



(86) Date de dépôt PCT/PCT Filing Date: 1992/12/04

(87) Date publication PCT/PCT Publication Date: 1993/06/24

(45) Date de délivrance/Issue Date: 2004/05/11

(85) Entrée phase nationale/National Entry: 1993/07/28

(86) N° demande PCT/PCT Application No.: US 1992/010491

(87) N° publication PCT/PCT Publication No.: 1993/011752

(30) Priorité/Priority: 1991/12/12 (806,581) US

(51) Cl.Int.⁵/Int.Cl.⁵ A61K 31/80, A61K 47/26, A61K 9/10

(72) Inventeurs/Inventors:

VALENTINE, WILLIAM, US;

VALENTINE, WILLIAM K., US

(73) Propriétaire/Owner:

ADVANCED TECHNOLOGY PHARMACEUTICALS

CORP., US

(74) Agent: OGILVY RENAULT

(54) Titre : COMPOSITION DE DEMOUSSAGE

(54) Title: DEFOAMING COMPOSITION

(57) **Abrégé/Abstract:**

A defoaming or antifoaming composition comprises a free flowing granular combinate of 50 to 90 weight percent of a water soluble carbohydrate-based agglomerate selected from the group consisting of maltodextrin agglomerates, maltodextrin/dextrose co-agglomerates, dextrose agglomerates; maltodextrin/sucrose co-agglomerates, maltodextrin/fructose co-agglomerates, sucrose agglomerates, fructose agglomerates, mannitol agglomerates, sorbitol agglomerates; agglomerates of hydrolyzed cereal solids, and agglomerates of corn syrup solids and about 10 to 50 weight percent of a liquid, non aqueous, defoaming or antifoaming composition such as simethicone, hydrocarbon-based oils or silicone oils. The composition may be combined with one or more suitable excipients and prepared as a unit dosage in the form of a compressed tablet, filled capsule, packet, or granule for various defoaming applications.

PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification	2101779	A1	(11) International Publication Number:	WO 93/11752
A61K 9/28, 9/14			(43) International Publication Date:	24 June 1993 (24.06.93)
(21) International Application Number: PCT/US92/10491 (22) International Filing Date: 4 December 1992 (04.12.92) (30) Priority data: 806,581 12 December 1991 (12.12.91) US (71) Applicant: VALENTINE ENTERPRISES, INC. [US/US]; 940 Collins Hill Road, Lawrenceville, GA 30243 (US). (72) Inventors: VALENTINE, William ; 667 New Hope Road, Lawrenceville, GA 30245 (US). VALENTINE, William, K. ; 732 Belmont Ridge Drive, Lawrenceville, GA 30243 (US).			(74) Agents: DELIO, Anthony, P. et al.; DeLio & Associates, 121 Whitney Avenue, New Haven, CT 06511 (US). (81) Designated States: CA, JP, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i>	

(54) Title: DEFOAMING COMPOSITION**(57) Abstract**

A defoaming or antifoaming composition comprises a free flowing granular combinate of 50 to 90 weight percent of a water soluble carbohydrate-based agglomerate selected from the group consisting of maltodextrin agglomerates, maltodextrin/dextrose co-agglomerates, dextrose agglomerates, maltodextrin/sucrose co-agglomerates, maltodextrin/fructose co-agglomerates, sucrose agglomerates, fructose agglomerates, mannitol agglomerates, sorbitol agglomerates, agglomerates of hydrolyzed cereal solids, and agglomerates of corn syrup solids and about 10 to 50 weight percent of a liquid, non aqueous, defoaming or antifoaming composition such as simethicone, hydrocarbon-based oils or silicone oils. The composition may be combined with one or more suitable excipients and prepared as a unit dosage in the form of a compressed tablet, filled capsule, packet, or granule for various defoaming applications.

-1-
DESCRIPTION

DEFOAMING COMPOSITION

5

Background of the Invention

1. Technical Field

This invention relates to a composition whereby fluid, nonaqueous, defoaming or antifoaming compositions
10 are prepared as relatively free flowing granular combines by intermixing them with a low density, highly porous, generally spherical, water soluble carbohydrate-based agglomerate such as maltodextrin to form adjuvant agglomerate combines suitable for addition to products
15 or processes wherever a rapid dispersion of the antifoaming or defoaming compound in an aqueous medium is indicated or desired.

2. Background Art

20 The following listing and characterization of fluid, nonaqueous, antifoaming or defoaming compositions or compounds used in the practice of this invention is given to more precisely and particularly illustrate applicable compositions and compounds. The listing is not meant to
25 limit or to specifically define the category of fluid, nonaqueous antifoaming or defoaming compositions, but rather to illustrate the scope of compositions applicable to the formation of the adjuvant agglomerate combines.

Fluid hydrocarbon oil-based antifoaming or defoaming
30 compositions containing a hydrocarbon-silicon copolymer, a hydrophobic filler, an organo-silicone surfactant, a hydrocarbon carrier oil, and, optionally, a silicone oil are disclosed in U.S. Patent No. 4,514,319 to Kulcarni et al.

35 Fluid antifoaming or defoaming compositions comprising mineral oil-containing dispersed hydrophobic solid particles are well known in the art. The use of hydrophobic silica in fluid hydrocarbon oil based

2101779

-2-

antifoam or defoaming compositions is disclosed in U.S. Patent Nos. 3,076,768; 3,207,698; 3,388,073; and 3,714,068.

Fluid antifoaming or defoaming compositions
5 comprising polyoxyethylene-polypropylene copolymers containing dispersed hydrophobic silica are disclosed in U.S. Patent Nos. 3,912,652 and 3,959,176.

Fluid antifoaming or defoaming compositions in a non-silicone oil and containing activated insitu
10 hydrophobic silica particles are disclosed in U.S. Patent No. 3,304,266.

Fluid antifoaming or defoaming compositions comprising a non-silicone water insoluble polyalkylene containing an alkoxysilicon chloride as the hydrophobic
15 agent are disclosed in G.B. Patent No. 1,166,877.

Fluid antifoaming or defoaming compositions employing the use of other intrinsically hydrophobic fillers in organic liquids are also well known. For example, Canadian Patent No. 508,856 discloses N,N'-distearyl
20 ethylene-diamide in white spirits, while the use of finely divided polyolefin polymers or polyesters dispersed in organic liquids is disclosed in U.S. Patent No. 3,705,859. The use of fatty acid salts is disclosed in G.B. Patent No. 1,267,482 and low molecular weight
25 polyethylenes in combination with mineral oil and conventional organic nonionic emulsifiers is disclosed in U.S. Patent No. 3,909,445.

Fluid antifoam or defoaming compositions comprising silicone oil-silica compounds containing organo silicone
30 compounds to improve performance are disclosed in U.S. Patent No. 3,691,091.

Fluid antifoam or defoaming compositions comprising the use of silicone-glycol copolymers in association with

-3-

silicone oil and silica are disclosed in U.S. Patent Nos. 3,746,653; 3,784,479; and 3,865,544.

Simethicone is a fluid antifoam or defoaming composition comprised of polydimethylsiloxane and silica
5 suitably purified for its intended application. The preparation of liquid methylsiloxane polymers is delineated in U.S. Patent No. 2,441,098, the disclosure of which is hereby incorporated by reference. The normal physical state of the simethicone is a water white to
10 grey translucent, viscous, oil-like liquid with a density of 0.965-0.970 grams/cubic centimeter having demonstrable immiscibility with water and alcohol.

The medically established therapeutic use for simethicone is as an ointment base ingredient, topical
15 drug vehicle, skin protectant, but most particularly as an antigas and antifatulent agent for human application as well as an antibloating agent for veterinary (animal) application. A combinate of simethicone and calcium silicate useful for such latter applications is disclosed
20 in U.S. Patent No. 4,906,478 to Valentine et al.

Various antigas or antifoam formulations, some containing simethicone, are disclosed in the prior art. The pharmaceutical and medicinal applications include U.S. Patent Nos. 4,605,551 to Buehler et al; 3,326,754 to
25 Prussin et al; 2,774,710 to Thompson et al; 4,115,553 to Rubino et al; 4,396,604 to Mitra; 3,767,794 to McVean et al; and 4,581,381 to Morris et al. Non-pharmaceutical and non-medicinal antifoaming applications, such as powdered cleaning agents, are disclosed in U.S. Patent
30 Nos. 3,843,558 to Farminer et al; 4,180,485 to Llenado; 4,264,465 to Abel; 4,102,823 to Matheson et al; and European Patent 213,953 to Iley et al.

