Office de la Propriété Intellectuelle du Canada
Un organisme d'Industrie Canada

Canadian Intellectual Property Office
An agency of Industry Canada

CA 2348024 C 2008/02/19

(11)(21) 2 348 024

(12) BREVET CANADIEN
CANADIAN PATENT

(13) C

(86) Date de dépôt PCT/PCT Filing Date: 1999/10/28
(87) Date publication PCT/PCT Publication Date: 2000/05/11
(45) Date de délivrance/Issue Date: 2008/02/19
(85) Entrée phase nationale/National Entry: 2001/04/26
(86) N° demande PCT/PCT Application No.: US 1999/025454
(87) N° publication PCT/PCT Publication No.: 2000/025744
(30) Priorité/Priority: 1998/10/30 (US60/106,302)

(51) Cl.Int./Int.Cl. *A61K 31/167* (2006.01), *A61K 47/12* (2006.01), *A61K 9/16* (2006.01)

(72) Inventeurs/Inventors:
MORRIS, JOSEPH M., US;
BEAHM, JAMES S., US

(73) Propriétaire/Owner:
MCNEIL-PPC, INC., US

(74) Agent: SMART & BIGGAR

(54) Titre : COMPOSITION PHARMACEUTIQUE COULANTE EN GRANULES ET FORME GALENIQUE SOUS FORME DE PAILLE POUR ADMINISTRATION ORALE

(54) Title: GRANULAR, FREE-FLOWING PHARMACEUTICAL COMPOSITION, AND STRAW-LIKE DOSAGE FORM FOR ORAL ADMINISTRATION THEREOF

(57) Abrégé/Abstract:
This invention provides a dry, granular, free-flowing, stable pharmaceutical composition for oral administration comprising particles of medicament or nutrient coated with a suitable taste-masking agent, a salivation-inducing agent, and a pharmaceutically acceptable carrier. This invention also provides dosage forms for oral administration comprising a closed, moisture-resistant container, either straw-like or non-straw-like, each having therein a single unit dose of the instant pharmaceutical composition, and having an opening means for permitting the dry oral administration thereof.

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : A61K 9/00, 31/165

A1

(11) International Publication Number: WO 00/25744

(43) International Publication Date: 11 May 2000 (11.05.00)

(21) International Application Number: PCT/US99/25454

(22) International Filing Date: 28 October 1999 (28.10.99)

(30) Priority Data:
60/106,302 30 October 1998 (30.10.98) US

(71) Applicant: MCNEIL–PPC, INC. [US/US]; Grandview Road, Skillman, NJ 08858 (US).

(72) Inventors: MORRIS, Joseph, M.; 180 Lafayette Road, Coatesville, NJ 19320 (US). BEAHM, James, S.; 122 Township Line Road, Exton, PA 19341 (US).

(74) Agents: CIAMPORCERO, Audley et al.; Johnson & Johnson, One Johnson Plaza, New Brunswick, NJ 08933–7003 (US).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: GRANULAR, FREE–FLOWING PHARMACEUTICAL COMPOSITION, AND STRAW–LIKE DOSAGE FORM FOR ORAL ADMINISTRATION THEREOF

(57) Abstract

This invention provides a dry, granular, free–flowing, stable pharmaceutical composition for oral administration comprising particles of medicament or nutrient coated with a suitable taste–masking agent, a salivation–inducing agent, and a pharmaceutically acceptable carrier. This invention also provides dosage forms for oral administration comprising a closed, moisture–resistant container, either straw–like or non–straw–like, each having therein a single unit dose of the instant pharmaceutical composition, and having an opening means for permitting the dry oral administration thereof.

GRANULAR, FREE-FLOWING PHARMACEUTICAL COMPOSITION, AND STRAW-LIKE DOSAGE FORM FOR ORAL ADMINISTRATION THEREOF

Field of the Invention

This invention relates to granular, free-flowing, pleasant tasting pharmaceutical compositions for oral administration, and also to straw-like dosage forms for administering same. These forms permit a more convenient and reliable way of administering a wide variety of medicaments and nutrients to those having difficulty in using other types of oral dosage forms.

