

Description

This invention relates to a medicament adsorbate which contains a complex magnesium aluminum silicate having sorbed therein a medicament drug and a surfactant.

The use of complex magnesium aluminum silicate has been taught in the literature as a method to render bitter drug principles tasteless in liquid, tablet and chewable dosage forms which become bioavailable when the adsorbate reaches the low pH acid media of the stomach.

U.S. Patent 3,337,402 to Zentner discloses the formation of a sedative composition using 7-chloro-1-methyl-5-phenyl-3H-1,4-benzodiazepin-2(1H)-one adsorbed on a complex magnesium aluminum silicate. Zentner notes that when the drug is first dissolved in a lower molecular weight monohydroxy aliphatic alcohol or in an aqueous alcohol mixture and then mixed with a complex magnesium aluminum silicate, the bitter taste and anesthetizing effect on the tongue associated with the drug is reduced or eliminated. Zentner also discloses that the adsorbate may be mixed with other ingredients to form lozenges, tablets, candies, capsules and suspensions.

U.S. Patent 3,567,819 to Idson, et al. discloses the formation of a decongestant composition using phenylpropanolamine hydrochloride adsorbed on a complex magnesium aluminum silicate. The objectionable taste of phenylpropanolamine hydrochloride is reduced or eliminated when the drug is first placed in solution and then mixed with complex magnesium aluminum silicate to form an adsorbate. The adsorbate is then dried and used to prepare a chewable multilayered tablet.

A procedure for preparing a good tasting medicament adsorbate which may contain up to about 35% by weight medicament compound has been unexpectedly discovered.

This has been achieved by sorbing a solution of medicament drug and surfactant into a complex magnesium aluminum silicate to form a mass which when dried is an essentially tasteless medicament adsorbate.

According to the present invention there is provided a medicament adsorbate which comprises: complex magnesium aluminum silicate having sorbed therein a solution of medicament drug and a surfactant.

In particular, it has been found that an essentially tasteless medicament adsorbate is produced by sorbing from 1% to 35% by weight of a medicament drug and from 0.05% to 4% by weight of a surfactant from a solution which has been admixed with a complex magnesium aluminum silicate sorbent to form a mass. The mass is dried to form an essentially tasteless adsorbate.

While the invention is not to be limited to theoretical considerations, it is believed that the presence of a surfactant in the sorbate solution permits deeper and more complete penetration of the sorbate solution into the sorbent. The surfactant acts by reducing the surface tension of sorbate solution thereby permitting the solution to wet and penetrate the sorbent. This effectively increases the interstitial sorbent surface area in contact with the medicament drug. The increased surface area and penetration of the sorbent by the medicament drug and surfactant solution results in the formation of an essentially tasteless medicament adsorbate.

The medicament and surfactant may be added to the sorbent as a single solution or as separate solutions. The sorbent may be added to the medicament and surfactant solution or to individual solutions of medicament and surfactant. The order of addition of the components of the adsorbate is not critical. It is critical, however, that the resultant mass of sorbent, solvent, medicament and surfactant be mixed thoroughly until uniform. This may be accomplished by pouring, spraying or related techniques known in the art.

It is believed that the sorbing of the medicament-surfactant solution into the complex magnesium aluminum silicate renders the medicament not available for organoleptic taste prior to passage into the digestive tract and subsequent desorption by the gastric fluid and enzymes. The taste masking sorption effect of this invention is superior to the taste masking found when a medicament drug is adsorbed merely from aqueous, organic or mixed solvents onto a complex magnesium aluminum silicate.

In the practice of the present invention, the complex magnesium aluminum silicate is a standard article of commerce. The typical average chemical analysis of complex magnesium aluminum silicate, conventionally expressed as oxides, may be represented as follows:

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	Percent by weight	Ratio to aluminum oxide	
5	Silicon dioxide	55 to 70	3.2 to 35
	Magnesium oxide	2.9 to 25	0.17 to 12.5
	Aluminum oxide	2.0 to 17	1
10	Ferric oxide	0.4 to 1.8	
	Calcium oxide	1.1 to 2.4	
15	Sodium oxide	1.0 to 3.8	
	Potassium oxide	0.2 to 1.9	
	Ignition loss	5.5 to 12.6	

In a preferred embodiment of the invention, the complex magnesium aluminum silicate has the following typical chemical analysis:

	Percent by weight	Ratio to aluminum oxide
25	Silicon dioxide	56 to 59 14.0 to 29.5
	Magnesium oxide	21 to 24 5.2 to 12.0
30	Aluminum oxide	2.0 to 4.0 1
	Ferric oxide	0.4 to 0.6
35	Calcium oxide	1.1 to 1.5
	Sodium oxide	2.5 to 3.5
	Potassium oxide	0.5 to 1.0
40	Ignition loss	5.5 to 12.6

The complex magnesium aluminum silicate of this invention is present in an amount from 70 to 90 percent by weight of the final adsorbate complex and more preferably from 75 to 85 percent.

It has been found that the particle size of the complex magnesium aluminum silicate is not critical in preparing the adsorbates of this invention. While not essential the average particle size of the complex magnesium aluminum silicate may range from about 10 to about 150 μ m. Such products have been found suitable to sorb sufficient quantities of the medicament-surfactant solution to prepare acceptable product.

Any solvent may be used in the inventive process to prepare the adsorbate providing it is capable of dissolving the medicament drug and surfactant. Representative solvents include water; polyhalogenated lower hydrocarbons such as chloroform, methylene chloride, ethylene chloride and the like; lower alcohols, such as methanol, ethanol, propanol, isopropanol, butanol and the like; aromatic solvents such as benzene and toluene, with water being the preferred solvent.

The medicament drugs used herein may be selected from a wide variety of drugs and their acid addition salts. Neutral compounds as well as organic and inorganic salts may be used provided the drug maintains its medicament value and is soluble in the solvent. Exemplary acid salts include hydrochloride, hydrobromide, orthophosphate, benzoate, maleate, tartrate, succinate, citrate, salicylate, sulfate and acetate.

The weight percent of the drug or its acid addition salt thereof based on the weight of the adsorbate is preferably from 1% to 30%, and most preferably 5% to 25%, which amounts will vary depending upon the therapeutic dosage permitted.

The medicament drug may be selected from a wide range of unpleasant tasting therapeutic agents and mixtures of therapeutic agents. Nonlimiting illustrative categories and specific examples include:

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- (a) Analgesics, such as acetaminophen, ibuprofen, phenacetin, and salicylamide;
(b) Antiasmatics, such as aminophylline, metaproterenol, epinephrine, and theophylline;
(c) Antitussives, such as dextromethorphan, dextromethorphan hydrobromide, noscapine, carbetapentane citrate, and chlorphedianol hydrochloride;
5 (d) Antihistamines, such as chlorpheniramine maleate, phenindamine tartrate, pyrillamine maleate, doxylamine succinate, phenyltoloxamine citrate, diphenhydramine hydrochloride, promethazine, and triprolidine;
(e) Antinauseants, such as dimenhydrinate, and meclizine;
(f) Decongestants, such as phenylephrine hydrochloride, phenylpropanolamine hydrochloride,
10 pseudoephedrine hydrochloride, ephedrine;
(g) Various alkaloids, such as codeine phosphate, codeine sulphate and morphine;
(h) Laxatives, such as phenolphthalein, danthron, pamabrom and bisocadyl;
(i) Anti-cholesterolemic and anti-lipid agents such as gemfibrozil;
(j) Appetite suppressants such as phenylpropanolamine hydrochloride, and caffeine;
15 (k) Central nervous system stimulants such as nicotine;
(l) Expectorants such as guaifenesin;
(m) Anti-inflammatory agents such as isoxicam, meclophenamic acid and naproxen; and
(n) Nutritional supplements, including vitamins and minerals, such as niacin, pantothenic acid, vitamin
B6, thiamine hydrochloride, riboflavin, potassium iodide, potassium chloride, cupric sulfate, and ferrous
20 sulfate.

Medicaments may be used alone or in combination within the ranges specified above to form the adsorbate.

In a preferred embodiment the medicament is the expectorant guaifenesin.

A surfactant is a surface active substance and as used herein is an organic compound consisting of two
25 parts: a hydrophobic portion, and a hydrophilic portion which renders the compound sufficiently soluble or dispersible in water or another polar solvent. The combined hydrophobic and hydrophilic portions render the compound surface-active and thus able to concentrate at the interface between a surfactant solution and another phase such as a solid sorbent. Surfactants function to allow solutions to penetrate and wet surfaces.

30 The weight percent of the surfactant based on the weight of the adsorbate is preferably from 0.05% to 2.5%, and most preferably 0.05% to 0.5% which amounts will vary depending upon the surfactant utilized.

