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Chewable pharmaceutical dosage forms

Abstract

One aspect of the present invention concerns compositions and methods of manufacturing translucent chewable gels that are pharmaceutically suitable for oral administration. The chewable gels includes an active pharmaceutical ingredient and a complexing agent. The active pharmaceutical ingredient has a bitter taste. The active pharmaceutical ingredient and the complexing agent are complexed in the form of an inclusion complex. The chewable gels are substantially devoid of bitter taste and/or a tendency to cause oral numbness when chewed.

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Background/Summary

RELATED APPLICATIONS (1) The present application is a continuation-in-part of U.S. patent application Ser. No. 16/515,982 filed Jul. 18, 2019, entitled CHEWABLE PHARMACEUTICAL DOSAGE FORMS, which claims the benefit of U.S. Provisional Patent Application Ser. No. 62/700,149, filed Jul. 18, 2018, entitled Chewable Pharmaceutical Dosage Forms and U.S. Provisional Patent Application Ser. No. 62/831,500, filed Apr. 9, 2019, entitled Chewable Pharmaceutical Dosage Forms, each of which is hereby incorporated in its entirety by reference herein.

BACKGROUND

1. Field

(1) The present invention relates generally to pharmaceutical products for human and animal use. More particularly, the present invention relates to orally consumable pharmaceutical products and methods of manufacturing the same. Even more particularly, the present invention relates to chewable pharmaceutical oral dosage forms, including chewable gels. As defined by the United States Pharmacopeia: “[c]hewable gels are used to deliver drug substances or dietary supplements via the oral route. In addition to drug substances(s) or dietary supplements, chewable gels can consist of all or some of the following components: gelling agent(s), sugars, water, sweeteners, and flavoring agents. The sweeteners and flavoring are intended to enhance patient acceptance and mask the taste of the delivered labeled drug substance or dietary supplement. Chewable gels maintain their molded shape, are elastic, and yield to mastication. They are intended to be chewed before swallowing. Chewable gels are also known as “gummies” in the confectionary and dietary supplement industries.”

2. Discussion of Prior Art

(2) Chewable oral dosage forms can be an effective way to administer drugs to those who are unable (or unwilling) to swallow traditional oral dosage forms. Known chewable dosage forms tend to lack certain organoleptic properties and are perceived by many patients as being dry, gritty, dusty, and/or bad tasting. Chewable gels could be a suitable alternative; however, chewable gels known in the art are difficult to manufacture (especially on a large scale) and/or suffer from an inability to consistently satisfy generally accepted regulatory standards. Further, many active pharmaceutical ingredients have tastes that are strongly disagreeable, something which manufactures of known chewable gels have failed to overcome. Thus, there is a need for pleasant

tasting chewable gels that: include active pharmaceutical ingredients; are capable of commercially viable manufacture; and consistently satisfy generally accepted regulatory standards.

SUMMARY OF THE INVENTION

- (3) One aspect of the present invention concerns chewable gels that can both be manufactured using commercially viable methods (e.g., in commercial batch sizes, etc.) and satisfy generally accepted regulatory standards (e.g., are pharmaceutically suitable) for chewable oral dosage forms.
- (4) One aspect of the present invention concerns compositions and methods of manufacturing a translucent chewable gel that is pharmaceutically suitable for oral administration. The chewable gel includes a water insoluble active pharmaceutical ingredient and a complexing agent. The water insoluble active pharmaceutical ingredient has a bitter taste. The water insoluble active pharmaceutical ingredient and the complexing agent are complexed in the form of an inclusion complex. The chewable gel is substantially devoid of bitter taste when chewed.
- (5) One aspect of the present invention concerns compositions and methods of manufacturing a translucent chewable gel that is pharmaceutically suitable for oral administration. The chewable gel includes a water soluble active pharmaceutical ingredient and a complexing agent. The water soluble active pharmaceutical ingredient has a bitter taste and a tendency to cause oral numbness. The water soluble active pharmaceutical ingredient and the complexing agent are complexed in the form of an inclusion complex. The chewable gel is substantially devoid of bitter taste and tendency to cause oral numbness when chewed.
- (6) This summary is provided to introduce a selection of concepts in a simplified form that are further described below in the detailed description. This summary is not intended to identify key features or essential features of the claimed subject matter, nor is it intended to be used to limit the scope of the claimed subject matter. Other aspects and advantages of the present invention will be apparent from the following detailed description of the embodiments and the accompanying drawing figures.
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Description

