second colon cleansing solution being a solution as claimed in any one of claims 1 to 10.

30. A kit as claimed in claim 26 comprising:

A) a first component being a composition for the preparation of a first colon cleansing solution, the first component consisting essentially of:

(i) 52.5 to 187.5 g PEG having an average molecular weight of 2500 to 4500 Da; and

(ii) 1.5 to 15 g of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof;

(iii) one or more electrolytes;

(iv) one or more flavouring agents; and

(v) one or more sweeteners,

and

B) a second component being a composition optionally presented in two or more parts for the preparation of a second colon cleansing solution, the second colon cleansing solution being a solution as claimed in any one of claims 1 to 10.

31. A kit as claimed in any one of claims 26 to 30 which comprises:

A) a first sachet comprising a first composition for the preparation of the first cleansing solution;

B1) a second sachet;

B2) a third sachet;

wherein the second and third sachets together provide a composition for the preparation of the second cleansing solution.

32. A kit as claimed in claim 31 wherein:

A) the first sachet comprises:

(i) 52.5 to 187.5 g PEG having an average molecular weight of 2500 to 4500 Da;

(ii) 1.5 to 15 g of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof;

(iii) optionally one or more electrolytes;

(iv) optionally one or more flavouring agents;

(v) optionally one or more sweeteners,

B1) the second sachet comprises:

(i) 5 to 100g PEG having an average molecular weight of 2500 to 4500 Da;

(ii) optionally one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof;

(iii) electrolytes and/or one or more salts of ascorbic acid; and

B2) the third sachet comprises ascorbic acid,

the one or more salts of ascorbic acid in the second sachet (B1) and the ascorbic acid in the third sachet (B2) together providing 150 to 1000 mmol ascorbate anion.

33. A solution as claimed in any one of claims 1 to 10 for use in cleansing the colon of a subject in combination with a colon cleansing solution comprising:

(i) 130 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da; and

(ii) 8.0 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof.

34. A solution as claimed in any one of claims 1 to 10 for use in cleansing the colon of a subject in combination with a colon cleansing solution consisting essentially of water and:

(i) 130 to 250 g per litre PEG having an average molecular weight of 2500 to 4500 Da;

(ii) 8.0 to 20 g per litre of one or more alkali metal sulphates, alkaline earth metal sulphates or a mixture thereof;

(iii 1) 1.0 to 3.0 g/L sodium chloride;

(iii 2) 0.5 to 1.5 g/L potassium chloride;

(iv) one or more flavouring agents;

(v) one or more sweeteners.

35. A solution that is hyper-osmotic and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, for use in a method of cleansing the colon of a subject comprising:

- administering to the subject an effective amount of a first cleansing solution; and then after a time interval

- administering to the subject an effective amount of a second cleansing solution,

wherein the second cleansing solution is a solution as claimed in any one of claims 1 to 10, is hyper-osmotic and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and wherein the first cleansing solution is either substantially free from ascorbic acid and salts thereof, or contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, in an amount providing a lower concentration of ascorbate anion than is present in the second cleansing solution.

36. A solution as for use in a method as claimed in claim 35 wherein the first cleansing solution is a bowel content suspending agent.

37. A solution for use in a method as claimed in claim 35 or 36 wherein the first cleansing solution comprises polyethylene glycol and/or an alkali metal sulphate, an alkaline earth metal sulphate or a mixture thereof.

38. A solution for use in a method as claimed in any one of claims 35 to 37 wherein the first cleansing solution is substantially free from ascorbic acid and salts thereof.

39. A solution for use in a method as claimed in any one of claims 35 to 38 wherein the first and/or second cleansing solution further comprises one or more of:

a) one or more electrolytes;

b) one or more flavouring agents;

c) one or more sweeteners.

40. A solution for use in a method as claimed in any one of claims 35 to 39 wherein the combined volume of the first and second cleansing solutions is less than 2 litres.

41. A solution for use in a method as claimed in any one of claims 35 to 40 wherein the subject takes from 250ml up to 1000ml of the second cleansing solution.