The surfactant may be selected from any of the groups of surface active agents. Nonlimiting illustrative categories and specific examples include:

35 (A) nonionic, which do not dissociate, but commonly derive their hydrophilic portion from polyhydroxy or polyethoxy structures; such as polyethylene oxides,

(B) anionic, where the hydrophilic portion of the molecule carries a negative charge: such as sodium lauryl sulfate, and linear alkyl sulfates, and

(C) cationic, where the hydrophilic portion of the molecule carries a positive charge: such as cetyl pyridinium chloride.

40 Surfactants may be used alone or in combination within the ranges specified above to form the adsorbate.

The medicament adsorbate of the invention is prepared by:

45 admixing a complex magnesium aluminum silicate with a medicament drug, a surfactant and a sufficient amount of solvent to dissolve the medicament drug and surfactant to form a mass containing the medicament drug and surfactant in an adsorbed condition, and recovering the medicament adsorbate.

In a preferred embodiment, the medicament adsorbate of the invention is prepared by:

(A) preparing a solution by dissolving the medicament drug and a surfactant in a solvent,

(B) sorbing the medicament drug and surfactant within a complex magnesium aluminum silicate by admixing the solution with the complex magnesium aluminum silicate to form a homogenous mass, and

50 (C) recovering the medicament adsorbate.

To form the medicament drug and surfactant solution, the medicament drug and surfactant are admixed with a solvent until they are dissolved. The solvent may be heated to aid dissolution. Preferably the solvent is heated from 65°C to 99°C.

55 The amount of solvent utilized to dissolve the medicament drug and surfactant will vary depending on the solubility of the particular medicament drug and surfactant used to form the adsorbate. The weight percent of the solvent used to form the solution based on the medicament adsorbate is from 10% to 60%, preferably 15% to 45%, and most preferably 20% to 35%.

In another preferred embodiment, the medicament adsorbate of the invention is prepared by:

60 admixing a complex magnesium aluminum silicate with a medicament drug, a surfactant and a sufficient amount of solvent to dissolve the medicament drug and hydrate the complex magnesium aluminum silicate to form a swollen mass containing the drug and surfactant in an adsorbed condition, the solvent having a water content of at least approximately 50% by weight of the solvent, and recovering the medicament adsorbate.

In a preferred embodiment, the medicament adsorbate of the invention is prepared by:

65 (A) preparing a blend by admixing a complex magnesium aluminum silicate with at least an equal

weight of solvent to form a swollen complex magnesium aluminum silicate.

(B) preparing a solution by dissolving the medicament drug and a surfactant in a solvent,

(C) sorbing the medicament drug and surfactant within the swollen complex magnesium aluminum silicate by admixing the blend with the solution to form a swollen mass having a homogeneous consistency and a water content of at least approximately 50% by weight of the total solvent content,

(D) recovering the medicament adsorbate.

To form the medicament drug solution, the medicament drug is admixed with a solvent until it is dissolved. The solvent may be heated to aid dissolution. Preferably the solvent is heated from 65°C to 99°C.

The amount of solvent utilized to dissolve the medicament drug will vary depending on the solubility of the particular medicament drug used to form the adsorbate. The weight percent of the solvent used to form the solution based on the medicament adsorbate is from 10% to 60%, preferably 15% to 45%, and most preferably 20% to 35% when the adsorbate is formed with swollen hydrated complex magnesium aluminum silicate.

When a complex magnesium aluminum silicate-solvent blend is used in the process the complex magnesium aluminum silicate and solvent are admixed until the silicate is swollen and the mixture is uniform. The solvent may be heated to aid formation of a uniform swollen blend. Preferably the solvent is heated from 35°C to 99°C.

The amount of solvent utilized to prepare the swollen complex magnesium aluminum silicate-solvent blend may vary widely but is generally from 1 to 20 times the weight of the complex magnesium aluminum silicate and preferably from 5 to 10 times the weight.

In another preferred embodiment, the medicament adsorbate of the invention is prepared by:

(A) preparing a solution by dissolving the medicament drug and surfactant in an amount of solvent at least equal in weight to the amount of complex magnesium aluminum silicate, said solvent having a water content of at least approximately 50% by weight of the solvent.

(B) sorbing the medicament drug and surfactant within a complex magnesium aluminum silicate by admixing the solution with the complex magnesium aluminum silicate to form a swollen homogeneous mass, and

(C) recovering the medicament adsorbate.

When the preferred procedure, described above is utilized, the medicament drug is dissolved in sufficient solvent to hydrate and swell the complex magnesium aluminum silicate sorbent. The amount of solvent utilized may vary widely but is generally from 1 to 20 times the weight of complex magnesium aluminum silicate and preferably from 5 to 10 times the weight. The solvent must have a water content of at least approximately 50% by weight of the solvent. A water content of less than approximately 50% will not sufficiently hydrate and swell the complex magnesium aluminum silicate.

The processes above involve the step of dissolving the medicament drug and surfactant in a suitable inert solvent. The resultant solution is then sorbed with mixing for 5 to 45 minutes into the complex magnesium aluminum silicate or the complex magnesium aluminum silicate solvent blend. The resulting product may be used as is or optionally removed and dried to a predetermined solvent content of up to approximately 20% and preferably 2% to 15% by weight of the medicament adsorbate.

The medicament adsorbate once prepared may be stored for future use or formulated with conventional additives, that is pharmaceutically acceptable carriers, to prepare medicated compositions which offer a variety of textures to suit particular applications. Such compositions may be in the form of a lozenge, tablet, toffee, nougat, chewy candy, chewing gum, suspension, and so forth. The pharmaceutically acceptable carriers may be prepared from a wide range of materials. Without being limited thereto, such materials include diluents, binders and adhesives, lubricants, disintegrants, colorants, bulking agents, flavorings, sweeteners and miscellaneous materials such as buffers and adsorbents in order to prepare a particular medicated composition. The preparation of confectionery and chewing gum products is well known and does not constitute an essential aspect of this invention.

As used herein, the term confectionery material means a product containing a bulking agent selected from a wide variety of materials such as sugar, corn syrup, and in the case of sugarless bulking agents, sugar alcohols such as sorbitol and mannitol and mixtures thereof. Confectionery material may include such exemplary substances as lozenges, tablets, toffee, nougat, chewy candy and so forth. In general, the bulking agent will comprise from 5% to 99% and preferably 20% to 95% by weight of the medicated confectionery product.

Lozenges are flavored medicated dosage forms intended to be sucked and held in the mouth. They may be in the form of various shapes, the most common being flat, circular, octagonal and biconvex forms. The lozenge bases are generally in two forms, hard, boiled candy lozenges and compressed tablet lozenges.

The hard boiled candy lozenges are prepared from a mixture of sugar and other carbohydrates that are kept in an amorphous or glassy condition. This form can be considered a solid syrup of sugars generally having from 0.5 to 1.5% moisture. Such materials normally contain up to approximately 92% corn syrup, up to approximately 70% sugar and from 0.1% to 5.0% water. The syrup component generally is prepared from corn syrups high in dextrose, but may include other materials. Further ingredients such as flavorings, sweeteners, acidulants, colorants and so forth may also be added.

Boiled candy lozenges may also be prepared from non-fermentable sugars such as sorbitol, mannitol,

and hydrogenated corn syrup. The candy lozenges may contain up to approximately 95% sorbitol, a mixture of sorbitol and mannitol at a ratio of 9.5 to 0.5 up to 7.5 to 2.5 and hydrogenated corn syrup up to approximately 55% of the syrup component.

In contrast, compressed tablet lozenges contain particulate materials and are formed into structures under pressure. They generally contain sugars in amounts up to 95% and typical tablet excipients such as binders and lubricants as well as flavors, colorants and so forth.

The lozenges may be made of soft confectionary materials such as those contained in nougat. These materials contain two primary components, namely a high boiling syrup such as corn syrup or the like, and a relatively light textured frappe, generally prepared from gelatin, egg albumen, milk proteins such as casein, and vegetable proteins such as soy protein, and the like. The frappe is generally relatively light, and may, for example, range in density from 0.5 to 0.7 g/cc.

By comparison, the high boiling syrup, or "bob syrup", is relatively viscous and possesses a higher density, and frequently contains a substantial amount of sugar. Conventionally, the final nougat composition is prepared by the addition of the "bob syrup" to the frappe under agitation, to form the basic nougat mixture. Further ingredients such as flavorings, oils, additional sugar and the like may be added thereafter also under agitation. A general discussion of the composition and preparation of nougat confections may be found in B. W. Minifie, *Chocolate, Cocoa and Confectionery: Science and Technology*, 2nd edition, AVI Publishing Co., Inc., Westport, Connecticut, (1980), at pages 424-425, which disclosure is incorporated herein by reference.

Pharmaceutical suspension of this invention may be prepared by conventional methods long established in the art of pharmaceutical compounding. Suspensions may contain conventional adjust materials employed in formulating the suspensions of the art. The suspensions of the present invention can comprise.