BRIEF DESCRIPTION OF THE DRAWING FIGURES

- (1) FIG. 1 is a chart showing the texture profiles (load in grams vs. time in seconds) for the chewable gel units formed in accordance with Example 4;
- (2) FIG. 2 is a chart showing the texture profiles (load in grams vs. time in seconds) for the chewable gel units formed in accordance with Example 6;
- (3) FIG. 3 is a chart showing the texture profiles (load in grams vs. time in seconds) for the chewable gel units formed in accordance with Example 7;
- (4) FIG. 4 is a chart showing the texture profiles (load in grams vs. time in seconds) for the chewable gel units formed in accordance with Example 9;
- (5) FIG. 5 is a chart showing the texture profiles (load in grams vs. time in seconds) for the chewable gel units formed in accordance with Example 16;
- (6) FIG. 6 is a chart showing the texture profiles (load in grams vs. time in seconds) for the chewable gel units formed in accordance with Example 18;
- (7) FIG. 7 is a chart showing the texture profiles (load in grams vs. time in seconds) for the chewable gel units formed in accordance with Example 21;
- (8) FIG. 8 is a chart showing the texture profiles (load in grams vs. time in seconds) for the chewable gel units formed in accordance with Example 22;
- (9) FIG. 9 is a chart showing the texture profiles (load in grams vs. time in seconds) for the chewable gel units formed in accordance with Example 23;
- (10) FIG. 10 is a chart showing the texture profiles (load in grams vs. time in seconds) for the chewable gel units formed in accordance with Example 24;

- (11) FIG. 11 is a chart showing the texture profiles (load in grams vs. time in seconds) for the chewable gel units formed in accordance with Example 25;
- (12) FIG. 12 is a chart showing the texture profiles (load in grams vs. time in seconds) for the chewable gel units formed in accordance with Example 27;
- (13) FIG. 13 is a chart showing the dissolution profile (% cumulative average drug released vs. time in minutes) of chewable gel units formed in accordance with Example 1;
- (14) FIG. 14 is a chart showing the dissolution profile (% cumulative average drug released vs. time in minutes) of chewable gel units formed in accordance with Example 2;
- (15) FIG. 15 is a chart showing comparative dissolution profiles (% cumulative average drug released vs. time in minutes) of chewable gel units formed in accordance with Example 4 after being stored for various durations and under various conditions;
- (16) FIG. 16 is a chart showing the dissolution profile (% cumulative average drug released vs. time in minutes) of chewable gel units formed in accordance with Example 5;
- (17) FIG. 17 is a chart showing the dissolution profile (% cumulative average drug released vs. time in minutes) of chewable gel units formed in accordance with Example 6;
- (18) FIG. 18 is a chart showing comparative dissolution profiles (% cumulative average drug released vs. time in minutes) of chewable gel units formed in accordance with Example 7 after being stored for various durations and under various conditions;
- (19) FIG. 19 is a chart showing comparative dissolution profiles (% cumulative average drug released vs. time in minutes) of chewable gel units formed in accordance with Example 9 after being stored for various durations and under various conditions;
- (20) FIG. 20 is a chart showing comparative dissolution profiles (% cumulative average drug released vs. time in minutes) of chewable gel units formed in accordance with Example 10 after being stored for various durations and under various conditions;
- (21) FIG. 21 is a chart showing the dissolution profile (% cumulative average drug released vs. time in minutes) of chewable gel units formed in accordance with Example 11;
- (22) FIG. 22 is a chart showing comparative dissolution profiles (% cumulative average drug released vs. time in minutes) of chewable gel units formed in accordance with Example 13 after being stored for various durations and under various conditions;
- (23) FIG. 23 is a chart showing comparative dissolution profiles (% cumulative average drug released vs. time in minutes) of chewable gel units formed in accordance with Example 14 analyzed using two (2) different apparatuses; and
- (24) FIG. 24 is a chart showing comparative mean serum drug concentrations over a 24-hour period with respect to the chewable gel units formed in accordance with Example 16 and a reference marketed product.
- (25) The figures do not limit the present invention to the specific embodiments disclosed and described herein. The emphasis instead being placed upon clearly illustrating certain principles of the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