The preferred pharmaceutical solid dose delivery system for simethicone is a chewable tablet. Such
35 chewable tablets often contain antacid ingredients such

2101779

-4-

as calcium carbonate, aluminum hydroxide, magnesium hydroxide and magnesium carbonate. The article by F. Maksond et al, "Simethicone use in Antacid Medications" as published in Manufacturing Chemist and Aerosol News, Vol. 47, No. 5, 1976, pp 36-36 discloses instability problems when simethicone is intermixed with aluminum or magnesium bases. It is extremely troublesome to distribute the oil-like, viscous, water and alcohol immiscible simethicone expeditiously and uniformly throughout a tablet granulation prior to compression. It is equally difficult to be certain that the simethicone is in a sufficiently divided and dispersed state so that its action will be quick and effective when administered per os as a chewable or swallowable tablet or powder filled capsule.

Similar problems are encountered in distributing the other anitfoaming compositions in an expeditious and uniform manner in their liquid form.

Bearing in mind the problems and deficiencies of the prior art, it is therefore an object of the present invention to provide an improved dry, granular combinate for dispersing liquid antifoaming or defoaming compounds in an aqueous medium.

It is another object of the present invention to provide an effective simethicone containing granule for use in gastric antacid, antigas, and/or antiflatulent formulations.

It is a further object of the present invention to provide granules to be added to aqueous based products or processes wherever antifoaming or defoaming is indicated or desired.

It is yet another object of the present invention to provide a facile method of producing an effective simethicone-containing foam controlling granule utilizing conventional equipment at relatively low cost.

It is a further object of the present invention to provide a free flowing simethicone containing granule for

2101779

-5-

use in conventional formulations which, after processing, retains acceptable defoaming activity.

It is yet another object of the present invention to provide an antifoaming or defoaming compound combine
5 which retains its properties and activity after extended storage and at elevated temperatures.

The present invention achieves these objects and satisfies the long felt need to overcome the difficulties in expeditious utilization of antifoaming or defoaming
10 compounds in an aqueous medium. A larger amount of antifoaming or defoaming compound can be incorporated with the carbohydrate-based agglomerate of this invention for dispersion than has previously been disclosed in the prior art. The carbohydrate-based agglomerate portion of
15 the combine makes it possible to effect rapid and uniform distribution of the antifoaming/defoaming compound by simple mixing.

Disclosure of Invention

20

The present invention relates to fluid, nonaqueous, antifoaming or defoaming compositions prepared as a dry, solid, flowable granule by intermixing a fluid, nonaqueous, antifoaming or defoaming compound or
25 composition and a low density, highly porous, generally spherical, water soluble, carbohydrate-based agglomerate such as a maltodextrin agglomerate, maltodextrin/dextrose co-agglomerate, dextrose agglomerate, maltodextrin/sucrose co-agglomerate, maltodextrin/fructose
30 co-agglomerate, sucrose agglomerate, fructose agglomerate, mannitol agglomerate, sorbitol agglomerate, agglomerated hydrolyzed cereal solids, agglomerated corn syrup solids, and combinations thereof to form a functional combine. The preferred agglomerate is
35 maltodextrin, a low conversion starch hydrolyzate having a D.E. (dextrose equivalent) less than 20. The fluid, nonaqueous, antifoaming or defoaming compound or

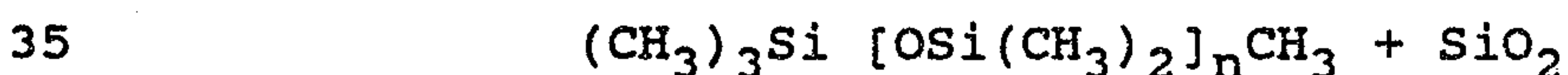
2101779

-6-

composition is added, in liquid form, to the water soluble carbohydrate agglomerate and blended to form a uniform, relatively free flowing combinate in which the base structure is water soluble. The combinate may be readily added to conventional products and processes where a rapid dispersion of the fluid, nonaqueous, antifoaming or defoaming compound is indicated. It is preferred that the fluid, nonaqueous, antifoaming or defoaming combinate have from about 10 to 50 weight percent antifoaming or defoaming composition or compound, and from about 90 to 50 weight percent carbohydrate agglomerate. It is more preferred that the fluid, nonaqueous, antifoaming or defoaming composition or compound represents 30 weight percent and the water soluble, highly porous, low density, generally spherical, carbohydrate agglomerate represents 70 weight percent of the admixture combinate. Unless otherwise specified, all references to percentages are in weight percent. The terms "antifoaming" and "defoaming" are generally used interchangeably throughout the specification. The antifoaming compositions or compounds useful in this invention may be any of those discussed in the background section of the specification, particularly simethicone (for pharmaceutical and medicinal applications) and silicone, mineral or other oils containing silica.

Modes for Carrying Out Invention

The preferred fluid, nonaqueous, antifoaming or defoaming compound prepared as a flowable granule used herein is simethicone and, more specifically, simethicone U.S.P. as defined in the United States Pharmacopeia, incorporated herein by reference, which has the chemical structure:



and the chemical formula:

-7-

Alpha(trimethylsilyl)-omega-methylpoly[oxy
(dimethylsilylene)] in mixture with silicon
dioxide.

5

Simethicone is a mixture of fully methylated linear
siloxane polymers containing repeating units of the
formula $[-(\text{CH}_3)_2\text{SiO-}]_n$, stabilized with
trimethylsiloxy end-blocking units of the formula
10 $[(\text{CH}_3)_3\text{SiO-}]$, and silicon dioxide. It is preferred
to contain not less than 90.5 percent and not more than
99.0 percent of polydimethylsiloxane ($[-(\text{CH}_3)_2\text{SiO-}]_n$),
and not less than 4.0 percent and not more
than 7.0 percent of silicon dioxide.

15 Maltodextrins are composed of water soluble glucose
polymers obtained from the reaction of starch with acid
and/or enzymes in the presence of water. The starch is
hydrolyzed to produce hydrolyzate products containing
sugars. The production of starch hydrolyzates, and, in
20 particular, low conversion starch hydrolyzates, is
described in U.S. Patent Nos. 3,663,369; 3,849,194;
4,298,400; and Re. 30,880, the disclosures of which are
hereby incorporated by reference. The starch used for
the preparation of maltodextrins can be any of a variety
25 of commercially available starches such as maize, potato,
or tapioca. Further, the U.S. Food and Drug Adminis-
tration defines maltodextrins, $(\text{C}_6\text{H}_{12}\text{O}_5)_n\text{H}_2\text{O}$,
as nonsweet nutritive saccharide polymers that consist of
D-glucose units linked primarily by alpha 1-4 bonds and
30 having a D.E. (total reducing sugars expressed as
dextrose equivalents) of less than 20.

Maltodextrin is usually produced as a fine, white
powder and is generally recognized as safe (gras) as a
direct human food ingredient at levels consistent with
35 good manufacturing practices. Agglomerated maltodextrin
is available from a variety of commercial sources and in

2101779

-8-

a larger, more porous, faster dissolving, and more free flowing form.

The preferred commercial source for low density, highly porous, generally spherical, water soluble maltodextrin agglomerates is the product family sold by Valentine Enterprises, Inc. of Lawrenceville, Georgia under the trademark VELite. The preferred VELite is VELite 20/40 which is prepared from 9-12 D.E. maltodextrin, derived from corn starch, and having the following typical analysis: a particle size distribution of about 100 percent less than 850 microns and a majority (98 percent) greater than 420 microns; an apparent density of from about 10 to about 12 pounds per cubic foot; a maximum moisture content of 6 percent; and a total surface area of between about 9.5 sq ft and 10.5 sq ft square meters per gram as determined by a 3 point nitrogen B.E.T. analysis.

A preferred embodiment of the present invention is directed toward the admixture of simethicone and maltodextrin agglomerate to form a uniform, relatively free flowing, granular combine containing 30 percent by weight of simethicone and 70 percent by weight maltodextrin for incorporation into tablets or for use "as is" for addition to an aqueous medium whenever antifoaming or defoaming is desired.

The 30 percent by weight simethicone/70 percent by weight agglomerated maltodextrin combine is readily formulated into, for example, antacid or antigas formulations by adding the 30% simethicone active granule combine to a compressible granule base without sacrificing or compromising the compressibility of the base granule. It is a further feature of the present invention that the simethicone is contained in or on a water soluble agglomerated maltodextrin and, as such, is available and stable in the formulations.

-9-

The process of the present invention may be practiced by obtaining desired quantities of agglomerated maltodextrin, such as VELite 20/40 available from Valentine Enterprises, Inc., and consumable simethicone, 5 such as Sentry simethicone available from Union Carbide Corporation. These two starting materials are then mixed employing low shear mixing such as that encountered in a planetary, ribbon or plow mixer in order to effect a uniform combinate agglomerate suitable for use without 10 further processing.