(a) preservatives such as benzoic acid, sorbic acid, methylparaben, propylparaben and ethylenediaminetetracetic acid (EDTA). Preservatives are generally present in amounts up to approximately 1% and preferably from 0.05% to 0.5% by weight of the suspension;

(b) buffers such as citric acid-sodium citrate, phosphoric acid-sodium phosphate, and acetic acid-sodium acetate in amounts up to approximately 1% and preferably from 0.05% to 0.5% by weight of the suspension;

(c) suspending agents or thickeners such as cellulose like methylcellulose, carageenans like alginic acid and its derivatives, xanthan gums, gelatin, acacia, and microcrystalline cellulose in amounts up to approximately 20% and preferably from 1% to 15% by weight of the suspension;

(d) antifoaming agents such as dimethyl polysiloxane in amounts up to approximately 0.2% and preferably from 0.01% to 0.1% by weight of the suspension;

(e) sweeteners includes those sweeteners both natural and artificial well known in the art.

Sweetening agents such as monosaccharides, disaccharides and polysaccharides such as xylose, ribose, glucose, mannose, galactose, fructose, dextrose, sucrose, maltose, partially hydrolyzed starch or corn syrup solids and sugar alcohols such as sorbitol, xylitol, mannitol and mixtures thereof may be utilized in amounts of 10% to 60% and preferably from 20% to 50% by weight of the suspension. Water soluble artificial sweeteners such as saccharin and saccharin salts such as sodium or calcium, cyclamate salts, acesulfame-K, aspartame and the like and mixtures thereof may be utilized in amounts from 0.001% to 5% by weight of the suspension;

(f) flavorants include both natural and artificial flavors, and mints such as peppermint, menthol, vanilla, artificial vanilla, chocolate, artificial chocolate, cinnamon, various fruit flavors, both individual and mixed may be utilized in amounts from 0.5% to 5% by weight of the suspension;

(g) colorants useful in the present invention include pigments which may be incorporated in amounts of up to approximately 6% by weight of the composition. A preferred pigment, titanium dioxide, may be incorporated in amounts up to approximately 1%. Also, the colorants may include other dyes suitable for food, drug and cosmetic applications, and known as F. D. & C. dyes and the like. Such dyes are generally present in amount up to approximately 0.25% and preferably from 0.05% to 0.2% by weight of the suspension;

(h) decolorizing agents such as sodium metabisulfite, ascorbic acid and the like may be incorporated into the suspension to prevent color changes due to aging. In general, amounts up to approximately 0.25% and preferably 0.05% to 0.2% by weight of the suspension are used;

(i) solubilizers such as alcohol, propylene glycol, polyethylene glycol and the like may be used to solubilize the flavors. Solubilizing agents are generally present in amounts up to approximately 10%; preferably from 2% to 5% by weight of the suspension.

Pharmaceutical suspensions of the present invention may be prepared as follows:

(A) admixing the thickener with water heated from 40°C to 95°C preferably 40°C to 70°C to form a dispersion if the thickener is not water soluble or a solution if the thickener is water soluble,

(B) admix the sweetener with water to form a solution,

(C) admix the medicament adsorbate with the thickener-water admixture to form a uniform thickener-adsorbate composition,

(D) combine the sweetener solution with the thickener-adsorbate composition and mix until uniform,

(E) admix optional ingredients such as colorants, flavors, decolorants, solubilizers, antifoaming agents,

buffers and additional water with the mixture of step (D) to form the suspension.

Adsorbates utilized in suspensions and other liquid formulations may be prepared *in situ*. That is, the medicament drug and adsorbent are added independently to the suspension or solution mixture to form the final product. The adsorbent then sorbs the medicament drug from solution to form the medicament adsorbate.

Pharmaceutical tablets of this invention may also be in chewable form. This form is particularly advantageous because of convenience and patient acceptance. To achieve acceptable stability and quality as well as good taste and mouth feel several considerations are important, namely amount of active substance per tablet flavor, compressibility and organoleptic properties of the drug.

The preparation of chewable medicated candy is by procedures similar to those used to make soft confectionary products. This procedure generally involves the formation of a boiled sugar-corn syrup blend to which is added a frappe mixture. The boiled sugar-corn syrup blend may be prepared from sugar and corn syrup blended in parts by weight ratio of 90 to 10 to 10 to 90. This blend is heated to temperatures above 121°C to remove water and to form a molten mass. The frappe is generally prepared from gelatin, egg albumen, milk proteins such as casein, and vegetable proteins such as soy protein, and the like which are added to a gelatin solution and rapidly mixed at ambient temperature to form an aerated sponge like mass. The frappe is then added to the molten candy base and mixed until homogeneous at temperatures between 65°C and 121°C.

The medicament adsorbate can then be added as the temperature of the mix is lowered to 65°C to 135°C whereupon additional ingredients are added such as flavors, and colorants. The formulation is further cooled and formed to pieces of desired dimensions.

A general discussion of the lozenge and chewable tablet forms of confectionary may be found in H. A. Lieberman and L. Lachman, *Pharmaceutical Dosage Forms: Tablets* Volume 1, Marcel Dekker, Inc., New York, N.Y. at pages 289 to 466 which disclosure is incorporated herein by reference.

As used herein, the term chewing gum product means a product containing a chewing gum formulation. In general, the chewing gum formulation will comprise from 5% to 99% and preferably 20% to 95% by weight of the medicated chewing gum product.

With regard to a chewing gum formulation, such formulations contain a gum base and various additives, such as sweeteners and flavors. The gum base employed will vary greatly depending on various factors such as the type of base used, consistency desired and other components used to make the final product. In general, amounts of 5% to 45% by weight of the final chewing gum composition are acceptable for use in chewing gum compositions with preferred amounts of 15% to 25% by weight. The gum base may be any water-insoluble gum base well known in the art. Illustrative examples of suitable polymers in gum bases include both natural and synthetic elastomers and rubbers. For example, those polymers which are suitable in gum bases, include, without limitation, substances of vegetable origin such as chicle, jelutong, gutta percha and crown gum. Synthetic elastomers such as butadiene-styrene copolymers, isobutylene-isoprene copolymers polyethylene, polyisobutylene and polyvinylacetate and mixtures thereof, are particularly useful.

The gum base composition may contain elastomer solvents to aid in softening the elastomer component. Such elastomer solvents may comprise methyl, glycerol or pentaerythritol esters of rosins or modified rosins, such as hydrogenated, dimerized or polymerized rosins or mixtures thereof. Examples of elastomer solvents suitable for use herein include the pentaerythritol ester of partially hydrogenated wood rosin, pentaerythritol ester of wood rosin, glycerol ester of wood rosin, glycerol ester of partially dimerized rosin, glycerol ester of polymerized rosin, glycerol ester of tall oil rosin, glycerol ester of wood rosin and partially hydrogenated wood rosin and partially hydrogenated methyl ester of rosin, such as polymers of alpha-pinene and beta-pinene; terpene resins including polyterpene and mixtures thereof. The solvent may be employed in an amount ranging from 10% to 75% and preferably 45% to 70% by weight to the gum base.

A variety of traditional ingredients such as plasticizers or softeners such as lanolin, stearic acid, sodium stearate, potassium stearate, glyceryl triacetate, glycerine and the like as well as natural and synthetic waxes, petroleum waxes, such as polyurethane waxes, paraffin waxes and microcrystalline waxes may also be incorporated into the gum base to obtain a variety of desirable textures and consistency properties. These individual additional materials are generally employed in amounts of up to 30% by weight and preferably in amounts from 3% to 20% by weight of the final gum base composition.

The chewing gum composition may additionally include the conventional additives of flavoring agents, coloring agents such as titanium dioxide, emulsifiers such as lecithin and glyceryl monostearate; and additional fillers such as aluminum hydroxide, alumina, aluminum silicates, calcium carbonate, and talc and combinations thereof. These fillers may also be used in the gum base in various amounts. Preferably the amount of fillers when used will vary from 4% to 30% by weight of the final chewing gum.

In the instance where auxiliary sweeteners are utilized, the present invention contemplates the inclusion of those sweeteners well known in the art, including both natural and artificial sweeteners. Thus, additional sweeteners may be chosen from the following non-limiting list:

A. Water-soluble sweetening agents such as monosaccharides, disaccharides and polysaccharides such as xylose, ribose, glucose, mannose, galactose, fructose, dextrose, sucrose, maltose, partially

hydrolyzed starch, or corn syrup solids and sugar alcohols such as sorbitol, xylitol, mannitol and mixtures thereof.

B. Water-soluble artificial sweeteners such as the soluble saccharin salts, i.e., sodium, or calcium saccharin salts, cyclamate salts, acesulfame-K and the like, and the free acid form of saccharin.

5 C. Dipeptide based sweeteners such as L-aspartyl-L-phenylalanine methyl ester and materials described in U.S. Patent No. 3,492,131 and the like.