- (26) The following description of the disclosure is provided as an enabling teaching of the disclosure in its best, currently known embodiment(s). To this end, those skilled in the relevant art will recognize and appreciate that many changes can be made to the various embodiments of the invention described herein, while still obtaining the beneficial results of the present disclosure. It will also be apparent that some of the desired benefits of the present disclosure can be obtained by selecting some of the features of the present disclosure without utilizing other features. Accordingly, those who work in the art will recognize that many modifications and adaptations to the present disclosure are possible and can even be desirable in certain circumstances and are a part of the present disclosure. Thus, the following description is provided as illustrative of the principles of the present disclosure and not in limitation thereof.
- (27) The terms and phrases “gummy pharmaceutical dosage form,” “gummy,” “gummy dosage

form,” “chewable gel,” and plural versions thereof as used herein have interchangeable meanings and shall be interpreted to have the same meaning as “chewable gel” as defined by United States Pharmacopeia and National Formulary General Chapter (1151), which is incorporated herein by reference in its entirety.

(28) In certain embodiments of the present invention, the composition of the chewable gel may include one or more the following components: functional ingredients; active ingredients; complexing agents; co-solvents; gelling agents; non-crystallizing polyol solutions; recrystallization inhibitors; lubricants (release agents); flavors; taste enhancing agents; and/or other additives.

(29) In certain embodiments of the present invention, the composition of the chewable gel has an active ingredient content ranging from about one-tenth of one percent-by-weight (0.1% w/w) to about ten percent-by-weight (10% w/w). As used herein, the phrase “percent-by-weight” (% w/w) refers to the amount/concentration of one or more components in a group of components. The percent-by-weight (% w/w) of one or more components in a group of components can be calculated by dividing the numerical value for the weight of one or more components in a group of components by the numerical value for the weight of all of the components in the group and multiplying the quotient by one-hundred (100).

(30) An active pharmaceutical ingredient (also referred to as active ingredient, pharmaceutically active agent, pharmaceutically acceptable active ingredient, drug, or active drug) for use in the process or product according to the current invention is a substance used in a pharmaceutical dosage form, intended to furnish pharmacological activity or to otherwise have direct effect in the diagnosis, cure, mitigation, treatment, and/or prevention of disease. Active ingredients also include compounds that have, or are thought to have, a direct effect in restoring, correcting, or modifying physiological functions in a patient population (humans or animals).

(31) As used herein, the phrase “functional ingredient” includes, but is not limited to, minerals, vitamins, nutraceutical agents, and other supplements; including derivatives, salts (and the like), and/or mixtures of the foregoing. A “functional/active” refers to both a functional ingredient and active pharmaceutical ingredient. As used herein, the phrase “pharmaceutically acceptable salt(s)” refers to salt(s) that retain the desired biological activity of the parent compound and exhibit minimal undesired toxicological effects.

(32) Although certain ingredients, such as acetaminophen, diphenhydramine hydrochloride (“diphenhydramine HCl”), azithromycin, ibuprofen, dimenhydrinate, amphetamine, fexofenadine hydrochloride (“fexofenadine HCl”), aspirin, dextromethorphan hydrobromide (“dextromethorphan HBr”), amoxicillin, cetirizine hydrochloride (“cetirizine HCl”), loratadine, phenylephrine hydrochloride (“phenylephrine HCl”), and/or methylphenidate, may appear in the examples provided below, it will be understood by those having ordinary skill in the art that other types of active ingredients (and/or functional ingredients) are within the scope of the present invention and that other active ingredients may be used without departing from the spirit of the present invention. For example, the present invention is equally applicable to gummy dosage forms where the active ingredient is selected from a group comprising of anti-inflammatory actives, coronary dilators, cerebral dilators, peripheral vasodilators, anti-infectives, psychotropics, antimanics, stimulants, gastro-intestinal sedatives, antidiarrheal active ingredients, anti-anginal drugs, vasodilators, anti-hypertensive drugs, vasoconstrictors and anti-migraine treatment actives, antibiotics, tranquilizers, antipsychotics, antitumor drugs, anticoagulants and antithrombotic drugs, hypnotics, sedatives, anti-emetics, antinauseants, anticonvulsants, neuromuscular drugs, hyper- and hypoglycemic agents, thyroid and antithyroid preparations, diuretics, antispasmodics, uterine relaxants, nutritional additives, anti-obesity drugs, anabolic drugs, erythropoietic drugs, antiasthmatics, expectorants, cough suppressants, mucolytics, anti-hyperuricemia drugs, antidepressants, and the like, or combinations of the foregoing.

(33) In certain embodiments of the present invention, the chewable gel formulation may include drugs used for treatment of Attention Deficit Hyperactivity Disorder (ADHD) selected from a

group comprising of methylphenidate, dexamethylphenidate, amphetamine, dextroamphetamine, and lisdexamfetamine dimesylate; including derivatives, salts (and the like), and/or mixtures of the foregoing.