The relative amounts of the simethicone and the maltodextrin agglomerate may range from about 10 to about 50 weight percent simethicone and from about 90 to about 50 percent by weight of agglomerated maltodextrin. This 15 range of the ingredients has been found to provide optimum performance of the final simethicone/agglomerated maltodextrin combinate. If more than about 50% by weight percent simethicone is used, the product tends to be too moist and exhibits poor flow. If more than 90% by weight 20 of agglomerated maltodextrin is used the product tends to exhibit non-uniform distribution of the simethicone. Exceeding either extreme will tend to result in less than optimum product performance, most particularly in final tableting. A 30% by weight simethicone to 70% by weight 25 agglomerated maltodextrin ratio represents the preferred product performance whether for tableting or for general purpose aqueous antifoaming or defoaming application.

The combinate maltodextrin and the antifoaming or defoaming composition preferably has a particle size in 30 which essentially all of the particles are less than about 20 mesh (-20 mesh) and greater than 40 mesh (+40 mesh) and a total typical surface area of less than about 1 square meter per gram.

While not wishing to be limited to a particular 35 combinate formation theory, it is believed that sorption, i.e., absorption or adsorption, takes place during the

2101779

-10-

blending whereupon the liquid simethicone or other defoaming compound or composition (the sorbate) is taken up by the agglomerated maltodextrin or other carbohydrate (the sorbent). It is further theorized that the rapid
5 water solubility of the carbohydrate moiety of the combinate helps to explain the speed of action of the product since the simethicone or other defoaming compound is liberated in dispersed particles.

The antifoaming and/or defoaming containing adjuvant
10 combinate granules of the present invention have been found to be equal in foam inhibition and foam breaking to an equivalent quantity of the starting simethicone. This means, for example, that 66.7 mg of the 30% simethicone combinate granule is equivalent in performance to 20 mg
15 of simethicone. The equivalent performance is demonstrable even after the simethicone/agglomerated maltodextrin combines have been stored at 45°C for a period of two months.

Defoaming activity of the simethicone/agglomerated
20 maltodextrin combinate or of the monadic simethicone or of the simethicone/agglomerated maltodextrin combinate contained as part of an antacid and/or antigas tablet, i.e., foam breaking (defoaming) and/or foam inhibition (antifoaming), may be defined and measured by the
25 procedure given in the United States Pharmacopeia. First, a foaming solution and test preparation are prepared as follows:

Foaming solution - dissolve 1g of octoxynol 9 in 100 ml of distilled water.

30 Test preparation - transfer 200 mg of simethicone to a 60 ml bottle, add 50 ml of tertiary butyl alcohol, cap the bottle, and shake vigorously. The preparation may be warmed slightly, if necessary, to effect the solution.

The procedure for determining defoaming activity as follows: For each test, a clean, unused 250 ml glass jar fitted with a 50 mm cap should be employed. Add,

-11-

dropwise, 0.5 ml of the test preparation (i.e., equivalent to 2.0 mg simethicone) to the 250 ml glass jar containing 100 ml of the foaming solution. Cap the jar and clamp it in an upright position on a wrist action shaker. Employing a radius of 13.3 ± 0.4 cm (measured from the center of the shaft to the center of the bottle), shake for 10 seconds through an arc of 10° at a frequency of 300 ± 30 strokes per minute. Record the time required for the foam to collapse. The time, in seconds, for foam collapse is determined at the instant the first portion of foam-free liquid surface appears, measured from the end of the shaking period. This time is the defoaming activity time and should not exceed 15 seconds for acceptable simethicone activity. To evaluate the simethicone/maltodextrin agglomerate combine activity, a quantity of the combine equivalent to 2.0 mg of simethicone (i.e. 6.7 mg of a 30% simethicone/maltodextrin combine) is introduced directly into the test solution and the defoaming time is determined as described above.

There is no fixed quantity of simethicone, supplied by the simethicone/maltodextrin combine, which must be used to prepare an antacid/antigas preparation. A typical formulation would contain:

Aluminum hydroxide dried gel 200 mg

Magnesium hydroxide, dried 200 mg

Simethicone/maltodextrin combine 85 mg

Not only will the simethicone/maltodextrin agglomerate release the simethicone by virtue of the water solubility of the malt extrin moiety, but, when the combine is added to tablet granulations, no deleterious compression effects are evidenced. Whether or not the foam inhibition attributes of the simethicone/maltodextrin agglomerate combines are measured from the combine alone or combined with standard antacid ingredients, in tablet or granule form,

2101779

-12-

defoaming results are obtained which are equivalent to simethicone alone. Significantly, the same defoaming test results are evidenced even after accelerated storage stability at 37°C, and 60°C, for periods up to 2 months.

Therefore, the simethicone/agglomerated maltodextrin adjuvant combinate demonstrates itself as a uniquely stable product capable of being combined with antacid ingredients such as aluminum and magnesium bases in a single layer tablet without compromising the acid neutralizing or the defoaming or antifoaming capacity of the dose form.

Standard excipients can be combined with the simethicone/agglomerated maltodextrin combinate granules in order to prepare pharmaceutical preparations in the form of tablets or capsules. In order to prepare tablets, the simethicone/agglomerated maltodextrin combinate may be combined and blended with standard compression granules comprising, for example, calcium carbonate, dextrose, sucrose, mannitol, sorbitol, aluminum hydroxide dried gel, magnesium hydroxide, any compatible spray dried flavor, and magnesium stearate. The blended preparation may be pressed by standard, well known techniques to form tablets of desired weight, potency, and hardness. A single layer homogeneous unit dosage tablet or capsule may preferably contain from about 80 mg to about 280 mg of the simethicone/agglomerated maltodextrin combinate (i.e., from about 25 to about 80 mg of simethicone), but any desired amount outside this range may be used for specific applications.

A general ranking order of the water soluble carbohydrate agglomerate/simethicone U.S.P. combines, beginning with the most satisfactory, is as follows:

- maltodextrin agglomerate
- maltodextrin/dextrose co-agglomerate
- dextrose agglomerate
- maltodextrin/sucrose co-agglomerate

-13-

maltodextrin/fructose co-agglomerate
sucrose agglomerate
fructose agglomerate

Additionally, mannitol agglomerate, sorbitol
5 agglomerate, agglomerated hydrolyzed cereal solids, and
agglomerated corn syrup solids, i.e., those having a D.E.
of 20 or greater, may be employed. Any of these
agglomerates, either alone or in combination, may be
obtained, combined with simethicone, and utilized in the
10 same manner as described above for the embodiment
utilizing agglomerated maltodextrin alone. The combine
will preferably comprise at least about 50 weight
percent, and up to about 90 weight percent, of the
carbohydrate-based agglomerate. The particle size of
15 substantially all of the carbohydrate-based agglomerate
is preferably less than about 850 microns, with the
majority (up to about 98 wt.%) greater than about 420
microns.

The maltodextrin/dextrose, maltodextrin/sucrose and
20 maltodextrin/fructose co-agglomerates are preferably
prepared by well known fluid bed agglomeration techniques
in which maltodextrin in solution (e.g., a 10% aqueous
solution or 5% povidone (K 29/32) U.S.P. solution) is
combined with the dextrose, sucrose or fructose in an
25 agglomerator bed. The specific ratio of maltodextrin to
dextrose, sucrose or fructose may vary according to use,
and may be determined without undue experimentation. The
co-agglomerate is produced by standard spray granulation
techniques. The carbohydrate-based agglomerates will
30 preferably have a particle size range of less than 20
mesh and greater than 60 mesh (U.S. Standard), more
preferably less than 20 mesh and greater than 40 mesh.

Other antifoaming compositions or compounds useful in
this invention with maltodextrin or any of the other
35 aforementioned carbohydrate-based agglomerates may be any
of those organic liquid defoamers discussed in the
background section of the specification, including

2101779

-14-

hydrocarbon-based liquids, such as mineral oils and other hydrocarbon oil-based liquids, and silicone oils. These liquids may optionally contain silica. The carbohydrate-based agglomerate and liquid antifoaming composition may be mixed by low shear mixing techniques in a planetary, ribbon or plow mixer in order to effect a uniform combine agglomerate suitable for use without further processing. The combine will preferably comprise at least about 10 weight percent, and no greater than about 50 weight percent, of the liquid antifoaming composition. Lower amounts of liquid antifoaming composition may be employed, although there tends to be non-uniform distribution of the antifoaming agent in amounts less than about 10 wt.%. The particle size range of the combine is not substantially different from the particle size range of the carbohydrate-based agglomerate prior to mixing with the liquid antifoaming composition.