In general, the amount of sweetener will vary with the desired amount of sweeteners selected for a particular chewing gum. This amount will normally be 0.001% to 90% by weight when using an easily extractable sweetener. The water-soluble sweeteners described in category A above, are preferably used in
10 amounts of 25% to 75% by weight, and most preferably from 50% to 65% by weight of the final chewing gum composition. In contrast, the artificial sweeteners described in categories B and C are used in amounts of 0.005% to 5.0% and most preferably 0.05% to 2.5% by weight of the final chewing gum composition. These amounts are ordinarily necessary to achieve a desired level of sweetness independent from the flavor level achieved from flavor oils. While water may be added independently with dry sweeteners, it will
15 generally be added as part of a corn syrup or corn syrup mixture.

Suitable flavorings include both natural and artificial flavors, and mints such as peppermint, spearmint, menthol, artificial vanilla, vanilla, artificial chocolate, chocolate, cinnamon, various fruit flavors, both individual and mixed, and the like are contemplated. The flavorings are generally utilized in amounts that will vary depending upon the individual flavor, and may, for example, range in amounts of 0.5% to 3%
20 by weight of the final composition.

The colorants useful in the present invention, include the pigments which may be incorporated in amounts of up to approximately 6% by weight of the composition. A preferred pigment, titanium dioxide, may be incorporated in amounts of up to approximately 1% by weight. Also, the colorants may include other dyes suitable for food, drug and cosmetic applications, and known as F.D. & C. dyes and the like. The
25 materials acceptable for the foregoing spectrum of use are preferably water-soluble. Illustrative examples include the indigo dye, known as F.D. & C. Blue No. 2, which is the disodium salt of 5,5-indigotindisulfonic acid. Similarly, the dye known as F.D. & C. Green No. 1, comprises a triphenylmethane dye and is the monosodium salt of 4-[4-N-ethyl-p-sulfobenzylamino]diphenylmethylene-[1-(N-ethyl-N-p-sulfonium--benzyl)-2,5-cyclohexadienimine]. A full recitation of all F.D. & C. and D. & C. colorants and their corresponding chemical structures may be found in the Kirk-Othmer Encyclopedia of Chemical Technology, 3rd
30 edition, in Volume 6, at pages 561-595, which text is accordingly incorporated herein by reference.

Suitable oils and fats that are usable would include partially hydrogenated vegetable or animal fats, such as coconut oil, palm kernel oil, beef tallow, lard, and the like. These ingredients are generally utilized in amounts with respect to the comestible product of up to approximately 7.0% by weight, and preferably
35 up to approximately 3.5% by weight of the final product.

It is generally believed that as the required amount of active substance per structure gets smaller and/or less bad tasting, the task at arriving at an acceptable formulation becomes easier due to the greater number of formulations available. Alternatively, extremely bad-tasting and/or high-dose drugs are difficult to formulate into medicament/chewable tablets. The medicament adsorbates of this invention overcome
40 these difficulties.

The quantity of adsorbate used may vary widely depending upon the particular medicament drug dosage. Amounts of medicament of 1.0 to 400 mg per medicated dosage are usable dependent upon the particular medicament. Naturally amounts of medicament adsorbate used will vary depending on the therapeutic dosage required and the amount of medicament sorbed on the substrate. Illustrative examples
45 are described below.

The usual dosage of dextromethorphan hydrobromide is between 10 and 30 mg per tablet. Incorporation of the adsorbate into, for example, a candy base is not difficult. It is compatible with most flavors and is stable over a wide pH range. The dextromethorphan HBr when added as the medicament adsorbate avoids its bitter taste and flavoring difficulty.

50 The usual dosage of phenylpropanolamine hydrochloride is 12.5 to 25 per tablet. The usual dosage of guaifenesin is 100 to 400 mg per tablet. The usual dosage of pseudoephedrine hydrochloride is 15 to 60 mg per tablet. The usual dosage range of chlorpheniramine maleate is 2 to 4 mg and lends itself easily to incorporation into a candy base. Naturally, the exact amount used will vary with the particular application and drug. These formulations are not difficult to flavor because the adsorbates formed with these
55 compounds substantially eliminate medicament after-taste.

The medicament adsorbate is generally present with the pharmaceutically acceptable carrier in an amount of from 1% to 60% by weight of the final composition. The exact amount will be dependent upon the particular medicament and dosage required.

60 The present invention is further illustrated by the following examples. All parts and percentages in the examples and throughout the specification and claims are by total weight of the medicament adsorbate unless otherwise indicated.

The complex magnesium aluminum silicate of Examples 1 to 5 has the following typical chemical analysis:

	Percent by weight	Ratio to Aluminum oxide	
5	Silicon dioxide	56 to 59	14.0 to 29.5
	Magnesium oxide	21 to 24	5.2 to 12.0
	Aluminum oxide	2.0 to 4.0	1
10	Ferric oxide	0.4 to 0.6	
	Calcium oxide	1.1 to 1.5	
15	Sodium oxide	2.5 to 3.5	
	Potassium oxide	0.5 to 1.0	
	Ignition loss	5.5 to 12.6	

20

Example 1 (Inventive Run 1)

This Example demonstrates a method for preparing a guaifenesin adsorbate according to the process of the invention.

25 To 1200 grams of heated water held at about 85°C to about 95°C is mixed 1200 grams of complex magnesium aluminum silicate. The mixing is continued for about 15 minutes until a uniform mixture results.

To 2000 grams of heated water held at about 85°C to about 95°C is mixed 270 grams of guaifenesin and 60 grams of sodium lauryl sulfate until a solution is formed.

30 The guaifenesin: sodium lauryl sulfate solution is mixed with the water: complex magnesium aluminum silicate mixture until a swollen homogeneous mass is obtained. The mass is then dried at about 75°C for about 16 hours. The resultant dried mass is then milled to produce a free flowing particulate material having a particle size of about 100 microns.

35 An organoleptic evaluation test was performed on the product to determine the presence or absence of bitterness. The instant product did not exhibit objectionable bitterness or off taste. The adsorbate of this example has significantly less bitterness than Comparative Example 2.

Example 2 (Non-Inventive Run A)

40 This Example demonstrates a guaifenesin adsorbate prepared by the procedure of Example 1 except that a surfactant is not present in solution with the guaifenesin.

To 1200 grams of heated water held at 85°C to about 95°C is mixed 1200 grams of complex magnesium aluminum silicate. The mixing is continued for about 15 minutes until a uniform mixture results.

45 To 2000 grams of heated water held at about 85°C to about 95°C is mixed 270 grams of guaifenesin until a solution is formed.

The guaifenesin solution is mixed with the water: complex magnesium aluminum silicate mixture until a homogeneous mass is obtained. The mass is then dried at about 75°C for about 16 hours. The resultant dried mass is then milled to produce a free flowing particulate material having a particle size of about 100 microns.

50 An organoleptic evaluation test was performed on the product to determine the presence or absence of bitterness. The instant product exhibited an acceptable level of bitterness.

Example 3 (Inventive Run 2)

55 This Example demonstrates a method of preparing a guaifenesin adsorbate according to the process of the invention.

60 To 1500 grams of heated water held at 85°C is mixed 750 grams of guaifenesin and 60 grams of sodium lauryl sulfate until a solution is formed. The resultant solution is then added with mixing to 3000 grams of complex magnesium aluminum silicate. Mixing is continued 10 minutes until a homogeneous mass is obtained. The mass is then dried at about 75°C for about 16 hours. The resultant dried mass is then milled to produce a free flowing particulate material having a particle size of about 100 microns.

An organoleptic evaluation test was performed on the product to determine the presence or absence of bitterness. The instant product did not exhibit objectionable bitterness or off taste. The adsorbate of this example has significantly less bitterness than Comparative Example 4.

65

Example 4**(Comparative Run B, No Surfactant)**

This Example demonstrates a guaifenesin adsorbate prepared by the procedure of Example 3 except that a surfactant is not present in solution with the guaifenesin.

To 1500 grams of heated water held at 85°C is mixed 750 grams of guaifenesin until a solution is formed. The resultant solution is then added with mixing to 3000 grams of complex magnesium aluminum silicate. Mixing is continued 10 minutes until a homogeneous mass is obtained. The mass is then dried at about 75°C for about 16 hours. The resultant dried mass is then milled to produce a free flowing particulate material having a particle size of about 100 microns.

An organoleptic evaluation test was performed on the product to determine the presence or absence of bitterness. The instant product exhibited an acceptable level of bitterness.

Example 5**(Inventive Run 4)**

This Example demonstrates a method for preparing a cold/sinus/asthma tablet formulation using an adsorbate prepared according to a process of the invention with pseudoephedrine HCl.

The adsorbate may be prepared as follows:

To 1200 grams of heated water held at about 85°C to about 95°C is mixed 1200 grams of complex magnesium aluminum silicate. The mixing is continued for about 15 minutes until a uniform mixture results.