(34) In certain embodiments of the present invention, the chewable gel formulation may include cannabis or hemp-based active/functional ingredients including, but not limited to, tetrahydrocannabinol, cannabidiol, and cannabis extracts, derivatives, salts (and the like), and/or mixtures of the foregoing.

(35) In certain embodiments of the present invention, the chewable gel formulation includes a complexing agent. A complexing agent is a pharmaceutical grade inactive ingredient which forms a complex with a functional/active ingredient.

(36) In certain embodiments of the present invention, the composition of the chewable gel has a complexing agent content ranging from about two-tenths of one percent-by-weight (0.2% w/w) to about twenty percent-by-weight (20% w/w).

(37) In certain embodiments of the present invention, cyclodextrins, such as hydroxypropyl-beta cyclodextrin ("HP.beta.CD"), can be used as complexing agents. Cyclodextrins are crystalline, homogeneous, non-hygroscopic substances built-up from glucopyranose units (oligomers of dextrose or its derivatives) joined by α -1,4-linkages. Typical examples include alpha-, beta-, and/or gamma-cyclodextrin; including derivatives and/or mixtures of the foregoing. Cyclodextrins form an active ingredient-cyclodextrin complex (i.e., an inclusion complex), which is an association between the active ingredient and the cyclodextrin and, preferably, takes the form of a clathrate-type inclusion complex, wherein the functional/active ingredient acts as the guest molecule in the enclosed tubular space of the cyclodextrin host, which facilitates increased solubility of functional/active ingredient. It is theorized that this enwrapping of functional/active ingredient (guest) inside cyclodextrin host may prevent interaction of functional/active ingredient with taste buds and/or interact with the gate-keeper proteins of taste buds affecting their functionality resulting in taste masking an unpleasant functional/active ingredient.

(38) In certain embodiments of the present invention, it is preferable to maintain a ratio of complexing agent to active ingredient whereby the active ingredient(s) remains substantially complexed with complexing agent (i.e., inclusion complex) to maintain high amounts of water insoluble active ingredient in solubilized form, which tends to minimize any disagreeable tastes, such as bitterness, and/or other unpleasant oral sensations, such as numbness of the mouth and tongue, and/or throat irritation that may be associated with the water insoluble (or poorly water soluble) active ingredient. Furthermore, maintaining a ratio of complexing agent to active ingredient whereby active ingredient remains substantially complexed with complexing agent (i.e., inclusion complex) facilitates the formation of a gummy dosage form with superior translucency and enhanced taste. For example, translucent gummy dosage forms that include acetaminophen can be difficult to formulate because acetaminophen has a strong bitter taste and is substantially insoluble in water, which is often a preferred solvent to make gummy dosage forms. When manufacturing such translucent gummy dosage form, it can be imperative to keep all components of the dosage form solubilized, or substantially solubilized, in water. Formation of an inclusion complex of acetaminophen and HP.beta.CD in the proper ratio helps to maintain acetaminophen in, or substantially in, solution, which also helps minimize the bitter taste of acetaminophen. In certain embodiments of the present invention, a ratio of complexing agent to active ingredient of at least about one-to-one (1:1) is preferred.

(39) Complexing agents can also facilitate minimization of disagreeable tastes, such as bitterness, and/or other unpleasant oral sensations with water soluble drugs. For example, diphenhydramine hydrochloride, an active ingredient, is known to cause numbness and/or tingling sensations in the mouth when taken via oral route. The inventors hereof found that when gummy dosage forms of the present invention were formulated using, among other ingredients, diphenhydramine hydrochloride complexed with HP.beta.CD in a ratio of complexing agent to active ingredient of

about two-to-one (2:1), no numbness or tingling sensation of mouth was perceived upon mastication of the gummy dosage form.

(40) It should be understood that other complexing agents may be used without departing from the spirit of the present invention. Furthermore, as will be understood by those having ordinary skill in the art, certain aspects of the present invention may apply to the use of complexing agents that form different kinds of complexes with functional/active ingredients. Additionally, it should be understood that certain aspects of the present invention are not limited to formulations that include a complexing agent.