Background of the Invention

Orally administered medicaments exist in many forms such as liquid solutions, emulsions, suspensions, capsules and tablets. Caplet and tablet forms are generally intended to be swallowed whole. Therefore, the often disagreeable taste of the medicament need not be taken into account when formulating such medicine, except in preventing any unpleasant taste while the medicine is in the mouth. This can be accomplished by placing a thin and quickly dissolving coating on the tablet, by using the gelatin capsule form, or by firmly compressing a tablet during manufacture so as to prevent its disintegration while in the mouth.

A common problem with chewable tablet forms is the often disagreeable taste of the active ingredient which manifests itself during chewing. In some cases, the taste of the medicament in a tablet can be overpowered by adding flavoring ingredients to the tablet so that when it is chewed, the taste of the medicament is simply overpowered. This has been done, for example, with children's aspirin, where the dosage is small enough so

that the amount of flavoring agents needed to mask the taste of the medicament is not so great that the tablet becomes unreasonably large.

A different approach is taken with a commercially available children's size tablet of acetaminophen, where the acetaminophen is present in granules coated with polymers such as ethyl cellulose, or cellulose acetate and polyvinyl pyrrolidone. While the tablet is in the mouth, a significant proportion of the acetaminophen remains shielded by the coating and thus does not contribute to taste, despite some breakage of the polymer coating upon compression of the tablet during manufacture, and additional breakage of the coating during chewing. The acetaminophen becomes bioavailable from the granules where the coating is broken, and from permeation through the coating. This phenomenon is due to the fact that ethylcellulose films are water-permeable, and combination films, such as cellulose acetate and polyvinyl pyrrolidone, contain one soluble component which dissolves in the gastrointestinal tract, rendering the film permeable to water and dissolved active components.

Despite the existing ability to mask unpleasant medicament taste in tablets and capsules, a need still exists for a more convenient way of administering these medicaments to those such as the very young and very old, who often have difficulty swallowing these types of dosage forms. Even among the broader population, a great many people report difficulty in swallowing tablets and capsules.

For pediatric medicines, the use of liquid and chewable dosage forms predominates until children reach

approximately 10-12 years of age. These dosages do not address all the needs of children in this age group. For example, problems with liquid dosage forms include uncertainty of delivered dose, limited stability after reconstitution (as seen with antibiotics), and poor taste. As for older patients, many require medicine tablets to be crushed because of swallowing difficulties. Indeed, the National Hospital Discharge Survey indicates that there is a 67% incidence of a discharge diagnosis of dysphagia among patients over age 65 (Department of Health and Human Services, National Center for Health Statistics (1989)). This incidence is almost five times higher than that seen among younger patients.

Summary of the Invention

This invention provides a dry, granular, free-flowing, stable pharmaceutical composition for oral administration comprising particles of medicament or nutrient coated with a suitable taste-masking agent, a salivation-inducing agent, and a pharmaceutically acceptable carrier.

This invention also provides a dosage form for oral administration comprising a closed, moisture-resistant, straw-like container having therein a single unit dose of the instant pharmaceutical composition, and having an opening means for permitting the dry oral administration thereof.

Finally, this invention provides a dosage form for oral administration comprising a closed, moisture-resistant, non-straw-like container having therein a single unit dose of the instant pharmaceutical composition, and having an opening means for permitting the dry oral administration thereof.

According to one aspect of the present invention, there is provided a dosage form for oral administration comprising: a closed, moisture resistant, straw-like container having therein a single unit dose of a pharmaceutical composition comprising a dry, granular, free flowing stable pharmaceutical composition for oral administration, said pharmaceutical composition comprising particles of medicament or nutrient coated with a suitable taste masking agent; particles of a salivation inducing agent in an amount sufficient to permit dry oral administration without any intake of water or other liquid; and particles of a pharmaceutically acceptable carrier, said container having an opening means for permitting the dry oral administration thereof.