To 2000 grams of heated water held at about 85°C to about 95°C is mixed 120 grams of pseudoephedrine HCl and 60 grams of sodium lauryl sulfate until a solution is formed.

The pseudoephedrine HCl:sodium lauryl sulfate solution is mixed with the water:complex magnesium aluminum silicate mixture until a homogeneous mass is obtained. The mass is then dried at about 75°C for about 16 hours. The resultant dried mass is then milled to produce a free flowing particulate material having a particle size of about 100 microns.

The following ingredients are mixed in the order indicated:

No. Ingredients	Mg/tablet
1. Chlorpheniramine maleate	4.0
2. Pseudoephedrine HCl-10% adsorbate (60.0mg drug/tablet)	600.0
3. Microcrystalline cellulose	37.3
4. Lactose	113.0
5. Modified cellulose gum	2.2
6. Fumed silica	1.1
7. Stearic acid	1.3
8. Magnesium stearate	1.1
	760.0

Procedure

Pass No. 2, No. 3 and No. 4 through a 40 mesh screen. Mix in a V-blender for 3 minutes. Pass No. 1, No. 5, No. 6, No. 7 and No. 8 through a No. 40 mesh screen. Add to the mixture in the V-blender and mix for 15 minutes. Compress powders using 16/22" flat faced punches to a hardness of 5—7 S.C. units.

Example 6**(Inventive Run 5)**

This Example demonstrates a method for preparing a chewable cough tablet formulation using an adsorbate prepared with guaifenesin prepared by the process of Example 1. The ingredients are mixed in the order indicated:

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No.	Ingredients	Mg/tablet
5	1. Guaifenesin—18.4% adsorbate (100 mg drug/tablet)	545.0
	2. Candy base	3630.5
	3. Frappe	130.0
10	4. Crystal sorbitol	123.0
	5. Vegetable fat (palm kernel oil)	265.0
	6. Sugar, granulated	138.0
15	7. Flavor	88.5
		4920.0

20 Procedure

Candy base cooked to 132°C is cooled in a kettle to a temperature of 110°C to 115°C. The frappe and sorbitol crystals are then mixed into the base to form a uniform mass. Mixing is continued until the mass is cooled to 73°C to 80°C. To the uniform mass is added with mixing the vegetable fat, color, and medicament adsorbate. The sugar and flavor are combined with mixing and added to the previous blend. Mixing is continued until a homogeneous mass is obtained. The product is removed from the kettle, cooled and then formed into 5 gram pieces. The tablet when chewed did not exhibit objectionable medicinal aftertaste due to the bitterness of the guaifenesin.

Claims for the Contracting States: AT, BE, FR, DE, IT, LU, NL, SE, CH, GB, LI

30

1. A medicament adsorbate which comprises:
a complex magnesium aluminum silicate having sorbed therein a solution of medicament drug and a surfactant.
2. A medicament adsorbate according to Claim 1, wherein the medicament drug is present in an amount of 1 to 35% by weight and the complex magnesium aluminum silicate is present in an amount of 70% to 90% by weight, all percents herein are by weight percent of the medicament adsorbate.
3. A medicament adsorbate according to the Claims 1 or 2, wherein the surfactant is present in an amount of 0.05% to 4% by weight of the medicament adsorbate.
4. A medicament adsorbate according to anyone of the Claims 1 to 3, further comprising a solvent content up to approximately 20% by weight of the medicament adsorbate.
5. A medicament adsorbate according to anyone of the Claims 1 to 3, further comprising a solvent content from 2% to 15% by weight of the medicament adsorbate.
6. A medicament adsorbate according to anyone of the Claims 1 to 5, wherein the surfactant is selected from sodium lauryl sulphate, pluronics and mixtures thereof.
7. A medicament adsorbate according to anyone of the Claims 1 to 6, wherein the complex magnesium aluminum silicate has the following typical chemical analysis:

		Percent by weight	Ratio to aluminum oxide
50	Silicon dioxide	55 to 70	3.2 to 35
	Magnesium oxide	2.9 to 25	0.17 to 12.5
	Aluminum oxide	2.0 to 17	1
55	Ferric oxide	0.4 to 1.8	
	Calcium oxide	1.1 to 2.4	
60	Sodium oxide	1.0 to 3.8	
	Potassium oxide	0.2 to 1.9	
65	Ignition loss	5.5 to 12.6	

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No.	Ingredients	Mg/tablet
1.	Guaifenesin—18.4% adsorbate (100 mg drug/tablet)	545.0
2.	Candy base	3630.5
3.	Frappe	130.0
4.	Crystal sorbitol	123.0
5.	Vegetable fat (palm kernel oil)	265.0
6.	Sugar, granulated	138.0
7.	Flavor	88.5
		4920.0

20 Procedure

Candy base cooked to 132°C is cooled in a kettle to a temperature of 110°C to 115°C. The frappe and sorbitol crystals are then mixed into the base to form a uniform mass. Mixing is continued until the mass is cooled to 73°C to 80°C. To the uniform mass is added with mixing the vegetable fat, color, and medicament adsorbate. The sugar and flavor are combined with mixing and added to the previous blend. Mixing is continued until a homogeneous mass is obtained. The product is removed from the kettle, cooled and then formed into 5 gram pieces. The tablet when chewed did not exhibit objectionable medicinal aftertaste due to the bitterness of the guaifenesin.

Claims for the Contracting States: AT, BE, FR, DE, IT, LU, NL, SE, CH, GB, LI

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1. A medicament adsorbate which comprises:
a complex magnesium aluminum silicate having sorbed therein a solution of medicament drug and a surfactant.

2. A medicament adsorbate according to Claim 1, wherein the medicament drug is present in an amount of 1 to 35% by weight and the complex magnesium aluminum silicate is present in an amount of 70% to 90% by weight, all percents herein are by weight percent of the medicament adsorbate.

3. A medicament adsorbate according to the Claims 1 or 2, wherein the surfactant is present in an amount of 0.05% to 4% by weight of the medicament adsorbate.

4. A medicament adsorbate according to anyone of the Claims 1 to 3, further comprising a solvent content up to approximately 20% by weight of the medicament adsorbate.

5. A medicament adsorbate according to anyone of the Claims 1 to 3, further comprising a solvent content from 2% to 15% by weight of the medicament adsorbate.

6. A medicament adsorbate according to anyone of the Claims 1 to 5, wherein the surfactant is selected from sodium lauryl sulphate, pluronics and mixtures thereof.

7. A medicament adsorbate according to anyone of the Claims 1 to 6, wherein the complex magnesium aluminum silicate has the following typical chemical analysis:

	Percent by weight	Ratio to aluminum oxide
Silicon dioxide	55 to 70	3.2 to 35
Magnesium oxide	2.9 to 25	0.17 to 12.5
Aluminum oxide	2.0 to 17	1
Ferric oxide	0.4 to 1.8	
Calcium oxide	1.1 to 2.4	
Sodium oxide	1.0 to 3.8	
Potassium oxide	0.2 to 1.9	
Ignition loss	5.5 to 12.6	



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8. A medicament adsorbate according to anyone of the Claims 1 to 6, wherein the complex magnesium aluminum silicate has the following typical chemical analysis:

	Percent by weight	Ratio to aluminum oxide
5		
	Silicon dioxide	56 to 59
		14.0 to 35
	Magnesium oxide	21 to 24
		5.2 to 12.0
10	Aluminum oxide	2.0 to 4.0
		1
	Ferric oxide	0.4 to 0.6
	Calcium oxide	1.1 to 1.5
15	Sodium oxide	2.5 to 3.5
	Potassium oxide	0.5 to 1.0
20	Ignition loss	5.5 to 12.6

9. A process for preparing a medicament adsorbate which comprises:
admixing a complex magnesium aluminum silicate with a medicament drug, a surfactant and a
25 sufficient amount of solvent to dissolve the medicament drug and surfactant to form a mass containing the medicament drug and surfactant in an adsorbed condition, and recovering the medicament adsorbate.

10. A process according to Claim 9, wherein the solvent is used in amounts from 10% to 60% by weight of the medicament adsorbate.

11. A process according to the Claims 9 or 10, wherein the medicament drug is present in an amount of
30 1% to 35% by weight and the complex magnesium aluminum silicate is present in an amount of 70% to 90% by weight, all percents herein are by weight percent of the medicament adsorbate.

12. A process according to anyone of the Claims 9 to 11, wherein the surfactant is present in an amount of 0.05% to 4% by weight of the medicament adsorbate.

13. A process according to anyone of the Claims 9 to 12, further comprising drying the mass to a final
35 solvent content up to approximately 20% by weight of the medicament adsorbate.

14. A process according to anyone of the Claims 9 to 13, wherein the solvent is used in an amount from 1 to 20 times by weight of the complex magnesium aluminum silicate.

15. A medicated composition which comprises a pharmaceutically acceptable carrier and from 1% to 60% by weight of the final composition of a medicament adsorbate according to any one of Claims 1 to 8.