The combine of carbohydrate-based agglomerate and antifoaming or defoaming composition of the present invention may be used by contacting the aqueous medium in which defoaming is desired with the combine. In the case of simethicone for use in pharmaceutical or medicinal applications, the carbohydrate-based agglomerate/simethicone combine would be ingested by the user in tablet, capsule, granule or other unit dose form to provide antigas and/or antiflatulent treatment. In the case of other defoaming compositions or compounds, the combine may be prepared as granules in bulk filled packages or in unit dose forms such as compressed tablets or water soluble pouches for application to the aqueous medium.

Acid neutralizing capacity may be measured by the procedure set forth in the United States Pharmacopeia. The analytical procedure, to be conducted at $37^{\circ}\text{C} \pm 3^{\circ}\text{C}$, is as follows:

First, standardize a pH meter using 0.05M potassium biphthalate and 0.05M potassium tetraoxalate

2101779

-15-

standardizing buffers. Next, transfer 100 ml of water to a 250 ml beaker containing a 40 x 10 mm magnetic stirring bar that is coated with solid perfluorocarbon and has a spin ring at its center. The power setting of the magnetic stirrer should be adjusted to produce a stirring rate of 300 rpm when the stirring bar is centered in the beaker, as determined by a suitable optical tachometer.

The test preparations are prepared as follows:

10 powders - transfer the accurately weighed portion of the substance to be tested to a 250 ml beaker, add 70 ml of water, and mix in the magnetic stirrer for one minute. Tablets - weigh not less than 20 tablets and determine the average tablet weight. Grind the tablets to a powder

15 that passes through a no. 20 sieve and is retained on a 100 sieve. Mix the material on the no. 100 sieve to obtain a uniform mixture, transfer an accurately weighed quantity of it, equivalent to the minimum dosage, to a 250 ml beaker. If wetting is desired, add not more than

20 5ml of alcohol (neutralized to an apparent pH of 3.5), and mix to wet the specimen thoroughly. Add 70 ml of water, and mix on the magnetic stirrer for one minute.

The test procedure is as follows: Pipet 30.0 ml of 1.0 N hydrochloric acid vs into the test preparation

25 prepared earlier while continuing to stir with the magnetic stirrer. Magnetic stirring should continue for 15 minutes (accurately timed) after the addition of the acid. Thereafter, begin to titrate immediately, in a period not to exceed 5 minutes, the excess hydrochloric

30 acid with 0.5 N sodium hydroxide vs to attain a stable pH of 3.5 for not less than 15 seconds. Calculate the number of mEq of acid consumed per gram of the substance tested. Each ml of 1.0 N hydrochloric acid is equal to 1 mEq of acid consumed.

2101779

-16-

EXAMPLES

The following illustrative examples are given to more precisely and particularly illustrate the specific details of the present invention. Equivalent procedures and quantities will occur to those skilled in the art and therefore, the following examples are not meant to define the limits of the present invention, these being defined by the scope of the appended claims.

10

Example 1

Starting Materials:

Simethicone U.S.P.

(Sentry simethicone) 40 g

15 Agglomerated Maltodextrin

(VELite 20/40) 160 g

The VELite 20/40 was charged into a 1000 cc stainless steel beaker and the simethicone was added. The total materials were blended with a spatula until uniform. The resulting granular combinate was lump free, less than 850 microns (20 mesh) in size, and contained 20% simethicone.

A portion of the sample was used to prepare chewable antacid tablets containing 125 mg of the simethicone/agglomerated maltodextrin combinate per tablet (equivalent to 25 mg of simethicone per tablet).

25

Example 2

Starting materials:

Simethicone U.S.P.

30 (Sentry simethicone) 300 g

Agglomerated maltodextrin

(VELite 20/40) 700 g

The VELite 20/40 was charged into a 5000 ml stainless steel beaker and the simethicone was added. The total materials were blended with a spatula until uniform. The resulting granular combinate was lump free, less than 850 microns (20 mesh) in size and contained 30% simethicone.

35

-17-

A portion of the sample was used to prepare chewable antacid tablets containing 84 mg of the simethicone/agglomerated maltodextrin combinate per tablet (equivalent to 25 mg simethicone per tablet).

5

Example 3

Starting materials:

Simethicone U.S.P.

(Sentry simethicone) 400 g

10 Agglomerated maltodextrin

(VELite 20/40) 600 g

VELite 20/40 was charged into a 5000 ml stainless steel beaker and the simethicone was added. The total materials were blended with a spatula until uniform. The
15 resulting granular combinate was lump free, less than 850 microns (20 mesh) in size and contained 40% simethicone.

A portion of the sample was used to prepare chewable antacid tablets containing 63 mg of the simethicone/agglomerated maltodextrin combinate per
20 tablet (equivalent to 25 mg of simethicone per tablet).

Example 4

Starting materials:

Simethicone U.S.P.

25 (Sentry simethicone) 1.5 kg

Agglomerated maltodextrin

(VELite 20/40) 3.5 kg

VELite 20/40 was charged into a 5 gallon stainless steel Hobart mixer and the simethicone was added. The mixer
30 was energized and mixing was effected for a period of 10 minutes. The resulting granular combinate was found to be lump free, less than 850 microns (20 mesh) in size, and contained 30% simethicone.

A portion of the product was used to prepare chewable
35 antacid tablets containing 84 mg of the simethicone/agglomerated maltodextrin combinate per tablet (equivalent to 25 mg of simethicone per tablet).

2101779

-18-

Example 5

Starting materials:

Simethicone U.S.P.

5 (Sentry simethicone) 30 kg

Agglomerated maltodextrin

(VELite 20/40) 70 kg

VELite 20/40 was charged into a 20 cubic foot capacity ribbon blender and the simethicone was added. 10 The mixer was energized and mixing was effected for a period of 10 minutes. The resulting granular combinate was discharged into drums and found to be lump free, less than 850 microns (20 mesh) in size, and contained 30% simethicone.

15 A portion of the product was used to prepare chewable antacid tablets containing 84 mg of the simethicone/agglomerated maltodextrin combinate per tablet (equivalent to 25 mg of simethicone per tablet).

20

Example 6

Starting materials:

Simethicone U.S.P.

(Sentry simethicone) 3.0 kg

Agglomerated maltodextrin

25 (VELite 20/40) 7.0 kg

VELite 20/40 was charged into a 3 cubic foot capacity stainless steel Lodige blender and the simethicone was added. The plow blades of the mixer were energized and mixing effected for a period of 10 minutes. The 30 resulting granular combinate was discharged into a drum and found to be lump free, less than 850 microns (20 mesh) in size, and contained 30% simethicone.

A portion of the product was used to prepare chewable antacid tablets containing 84 mg of the simethicone/ 35 agglomerated maltodextrin combinate per tablet (equivalent to 25 mg of simethicone per tablet).

2101779

-19-

Example 7

Starting materials:

Simethicone U.S.P.

(Sentry simethicone)

90 kg

Agglomerated maltodextrin

(VELite 20/40)

210 kg

VELite 20/40 was charged into a 1200 l stainless steel Lodige blender and the simethicone added. The plow blades of the mixer were energized and mixing was effected for a period of 10 minutes. The resulting granular combinate was discharged into drums and found to be lump free, less than 850 microns (20 mesh) in size, and contained 30% simethicone.

A portion of the product was used to prepare chewable antacid tablets containing 84 mg of the simethicone/agglomerated maltodextrin combinate per tablet (equivalent to 25 mg of simethicone per tablet).

Example 8

Each of the simethicone/maltodextrin combines produced in Examples 1-7 were evaluated in the following manner:

A quantity of the simethicone/agglomerated maltodextrin combines were evaluated in the standard U.S.P. defoaming test at a level equivalent to 2 mg of simethicone.

<u>Example No.</u>	<u>Quantity of the Combine Used</u> (mg)	<u>Simethicone Equivalent</u> (mg)	<u>Time to Defoam</u> (sec.)
1	10.0	2	3-4
2	6.7	2	3-4
3	5.0	2	3-4
4	6.7	2	3-4
5	6.7	2	3-4
6	6.7	2	3-4
7	6.7	2	3-4
Controls-			
Simethicone U.S.P	2.0	2	3-4
Simethicone U.S.P (as 30% emulsion)	6.7	2	3-4

2101779

-20-

The data suggests that equivalent quantities of simethicone derived from either the simethicone/maltodextrin combines or from the simethicone U.S.P. or from the commercial 30% silicone emulsion demonstrate equivalent defoaming action.