According to another aspect of the present invention, there is provided a dosage form for oral administration comprising: a closed, moisture resistant, non-straw-like container having therein a single unit dosage of a pharmaceutical composition consisting essentially of a dry, granular, free flowing stable pharmaceutical composition for oral administration, said pharmaceutical composition comprising particles of medicament or nutrient coated with a suitable polymeric taste masking agent; particles of a salivation inducing agent in an amount sufficient to permit dry oral administration without any intake of water or other liquid; and particles of a pharmaceutically acceptable carrier, said container having an opening means for permitting the dry oral administration thereof.

According to still another aspect of the present invention, there is provided a dosage form for oral administration comprising: a closed, moisture-resistant, non-straw-like container having therein a single unit dose

of a pharmaceutical composition consisting essentially of a dry, granular, free-flowing pharmaceutical composition for oral administration, said pharmaceutical composition comprising particles of a pharmaceutically effective amount of acetaminophen coated with a suitable polymeric taste-masking agent; particles of citric acid in an amount sufficient to permit dry oral administration without any intake of water or other liquid; particles of mannitol at a level of from about 30 to about 60% by weight, and particles of a sweetener, and having an opening means for permitting the dry oral administration thereof.

According to yet another aspect of the present invention, there is provided a dosage form for oral administration comprising a closed, moisture resistant container having a drinking straw shape and having therein a single unit dose of a pharmaceutical composition comprising a dry, granular, free flowing stable pharmaceutical composition for oral administration, said pharmaceutical composition comprising: a) particles of acetaminophen coated with a suitable taste masking agent; b) particles of an edible carboxylic acid selected from the group consisting of citric acid, malic acid, fumaric acid, benzoic acid, sorbic acid, adipic acid, and mixtures thereof in an amount sufficient to permit dry oral administration without any intake of water or other liquid; and c) particles of a pharmaceutically acceptable carrier, said container having an opening means for permitting the dry oral administration thereof and wherein the pharmaceutical composition has a total water content of less than about 10% by weight.

Brief Description of the Figures

Figure 1 shows examples of the instant dosage forms, i.e., a straw dosage form, a pouch dosage form, and a blister pack dosage form.

Detailed Description of the Invention

This invention provides dry, granular, free-flowing, stable, pleasant tasting pharmaceutical compositions for oral administration. The invention also provides dosage forms employing both straw-like and non-straw-like containers for administering same. These forms are a convenient and reliable way of administering a wide variety of medicaments and nutrients to those having difficulty using other types of oral dosage forms, especially tablets and capsules.

More specifically, this invention provides a dry, granular, free-flowing, stable pharmaceutical composition for oral administration comprising particles of medicament or nutrient coated with a suitable taste-masking agent, a salivation-inducing agent, and a pharmaceutically acceptable carrier.

In one embodiment, the instant dry composition has a total water content of less than 10% by weight. In the preferred embodiment, the instant dry composition has a total water content of less than 3% by weight. As used herein, the term "stable" shall mean physically as well as chemically stable. This term is well understood in the art and includes, but is not limited to, having a shelf life of at least about two years.

The medicament or nutrient used in this invention can be any medicament or nutrient suitable for oral administration. The types of medicaments envisioned for use in this invention include, without limitation, analgesics, antacids, antibiotics, decongestants, antitussives, expectorants, local anaesthetics, antihistamines, sympathomimetics, laxatives, and

antidiarrheals. The types of nurients envisioned for use in this invention include, without limitation, minerals such as iron, and vitamins such as B_6, B_{12}, thiamin and folic acid.

Numerous analgesics are known in the art and include, by way of example, acetaminophen, acetyl salicylic acid, indomethacin and optically active isomers or racemates of ibuprofen, naproxen, flurbiprofen, carprofen, tiaprofenic acid, cicloprofen, ketoprofen, ketorolac, etodolac, indomethacin, sulindac, fenoprofen, diclofenac, piroxicam, benzydomine, nabumetone, their pharmaceutically acceptable salts and mixtures thereof. In the preferred embodiment, the analgesic is acetaminophen.

