(11) Application No. AU 2003205868 B2

(19) AUSTRALIAN PATENT OFFICE

(54) Title

Improvements in or relating to compositions

(51)[6] International Patent Classification(s)

A61K 47/02 (2006.01) 0BMJP **A61K** 31/734 20060101ALI2005100

A61K 9/00 (2006.01) 8BMEP **A61K** 33/00 20060101ALI2005100

A61K 9/20 (2006.01) 8BMEP **A61K** 47/34 20060101ALI2005122

A61K 31/734 (2006.01) 0BMJP **A61K** 47/36 20060101ALI2005122

A61K 33/00 (2006.01) 0BMJP **A61P** 1/04 20060101ALI2006052

A61K 47/34 (2006.01) 1BMGB PCT/GB03/00593

A61K 47/36 (2006.01)

A61P 1/04 (2006.01)

A61K 47/02 20060101AFI2005122

0BMJP **A61K** 9/00 20060101ALI2005100

8BMEP **A61K** 9/20 20060101ALI2005122

(21) Application No: 2003205868 (22) Application Date: 2003.02.07

(87) WIPO No: WO03/068246

(30) Priority Data

(31) Number	(32) Date	(33) Country
0203269.6	2002.02.12	GB

(43) Publication Date : 2003.09.04

(43) Publication Journal Date : 2003.10.02

(71) Applicant(s)

Reckitt Benckiser Healthcare (UK) Limited

(72) Inventor(s)

Myrvold, Rolf; Dickson, Paul Andrew; Axford, Sophie Eugenie; Marshall, Paul; Jolliffe, Ian Gordon

(74) Agent/Attorney

FB Rice & Co, Level 23 44 Market Street, SYDNEY, NSW, 2000

(56) Related Art

WO 1995/11668 A

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 August 2003 (21.08.2003)

PCT

(10) International Publication Number
WO 03/068246 A3

(51) International Patent Classification[7]: A61K 31/734, 9/00, 9/48

(21) International Application Number: PCT/GB03/00593

(22) International Filing Date: 7 February 2003 (07.02.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0203269.6 12 February 2002 (12.02.2002) GB

(71) Applicant *(for all designated States except US)*: **RECKITT BENCKISER HEALTHCARE (UK) LIMITED** [GB/GB]; 103-105 Bath Road, Slough, Berkshire SL1 3UH (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **AXFORD, Sophie, Eugenie** [GB/GB]; 39 Redwing Close, Bicester, Oxfordshire OX26 6SR (GB). **DICKSON, Paul, Andrew** [GB/GB]; Reckitt Benckiser Healthcare (UK) Limited, Dansom Lane, Hull HU8 7DS (GB). **JOLLIFFE, Ian, Gordon** [GB/GB]; Reckitt Benckiser Healthcare (UK) Limited, Dansom Lane, Hull HU8 7DS (GB). **MYRVOLD, Rolf** [NO/NO]; Ovre Gjellum vei 28, N-1389 Heggedal (NO). **MARSHALL, Paul** [GB/GB]; 30 Donington Drive, Ashby-de-la-Zouch, Leicestershire LE65 2NT (GB).

(74) Agents: **HALL, Marina** et al.; Reckitt Benckiser PLC, Group Patents Department, Dansom Lane, Hull HU8 7DS (GB).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for all designations*
of inventorship (Rule 4.17(iv)) for US only

Published:

with international search report

(88) Date of publication of the international search report:
18 December 2003

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 03/068246 A3

(54) Title: IMPROVEMENTS IN OR RELATING TO COMPOSITIONS

(57) Abstract: A solid, ingestible composition comprising: a) an alginate; b) a bicarbonate and/or carbonate; and c) a C_2-C_5 polyol or poly (C_2-C_5 alkylene glycol).

IMPROVEMENTS IN OR RELATING TO COMPOSITIONS

Field of the Invention

The present invention relates to pharmaceutical compositions, and in particular to composition for the treatment of reflux oesophagitis, gastritis, dyspepsia or peptic ulceration or for use as a sustained releasing or targeted delivery compositions.