40 16. A medicated composition according to Claim 15, wherein the pharmaceutically acceptable carrier is selected from a lozenge, a tablet, suspension, toffee, nougat, chewy candy and chewing gum.

17. A medicated confectionery product comprising:

a bulking agent of up to approximately 99%;

45 a therapeutically effective amount of a medicament adsorbate according to one of Claims 1 to 8, the medicament adsorbate being admixed in the confectionery product, all percents herein are by weight of the medicated confectionery product.

18. A medicated chewing gum product containing a therapeutically effective amount of medicament drug which comprises:

50 a chewing gum composition in an amount up to approximately 99% containing, a gum base, and a sweetener; and

a therapeutically effective amount of a medicament adsorbate according to any one of Claims 1 to 8, the medicament adsorbate being admixed in the chewing gum composition, all percents herein are by weight of the medicated chewing gum product.

55 **Claims for the Contracting State: ES**

1. A process for preparing a medicament adsorbate which comprises:

60 admixing a complex magnesium aluminum silicate with a medicament drug, a surfactant and a sufficient amount of solvent to dissolve the medicament drug and surfactant to form a mass containing the medicament drug and surfactant in an adsorbed condition, and recovering the medicament adsorbate.

2. A process according to Claim 1, wherein the medicament drug is present in an amount of 1 to 35% by weight and the complex magnesium aluminum silicate is present in an amount of 70% to 90% by weight, all percents herein are by weight percent of the medicament adsorbate.

65 3. A process according to the Claims 1 or 2, wherein the surfactant is present in an amount of 0.05% to 4% by weight of the medicament adsorbate.



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4. A process according to any one of the Claims 1 to 3, wherein the surfactant is selected from sodium lauryl sulphate, pluronics and mixtures thereof.

5. A process according to any one of the Claims 1 to 4, wherein the complex magnesium aluminum silicate has the following typical chemical analysis:

	Percent by weight	Ratio to aluminum oxide
10 Silicon dioxide	55 to 70	3.2 to 35
Magnesium oxide	2.9 to 25	0.17 to 12.5
Aluminum oxide	2.0 to 17	1
15 Ferric oxide	0.4 to 1.8	
Calcium oxide	1.1 to 2.4	
20 Sodium oxide	1.0 to 3.8	
Potassium oxide	0.2 to 1.9	
Ignition loss	5.5 to 12.6	

6. A process according to any one of the Claims 1 to 4, wherein the complex magnesium aluminum silicate has the following typical chemical analysis:

	Percent by weight	Ratio to aluminum oxide
30 Silicon dioxide	56 to 59	14.0 to 35
Magnesium oxide	21 to 24	5.2 to 12.0
35 Aluminum oxide	2.0 to 4.0	1
Ferric oxide	0.4 to 0.6	
40 Calcium oxide	1.1 to 1.5	
Sodium oxide	2.5 to 3.5	
Potassium oxide	0.5 to 1.0	
45 Ignition loss	5.5 to 12.6	

7. A process according to any preceding claim, wherein the amount of solvent used in the process is from 10% to 60% by weight of the medicament adsorbate.

8. A process according to any one of the preceding claims, wherein the amount of solvent used in the process is from 1 to 20 times by weight of the complex magnesium aluminum silicate.

9. A process according to any one of the preceding claims, which further includes drying the mass to a final solvent content of up to approximately 20% by weight of the medicament.

10. A process according to Claim 9, wherein the mass is dried to a final solvent content of 2% to 15% by weight of the medicament adsorbate.

11. A process for the preparation of a medicated composition which comprises admixing a pharmaceutically acceptable carrier and from 1% to 60% by weight of the final composition of a medicament adsorbate made according to any one of Claims 1 to 10.

12. A process according to Claim 11, wherein the pharmaceutically acceptable carrier is selected from a lozenge, a tablet, suspension, toffee, nougat, chewy candy and chewing gum.

13. A process for the preparation of a medicated confectionery product which process comprises: admixing up to approximately 99% of a bulking agent; and a therapeutically effective amount of a medicament adsorbate made according to any one of Claims 1

to 10.



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14. A process for the preparation of a medicated chewing gum product which comprises admixing: a chewing gum composition in an amount up to approximately 99% containing a gum base, and a sweetener; and

a therapeutically effective amount of a medicament adsorbate made according to any one of Claims 1 to 10, all percents herein are by weight of the medicated chewing gum product.

Patentansprüche für die Vertragsstaaten: AT, BE, FR, DE, IT, LU, NL, SE, CH, GB, LI

1. Arzneimitteladsorbat, welches umfaßt:
10 ein komplexes Magnesiumaluminiumsilicat, worin eine Lösung von Arzneimittelwirkstoff und eines grenzflächenaktiven Mittels sorbiert sind.
2. Arzneimitteladsorbat nach Anspruch 1, worin der Arzneimittelwirkstoff in einer Menge von 1 bis 35 Gew.-% anwesend ist, und das komplexe Magnesiumaluminiumsilicat in einer Menge von 70 bis 90 Gew.-% anwesend ist, wobei alle Prozentangaben hierin auf Gewichtsprozent des Arzneimitteladsorbats
15 bezogen sind.
3. Arzneimitteladsorbat nach den Ansprüchen 1 oder 2, worin das grenzflächenaktive Mittel in einer Menge von 0,05 bis 4 Gew.-% des Arzneimitteladsorbats anwesend ist.
4. Arzneimitteladsorbat nach irgendeinem der Ansprüche 1 bis 3, welches weiters einen Lösungsmittelgehalt bis etwa 20 Gew.-% des Arzneimitteladsorbats umfaßt.
20 5. Arzneimitteladsorbat nach irgendeinem der Ansprüche 1 bis 3, welches weiters einen Lösungsmittelgehalt von 2 bis 15 Gew.-% des Arzneimitteladsorbats umfaßt.
6. Arzneimitteladsorbat nach irgendeinem der Ansprüche 1 bis 5, worin das grenzflächenaktive Mittel ausgewählt ist aus Natriumlaurylsulfat, Pluronic und Mischungen davon.
7. Arzneimitteladsorbat nach irgendeinem der Ansprüche 1 bis 6, worin das komplexe
25 Magnesiumaluminiumsilicat die folgende typische chemische Analyse aufweist:

		Gewichtsprozent	Verhältnis zu Aluminiumoxid
30	Siliciumdioxid	55 to 70	3,2 bis 35
	Magnesiumoxid	2,9 to 25	0,17 bis 12,5
	Aluminiumoxid	2,0 bis 17	1
35	Eisen(III)-oxid	0,4 bis 1,8	
	Calciumoxid	1,1 bis 2,4	
40	Natriumoxid	1,0 bis 3,8	
	Kaliumoxid	0,2 bis 1,9	
45	Glühverlust	5,5 bis 12,6	

8. Arzneimitteladsorbat nach irgendeinem der Ansprüche 1 bis 6, worin das komplexe Magnesiumaluminiumsilicat die folgende typische chemische Analyse aufweist:

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	Gewichtsprozent	Verhältnis zu Aluminiumoxid	
5	Siliciumdioxid	56 bis 59	14,0 bis 35
	Magnesiumoxid	21 bis 24	5,2 bis 12,0
	Aluminiumoxid	2,0 bis 4,0	1
10	Eisen(III)-oxid	0,4 bis 0,6	
	Calciumoxid	1,1 bis 1,5	
15	Natriumoxid	2,5 bis 3,5	
	Kaliumoxid	0,5 bis 1,0	
	Glühverlust	5,5 bis 12,6	

20 9. Verfahren zur Herstellung eines Arzneimitteladsorbats, welches Verfahren umfaßt:

Mischen eines komplexen Magnesiumaluminiumsilicats mit einem Arzneimittelwirkstoff, einem grenzflächenaktiven Mittel und einer ausreichenden Menge Lösungsmittel zur Lösung des Arzneimittelwirkstoffs und grenzflächenaktiven Mittels zur Bildung einer den Arzneimittelwirkstoff und das grenzflächenaktive Mittel in einem adsorbierten Zustand enthaltenden Masse und Gewinnung des Arzneimitteladsorbats.

10. Verfahren nach Anspruch 9, worin das Lösungsmittel in Mengen von 10 bis 60 Gew.-% des Arzneimitteladsorbats verwendet wird.

11. Verfahren nach den Ansprüchen 9 bis 10, worin der Arzneimittelwirkstoff in einer Menge von 1 bis 35 Gew.-% anwesend ist, und das komplexe Magnesiumaluminiumsilicat in einer Menge von 70 bis 90 Gew.-% anwesend ist, wobei alle Prozentangaben hierin auf Gewichtsprozent des Arzneimitteladsorbats bezogen sind.

12. Verfahren nach irgendeinem der Ansprüche 9 bis 11, worin das grenzflächenaktive Mittel in einer Menge von 0,05 bis 4 Gew.-% des Arzneimitteladsorbats anwesend ist.