Decongestants for use in the present invention include, for example, pseudoephedrine, phenylpropanolamine, phenylephrine and ephedrine, their pharmaceutically acceptable salts, and mixtures thereof. Antitussives for use in this invention include, for example, dextromethorphan, chlophedianol, carbetapentane, caramiphen, noscapine, diphenhydramine, codeine, hydrocodone, hydromorphone, fominoben, benzonatate, their pharmaceutically acceptable salts, and mixtures thereof. Expectorants (also known as mucolytic agents) useful in this invention include, for example, glyceryl guaiacolate, guaifenesin, terpin hydrate, ammonium chloride, N-acetylcysteine and bromhexine, ambroxol, their pharmaceutically acceptable salts, and mixtures thereof. Local anaesthetics useful in this invention include, for example, hexylresorcinol, dyclonine, benzocaine, phenol, their pharmaceutically acceptable salts, and mixtures thereof.

Antihistamines useful in the present invention include, for example, chlorpheniramine, brompheniramine, diphenhydramine, dexchlorpheniramine, dexbromphreniramine, triprolidine, azatadine, doxylamine, tripelennamine, cyproheptadine, hydroxyzine, carbinoxamine, phenindamine, bromodiphenhydramine, pyrilamine, their pharmaceutically acceptable salts and mixtures thereof, as well as the non-sedating antihistamines such as acrivastine, AHR-11325, astemizole, azatadine, azelastine, cetirizine, ebastine, ketotifen, lodoxamide, loratidine, levocabastine, mequitazine, oxatomide, setastine, tazifylline, temelastine, and terfenadine, their pharmaceutically acceptable salts and mixtures thereof.

Sympathomimetics suitable for use in this invention include, for example, pseudoephedrine, phenylpropanolamine, pharmaceutically acceptable salts thereof (e.g., pseudoephedrine hydrochloride), and mixtures thereof. Laxatives which can be used in the present invention include, for example, sennosides A and B. Suitable antidiarrheals include, for example, loperamide and pharmaceutically acceptable salts thereof (e.g., loperamide HCl).

As used herein, the term "pharmaceutically acceptable salts" refers to salts prepared from pharmaceutically acceptable non-toxic bases including inorganic bases and organic bases. Salts derived from inorganic bases include sodium, potassium, lithium, ammonia, calcium, magnesium, ferrous, zinc, manganous, aluminum, ferric, manganic salts and the like. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary,

tertiary and quaternary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins such as triethylamine, tripropylamine, 2-dimethylaminoethanol, 2-diethylaminoethanol, amino acids generally and lysine, arginine and histidine specifically, caffeine, procaine, N-ethylpiperidine, hydrabamine, choline, betaine, ethylenediamine, glucosamine, methylglycamine, theobromine, purines, piperazine, piperidine, polyamine resins and the like.

All of these medicaments, as well as their acceptable dosage ranges, are described in U.S. Patent Nos. 4,783,465 and 4,619,934. Additional antitussives, expectorants, antihistamines, sympathomimetics, laxatives, antidiarrheals and analgesics suitable for use in the present invention are described in Remington's Pharmaceutical Sciences (Mack Publishing Co., Easton, PA, 18th ed., Chapters 39, 42, 43, 58 and 59 (1990)).

Methods of coating medicament and nutrient particles used in this invention with taste-masking agents are well known and commercially available in the pharmaceutical industry. Such methods are taught, for example, in U.S. Patent Nos. 5,489,436, 5,260,072, 5,215,755, 5,489,436, 5,460,825, and 4,851,224. These taste-masking agents include, for example, ethyl cellulose ("EC"); cellulose acetate ("CA"); cellulose acetate butyrate ("CAB"); polymethacrylates such as dimethylaminoethyl methacrylate and neutral methacrylic acid ester (Eudragit® E-100); hydroxypropyl cellulose ("HPC"); hydroxyethyl cellulose ("HEC"); and hydroxypropyl methyl cellulose ("HPMC").