Background Art

Reflux oesophagitis occurs when small amounts of gastric juice, food and/or bile acids pass into the lower part of the oesophagus and cause oesophageal inflammation accompanied by pain which may manifest itself in the form of heartburn.

One approach to the problem of reflux oesophagitis has been to administer a preparation which on contact with gastric acid generates a carbonated gelatinous foam or raft which floats on the stomach contents. When reflux occurs it is this raft which precedes the stomach contents into the oesophagus, thus protecting the mucosa from further irritation. Known preparations of this type include liquid preparations comprising sodium alginate, sodium or potassium bicarbonate and calcium carbonate. Such compositions are sold under the trade marks GAVISCON and GAVISCON ADVANCE and are described in GB-A-1,524,740 and WO 95/11668.

Other such preparations are those in solid form, for example in the form of powders or tablets, such as those which again are sold under the trade mark GAVISCON. Such preparations comprise alginic acid, sodium bicarbonate

and calcium carbonate. The alginic acid and the bicarbonate and carbonate react in the aqueous environment of the mouth to form an alginate foam, which is then swallowed. In the acidic stomach environment the alginate is converted back into insoluble alginic acid, which then forms the raft on top of the stomach contents.

It has been found that solid compositions which foam in the mouth are difficult, and sometimes unpleasant, to swallow. In order to provide a non-foaming, solid composition we have tried to replace the alginic acid by an alginate. However, we have found that such compositions have extremely poor mouth feel. The alginate is sticky and causes the composition to stick to the palate, and especially to the teeth.

Any discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is solely for the purpose of providing a context for the present invention. It is not to be taken as an admission that any or all of these matters form part of the prior art base or were common general knowledge in the field relevant to the present invention as it existed before the priority date of each claim of this application.

Disclosure of the Invention

The present inventors have surprisingly found that the mouth feel and stickiness of such compositions can be improved by including a further component in the composition.

Throughout this specification the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

In one aspect, the present invention provides a solid, ingestible composition comprising:

a) an alginate;

b) a bicarbonate and/or carbonate; and

c) a C_2-C_5 polyol or poly (C_2-C_5 alkylene glycol) having a molecular weight of at least 6000.

The composition of the present invention has less foaming than the tablets currently sold under the trade mark GAVISCON since it comprises an alginate rather than alginic acid. It also has a good mouth feel and does not

stick to the teeth as much as a composition which does not comprise a polyol or polyalkylene glycol.

The composition of the present invention comprises an alginate. Any alginate may be used, but it is especially desirable to use an alkali metal salt of an alginate, such as sodium or potassium alginate. Preferably a low viscosity grade of the alginate is used. These are generally grades of alginate for which the viscosity of a 10% weight/volume aqueous solution, when determined on a Brookfield RVT viscometer using spindle number 3 at 20 r.p.m. at 20 °C, falls within the range of 200 to 1,500 mPa.s. An example of a suitable commercial grade of low viscosity sodium alginate is Protanal LFR 5/60, obtainable from FMC BioPolymer. High viscosity grades of alginate may also be used. These are generally grades alginate for which the viscosity of a 1% weight/volume aqueous solution, when determined on a Brookfield RVT viscometer using spindle number 3 at 20 r.p.m. at 20 °C, is above 500 mPa.s. An example of a suitable commercial grade of high viscosity sodium alginate is Protanal SF200, also obtainable from FMC BioPolymer

The compositions of the present invention generally have a content of alginate of from 2 to 90 wt%, preferably 5 to 50 wt%, based on the total weight of the composition.

The compositions of the present invention also comprise a bicarbonate and/or carbonate. Examples of bicarbonates are alkali metal bicarbonates such as sodium and potassium bicarbonate and alkaline earth metal

bicarbonates. One or two or more different bicarbonates may be used. Examples of carbonates are alkali metal carbonates such as sodium and potassium carbonate and alkaline earth metal carbonates such as calcium and magnesium carbonate. Further examples are aluminium carbonate and mixed alkali metal carbonates such as sodium glycine carbonate. One or two or more different carbonates may be used. Furthermore one or more bicarbonates may be used with one or more carbonates. Especially preferred combinations are sodium and/or potassium bicarbonate and calcium carbonate.