Stability samples stored for periods up to 2 months at 37°C and 45°C evidence no change in defoaming times and are unchanged in physical appearance.

It is observed that when the simethicone/agglomerated maltodextrin combines (Examples 1-7) are added to water at a level calculated to liberate 100 mg of simethicone, the maltodextrin moiety dissolves in the water and the silicone forms a surface oil layer.

Example 9

Each of the simethicone/agglomerated maltodextrin combines produced in Examples 1-7 were evaluated in a typical chewable antacid tablet formulation as follows (all values in mg):

	<u>EX.1</u>	<u>EX.2</u>	<u>EX.3</u>	<u>EX.4</u>	<u>EX.5</u>	<u>EX.6</u>	<u>EX.7</u>
Compression							
Dextrose	661	702	723	702	702	702	702
Aluminum							
Hydroxide							
Dried Gel	200	200	200	200	200	200	200
Magnesium							
Hydroxide							
Powder	200	200	200	200	200	200	200
Simethicone/ Maltodextrin Combine							
Equivalent to 25 mg of Simethicone	125	84	63	84	84	84	84
Spray Dried							
Flavor	5	5	5	5	5	5	5
Magnesium							
Stearate	9	9	9	9	9	9	9

Each of the formulations were produced as single layer 9/16 inch, flat-faced, beveled edge chewable tablets, compressed at a weight of 1200 mg and a hardness

-21-

of 7-9 Kp. Tablets without simethicone were also produced under the same conditions to serve as a control.

All of the tablets produced for the trials satisfied the criteria for taste acceptance, mouth feel, hardness, friability, and acid neutralization.

Each of the tablet formulations were evaluated for defoaming in accordance with the U.S.P. method for antacid tablets with the following results:

Test Storage Condition:	<u>Initial</u>	<u>45° for 2 Months</u>
Tablets produced with Simethicone/Malto- dextrin Combine From:	<u>Time to Defoam (In Seconds)</u>	<u>Time to Defoam (In Seconds)</u>
EX.1	5-7	5-7
EX.2	5-7	5-7
EX.3	5-7	5-7
EX.4	5-7	5-7
EX.5	5-7	5-7
EX.6	5-7	5-7
EX.7	5-7	5-7
Control	No Defoaming	No Defoaming

After storage at 45°C for a period of two months all of the tablets still satisfied the acid neutralization criteria for extra strength antacid tablets.

Example 10

Calcium carbonate-based antacid tablets were prepared with and without simethicone/agglomerated maltodextrin combine as follows (all values in mg):

Formula:	<u>With Combine</u>	<u>Without Combine</u>
Calcium Carbonate		
Compression Granules		
(53% Calcium Carbonate		
47% Dextrose)	1000	1000
Compression Dextrose	104	188
Simethicone/Agglomerated		
Maltodextrin Combine		
From Example #7	84	- -
Spray Dried Flavor	3	3
Magnesium Stearate	9	9

2101779

-22-

Each of the formulations were processed into single layered 9/16 inch, flat faced, beveled edge chewable tablets compressed at a weight of 1200 mg and a hardness of 7-9 Kp.

Each of the chewable tablet formulations produced for the trials satisfied the criteria for chewable tablets with respect to taste acceptance, mouth feel, hardness, friability, and acid neutralization.

Each of the chewable tablet formulations were evaluated for defoaming in accordance with the U.S.P. method for antacid tablets with the following results:

	<u>Defoaming Time</u>
Formulation With Combinate	4-6 sec.
Formulation Without Combinate	No Defoaming

Example 11

Magaldrate (aluminum magnesium hydrate with magnesium sulfate) based antacid tablets were prepared with and without simethicone/agglomerated maltodextrin combinate as follows (all values in mg):

<u>Formula</u>	<u>With Combinate</u>	<u>Without Combinate</u>
Dextrose Compression Granules	702	786
Magaldrate	400	400
Simethicone/Agglomerated Maltodextrin Combinate From Example 7	84	---
Spray Dried Flavor	5	5
Magnesium Stearate	9	9,

Both of the formulations were processed into single layered 9/16 inch, flat-faced, beveled edge chewable antacid tablets at a weight of 1200 mg and a hardness of 7-9 Kp.

2101779

-23-

The chewable antacid tablets produced for the trials, i.e., with and without the simethicone/agglomerated maltodextrin combinate, satisfied the criteria for taste acceptance, mouth feel, hardness, friability, and acid neutralization.

Each of the formulations were evaluated for defoaming in accordance with the U.S.P. method for antacid tablets with the following results:

Defoaming Time

10

Formulation With Combinate	4-6 sec.
Formulation Without Combinate	No Defoaming

Example 12

15 An antigas chewable tablet formulation was prepared to demonstrate the utility of simethicone/agglomerated maltodextrin combinate in such an application as follows (all values in mg):

20 Compression Dextrose	946
-------------------------	-----

Simethicone/Agglomerated Maltodextrin Combinate From Example 7	240
--	-----

25

Spray Dried Flavor	5
--------------------	---

Magnesium Stearate	9,
--------------------	----

30 The formulation was produced as a single layered 9/16 inch, flat-faced, beveled edged chewable tablet compressed at a weight of 1200 mg and a hardness of 7-9 Kp.

35 The tablets produced satisfied the criteria for taste acceptance, mouth feel, hardness, friability, and foam suppression.

2101779

-24-

Example 13

To further illustrate the utility of the invention, a general standard fluid silicone oil defoamer/ agglomerated maltodextrin combinate was prepared:

Starting Materials Used:

Fluid Silicone Oil
10 Containing Silica 1.05 kg

Agglomerated Maltodextrin
(VELite 20/40) 2.45 kg

15 The VELite 20/40 was charged into a 5 gallon stainless steel Hobart mixer and the fluid silicone oil containing silica added. The mixer was energized and mixing was effected for a period of 10 minutes. The resulting granular combinate was lump free, less than 850 microns (20 mesh) in size and
20 contained 30% of the fluid silicone oil containing silica defoaming compound.

The above described combinate demonstrated satisfactory antifoaming/defoaming properties when subjected to the standard U.S.P. defoaming test.

25

Example 14

To further illustrate the utility of the invention, a general standard fluid mineral oil defoamer/agglomerated maltodextrin combinate was prepared as follows:

30

Starting Materials Used:

Fluid Mineral Oil
Containing Silica 1.05 kg

35

-25-

Agglomerated Maltodextrin
(VELite 20/40)

2.45 kg

5 The VELite 20/40 was charged into a 5 gallon stainless steel Hobart mixer and the fluid mineral oil containing silica added. The mixer was energized and mixing was effected for a period of 10 minutes. The resulting granular combinate was lump free, less than 850 microns (20 mesh) in size and
10 contained 30% of the fluid silicone oil containing silica defoaming compound.

The above described combinate demonstrated satisfactory antifoaming/defoaming properties when subjected to the standard U.S.P. defoaming test.

15 The following Examples illustrate the use of other water soluble carbohydrate-based agglomerates in combination with simethicone.

Example 15

20 A granular or agglomerated product comprised of dextrose monohydrate 95% and maltodextrin (10 D.E.) 5% was obtained from Corn Products Corporation under the trademark Unidex 2034. The Unidex product had a particle size range of -20/+60 mesh and an apparent bulk density of 0.58 g/cc.

25 Sample products were prepared by adding simethicone U.S.P. to the Unidex dextrose monohydrate/maltodextrin mixture in the following amounts, followed by 10 minute mixing to produce relatively free flowing Unidex product/simethicone combines:

30	<u>1</u>	<u>2</u>	<u>3</u>
Unidex 2034			
(-20/+60 Mesh)	80% w/w	70% w/w	60% w/w

2101779

-26-

Sentry Simethicone U.S.P.

(Union Carbide)

20% w/w 30% w/w 40% w/w

The Unidex product/simethicone U.S.P. combines
5 evidenced rapid defoaming characteristics, i.e., 2 seconds
by the U.S.P. test.

Standard antacid tablets containing 200 mg of aluminum
hydroxide, 200 mg of magnesium hydroxide, and 25 mg of
simethicone, in the form of the Unidex product/
10 simethicone combinate, also evidenced satisfactory
defoaming characteristics when tested by the U.S.P.
defoaming method, i.e. 6-8 seconds.