(41) In certain embodiments of the present invention, the chewable gel formulation includes a buffering agent. A buffering agent is a weak acid or base used to maintain the pH of a dispersion near a desired value during the manufacturing process, which, in the context of the present invention, can help minimize molding times (i.e., the amount of time necessary to form a product from a gummy mixture and to remove the formed product from the mold) to less than one (1) hour and/or reduce (or in some instances eliminate) the amount of time needed to cure the gummies after they are removed from a forming device.

(42) In certain embodiments of the present invention, trisodium citrate is used in an amount of up to about one percent-by-weight (1% w/w) to maintain the pH of the gummy mixture in the range of about five (5) to about eight (8). It should be understood that other buffering agents may be used without departing from the spirit of the present invention. Furthermore, it should be understood that certain embodiments of the present invention are not limited to formulations that include a buffering agent.

(43) In certain embodiments of the present invention, the chewable gel formulation includes a non-acidic antimicrobial agent, such as a tonicity modifying agent. As discussed in greater detail below, the use of tonicity modifying agents reduce the need for acidic antimicrobial agents (e.g., citric acid, fumaric acid, benzoic acid, acetic acid, etc.) to inhibit microbial growth.

(44) In certain embodiments of the present invention, the composition of the chewable gel has a tonicity modifying agent content of less than about two percent-by-weight (2% w/w). In certain embodiments of the present invention, sodium chloride is used as a tonicity modifying agent (and may also facilitate improved taste of gummy dosage forms of the present invention).

(45) It should be understood that other antimicrobial agents may be used without departing from the spirit of the present invention. Additionally, it should be understood that certain embodiments of the present invention are not limited to formulations that include a non-acidic antimicrobial agent.

(46) A gelling agent provides structural integrity to the chewable gels of the present invention. More particularly, chewable gels can be described as a two-phase system consisting of suspended particles in a dispersion medium. The suspended particles (i.e., gelling agents) undergo a high degree of cross-linking or association when hydrated, forming an interlaced three-dimensional structure that provides structural integrity to the chewable gel.

(47) In certain embodiments of the present invention, the composition of the chewable gel has a gelling agent content ranging from about one-tenth of one percent-by-weight (0.1% w/w) to about twenty percent-by-weight (20% w/w).

(48) Gelling agents of the present invention may include, but are not limited to, the group comprising of gelatin, alginate, carrageenan, dextran, gellan, guar gum, hyaluronic acid, pullulan, xanthan, xyloglucan, pectins, chitosan, tapioca, and the like; including combinations of the foregoing. It should be understood that other gelling agents may be used without departing from the spirit of the present invention.

(49) Carrageenan is a naturally occurring polysaccharide derived from different species of Rhodophyceae (red seaweed). There are three primary families of carrageenan based on the position of sulfate groups and the presence or absence of anhydrogalactose: lambda, iota, and kappa, with iota-carrageenan being preferred in certain embodiments of the present invention.

Carrageenan does not exhibit a thermo-reversible gelling property and is stable in accelerated conditions of temperature (e.g., about thirty-seven degrees Celsius (37° C.) to about forty-three degrees Celsius (43° C.)) and relative humidity (about seventy percent relative humidity (70% RH) to about eighty percent relative humidity (80% RH)) in accordance with guidelines set by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH).

(50) In some embodiments of the present invention, the dosage form contains carrageenan in a concentration of at least one percent-by-weight (1.0% w/w).

(51) Additional information relating to gelling agents can be found in the Handbook of Pharmaceutical Excipients (Raymond C Rowe et al. eds., 6th ed. 2009), which is incorporated herein by reference in its entirety. Additional information concerning carrageenan can be found in the Handbook of Hydrocolloids (Glyn O. Phillips et al., eds., 2nd ed. 2009), which is incorporated herein by reference in its entirety.

(52) In certain embodiments of the present invention, the chewable gel formulation includes a co-solvent. A co-solvent is either a water-miscible or partially miscible organic solvent, that facilitates reduction of strong interactions between water molecules and hence reduces the ability of water to precipitate-out non-polar solute. Co-solvents work synergistically with complexing agents like cyclodextrins to increase the solubility of the functional/active ingredient, which, as discussed above, facilitates the formation of a chewable gel with improved translucency and taste. The exact mechanism of synergism between co-solvent and cyclodextrins is not clear; however, it is assumed that when a co-solvent is introduced into solution containing the inclusion complex, co-solvents facilitate formation of a drug bearing binary/ternary complex increasing solubility of the functional/active ingredient.

(53) In certain embodiments of the present invention, the composition of the chewable gel has a co-solvent content ranging from about one-half of one percent-by-weight (0.5% w/w) to about fifty percent-by-weight (50% w/w).