Alternatively, medicament particles that are already

taste-masked can be purchased commercially. For example, taste-masked acetaminophen particles are commercially available from Eurand America, Inc. (845 Center Drive, Vandalia, OH 45377), and taste-masked pseudoephedrine ("PE") and chlorpheniramine maleate ("CPM") particles are available from Particle Dynamics, Inc. (2503 South Hanley Road, St. Louis, MO 63144).

Pharmaceutically acceptable carriers are generally water-disintegratable carbohydrates which are described in Lieberman et al., Pharmaceutical Dosage Forms (Marcel Dekker, Inc., New York, 2 Ed. Vol. 1, pp. 205-209 (1990)). Preferred carriers include dextrose, sucrose, lactose, maltose, xylose, maltodextrins, dextrates, mannitol, sorbitol, and xylitol.

One or more salivation-inducing agents are appropriate for the proper ingestion of the instant pharmaceutical composition, given its dry, granular nature. Such agents are routinely used in the art, and are usually carboxylic acids. In one embodiment, the salivation-inducing agent is an edible carboxylic acid such as citric acid, malic acid, fumaric acid, benzoic acid, sorbic acid, or adipic acid. Preferably, anhydrous carboxylic acids are used. The use of carboxylic acids in specific formulations is shown in the Examples section below.

In order to enhance its taste, mouth-feel and other physical properties, the instant pharmaceutical composition ideally includes components additional to the medicament, salivation-inducing agent, and carrier. Thus, in one embodiment, the pharmaceutical composition further comprises one or more of a soothing agent, a sweetener, and a flavoring agent. In the preferred

embodiment, the composition comprises all of these additional components.

Soothing agents create a "cooling" sensation in the mouth due to their negative heat of hydration. These are widely used in the art and include, for example, mannitol, sorbitol, and xylitol. Suitable sweeteners include, for example, aspartame, sucralose, saccharine, cyclamate, acesulfame potassium, manitol, sorbitol, and xylitol. Suitable flavoring agents include, for example, fruit flavoring (e.g. lemon flavor) and cream flavoring. A more extensive list of soothing agents, sweeteners, and flavoring agents is provided in Handbook of Pharmaceutical Excipients, 2nd ed. (American Pharmaceutical Association, Washington, D.C. (1994)).

In one embodiment, the pharmaceutical composition comprises coated acetaminophen particles, citric acid, mannitol, a sweetener, and lemon flavoring. Additional, more specific embodiments of this composition are provided in the Examples section below.

In another embodiment, the coated particles of the instant pharmaceutical composition comprise a plurality of medicaments and/or nutrients. Here, two possibilities exist, i.e., (i) the composition has one type of coated particle containing a plurality of medicaments and/or nutrients, and (ii) the composition has more than one type of coated particle, each type containing a one or more medicaments and/or nutrients. In one example, the composition comprises coated acetaminophen particles and coated particles of either chlorpheniramine maleate or pseudoepheddrine (Descote®, Particle Dynamics, Inc.).

This invention also provides two dosage forms for oral administration. The first form comprises a closed, moisture-resistant, straw-like container having therein a single unit dose of the instant pharmaceutical composition, and having an opening means for permitting the dry oral administration thereof. The second form comprises a closed, moisture-resistant, non-straw-like container having therein a single unit dose of the instant pharmaceutical composition, and having an opening means for permitting the dry oral administration thereof. As used herein, "dry oral administration" means oral administration that does not require the concomitant intake of water or other liquid. In the preferred embodiment of the instant dosage forms, the coated medicament is acetaminophen, whose single unit dosages include, for example, 50 mg, 80 mg, 160 mg, 300 mg, 325 mg, 500 mg and 1000 mg.