The carbonate and/or bicarbonate are present in amounts such that they provide an adequate volume of gas (carbon dioxide) to float the gel produced when the alginate contacts the gastric acid in the stomach. The rigidity and thickness of the carbonate raft will depend, for example, upon the relative amounts of carbonate and/or bicarbonate and on the grade of the alginate.

If used alone, the bicarbonate is generally present in the compositions of the present invention in an amount of from 1.5 to 35 wt%, preferably 2 to 15 wt%, most preferably 3 to 10 wt%. If used alone, the carbonate is generally present in the compositions of the present invention in an amount of from 0.2 to 55 wt%, preferably 0.5 to 10 wt%, most preferably 1 to 4 wt%.

Preferably the bicarbonate and carbonate may also be present together in the composition, preferably from 1 to 20 wt%, for example in a total amount of from 1 to 40 wt%,

preferably 1 to 12 wt%. Approximately equal amounts of the bicarbonate and carbonate may be present in the composition. Alternatively, the composition may comprise more bicarbonate than carbonate. The weight ratio of bicarbonate to carbonate in the composition may be from 1:1 to 2:1.

The compositions of the present invention also comprise a C_2-C_5 polyol or poly(C_2-C_5 alkylene glycol). Suitable polyols have 2, 3, 4 or 5 carbon atoms and contain 2 or more hydroxy groups, for example 2, 3, 4 or 5 hydroxy groups. Examples of suitable compounds are ethylene glycol, propylene glycol, glycerol and erythritol.

The poly(C_2-C_5 alkylene glycol) is preferably a polyethylene glycol or polypropylene glycol. The polyalkylene glycol may comprise any number of alkylene glycol units, for example having a molecular weight of at least 6000. Polyalkylene glycols may be liquid or solid at room temperature (20°C). It is preferred to use the solid form, particularly in the form of a free-flowing powder, for ease of handling and incorporation into the blend.

The polyol or poly(C_2-C_5 alkylene glycol) is generally present in the compositions of the present invention in an amount of from 1 to 50 wt%, preferably from 1 to 15 wt%, preferably 1.5 to 10 wt%, most preferably 2 to 6 wt%.

The polyol or poly(C_2-C_5 alkylene glycol) and the alginate may, for example, be present in the composition

of the present invention in a weight ratio of from 2:1 to 1:25, preferably from 1:4 to 1:12.5.

The compositions of the present invention may also comprise further, optional components.

For example, the compositions of the present invention preferably comprise a source of divalent and/or trivalent metal ions. Such ions strengthen the raft formed in the stomach. Suitable metal ions are calcium and aluminium. The ions may be provided as part of the bicarbonate and/or carbonate, but may also comprise other anions if desired. For example, suitable sources of calcium ions are calcium carbonate, lactate, chloride, gluconate, phosphate, hydrogen phosphate, sulfate, tartrate or citrate, and suitable sources of aluminium ions are aluminium carbonate, lactate, glycinate or phosphate, aluminium magnesium carbonate, hydroxide or magaldrate, aluminium sodium carbonate hydroxide or aluminium sodium silicate. If used, the calcium ions are preferably present in an amount of from 8 to 800 parts, and the aluminium ions are preferably present in an amount of from 2 to 500 parts, per 500 parts by weight of alginate.

The compositions of the present invention may also comprise a preservative to prevent contamination and subsequent deterioration by micro-organisms. Examples of suitable preservatives are methyl, ethyl, propyl and butyl para-hydroxybenzoates and their salts, which are preferably used in combinations, for example methyl and propyl or ethyl and butyl. The compositions of the present invention do not need to include such a preservative, but if a preservative is present it may be

used in an amount of, for example, up to 0.5 wt%, based on the total weight of the composition.