(54) In certain embodiments of the present invention, the co-solvent is selected from a group comprising of polyethylene glycol ("PEG"), propylene glycol, glycerin/glycerol, sorbitol, maltitol, and the like; including combinations of the foregoing. However, it should be understood that other co-solvents may be used without departing from the spirit of the present invention.

(55) In certain embodiments of the present invention, the chewable gel formulation includes a recrystallization inhibitor. Recrystallization inhibitors aid to inhibit recrystallization of certain ingredients in the composition and can also reduce irritability of the functional/active ingredient on oral mucosa, which aids in masking unpleasant taste of active/functional ingredients and mixtures thereof.

(56) Formulations of the present invention may include one or more recrystallization inhibitors selected from the group consisting of polyvinyl alcohol ("PVA"), mannitol, sodium carboxymethyl cellulose ("CMCNa"), hydroxypropyl methylcellulose ("HPMC"), and povidone (also known as polyvinylpyrrolidone, "PVP"), and the like; including combinations of the foregoing. However, it should be understood that other recrystallization inhibitors may be used without departing from the spirit of the present invention.

(57) In certain embodiments of the present invention, the composition of the chewable gel may have a recrystallization inhibitor content ranging from about one-tenth of one percent-by-weight (0.1% w/w) to about five percent-by-weight (5% w/w).

(58) In certain embodiments of the present invention, the chewable gel formulation includes a non-crystallizing polyol solution. Non-crystallizing polyol solutions provide a sweet taste and will not, under conditions presented herein, precipitate out of solution. Additionally, non-crystallizing polyol solutions may contribute to an increased solubility of the chewable gel formulation; for instance, in formulations containing sugar, non-crystallizing polyol solutions can prevent or reduce recrystallization of solubilized sugar from the gummy composition. If solubilized sugar

recrystallizes from the gummy composition, the chewable gels formed therefrom may not have the translucent appearance that is preferred in many embodiments of the present invention.

(59) Formulations of the present invention may also include one or more non-crystallizing polyol solutions selected from the group consisting of non-crystallizing sorbitol solution, maltitol solution, and the like; including combinations of the foregoing. Other non-crystallizing polyol solutions may be used without departing from the spirit of the present invention.

(60) In certain embodiments of the present invention, the chewable gel formulation includes lubricating agents (also referred to as release agents). Lubricating agents facilitate formation of the chewable gel by preventing the occurrence of damaging contact between the gummy and surfaces of dosage form forming devices. In certain embodiments of the present invention, the chewable gel formulation may have a lubricant content ranging from about one-tenth of one percent-by-weight (0.1% w/w) to about five percent-by-weight (5% w/w).

(61) Formulations of the present invention may include at least one lubricating agent selected from the group consisting of mineral oil, light mineral oil, and the like; including combinations of the foregoing. Both mineral oil and light mineral oil are transparent, colorless, viscous oily liquids, without fluorescence in daylight. They are practically tasteless and odorless when cold, and have a faint odor when heated. It should be understood that other lubricating agents may be used without departing from the spirit of the present invention. Furthermore, it should be understood that certain embodiments of the present invention are not limited to formulations that include a lubricating agent.

(62) Formulations of the present invention may also include one or more flavor compositions, for example, fruit flavor compositions, botanical flavor compositions, or mixtures thereof. The particular amount of the flavor component useful for imparting flavor characteristics to the composition of the present invention will depend upon the flavor(s) selected, the flavor impression desired, and the form of the flavor component. Those skilled in the art are readily able to determine the amount of any flavor component(s) used to achieve the desired flavor impression. It should be understood that a wide range of flavor compositions may be used without departing from the spirit of the present invention. Furthermore, it should be understood that certain embodiments of the present invention are not limited to formulations that include a flavor composition.

(63) In certain embodiments of the present invention, the chewable gel formulation may include taste enhancing agents. Taste enhancing agents are substances that may enhance or suppress perceived tastes and/or smells. Also, taste enhancing agents may provide a perceived flavor.

(64) In certain embodiments of the present invention, taste enhancing agents may include taste masking powders, bitter blocker powders, and/or sweetening agents such as dextrose, neotame, and sucralose. It should be understood that other taste enhancing agents may be used without departing from the spirit of the present invention.

(65) In certain embodiments of the present invention, the composition of the chewable gel includes coloring agents such as dyes and pigments. It should be understood that a wide range of coloring agents may be used without departing from the spirit of the present invention. Furthermore, it should be understood that certain embodiments of the present invention are not limited to formulations that include a coloring agent.