As used herein, the term "straw-like container" means any container having a cylindrical shape whose length is greater than its width. The dimensions of the straw-like container used in this invention can vary widely. In one embodiment, its dimensions are those of an ordinary drinking straw, e.g., having a length of about 200 mm and a width of about 6 mm. The straw-like container can be made from any non-toxic moisture-resistant material such as plastic (e.g. polyethylene) or wax-coated paper. Finally, the opening means on the straw-like container includes, for example, an end that is opened by tearing, or by removing a cap (via twisting or otherwise). Once open, the contents of the container are simply emptied directly into the user's mouth. The straw-like container used in this invention is intended to

function like the straw-like container used in the PIXIE STICK™ children's granular candy dispenser.

As used herein, the term "non-straw-like container" means any container that does not have a cylindrical shape whose length is greater than its width. As with the straw-like container, the dimensions of the non-straw-like container used in this invention can vary widely. For example, the non-straw-like container can be a "blister pack", which is a widely used type of pharmaceutical container typically made from polymers such as polyvinyl chloride, polyvinylidine chloride ("PVDC") and polychlorotrifluoroethylene ("Aclar®"). Alternatively, the non-straw-like container can be oblong and non-cylindrically shaped, oblong and having only a portion which is cylindrically shaped, or cylindrically shaped wherein the width is greater than the length. Moreover, non-straw-like container can be a pouch, such as a foil/foil pouch, a foil/paper pouch, or a paper/paper pouch. As with the straw-like container, the non-straw-like container can be made from any non-toxic moisture-resistant material such as plastic or wax-coated paper, and the opening means includes, for example, an end which is opened by tearing, or by removing a cap.

In one embodiment (and in the case of straw dosage forms the preferred embodiment), the instant dosage forms are packaged, along with a desiccant, within an outer, child-resistant container. Child-resistant containers (which meet the requirements of the Poison Prevention Packaging Act of 1970 (16 C.F.R. 1700, et seq.)) and their methods of manufacture are standard in the art. Ideally, within each outer container is a

plurality of individual dosage forms to be administered either on an "as needed" basis, or periodically over a prescribed length of time. An example of the former "as needed" scenario is the use of analgesics, such as acetaminophen, for pain relief. An example of the latter "periodic" scenario is the use of antihistamines, such as brompheniramine, for relief of symptoms of seasonal allergies.

This invention will be better understood by reference to the Examples that follow, but those skilled in the art will readily appreciate that they are only illustrative of the invention as described more fully in the claims which follow thereafter. In addition, various publications are cited throughout this application. The disclosure of these publications is hereby incorporated by reference into this application to describe more fully the state of the art to which this invention pertains.

Example 1

TYLENOL (Acetaminophen) Granules - I

Ingredient	Unit Weight Mg	Weight Percent
Encapsulated Acetaminophen*	1075.3	59.74
Citric Acid USP (Anhydrous Powder)	20.0	1.11
Aspartame NF (Powder)	46.0	2.55
Alpine Cream Flavor Power	6.6	0.37
Natural and Artificial Lemon Juice Flavor	6.6	0.37
Mannitol (Granular)	645.5	35.86
Total	1800.0	100.00

*Equivalent to 1,000 mg of acetaminophen.

Physicals	Actual	
	Mesh Size	% Retained
Particle Size Analysis	20	0.1%
	30	2.0%
	40	16.0%
	60	62.9%
	80	11.8%
	100	2.5%
	Pan	4.8%
Bulk Density	0.60g/mL	
Tap Density	0.74 g/mL at 250 taps	
	0.74 g/mL at 500 taps	

Note: the following acronyms are used in the Examples.
"NF" means National Formulary.
"USP" means United States Pharmacopeia.
"JP" means Japan Pharmacopeia.
"JPE" means Japan Pharmaceutical Excipient.

Example 2
TYLENOL (Acetaminophen) Granules - II

Ingredient	Unit Weight Mg	Weight Percent
Encapsulated Acetaminophen*	1070.1	58.48
Fumaric Acid NF (Powder)	60.0	3.28
Aspartame NF (Powder)	46.0	2.51
Alpine Cream Flavor	6.6	0.36
Natural and Artificial Lemon Juice Flavor	6.6	0.36
Mannitol (Granular)	640.7	35.01
Total	1830.0	100.00

*Equivalent to 1,000 mg of acetaminophen.