The compositions of the present invention may also comprise one or more colourings, sweetenings, flavourings, pH adjusting ingredients and fillers. When the compositions of the present invention are intended for use as sustained releasing compositions they will also comprise at least one active ingredient suitable for specific delivery to the stomach, such as a drug. Examples of suitable drugs are analgesics (e.g. sucacetaminophen, ibuprofen, naproxen, diclofenac, ketoprofen, choline salicylate, benzydamine, buprenorphine, hydrocortisone, betamethasone); decongestants (e.g. pseudoephedrine, phenylephrine, oxymetazoline, xylometazoline); cough suppressants (e.g. dextromethorphan, codeine, pholocodine); expectorants (e.g. guaiphenesin, n-acetylcysteine, bromhexine); antiseptics (e.g. triclosan, chloroxylenol, amylmetacresol, hexylresorcinol, dichlorobenzyl alcohol, benzyl alcohol); cardiovascular agents (e.g. glyceryl trinitrate); local anaesthetics (e.g. benzocaine, lignocaine); antacid agents (e.g. calcium carbonate, sodium bicarbonate, magnesium trisilicate, aluminium hydroxide, magaldrate,); antiulcer agents (e.g. carbenoxolone, sucralfate, cimetidine, ranitidine, nizatidine, famotidine, omeprazole, pantoprazole); antihistamines (e.g. loratidine, terfenadine, diphenhydramine, chlorphenhydramine, triprolidine, acrivastine); antinausea agents (e.g. prochlorperazine, sumatriptan); bowel regulatory agents (e.g. diphenoxylate, loperamide, sennosides); antifungal agents

(e.g. clotrimazole); antimicrobial agents and antibiotics (e.g. fusafungine, tyrothricin).

It is also possible for the compositions of the present invention to comprise alginic acid, although this is not preferred since it could cause undesirable foaming in the mouth.

The compositions of the present invention may be in any solid form. For example they may be in the form of a tablet, such as a chewable tablet. They may also be in the form of a chewable gum, a confectionary such as a fudge or boiled sweet or in the form of particles or granules, for example free-flowing or packed in a capsule, for example a soft or hard gel capsule.

The composition of the present invention may be used in a method of treatment of the human or animal body by therapy, especially use in the treatment of reflux oesophagitis, gastritis, dyspepsia or peptic ulceration or for use as a sustained releasing or targeted delivery composition.

The composition of the present invention may be used in the manufacture of a medicament for the treatment of reflux oesophagitis, gastritis, dyspepsia or peptic ulceration or for use as a sustained releasing or targeted delivery composition.

The composition of the present invention may be used in a method of treating reflux oesophagitis, gastritis, dyspepsia or peptic ulceration or for sustained releasing or targeting a delivery composition, which comprises

orally administering to a subject in need thereof or liable to need an effective amount of the composition.

The composition is generally administered in an amount of from 100 to 2000 mg alginate per dose.

The compositions of the present invention may be prepared by simply mixing the ingredients. It is especially preferred to mix the ingredients together in particulate form and then granulate or agglomerate the particles using a suitable granulating agent such as water, a C_2 to C_4 alcohol such as ethanol or isopropanol, or a mixture thereof. This is especially suitable when the PEG used is naturally a solid. It is also possible to granulate the remaining ingredients with PEG as a granulating agent when it is in liquid form. Additional granulating binders may also be used, for example povidone, a cellulose derivative such as HPMC or starch paste. A preferred starch paste uses water as the granulating solvent, and povidone is generally used with an ethanol or isopropanol solvent. We have surprisingly found that when a wet granulation is carried out, the amount of polyol or polyalkylene glycol can be reduced while retaining a satisfactory mouthfeel. A normal granulation process may need a weight ratio of polyol or polyalkylene glycol to aliginate of up to about 1:1. However, using a wet granulation process enables the weight ratio of polyol or polyalkylene glycol to alginate to be reduced to less than 0.25:1, especially less than 0.15:1, while retaining a satisfactory mouthfeel.