Example 16

15 Dextrose monohydrate-maltodextrin agglomerates were
prepared by fluid bed agglomeration as follows:

In the fluid bed agglomerator bed:

Dextrose Monohydrate 95%
(Clintose 'F' Granulation,
20 Archer Daniels Midland)

In aqueous solution:

Maltodextrin, 10 D.E. 5%
(Maltrin M-100,
25 Grain Processing Corporation)

The dextrose monohydrate-maltodextrin co-agglomerate
was processed by standard spray granulation techniques to
produce an agglomerate for sorption trials. After
30 processing, the agglomerated dextrose-maltodextrin
particles had a particle size range of about -20/+60 mesh
and an apparent density of 0.42 g/cc.:

Sample products were prepared by adding the
simethicone U.S.P. to the agglomerated dextrose-

2101779

-27-

maltodextrin in the following amounts (percentages by weight):

	<u>1</u>	<u>2</u>	<u>3</u>
Dextrose/maltodextrin			
5 Co-agglomerate (-20/+60 Mesh)	80%	70%	60%
Sentry Simethicone U.S.P. (Union Carbide)	20%	30%	40%

10 The samples were mixed for 10 minutes to produce relatively free flowing simethicone/dextrose-maltodextrin agglomerate combines.

The agglomerated dextrose-maltodextrin/simethicone combines evidenced rapid defoaming characteristics,
15 i.e., 2 seconds by the U.S.P. defoaming test.

Standard single layer antacid tablets containing 200 mg of aluminum hydroxide, 200 mg of magnesium hydroxide, and 25 mg of simethicone, in the form of the dextrose agglomerate/simethicone U.S.P. combine, evidenced rapid
20 defoaming characteristics, i.e. 6-8 seconds by the U.S.P. defoaming test.

Example 17

Sucrose-maltodextrin co-agglomerates were prepared by
25 fluid bed agglomeration as follows:

In fluid bed agglomerator bed:

Milled sucrose (-50 Mesh) 95%

In pump solution:

30 Maltodextrin, 10 D.E.
(as 10% aqueous solution) 5%

The sucrose-maltodextrin co-agglomerate was effected by standard spray granulation techniques to produce an
35 agglomerate for sorption trials. After processing, the

2101779

-28-

sucrose-maltodextrin particles had a particle size range of about -20/+60 mesh and an apparent density of 0.45 g/cc.

Sample products were prepared by adding simethicone U.S.P. to the sucrose-maltodextrin co-agglomerates in the following amounts:

	<u>1</u>	<u>2</u>	<u>3</u>
Sucrose-maltodextrin			
10 co-agglomerate			
(-20/+60 Mesh)	80%	70%	60%
Sentry Simethicone U.S.P.			
(Union Carbide)	20%	30%	40%

15

The samples were mixed for 10 minutes to produce relatively free flowing simethicone/sucrose-maltodextrin agglomerate combinates.

The agglomerated sucrose-maltodextrin/simethicone combinates evidenced rapid defoaming characteristics, i.e., 2 seconds by the U.S.P. defoaming test.

Standard single layer chewable antacid tablets containing 200 mg aluminum hydroxide, 200 mg magnesium hydroxide, and 25 mg of simethicone in the form of the sucrose-maltodextrin co-agglomerate/simethicone combinate, also evidenced satisfactory defoaming characteristics when tested by the U.S.P. defoaming method, i.e., 6-8 seconds.

30

Example 18

Sucrose 10x-maltodextrin co-agglomerates were prepared by fluid bed agglomeration as follows. Sucrose 10X is a widely available finely milled sucrose which contains 2% corn starch to assure free-flow:

35

-29-

In fluid bed agglomerator bed:

Sucrose 10x 95%

In pump solution:

5 Maltodextrin, 10 D.E. 5%
(as aqueous solution)

The sucrose 10X-maltodextrin co-agglomerate was effected by standard spray granulation techniques to produce an agglomerate for sorption trials. After processing, the agglomerated sucrose 10X-maltodextrin particles had a particle size range of about -20/+60 mesh and an apparent density of 0.40 g/cc.

Sample products were prepared by adding the simethicone U.S.P. to the sucrose 10X-maltodextrin co-agglomerate in the following amounts:

	<u>1</u>	<u>2</u>	<u>3</u>
Sucrose 10X-maltodextrin			
Co-agglomerate (-20/+60 Mesh)	80%	70%	60%
Sentry Simethicone U.S.P.			
(Union Carbide)	20%	30%	40%

The samples were produced by mixing for 10 minutes to produce relatively free flowing simethicone/sucrose 10X-maltodextrin agglomerate combinates.

The agglomerated sucrose 10X-maltodextrin/simethicone U.S.P. combinates evidenced rapid defoaming characteristics, i.e. 2 seconds by the U.S.P. defoaming test.

Example 19

Dextrose monohydrate-maltodextrin co-agglomerates were prepared by fluid bed agglomeration as follows:

2101779

-30-

In fluid bed agglomerator bed:

Dextrose monohydrate 42.5%

Maltodextrin, 10 D.E. 42.5%

In pump solution:

5 Maltodextrin, 10 D.E. 5.0%
(in aqueous solution)

The dextrose monohydrate-maltodextrin co-agglomerate was effected by standard spray granulation techniques to produce an agglomerate for sorption trials. After processing, the dextrose-maltodextrin co-agglomerate particles had a particle size range of about -20/+60 mesh and an apparent density of 0.30 g/cc.

Sample products were prepared by adding the simethicone U.S.P. to the dextrose-maltodextrin co-agglomerate in the following amounts:

	<u>1</u>	<u>2</u>	<u>3</u>
Dextrose-maltodextrin			
Co-agglomerate (-20/+60 Mesh)	80%	70%	60%
Sentry simethicone U.S.P. (Union Carbide)	20%	30%	40%

The samples were produced by mixing for 10 minutes to produce relatively free flowing simethicone/dextrose-maltodextrin co-agglomerate combines.

The agglomerated dextrose-maltodextrin/simethicone U.S.P. combines evidenced rapid defoaming characteristics, i.e. 2 seconds by the U.S.P. defoaming test.

Standard single layer chewable antacid tablets containing 200 mg of aluminum hydroxide, 200 mg of magnesium hydroxide and 25 mg of simethicone, in the form of agglomerated dextrose-maltodextrin/simethicone U.S.P. combines, evidenced rapid defoaming characteristics, i.e. 6-8 seconds by the U.S.P. defoaming test.

2101779

-31-

Example 20

Sucrose-maltodextrin co-agglomerates were prepared by fluid bed agglomeration as follows:

In fluid bed agglomerator bed:

5	Sucrose 10X	42.5%
	Maltodextrin, 10 D.E.	42.5%

In pump solution:

	Maltodextrin, 10 D.E.	5.0%
10	(in aqueous solution)	

The sucrose-maltodextrin co-agglomerate was effected by standard spray granulation techniques to produce an agglomerate for sorption trials. After processing, the
15 sucrose-maltodextrin co-agglomerate particles had a particle size range of about -20/+60 mesh and an apparent density of 0.32 g/cc.

Sample products were prepared by adding simethicone U.S.P. to the sucrose-maltodextrin co-agglomerates in the
20 following amounts:

	<u>1</u>	<u>2</u>	<u>3</u>
Sucrose-maltodextrin co-agglomerate (-20/+60 Mesh)	80%	70%	60%
25 Sentry Simethicone (Union Carbide)	20%	30%	40%

The samples were produced by mixing for 10 minutes to
30 produce relatively free flowing simethicone/sucrose-maltodextrin co-agglomerate combinates.

The sucrose-maltodextrin co-agglomerate/simethicone combinates evidenced rapid defoaming characteristics, i.e. 2 seconds by the U.S.P. defoaming test.

2101779

-32-

Standard single layer chewable antacid tablets containing 200 mg of aluminum hydroxide, 200 mg of magnesium hydroxide and 25 mg of simethicone, in the form of the sucrose 10X-maltodextrin/simethicone combinate, 5 evidenced rapid defoaming characteristics, i.e. 6-8 seconds by the U.S.P. defoaming test.

Example 21

Dextrose monohydrate-maltodextrin co-agglomerates were 10 prepared as in Example 19 except that the pump solution was 5% povidone (K 29/32) U.S.P.

Similar trial products were prepared and similar results were observed as in Example 19.

15

Example 22

Sucrose-maltodextrin co-agglomerates were prepared as in example 20 except that the pump solution was 5% povidone (K 29/32) U.S.P.

Similar trial products were prepared and similar 20 results were observed as in example 20.

Example 23

Fructose-maltodextrin co-agglomerates were prepared by fluid bed agglomeration as follows:

25

In fluid bed agglomerator bowl:

Fructose (powder)	50%
Maltodextrin, 10 D.E.	47.5%

In pump solution:

30

Maltodextrin, 10 D.E.	
(as 10% water solution)	2.5%

2101779

-33-

A fructose-maltodextrin co-agglomerate was effected by standard spray granulation techniques to produce an agglomerate for sorption trials. After processing, the fructose-maltodextrin co-agglomerate particles had a particle size range of about -20+60 mesh and an apparent density of 0.42 g/cc.