Physicals	Actual	
	Mesh Size	% Retained
Particle Size Analysis	20	0.2%
	30	1.8%
	40	13.2%
	60	63.4%
	80	10.2%
	100	7.0%
	Pan	4.1%
Bulk Density	0.63g/mL	
Tap Density	0.80g/mL at 50 taps	

Example 3
TYLENOL (Acetaminophen) Granules - III

Ingredient	Unit Weight (mg)	Max. Daily Dose (mg)	Weight Percent (%)
JP Mannitol	358.70	1076.10	51.24
JP Citric Acid Anhydrous	3.70	11.10	0.53
Lemon Juice Flavor	2.30	6.90	0.33
JP Magnesium Stearate	2.00	6.00	0.28
JP Acetaminophen	300.00	900.00	42.86
JPE Ethylcellulose	33.30	99.90	4.76
Total Weight	700.00	2100.00	100.00

Physicals	Actual	
	Mesh Size	% Retained
Particle Size Analysis	20	0%
	35	1.8%
	200	97.6%
	Pan	0.6%

Example 4

Sore Throat Granules

Ingredient	Unit Weight Mg	Weight Percent
Encapsulated Acetaminophen*	571.4	56.95
Citric Acid USP (Anhydrous Powder)	7.0	0.7
Aspartame NF (Powder)	15.0	1.5
Prosweet Power	4.0	0.4
Artificial Cherry Flavor	2.5	0.25
Mixed Berry Flavor	1.0	0.1
Mannitol (Granular)	399.1	39.8
Dyclonine HCl	3.0	0.3
Total	1003.0	100.0

*Equivalent to 500 mg of acetaminophen.

74374-4

CLAIMS:

1. A dosage form for oral administration comprising: a closed, moisture resistant, straw-like container having therein a single unit dose of a pharmaceutical composition comprising a dry, granular, free flowing stable pharmaceutical composition for oral administration, said pharmaceutical composition comprising particles of medicament or nutrient coated with a suitable taste masking agent; particles of a salivation inducing agent in an amount sufficient to permit dry oral administration without any intake of water or other liquid; and particles of a pharmaceutically acceptable carrier, said container having an opening means for permitting the dry oral administration thereof.

2. The dosage form of claim 1, wherein the medicament is acetaminophen.

3. The dosage form of claim 1 or 2, wherein the form is packaged, along with a desiccant, within an outer, child-resistant container.

4. The dosage form of any one of claims 1 to 3, wherein the salivation-inducing agent is an edible carboxylic acid.

5. The dosage form of any one of claims 1 to 3, wherein the salivation-inducing agent is selected from the group consisting of citric acid, malic acid, fumaric acid, benzoic acid, sorbic acid, adipic acid, and mixtures thereof.

6. The dosage form of any one of claims 1 to 5, further comprising a soothing agent and a sweetener.

7. The dosage form of claim 6, wherein the soothing agent exhibits a negative heat of hydration.

8. The dosage form of claim 7, wherein the soothing agent is selected from the group consisting of mannitol, sorbitol, and xylitol.

9. The dosage form of claim 6, wherein said sweetener is selected from the group consisting of aspartame, sucralose, saccharine, cyclamate, acesulfame potassium, mannitol, sorbitol, and xylitol.

10. The dosage form of any one of claims 1 to 9, wherein the pharmaceutical composition has a total water content of less than about 10% by weight.

11. A dosage form for oral administration comprising: a closed, moisture resistant, non-straw-like container having therein a single unit dosage of a pharmaceutical composition consisting essentially of a dry, granular, free flowing stable pharmaceutical composition for oral administration, said pharmaceutical composition comprising particles of medicament or nutrient coated with a suitable polymeric taste masking agent; particles of a salivation inducing agent in an amount sufficient to permit dry oral administration without any intake of water or other liquid; and particles of a pharmaceutically acceptable carrier, said container having an opening means for permitting the dry oral administration thereof.