One or more of the components may be added after granulation. In particular the polyol or polyalkylene

glycol may be added after granulation, although this is not preferred since an increased amount of this component may be required to achieve a suitable mouth feel. It is preferred to avoid the use of excessive amounts of polyol or polyalkylene glycol since the amount of this component which can be ingested may be limited by regulatory authorities.

In a preferred process for preparing the composition of the present invention, the alginate, carbonate and/or bicarbonate and polyol or polyalkylene glycol are granulated together, dried and screened prior to mixing in any further components. It is also possible, for example, to granulate only the alginate and the polyol or polyalkylene glycol prior to adding the remaining components.

The present invention is further described in the following Examples.

EXAMPLES

EXAMPLE 1

The following particulate components (each having a maximum particle size of 1mm) were mixed together in a high shear mixer for 1 minute:

Sodium Alginate LFR 5/60	250g
Sodium bicarbonate	133.5g
Calcium carbonate	80g
PEG 20,000	30g

The mixture was then granulated in a granulator using 75ml distilled, deionised water as a granulating agent.

The granules were then dried in a fluid bed drier at 40°C for 20 minutes and subsequently milled firstly through a 610µm screen and secondly through a 457µm screen using a Quadro Comill. The milled granulate was then blended with the following ingredients in a low shear tumble blender for 5 minutes:

Mannitol	522.75g
Crospovidone (dispersant)	55g
Flavour 1	5.5g
Flavour 2	1.1g
Acesulfame K	5.5g
Aspartame	1.65g

Finally, 15g magnesium stearate was added to the blender, and blending was continued for a further 2 minutes.

The granules were then compressed into tablets each containing 250mg or 500mg sodium alginate. The tablets were found to have a smooth, slightly chewy texture with no significant toothpacking or gummy residue.

EXAMPLE 2

250 and 500 mg tablets were prepared following the procedure of Example 1 except for using the following components:

Sodium Alginate LFR 5/60	250g
Sodium bicarbonate	133.5g

Calcium carbonate	80g
PEG 20,000	30g
Mannitol	516.5g
Crospovidone	55g
Flavour	10g
Aspartame	10g
Magnesium stearate	15g

COMPARATIVE EXAMPLE 1 AND EXAMPLES 3 TO 7

A Comparative test was carried out to illustrate the beneficial effects of a polyalkylene glycol on the mouthfeel of a composition.

The following compositions were prepared:

	EXAMPLES					
Ingredient (mg)	Comparative 1	3	4	5	6	7
Protanal LFR 5/60	520	500	500	500	500	500
$NaHCO_3$	177	170	170	170	170	170
Mannitol	1178	950	600	950	1125	300
Mg-stearate	31	30	30	30	30	30
Kollidon 90F	104	-	-	-	-	-
PEG 20000	-	-	700	350	175	1000
PEG 3000	-	350	-	-	-	-
Total weight (mg)	2010	2000	2000	2000	2000	2000
PEG: Alginate	-	1:1.43	1:0.71	1:1.43	1:2.86	1:0.5
Mouthfeel	Very sticky in mouth + tooth-packing	Satisfac-tory for not sticking	Not sticking or tooth-packing. Slightly oily/creamy	Drying initially, slightly gritty. Then creamy. Not sticky	Creamy, not sticky	Quick disper-sing. Very clean in the mouth i.e.not sticky or tooth-packing

COMPARATIVE EXAMPLE 2 AND EXAMPLE 8

Tablets produced by the method set out below were then evaluated for their mouthfeel.

Ingredient	Example	
	Comparative 2	8
	mg/tablet	mg/tablet
Sodium alginate LFR5/60	250.00	250.00
Sodium bicarbonate	133.50	133.50
Calcium carbonate	80.00	80.00
Mannitol	607.75	432.75
Polyethylene Glycol 20000	0.00	175.00
Flavour 1	5.50	5.50
Flavour 2	1.10	1.10
Sweetener 1	5.50	5.50
Sweetener 2	1.65	1.65
Magnesium stearate	15.00	15.00
Tablet weight	1100mg	1100mg

Processing

Batch size produced 550g

1. Blend together ingredients except magnesium stearate for 5 minutes using a Turbula T2C tumble mixer.
2. Add the magnesium stearate and blend for a further 2 minutes.
3. Compress into tablets using the Riva Piccola tablet press fitted with 16mm FBE punches.