13. Verfahren nach irgendeinem der Ansprüche 9 bis 12, welches weiters das Trocknen der Masse bis zu einem endgültigen Lösungsmittelgehalt bis etwa 20 Gew.-% des Arzneimitteladsorbats umfaßt.

14. Verfahren nach irgendeinem der Ansprüche 9 bis 13, worin das Lösungsmittel in einer ein- bis zwanzigfachen Gewichtsmenge des komplexen Magnesiumaluminiumsilicats verwendet wird.

15. Arzneimittelzusammensetzung, welche einen pharmazeutisch akzeptablen Träger und ein Arzneimitteladsorbat nach irgendeinem der Ansprüche 1 bis 8 in einer Menge von 1 bis 60 Gew.-% der Enzusammensetzung umfaßt.

16. Arzneimittelzusammensetzung nach Anspruch 15, worin der pharmazeutisch akzeptable Träger ausgewählt ist aus einer Pastille, Tablette, Suspension, Karamelle, einem Nougat, Kaukonfekt und Kaugummi.

17. Arzneimittelkonfektprodukt, welches umfaßt:

45 ein Quellmittel bis zu etwa 99%;

eine therapeutisch wirksame Menge eines Arzneimitteladsorbats nach irgendeinem der Ansprüche 1 bis 8,

wobei das Arzneimitteladsorbat in das Konfektprodukt gemischt ist,

alle Prozentangaben hierin sind auf das Gewicht des Arzneimittelkonfektprodukts bezogen.

18. Arzneimittelkaugummiprodukt, welches eine therapeutisch wirksame Menge eines Arzneimittelwirkstoffs enthält, welches Produkt umfaßt:

eine Kaugummizusammensetzung in einer Menge bis etwa 99%, welche eine Gummibasis und einen Süßstoff enthält, und eine therapeutisch wirksame Menge eines Arzneimitteladsorbats nach irgendeinem der Ansprüche 1 bis 8,

55 wobei das Arzneimitteladsorbat in die Kaugummizusammensetzung gemischt ist,

alle Prozentangaben hierin sind auf das Gewicht des Arzneimittelkaugummiprodukts bezogen.

Patentansprüche für den Vertragsstaat: ES

60 1. Verfahren zur Herstellung eines Arzneimitteladsorbats, welches umfaßt:

Mischen eines komplexen Magnesiumaluminiumsilicats mit einem Arzneimittelwirkstoff, einem grenzflächenaktiven Mittel und einer ausreichenden Menge Lösungsmittel zur Lösung des Arzneimittelwirkstoffs und des grenzflächenaktiven Mittels zur Bildung einer den Arzneimittelwirkstoff und das grenzflächenaktive Mittel in einem adsorbierten Zustand enthaltenden Masse und Gewinnung des Arzneimitteladsorbats.



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2. Verfahren nach Anspruch 1, worin der Arzneimittelwirkstoff in einer Menge von 1 bis 35 Gew.-% anwesend ist, und das komplexe Magnesiumaluminiumsilicat, in einer Menge von 70 bis 90 Gew.-% anwesend ist, wobei alle Prozentangaben hierin auf Gewichtsprozent des Arzneimitteladsorbats bezogen sind.

3. Verfahren nach irgendeinem der Ansprüche 1 bis 2, worin das grenzflächenaktive Mittel in einer Menge von 0,05 bis 4 Gew.-% des Arzneimitteladsorbats anwesend ist.

4. Verfahren nach irgendeinem der Ansprüche 1 bis 3, worin das grenzflächenaktive Mittel ausgewählt ist aus Natriumlaurylsulfat, Pluronic und Mischungen davon.

5. Verfahren nach irgendeinem der Ansprüche 1 bis 4, worin das komplexe Magnesiumaluminiumsilicat die folgende typische chemische Analyse aufweist:

		Gewichtsprozent	Verhältnis zu Aluminiumoxid
15	Siliciumdioxid	55 bis 70	3,2 bis 35
	Magnesiumoxid	2,9 bis 25	0,17 bis 12,5
	Aluminiumoxid	2,0 bis 17	1
20	Eisen(III)-oxid	0,4 bis 1,8	
	Calciumoxid	1,1 bis 2,4	
25	Natriumoxid	1,0 bis 3,8	
	Kaliumoxid	0,2 bis 1,9	
30	Glühverlust	5,5 bis 12,6	

6. Verfahren nach irgendeinem der Ansprüche 1 bis 4, worin das komplexe Magnesiumaluminiumsilicat die folgende typische chemische Analyse aufweist:

		Gewichtsprozent	Verhältnis zu Aluminiumoxid
35	Siliciumdioxid	56 bis 59	14,0 bis 35
40	Magnesiumoxid	21 bis 24	5,2 bis 12,0
	Aluminiumoxid	2,0 bis 4,0	1
	Eisen(III)-oxid	0,4 bis 0,6	
45	Calciumoxid	1,1 bis 1,5	
	Natriumoxid	2,5 bis 3,5	
50	Kaliumoxid	0,5 bis 1,0	
	Glühverlust	5,5 bis 12,6	

7. Verfahren nach irgendeinem vorhergehenden Anspruch, worin die Menge des im Verfahren verwendeten Lösungsmittels 10 bis 60 Gew.-% des Arzneimitteladsorbats beträgt.

8. Verfahren nach irgendeinem der vorhergehenden Ansprüche, worin die Menge des im Verfahren verwendeten Lösungsmittels das ein- bis zwanzigfache Gewicht des komplexen Magnesiumaluminiumsilicats beträgt.

9. Verfahren nach irgendeinem der Ansprüche 9 bis 12, welches weiters das Trocknen der Masse zu einem endgültigen Lösungsmittelgehalt bis etwa 20 Gew.-% des Arzneimittels umfaßt.

10. Verfahren nach Anspruch 9, worin die Masse bis zu einem endgültigen Lösungsmittelgehalt von 2 bis 15 Gew.-% des Arzneimitteladsorbats getrocknet wird.

11. Verfahren zur Herstellung einer Arzneimittelzusammensetzung, welches das Mischen eines pharmazeutisch akzeptablen Trägers und eines nach einem der Ansprüche 1 bis 10 hergestellten



Arzneimitteladsorbats in einer Menge von 1 bis 60 Gew.-% der Enzusammensetzung umfaßt.

12. Verfahren nach Anspruch 11, worin der pharmazeutisch akzeptable Träger ausgewählt ist aus einer Pastille, Tablette, Suspension, Karamelle, einem Nougat, Kaukonfekt und Kaugummi.

13. Verfahren zur Herstellung eines Arzneimittelkonfektprodukts, welches Verfahren umfaßt:

5 Mischen von bis zu etwa 99% eines Quellmittels und einer therapeutisch wirksamen Menge eines Arzneimitteladsorbats, welches nach irgendeinem der Ansprüche 1 bis 10 hergestellt wurde.

14. Verfahren zur Herstellung eines Arzneimittelkaugummiprodukts, welches Verfahren das Mischen von einer Kaugummizusammensetzung in einer Menge bis zu etwa 99%, welche eine Gummibasis und einen Süßstoff enthält, und einer therapeutisch wirksamen Menge eines Arzneimitteladsorbats, welches nach irgendeinem der Ansprüche 1 bis 10 hergestellt wurde, wobei alle Prozentangaben hierin auf das Gewichts des Arzneimittelkaugummiprodukts bezogen sind, umfaßt.

Revendications pour les Etats Contractants: AT, BE, FR, DE, IT, LU, NL, SE CH, GB, LI

15 1. Adsorbat médicamenteux, qui comprend un silicate complexe de magnésium et d'aluminium dans lequel est sorbée une solution d'un médicament et d'un tensioactif.

2. Adsorbat médicamenteux selon la revendication 1, dans lequel le médicament est présent en une quantité de 1 à 35% en poids et le silicate complexe de magnésium et d'aluminium est présent en une quantité de 70 à 90% en poids, tous les pourcentages étant exprimés en pourcentages en poids par rapport à l'adsorbat médicamenteux.

3. Adsorbat médicamenteux selon la revendication 1 ou 2, dans lequel le tensioactif est présent en une quantité de 0,05 à 4% en poids par rapport à l'adsorbat médicamenteux.

4. Adsorbat médicamenteux selon l'une quelconque des revendications 1 à 3, contenant en outre jusqu'à environ 20% en poids d'un solvant, par rapport à l'adsorbat médicamenteux.

25 5. Adsorbat médicamenteux selon l'une quelconque des revendications 1 à 3, comprenant en outre de 2 à 15% en poids d'un solvant, par rapport à l'adsorbat médicamenteux.

6. Adsorbat médicamenteux selon l'une quelconque des revendications 1 à 5, dans lequel le tensioactif est choisi entre le laurylsulfate de sodium, les tensioactifs anioniques du type Pluronic et leurs mélanges.