12. The dosage form of claim 11, wherein the medicament is acetaminophen.

13. The dosage form of claim 11 or 12, wherein said container is a pouch.

14. The dosage form of any one of claims 11 to 13, wherein said pharmaceutical composition remains physically and chemically stable in said container for at least about two years.

15. The dosage form of any one of claims 11 to 14, wherein the form is packaged, along with a desiccant, within an outer, child-resistant container.

16. The dosage form of any one of claims 11 to 15, wherein the salivation-inducing agent is an edible carboxylic acid.

17. The dosage form of any one of claims 11 to 15, wherein the salivation-inducing agent is selected from the group consisting of citric acid, malic acid, fumaric acid, benzoic acid, sorbic acid, adipic acid, and mixtures thereof.

18. The dosage form of any one of claims 11 to 17, further comprising a soothing agent and a sweetener.

19. The dosage form of claim 18, wherein the soothing agent exhibits a negative heat of hydration.

20. The dosage form of claim 19, wherein the soothing agent is selected from the group consisting of mannitol, sorbitol, and xylitol.

21. The dosage form of claim 18, wherein said sweetener is selected from the group consisting of aspartame, sucralose, saccharine, cyclamate, acesulfame potassium, mannitol, sorbitol, and xylitol.

22. The dosage form of any one of claims 11 to 21, wherein the pharmaceutical composition has a total water content of less than 10% by weight.

23. A dosage form for oral administration comprising: a closed, moisture-resistant, non-straw-like container having therein a single unit dose of a pharmaceutical composition consisting essentially of a dry, granular, free-flowing pharmaceutical composition for oral administration, said pharmaceutical composition comprising particles of a pharmaceutically effective amount of acetaminophen coated with a suitable polymeric taste-masking agent; particles of citric acid in an amount sufficient to permit dry oral administration without any intake of water or other liquid; particles of mannitol at a level of from about 30 to about 60% by weight, and particles of a sweetener, and having an opening means for permitting the dry oral administration thereof.

24. The dosage form of claim 23, wherein the pharmaceutical composition has a total water content of less than about 10% by weight.

25. The dosage form of claim 23 or 24, wherein said container is a pouch.

26. The dosage form of any one of claims 23 to 25, wherein said pharmaceutical composition remains physically and chemically stable in said container for at least about two years.

27. A dosage form for oral administration comprising a closed, moisture resistant container having a drinking straw shape and having therein a single unit dose of a pharmaceutical composition comprising a dry, granular, free flowing stable pharmaceutical composition for oral administration, said pharmaceutical composition comprising:

a) particles of acetaminophen coated with a suitable taste masking agent;

b) particles of an edible carboxylic acid selected from the group consisting of citric acid, malic acid, fumaric acid, benzoic acid, sorbic acid, adipic acid, and mixtures thereof in an amount sufficient to permit dry oral administration without any intake of water or other liquid; and

c) particles of a pharmaceutically acceptable carrier,

said container having an opening means for permitting the dry oral administration thereof and wherein the pharmaceutical composition has a total water content of less than about 10% by weight.

28. The dosage form of claim 27, wherein the form is packaged, along with a desiccant, within an outer, child-resistant container.

29. The dosage form of claim 27 or 28, further comprising a soothing agent and a sweetener.

30. The dosage form of claim 29, wherein the soothing agent exhibits a negative heat of hydration.

31. The dosage form of claim 30, wherein the soothing agent is selected from the group consisting of mannitol, sorbitol, and xylitol.

32. The dosage form of claim 31, wherein said sweetener is selected form the group consisting of aspartame, sucralose, saccharine, cyclamate, acesulfame potassium, mannitol, sorbitol, and xylitol.

33. The dosage form of any one of claims 27 to 32, wherein said pharmaceutical composition remains physically

and chemically stable in said container for at least about two years.

SMART & BIGGAR

OTTAWA, CANADA

PATENT AGENTS

FIG. 1