Tableting of the composition of Comparative Example 2 that did not contain PEG was poor, with evidence of lamination and capping.

The organoleptic properties of these tablets were assessed in the laboratory:

Example	Toothpacking	Mouthfeel	Taste	After taste	Overall
Example 8	Very slight	Drier, crisper. Tablet broke up quickly.	Pleasant, mint	None	OK - acceptable
Compara-tive 2	Worst of all batches	Drying, cloying pasty, chewy & sticky	Pleasant, mint	None	Poor - unacceptable

To check for raft formation properties and the appearance of the rafts, four crushed tablets (total 1g sodium alginate) were mixed with 20ml of water and poured into a 250ml beaker containing 150ml 0.1M HCl at 37°C. The ability to form a coherent foamy floating gel "raft" on the surface of the acid over 30 minutes was observed.

In both cases a floating raft was rapidly formed. This was continuous across the beaker surface and was resistant to rupture. No difference was observed between the two formulations.

Addition of PEG to the composition therefore has a significant effect on the mouthfeel of the product

without affecting the ability to form a reflux-suppressing raft.

EXAMPLE 9

Tablets containing the following components were prepared.

Sodium aliginate LFR5/60	250.00 mg
Sodium bicarbonate	133.50 mg
Calcium carbonate	80.00 mg
Mannitol	516.50 mg
Polyethylene Glycol 20000	30.00 mg
Crospovidone	55.00 mg
Mint Flavour	10.00 mg
Sweetener	10.00 mg
Magnesium stearate	15.00 mg
Tablet weight	1100 mg

Process

1. Granulate components

1.1 Add Sodium alginate LFR5/60, Sodium bicarbonate, Calcium carbonate, and Polyethylene Glycol 20000 to food processor Bowl (Magimix 3000 mixer fitted with large bowl).

1.2. Turn on processor and blend the powders for 2 minutes.

1.3 Granulate by spraying in water until a wet mass begins to form (approximately 70-110g water).

1.4 Dry the granules in a fluid bed drier (Aeromatic Strea 1) at 40°C inlet air temperature.

1.5 screen the dried granules using Quadro Comil mill fitted with a 457µm screen.

1.6 sieve the granules through a 850µm sieve

2. Tableting mix

2.1 Take the granules and the appropriate amount of the remaining ingredients except the magnesium stearate and tumble mix for 5 minutes.

2.2 Add the magnesium stearate and tumble mix for a further 2 minutes.

3. Tableting

3.1 Tablet the resulting tablet blend using the Riva Piccola bench top rotary tablet press fitted with 16mm FBE punches.

It was found that wet granulation of the components with the PEG enabled a reduced amount of PEG to be used as compared with the dry granulation of Example 8, while still retaining an acceptable mouthfeel.

Example 10

Tablets were prepared from the following compositions, using the process described in Example 9.

Sodium alginate LFR5/60 (sorbitol free)	500.00mg
Potassium bicarbonate, medium granular	100.00mg
Calcium carbonate	100.00mg
Polyethylene glycol 20,000	60.00mg
Mannitol	1260.00mg
Crospovidone	110.00mg
Mint flavour	20.00mg
Sweetener	20.00mg
Magnesium stearate	30.00mg
Total	2200.00mg

The tablets were produced to a weight of 500mg using 22mm flat bevel edge tooling.

These tablets gave satisfactory mouthfeel and raft formation and texture were at least as good as those of Example 9.

Example 11

Example 10 was repeated but using the following compositions:

Sodium Alginate LFR 5/60	250g
Sodium bicarbonate	133.5g
Calcium carbonate	80g
PEG 20,000	30g
Mannitol	571.5g
Mint flavour	10g

Sweetener	10g
Magnesium stearate	15g

The tablets produced were considered to have a better mouthfeel than those of Example 10, even though they did not contain Crospovidone.