Sample products were prepared by adding simethicone U.S.P. to the fructose-maltodextrin agglomerates in the following amounts:

	<u>1</u>	<u>2</u>	<u>3</u>
Fructose/maltodextrin co-agglomerate (-20/+60 Mesh)	80%	70%	60%
Sentry Simethicone U.S.P. (Union Carbide)	20%	30%	40%

The samples were produced by mixing for 10 minutes to produce relatively free flowing simethicone/fructose-maltodextrin co-agglomerate combines.

The co-agglomerated fructose-maltodextrin/simethicone combines evidenced rapid defoaming characteristics, i.e. 2 seconds by the U.S.P. defoaming test.

Single layer chewable antacid tablets containing 200 mg of aluminum hydroxide, 200 mg of magnesium hydroxide and 25 mg of simethicone, in the form of the fructose-maltodextrin/simethicone U.S.P. combine, evidenced rapid defoaming characteristics, i.e. 6-8 seconds by the U.S.P. defoaming test.

While the invention has been described with reference to specific embodiments, it will be recognized by those skilled in the art that variations are possible without

2101779

-34-

departing from the spirit and scope of the invention, and that it is intended to cover all changes and modifications of the invention disclosed herein for the purposes of illustration which do not constitute
5 departure from the spirit and scope of the invention.

Having thus described the invention, what is claimed is:

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. An antifoaming or defoaming composition comprising a dry, uniform, free flowing granular combinate of a water soluble carbohydrate-based agglomerate and a liquid, nonaqueous, antifoaming or defoaming composition selected from the group consisting of hydrocarbon-based oils and silicone oils, wherein said carbohydrate-based agglomerate is selected from the group consisting of maltodextrin/dextrose co-agglomerates, dextrose agglomerates, maltodextrin/sucrose co-agglomerates, maltodextrin/fructose co-agglomerates, sucrose agglomerates, fructose agglomerates, mannitol agglomerates, sorbitol agglomerates, agglomerates of hydrolyzed cereal solids and agglomerates of corn syrup solids having a D.E. of at least 20.

2. The composition of claim 1, wherein said carbohydrate-based agglomerate is selected from the group consisting of dextrose agglomerates, sucrose agglomerates, fructose agglomerates, mannitol agglomerates, sorbitol agglomerates, agglomerates of hydrolyzed cereal solids, and agglomerates of corn syrup solids having a D.E. of at least 20.

3. The composition of claim 1, wherein said liquid antifoaming or defoaming composition is taken up by the agglomerated carbohydrate particles by sorption.

4. The composition of claim 1, wherein said combinate is comprised of one or more carbohydrate-based agglomerates having a particle size of less than about

850 microns with a majority greater than about 420 microns.

5. The composition of claim 1, wherein said combinate further includes one or more excipients.

6. The composition of claim 1, comprising about 50 to 90 weight percent carbohydrate-based agglomerate and about 10 to 50 weight percent liquid antifoaming or defoaming composition.

7. The composition of claim 1, wherein said liquid antifoaming or defoaming composition comprises a hydrocarbon-based oil.

8. The composition of claim 1, wherein said liquid antifoaming or defoaming composition comprises mineral oil.

9. The composition of claim 1 wherein said liquid antifoaming or defoaming composition comprises silicone oil.

10. The composition of claim 1, wherein said liquid, nonaqueous, antifoaming or defoaming composition is a silicone oil containing silica in an amount up to about 50 weight percent of the composition.

11. The composition of claim 1, wherein said liquid, nonaqueous, antifoaming or defoaming composition is a hydrocarbon-based oil containing silica in an amount up to about 50 weight percent of the composition.

12. An antifoaming or defoaming composition comprising a dry, uniform, free flowing granular combinate of at least about 50 weight percent water soluble carbohydrate-based agglomerate selected from the group consisting of maltodextrin/dextrose co-agglomerates, dextrose agglomerates, maltodextrin/sucrose co-agglomerates, maltodextrin/fructose co-agglomerates, sucrose agglomerates, fructose agglomerates, mannitol agglomerated sorbitol agglomerates, agglomerates of hydrolyzed cereal solids, and agglomerates of corn syrup solids having a D.E. of least 20, substantially having a particle size of less than about 850 microns and simethicone in an amount up to about 50 weight percent.

13. The composition of claim 12, wherein said simethicone is taken up by the agglomerated carbohydrate-based particles by sorption.

14. The composition of claim 12, comprising about 50 to 90 weight percent carbohydrate-based agglomerate and about 10 to 50 weight percent simethicone.

15. The composition of claim 12, wherein said combinate further includes one or more excipients.

16. The composition of claim 12, wherein said combinate is prepared as a unit dose compressed tablet, capsule, or granule.

17. The composition of claim 12, wherein said water soluble carbohydrate-based agglomerate is selected from the group consisting of maltodextrin/dextrose co-

agglomerates, maltodextrin/sucrose co-agglomerates, and maltodextrin/fructose co-agglomerates.

18. The composition of claim 12, wherein said water soluble carbohydrate-based agglomerate is selected from the group consisting of dextrose agglomerates, sucrose agglomerates, fructose agglomerates, mannitol agglomerates, sorbitol agglomerates, agglomerates of hydrolyzed cereal solids, and agglomerates of corn syrup solids having a D.E. of at least 20.

19. An antifoaming or defoaming composition consisting essentially of a dry, uniform, free flowing granular combinate of: 1) a water soluble carbohydrate-based agglomerate selected from the group consisting combinations of maltodextrin with dextrose, sucrose or fructose, and 2) a liquid, nonaqueous, antifoaming or defoaming composition selected from the group consisting of hydrocarbon-based oils containing silica and silicone oils containing silica in an amount up to about 50 weight percent of the composition.

20. The composition of claim 19, wherein said combinate is comprised of one or more carbohydrate-based agglomerates having a particle size of less than about 850 microns with a majority greater than about 420 microns.

21. The composition of claim 19, comprising about 50 to 90 weight percent carbohydrate-based agglomerate and about 10 to 50 weight percent liquid antifoaming or defoaming composition.

22. An antifoaming or defoaming composition consisting essentially of a dry, uniform, free flowing granular combinate of at least about 50 weight percent water soluble carbohydrate-based agglomerate selected from the group consisting of maltodextrin/dextrose co-agglomerates, maltodextrin/sucrose co-agglomerates, and maltodextrin/fructose co-agglomerates, substantially having a particle size of less than about 850 microns and simethicone in an amount up to about 50 weight percent.

23. An antifoaming or defoaming composition consisting essentially of: 1) a dry, uniform, free flowing granular combinate of a water soluble carbohydrate-based agglomerate selected from the group consisting of maltodextrin/dextrose co-agglomerates, dextrose agglomerates, maltodextrin/sucrose co-agglomerates, maltodextrin/fructose co-agglomerates, sucrose agglomerates, fructose agglomerates, mannitol agglomerates, sorbitol agglomerates of hydrolyzed cereal solids, and agglomerates of corn syrup solids having a D.E of a least 20; and 2) an antifoaming or defoaming composition comprising silicone oil.

24. The composition of claim 23, wherein said antifoaming or defoaming composition comprises silicone oil containing silica.

25. The composition of claim 23, wherein said combinate comprised of one or more carbohydrate-based agglomerates having a particle size of less than about 850 microns with a majority greater than about 420 microns.

26. The composition of claim 23, comprising about 50 to 90 weight percent carbohydrate-based agglomerate and about 10 to 50 weight percent liquid antifoaming or defoaming composition.

27. A process for producing an antifoaming or defoaming combinate, comprising mixing a water soluble carbohydrate-based agglomerate selected from the group consisting of maltodextrin/dextrose co-agglomerates, dextrose agglomerates, maltodextrin/sucrose co-agglomerates, maltodextrin/fructose co-agglomerates, sucrose agglomerates, fructose agglomerates, mannitol agglomerates sorbitol agglomerates, agglomerates of hydrolyzed cereal solids and agglomerates of corn syrup solids having a D.E. of at least 20, with a liquid, nonaqueous, antifoaming or defoaming composition selected from the group consisting of hydrocarbon-based oils, mineral oils and silicone oils to form a dry, uniform, free flowing granular combinate.