42. A solution for use in a method as claimed in any one of claims 35 to 41 wherein first cleansing solution has a volume of 750ml and the second cleansing solution has a volume of 500ml.

43. A solution as for use in a method as claimed in any one of claims 35 to 42 wherein the measured osmolality of the first cleansing solution is in the range 200 to 1500 mOsmol/kg.

44. A solution as for use in a method as claimed in any one of claims 35 to 43 wherein the measured osmolality of the second cleansing solution is in the range 500 to 2000 mOsmol/kg.

45. A kit comprising:

- a first colon cleansing solution; and

- a second colon cleansing solution,

wherein the second colon cleansing solution is a solution as claimed in any one of claims 1 to 10, is hyper-osmotic and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and wherein the first colon cleansing solution is either substantially free from ascorbic acid and salts thereof, or contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, in an amount providing a lower concentration of ascorbate anion in the first colon solution than is present in the second colon cleansing solution.

46. A kit as claimed in claim 45 wherein the first and/or second solution is as described in any one of claims 35 to 44.

47. A kit as claimed in claim 45 or 46, for use in a method of cleansing the colon of a subject, said method comprising:

- the subject taking an effective amount of a first cleansing solution; and then after a time interval

- the subject taking an effective amount of a second cleansing solution.

48. A kit comprising:

a) a first component, being a composition for the preparation of a first colon cleansing solution by admixture with water; and

b) a second component, being a composition for the preparation of a second colon cleansing solution by admixture with water,

and instructions for use that specify the volume to which each component is to be made up with water,

wherein the second colon cleansing solution, when made up to the instructed specified volume with water, is a solution as claimed in any one of claims 1 to 10, is hyper-osmotic and contains ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof; and wherein the first colon cleansing solution is either substantially free from ascorbic acid and salts thereof, or contains, when made up to the instructed specified volume with water, ascorbic acid, one or more salts of ascorbic acid, or a mixture thereof, in an amount providing, a lower concentration of ascorbate anion in the first colon solution than in the second colon cleansing solution.

49. A kit as claimed in claim 48 wherein one or both of components a) and b) are dry powders.

50. A kit as claimed in claim 48 or 49 wherein the specified volume of water for each solution is less than one litre.

51. A kit as claimed in any one of claims 48 to 50 wherein the specified volume for the first component is 750ml.

52. A kit as claimed in any one of claims 48 to 51 wherein the specified volume for the second component from 500ml.

53. A kit as claimed in any one of claims 48 to 52 wherein the instructions specify that the first colon cleansing solution is ingested first followed, after a time interval, by ingestion of the second colon cleansing solution.

54. A kit as claimed in any one of claims 48 to 53 wherein the first and/or second component is each contained in one or more containers.

55. A kit as claimed in claim 54 wherein the second component is contained in more than one container.

56. A kit as claimed in claim 55 wherein the second component comprises both ascorbic acid and PEG and the ascorbic acid and PEG are contained in separate containers.

57. A kit as claimed in any one of claims 54 to 56 wherein each container is a sachet.

58. A kit as claimed in any one of claims 48 to 57 wherein the first component comprises one dose of the first colon cleansing solution, and the second component comprises one dose of the second colon cleansing solution.

59. A kit as claimed in any one of claims 48 to 58 comprising:

a) a first sachet comprising a first composition for the preparation of a first colon cleansing solution;

b) a second sachet;

c) a third sachet;

wherein the second and third sachets together provide a composition for the preparation of a second colon cleansing solution.

60. A kit as claimed in claim 59 wherein:

a) the first sachet comprises polyethylene glycol and/or sodium sulphate, optional flavouring and/or optional sweetener;

b) the second sachet comprises polyethylene glycol, and optionally further components including one or more selected from an alkali metal sulphate, an alkaline earth metal sulphate, or a mixture thereof, electrolytes, one or more salts of ascorbic acid, flavouring and sweetener; and

c) the third sachet comprises ascorbic acid and optionally one or more salts of ascorbic acid.