Examples 12 to 17

Tablets were prepared from the following compositions:

Ingredient						
	12	13	14	15	16	17
	mg/ tablet	mg/ tablet	mg/ tablet	mg/ tablet	mg/ tablet	mg/ tablet
Sodium alginate LFR5/60	250.00	250.00	250.00	250.00	250.00	250.00
Sodium bicarbonate	50.00	250.00	50.00	133.00	133.00	50.00
Calcium carbonate	25.00	10.00	100.00	20.00	80.00	100.00
Polyethylene Glycol 20000	175.00	175.00	175.00	175.00	-	-
Polyethylene Glycol 3000	-	-	-	-	175.00	175.00
Crospovidone	1.10	1.10	1.10	1.10	1.10	1.10
Flavour	5.50	5.50	5.50	5.50	5.50	5.50
Sweetener	1.65	1.65	1.65	1.65	1.65	1.65
Magnesium stearate	15.00	15.00	15.00	15.00	15.00	15.00
Mannitol	Qs	qs	qs	qs	qs	qs
Tablet weight	1100mg	1100mg	1100mg	1100mg	1100mg	1100mg

Example 18

Tablets were prepared from the following compositions:

Ingredient	mg/tablet
Sodium alginate	500.00
Potassium bicarbonate	100.00
Calcium carbonate	100.00
Polyethylene glycol 20,000	60.00
Mannitol	1370.00
Flavouring	20.00
Sweetener	20.00
Magnesium Stearate	30.00
Total	2200.00

CLAIMS

1. A solid, ingestible composition comprising:
   a. an alginate;
   b. a bicarbonate and/or carbonate; and
   c. a C_2-C_5 polyol or poly(C_2-C_5 alkylene glycol) having a molecular weight of at least 6,000 and present in the composition in an amount of from 1 to 50 weight %.

2. A composition according to claim 1 wherein the polyalkylene glycol is polyethylene glycol (PEG).

3. A composition according to any one of the preceding claims wherein the alginate is sodium alginate.

4. A composition according to any one of the preceding claims wherein the bicarbonate is sodium bicarbonate.

5. A composition according to any one of the preceding claims wherein the carbonate is calcium carbonate.

6. A composition according to any one of the preceding claims which is in the form of a tablet.

7. A composition as defined in any one of the preceding claims for use in a method of treatment of the human or animal body by therapy.

8. A composition as defined in any one of claims 1 to 6 for use in the treatment of reflux oesophagitis, gastritis, dyspepsia or peptic ulceration or for use as a sustained releasing or targeted delivery composition.

9. Use of a composition as defined in any one of claims 1 to 6 in the manufacture of a medicament for the treatment of reflux oesophagitis, gastritis, dyspepsia or peptic ulceration or for use as a sustained releasing or targeted delivery composition.

10. Use of a composition s defined in any one of claims 1 to 6 for the treatment of reflux oesophagitis, gastritis, dyspepsia or peptic ulceration or for use as a sustained releasing or targeted delivery composition.

11. A method of treating reflux oesophagitis, gastritis, dyspepsia or peptic ulceration or for sustained releasing or targeting a delivery composition, which comprises orally administering to a subject in need thereof or liable to need an effective amount of a composition as defined in any one of claims 1 to 6.

12. A process for preparing a composition as defined in any one of claims 1 to 6 which comprises mixing together the alginate, the bicarbonate and/or carbonate and the polyol or polyalkylene glycol.

13. A process according to claim 12 wherein the components are granulated together in a wet granulation process.

14. A process according to claim 13 wherein the weight ratio of the polyol or polyalkylene glycol to the alginate is less than 0.25:1.

15. A solid, ingestible composition substantially as hereinbefore described with reference to any one of the Examples, excluding the Comparative Examples.

Dated this twenty sixth day of August 2004

Reckitt Benckiser Healthcare (UK) Limited
Patent Attorneys for the Applicant:

F B RICE & CO