7. Adsorbat médicamenteux selon l'une quelconque des revendications 1 à 6, dans lequel le silicate complexe de magnésium et d'aluminium présente l'analyse chimique typique suivante:

		% en poids	Proportion à l'oxyde d'aluminium
35	Silice	55 à 70	3,2 à 35
	Oxyde de magnésium	2,9 à 25	0,17 à 12,5
	Oxyde d'aluminium	2,0 à 17	1
40	Oxyde ferrique	0,4 à 1,8	
	Oxyde de calcium	1,1 à 2,4	
45	Oxyde de sodium	1,0 à 3,8	
	Oxyde de potassium	0,2 à 1,9	
50	Perte au feu	5,5 à 12,6	

8. Adsorbat médicamenteux selon l'une quelconque des revendications 1 à 6, dans lequel le silicate complexe de magnésium et d'aluminium présente l'analyse chimique typique suivante:



	% en poids	Proportion à l'oxyde d'aluminium
5 Silice	56 à 59	14,0 à 35
Oxyde de magnésium	21 à 24	5,2 à 12,0
Oxyde d'aluminium	2,0 à 4,0	1
10 Oxyde ferrique	0,4 à 0,6	
Oxyde de calcium	1,1 à 1,5	
15 Oxyde de sodium	2,5 à 3,5	
Oxyde de potassium	0,5 à 1,0	
Perte au feu	5,5 à 12,6	

9. Procédé pour la préparation d'un adsorbat médicamenteux, qui consiste à mélanger un silicate complexe de magnésium et d'aluminium à un médicament, un tensioactif et une quantité d'un solvant suffisante pour dissoudre le médicament et le tensioactif pour former une masse contenant le médicament et le tensioactif à l'état adsorbé, et à récupérer l'adsorbat médicamenteux.

10. Procédé selon la revendication 9, dans lequel le solvant est utilisé en des quantités de 10 à 60% en poids par rapport à l'adsorbat médicamenteux.

11. Procédé selon la revendication 9 ou 10, dans lequel le médicament est présent en une quantité de 1 à 35% en poids, et le silicate complexe de magnésium et d'aluminium est présent en une quantité de 70 à 90% en poids, tous les pourcentages étant exprimés par rapport à l'adsorbat médicamenteux.

12. Procédé selon l'une quelconque des revendications 9 à 11, dans lequel le tensioactif est présent en une quantité de 0,05 à 4% en poids par rapport à l'adsorbat médicamenteux.

13. Procédé selon l'une quelconque des revendications 9 à 12, consistant en outre à sécher la masse jusqu'à ce que la teneur finale en solvant aille jusqu'à environ 20% en poids par rapport à l'adsorbat médicamenteux.

14. Procédé selon l'une quelconque des revendications 9 à 13, dans lequel la quantité de solvant utilisée est d'environ 1 à environ 20 fois le poids du silicate complexe de magnésium et d'aluminium.

15. Composition médicamenteuse, qui comprend un excipient pharmaceutiquement acceptable et de 1 à 60% en poids, par rapport à la composition finale, d'un adsorbat médicamenteux selon l'une quelconque des revendications 1 à 8.

16. Composition médicamenteuse selon la revendication 15, dans laquelle l'excipient pharmaceutiquement acceptable est choisi parmi les pastilles, les comprimés, les suspensions, les caramels, les nougats, les bonbons à mâcher et la gomme à mâcher.

17. Produit médicamenteux de confiserie, comprenant:

un diluant, en une quantité allant jusqu'à environ 99%;

une quantité thérapeutiquement efficace d'un adsorbat médicamenteux selon l'une quelconque des revendications 1 à 8,

ledit adsorbat médicamenteux étant mélangé dans le produit de confiserie,

tous les pourcentages étant exprimés en poids par rapport au produit médicamenteux de confiserie.

18. Produit médicamenteux de type gomme à mâcher, contenant une quantité d'un médicament à effet thérapeutique, comprenant:

une composition de gomme à mâcher, en une quantité allant jusqu'à environ 99%, et contenant une base de gomme et un édulcorant; et

une quantité à effet thérapeutique, d'un adsorbat médicamenteux selon l'une quelconque des revendications 1 à 8,

ledit adsorbat médicamenteux étant mélangé à la composition de gomme à mâcher,

tous les pourcentages étant en poids par rapport au produit médicamenteux du type gomme à mâcher.

Revendications pour l'Etat Contractant: ES

1. Procédé pour la préparation d'un adsorbat médicamenteux, qui consiste à mélanger un silicate complexe de magnésium et d'aluminium à un médicament, un tensioactif et une quantité d'un solvant suffisante pour dissoudre le médicament et le tensioactif pour former une masse contenant le médicament et le tensioactif à l'état adsorbé, et à récupérer l'adsorbat médicamenteux.

2. Procédé selon la revendication 1, dans lequel le médicament est présent en une quantité de 1 à 35% en poids, et le silicate complexe de magnésium et d'aluminium est présente en une quantité de 70 à 90%



en poids, tous les pourcentages étant exprimés par rapport à l'adsorbat médicamenteux.

3. Procédé selon la revendication 1 ou 2, dans lequel le tensioactif est présent en une quantité de 0,05 à 4% en poids par rapport à l'adsorbat médicamenteux.

4. Procédé selon l'une quelconque des revendications 1 à 3, dans lequel le tensioactif est choisi entre le laurylsulfate de sodium, les tensioactifs anioniques du type Pluronic et leurs mélanges.

5. Procédé selon l'une quelconque des revendications 1 à 4, dans lequel le silicate complexe de magnésium et d'aluminium présente l'analyse chimique typique suivante:

		% en poids	Proportion à l'oxyde d'aluminium
10	Silice	55 à 70	3,2 à 35
	Oxyde de magnésium	2,9 à 25	0,17 à 12,5
15	Oxyde d'aluminium	2,0 à 17	1
	Oxyde ferrique	0,4 à 1,8	
20	Oxyde de calcium	1,1 à 2,4	
	Oxyde de sodium	1,0 à 3,8	
	Oxyde de potassium	0,2 à 1,9	
25	Perte au feu	5,5 à 12,6	

6. Procédé selon l'une quelconque des revendications 1 à 4, dans lequel le silicate complexe de magnésium et d'aluminium présente l'analyse chimique typique suivante:

		% en poids	Proportion à l'oxyde d'aluminium
35	Silice	56 à 59	14,0 à 35
	Oxyde de magnésium	21 à 24	5,2 à 12,0
	Oxyde d'aluminium	2,0 à 4,0	1
40	Oxyde ferrique	0,4 à 0,6	
	Oxyde de calcium	1,1 à 1,5	
45	Oxyde de sodium	2,5 à 3,5	
	Oxyde de potassium	0,5 à 1,0	
50	Perte au feu	5,5 à 12,6	

7. Procédé selon l'une quelconque des revendications précédentes, dans lequel la quantité de solvant utilisée dans le procédé est comprise entre 10 et 60% en poids par rapport à l'adsorbat médicamenteux.

8. Procédé selon l'une quelconque des revendications précédentes, dans lequel la quantité de solvant utilisée dans le procédé est comprise entre 1 et 20 fois le poids du silicate complexe de magnésium et d'aluminium.

9. Procédé selon l'une quelconque des revendications 9 à 12, qui consiste en outre à sécher la masse jusqu'à une teneur finale en solvant allant jusqu'à environ 20% en poids par rapport au médicament.

10. Procédé selon la revendication 9, dans lequel la masse est séchée jusqu'à une teneur finale en solvant de 2 à 15% en poids par rapport à l'adsorbat médicamenteux.

11. Procédé pour la préparation d'une composition médicamenteuse, qui consiste à mélanger un excipient pharmaceutiquement acceptable et de 1 à 60% en poids, par rapport à la composition finale, d'un adsorbat médicamenteux préparé selon l'une quelconque des revendications 1 à 10.



12. Procédé selon la revendication 11, dans lequel l'excipient pharmaceutiquement acceptable est choisi parmi les pastilles, les comprimés, les suspensions, les caramels, les nougats, les bonbons à mâcher et la gomme à mâcher.

5 13. Procédé pour la préparation d'un produit médicamenteux de confiserie, qui consiste:
à ajouter jusqu'à environ 99% d'un diluant; et
une quantité à effet thérapeutique d'un adsorbat médicamenteux préparé selon l'une quelconque des revendications 1 à 10.

10 14. Procédé pour la préparation d'un produit médicamenteux du type gomme à mâcher, qui consiste à mélanger une composition de gomme à mâcher en une quantité allant jusqu'à environ 99% et contenant une base de gomme, et un édulcorant; et
une quantité à effet thérapeutique d'un adsorbat médicamenteux préparé selon l'une quelconque des revendications 1 à 10, tous les pourcentages étant en poids par rapport au produit médicamenteux du type gomme à mâcher.

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