(66) In some embodiments of the present invention, a single excipient has more than one function in the gummy formulation. In certain embodiments of the present invention glycerol may serve a multi-purpose role as a co-solvent and a humectant. In certain embodiments of the present invention, maltitol solution may serve a multi-purpose role as a co-solvent and re-crystallization inhibitor. In certain embodiments of the present invention, caster sugar may serve a multi-purpose role as a sweetener and humectant.

(67) In certain embodiments of the present invention, it may be preferable to maintain a product temperature below about one hundred five degrees Celsius (105° C.). Product temperature generally refers to actual temperature at which product is maintained during different stages of

manufacturing. Processing temperature refers to a temperature that enables the product temperature to be maintained during various stages of manufacturing. Known processes of manufacturing gummy dosage forms and/or gummy products require higher product temperatures, which can be problematic and/or impractical for the manufacture of pharmaceutical grade gummy dosage forms. For instance, satisfaction of regulatory requirements for pharmaceuticals including, but not limited to, efficacy and safety, is problematic using known processes because of, among other things, difficulties relating to controlling the assay of active ingredient; providing a unit dosage form having acceptable content uniformity and achieving acceptable drug degradation limits.

Additionally, known processes of manufacturing gummy dosage forms do not enable addition of the active/functional ingredient near the end of the heating process based on the viscosity and dynamic solid content (% w/w) of the heated gummy mixture, which may result in a unit dosage form having unacceptable content uniformity. Furthermore, known processes of manufacturing gummy dosage forms and/or gummy products at higher product temperatures often require that the higher product temperature of the final gummy mixture be maintained, or substantially maintained, until the final gummy mixture is transferred to a mold or other forming device. Moreover, such known processes often require substantial conditioning at considerably lower temperatures for formation of and/or curing of the final dosage form (i.e., final formed structure), which adds to the duration of processing time (negatively impacting commercial viability). The foregoing limitations of known processes can be overcome by, among other things, maintaining a constant solid content (% w/w) of the gummy mixture during manufacture by proper control of product temperature below about one hundred five degrees Celsius (105° C.) during certain/specific stages of manufacturing.

(68) In certain embodiments of the present invention, it may be preferable to maintain the pH of the gummy mixture in the range of about five (5) to about eight (8). Preferably, the pH of the gummy mixture according to the present invention is maintained in the range of about five (5) to about eight (8) without the use of acid preservatives (e.g., citric acid, fumaric acid, benzoic acid, acetic acid, etc.). Gummies formed by known processes typically have a high-water content (e.g., twenty (20) to thirty-five (35) percent-by-weight), which often requires the addition of acid preservatives to the gummy mixture to prevent microbial spoilage. Characteristically, acid preservatives do not kill micro-organisms but inhibit their growth by extending lag phases. Generally, acid preservatives are more effective at low pH values (where solutions contain increased concentrations of undissociated acids), where they become increasingly potent as antimicrobial agents. In gummy formulations that include carrageenan, the use of acid preservatives may be problematic due to autohydrolysis of carrageenan in gummy mixtures having lower pH levels (and higher temperatures), which can result in, among other things: an increased molding time; and/or a prolonged curing period. In certain embodiments of the present invention, use of a buffering agent (e.g., trisodium citrate) can facilitate a pH of the gummy mixture in a range of about five (5) to about eight (8), which can lead to faster molding times (i.e., less than one (1) hour).

(69) In certain embodiments of the present invention, non-acidic antimicrobial agents, such as tonicity modifying agents, can be used to control microbial content. For instance, sodium chloride can be used to provide a chewable gel composition with a relatively high osmotic pressure gradient (hypertonic), which inhibits microbial growth. This inhibition of microbial growth can be corroborated by the low water activity (a.sub.w) of the product. Water activity (a.sub.w) of a product is the ratio between the vapor pressure of the product itself, when in a completely undisturbed balance with the surrounding air media, and the vapor pressure of distilled water under identical conditions. Water activity (a.sub.w) has its most useful application in predicting the growth of bacteria, yeast, and mold. It is well known that for an orally consumable product to have a useful shelf life without relying on refrigerated storage, it is necessary to control either its acidity level (pH) or the level of water activity (a.sub.w) or a suitable combination of the two. This can effectively increase the product's stability and make it possible to predict its shelf life under known

ambient storage conditions. In certain embodiments of the present invention, the average water content in the chewable gel unit is about eighteen percent (18%) to about twenty-two percent (22%), with a water activity (a.sub.w) of up to 0.75, which provides, among other things, a chewable gel unit having a longer shelf life than what is known in the art.