28. The process of claim 27, wherein said carbohydrate-based agglomerate is selected from the group consisting of dextrose agglomerates, sucrose agglomerates, fructose agglomerates, mannitol agglomerates, sorbitol agglomerates, agglomerates of hydrolyzed cereal solids, and agglomerates of corn syrup solids having a D.E. of at least 20.

29. The process of claim 27, wherein said liquid antifoaming or defoaming composition is taken up by the carbohydrate-based agglomerate particles by sorption.

30. The process of claim 27, wherein said combinate is comprised of one or more carbohydrate-based agglomerates having a particle size of less than about 850 microns with a majority greater than about 420 microns.

31. The process of claim 27, further including the step of blending one or more excipients with said combinate.

32. The process of claim 27, comprising mixing about 50 to 90 weight percent carbohydrate-based agglomerate and about 10 to 50 weight percent liquid antifoaming or defoaming composition.

33. The process of claim 27, wherein said liquid antifoaming or defoaming composition comprises a hydrocarbon-based oil.

34. The process of claim 27, wherein said liquid antifoaming or defoaming composition comprises mineral oil.

35. The process of claim 27, wherein said liquid antifoaming or defoaming composition comprises silicone oil.

36. The process of claim 27, wherein said liquid, nonaqueous, antifoaming or defoaming composition is a silicone oil containing silica in an amount up to about 50 weight percent of the composition.

37. The process of claim 27, wherein said liquid, nonaqueous, antifoaming or defoaming composition is a hydrocarbon-based oil containing silica in an amount up to about 50 weight percent of the composition.

38. A process for producing an antifoaming or defoaming combinate, comprising mixing at least about 50 weight percent of a water soluble carbohydrate-based agglomerate selected from the group consisting of maltodextrin/dextrose co-agglomerates, dextrose agglomerates, maltodextrin/sucrose co-agglomerates, maltodextrin/fructose co-agglomerates, sucrose agglomerates, fructose agglomerates, mannitol agglomerates, sorbitol agglomerates, agglomerates of hydrolyzed cereal solids, and agglomerates of corn syrup solids having a D.E. of at least 20, substantially having a particle size of less than 850 microns with simethicone in an amount up to about 50 weight percent to form a dry, uniform, free flowing granular combinate.

39. The process of claim 38, wherein said simethicone is taken up by the carbohydrate-based agglomerate particles by sorption.

40. The process of claim 38, further including the step of blending one or more excipients with said combinate.

41. The process of claim 38, comprising mixing about 50 to 90 weight percent carbohydrate-based agglomerate and about 10 to 50 weight percent simethicone.

42. The process of claim 38, further including the step of preparing said combinate as a unit dose compressed tablet, capsule, or granule.

43. The process of claim 38, wherein said water soluble carbohydrate-based agglomerate is selected from the group consisting of maltodextrin/dextrose co-agglomerates, maltodextrin/sucrose co-agglomerates, and maltodextrin/fructose co-agglomerates.

44. The process of claim 38, wherein said water soluble carbohydrate-based agglomerate is selected from the group consisting of dextrose agglomerates, sucrose agglomerates, fructose agglomerates, mannitol agglomerates, sorbitol agglomerates, agglomerates of hydrolyzed cereal solids, and agglomerates of corn syrup solids having a D.E. of at least 20.

45. A process for producing an antifoaming or defoaming combinate consisting essentially of mixing a water soluble carbohydrate-based agglomerate selected from the group consisting of combinations of maltodextrin with dextrose, sucrose or fructose, with a liquid, nonaqueous, antifoaming or defoaming composition selected from the group consisting of hydrocarbon-based oils containing silica and silicone oils containing silica in an amount up to about 50 weight percent of the composition to form a dry, uniform, free flowing granular combinate.

46. The process of claim 45, wherein said combinate is comprised of one or more carbohydrate-based agglomerates having a particle size of less than about

850 microns with a majority greater than about 420 microns.

47. The process of claim 46, comprising about 50 to 90 weight percent carbohydrate-based agglomerate and about 10 to 50 weight percent liquid antifoaming or defoaming composition.

48. A process for producing an antifoaming or defoaming combinate consisting essentially of mixing at least about 50 weight percent of a water soluble carbohydrate-based agglomerate selected from the group consisting of maltodextrin/dextrose co-agglomerates, maltodextrin/sucrose co-agglomerates, and maltodextrin/fructose co-agglomerates, substantially having a particle size of less than 850 microns with simethicone in an amount up to about 50 weight percent to form a dry, uniform, free flowing granular combinate.

49. A process for producing an antifoaming or defoaming combinate consisting essentially of mixing a water soluble carbohydrate-based agglomerate selected from the group consisting of maltodextrin/fructose co-agglomerates, dextrose agglomerates, maltodextrin-sucrose co-agglomerates, maltodextrin/fructose co-agglomerates, sucrose agglomerates, fructose agglomerates, mannitol agglomerates, sorbitol agglomerates, agglomerates of hydrolyzed cereal solids, and agglomerates of corn syrup solids having a D.E of at least 20 with a liquid, nonaqueous, antifoaming or defoaming composition comprising silicone oil to form a dry, uniform, free flowing granular combinate.

50. The process of claim 49, wherein said antifoaming or defoaming composition comprises silicone oil containing silica.

51. The process of claim 49, wherein said combinate is comprised of one or more carbohydrate-based agglomerates having a particle size of less than about 850 microns with a majority greater than about 420 microns.

52. The process of claim 49, comprising about 50 to 90 weight percent carbohydrate-based agglomerate and about 10 to 50 weight percent liquid antifoaming or defoaming composition.

53. A method of defoaming an aqueous medium comprising contacting said aqueous medium with an antifoaming or defoaming composition comprising a dry, uniform, free flowing granular combinate of a water soluble carbohydrate-based agglomerate and a liquid, nonaqueous, antifoaming or defoaming composition selected from the group consisting of hydrocarbon-based oils and silicone oils, wherein said carbohydrate-based agglomerate is selected from the group consisting of maltodextrin/dextrose co-agglomerates, dextrose agglomerates, maltodextrin/sucrose co-agglomerates, maltodextrin/fructose co-agglomerates, sucrose agglomerates, fructose agglomerates, mannitol agglomerates, sorbitol agglomerates, agglomerates of hydrolyzed cereal solids and agglomerates of corn syrup solids having a D.E. of at least 20.

54. The method of claim 53, wherein said carbohydrate-based agglomerate is selected from the group consisting of dextrose agglomerates, sucrose agglomerates, fructose agglomerates, mannitol agglomerates, sorbitol agglomerates, agglomerates of hydrolyzed cereal solids, and agglomerates of corn syrup solids having a D.E. of at least 20.

55. The method of claim 53, wherein said liquid, nonaqueous, antifoaming or defoaming composition is selected from the group consisting of hydrocarbon-based oils containing silica and silicone oils containing silica.

56. The method of claim 55, wherein said liquid, nonaqueous, antifoaming or defoaming composition is a silicone oil containing silica.

57. The method of claim 55, wherein said liquid, nonaqueous, antifoaming or defoaming composition is a hydrocarbon-based oil, containing silica.

58. A method of defoaming an aqueous medium comprising contacting said aqueous medium with an antifoaming or defoaming composition comprising a dry, uniform, free flowing granular combinate of at least about 50 weight percent water soluble carbohydrate-based agglomerate selected from the group consisting of maltodextrin/dextrose co-agglomerates, dextrose agglomerates, maltodextrin/sucrose co-agglomerates, maltodextrin/fructose co-agglomerates, sucrose agglomerates, fructose agglomerates, mannitol agglomerates, sorbitol agglomerates, agglomerates of

hydrolyzed cereal solids, and agglomerates of corn syrup solids having a D.E. of at least 20, substantially having a particle size of less than about 850 microns and simethicone in an amount up to about 50 weight percent.

59. The method of claim 58, wherein said combinate further includes one or more excipients.

60. The method of claim 58, wherein said combinate is in the form of a unit dose compressed tablet, capsule, or free flowing granules.

61. Use of an antifoaming or defoaming composition of an antifoaming or defoaming composition for treating flatulence, wherein said antifoaming or defoaming composition comprises a dry, uniform, free flowing granular combinate of at least about 50 weight percent water soluble carbohydrate-based agglomerate selected from the group consisting of maltodextrin/dextrose co-agglomerates, dextrose agglomerates, maltodextrin/sucrose co-agglomerates, maltodextrin/fructose co-agglomerates, sucrose agglomerates, fructose agglomerates, mannitol agglomerates, sorbitol agglomerates, agglomerates of hydrolyzed cereal solids, and agglomerates of corn syrup solids having a D.E of at least 20, substantially having a particle size of less than about 850 microns and simethicone in an amount up to about 50 weight percent.