(70) Solid content is the percentage of solid/dry matter in the formulation. Solid content (SC) can be computed using the following equation: $SC = 100 - (((\text{mass of the wet sample}) - (\text{mass of the dry sample})) \div (\text{mass of the wet sample})) \times 100$. For example, if the mass of the dry sample is thirty grams (30 g) and the mass of the wet sample is forty-five grams (45 g), then the solid content would be approximately sixty-six and seven-tenths percent-by-weight (66.7% w/w). Solid content can be measured using various instruments, including refractometer meters. A refractometer is an optical instrument that employs the measurement of refractive index of a composition to determine the solid content of the composition. In certain embodiments of the present invention, it is preferable for the gummy mixture to have a solid content ranging from about seventy percent-by-weight (70% w/w) to about eighty percent-by-weight (80% w/w); and more preferably ranging from about seventy-four percent-by-weight (74% w/w) to about eighty percent-by-weight (80% w/w). If the solid content is too high or too low, then the gummy dosage forms (gummies) formed may be too sticky or too brittle, respectively. Gummy dosage forms that are too sticky or too brittle will not have the preferred organoleptic properties of the present invention. Further, gummy dosage forms that are too sticky can be difficult to remove from molds (e.g., sticking to the mold), and dosage forms that are too brittle tend to be easily breakable.

(71) As discussed above, the present invention is not limited to any particular dosage form forming device. Many different devices and methods may be used to facilitate shaping the gummy dosage forms without departing from the spirit of the present invention.

(72) The present invention is not limited to any particular means of transferring the gummy mixture to the dosage form forming device(s). With reference to certain manufacturing processes of the present invention, in some embodiments, the gummy mixture may be transferred to the dosage form forming device(s) by pouring or other means of transfer whereby gravity is the primary motive force inducing flow. With reference to certain manufacturing processes of the present invention, in some embodiments, it is preferable to mechanically induce flow of the gummy mixture to facilitate transfer of the mixture to the dosage form forming device(s). For example, a wide range of pumping devices may be used to facilitate transfer of the gummy mixture to the dosage form forming device or other means of transfer whereby gravity is the primary motive force inducing flow are not sufficient. It should be understood by those having ordinary skill in the art that transferring the gummy mixture to the dosage form forming device(s) may be accomplished by many different ways, including the use of many different types of devices, without departing from the spirit of the present invention. Additionally, it should be understood that gummy dosage forms of the present invention may be made using a continuous process including, but not limited to, mogul-type production systems.

(73) With reference to certain manufacturing processes of the present invention, in some embodiments, the gummy mixture is removed from the dosage form forming device after drying. Drying the gummy mixture may be accomplished in several different ways without departing from the spirit of the present invention. For example, in certain embodiments of the present invention, the gummy mixture is allowed to dry in the dosage form forming device at ambient temperature (also referred to as room temperature, around 20° C.) for a duration of time ranging from about twenty (20) to about thirty (30) minutes (dry time) before the chewable gels are removed. The dry time may be reduced by adjusting a dry time parameter. For example, in certain embodiments of the present invention, the gummy mixture is dried at a temperature ranging from about two degrees Celsius (2° C.) to about five degrees Celsius (5° C.) for a duration of time ranging from about ten (10) minutes to about fifteen (15) minutes before the chewable gels are removed.

Different/additional drying parameters (e.g., temperature, etc.) may be used without departing from

the spirit of the present invention. As will be discussed in greater detail below, in certain embodiments of the present invention, the chewable gels are cured after being removed from the dosage form forming device. In certain embodiments of the present invention, the chewable gels are cured within the dosage form forming device.

(74) The means of removing the dosage forms from the dosage form forming device may vary depending on the type of dosage form forming device being used. It should be understood by those having ordinary skill in the art that many different types of dosage form forming devices may be used without departing from the spirit of the present invention.

(75) Preferably, once the gummy mixture has sufficiently dried in the dosage form forming device, the individual chewable gels of the present invention are removed. Undesired defects to the appearance and/or shape of the individual chewable gel units of the present invention may occur if improperly removed. Those having ordinary skill in the art will appreciate that such defects can increase manufacturing costs.

(76) In certain embodiments of the present invention, the chewable gel units may optionally include a dusting of polishing agents on the outer surface. When packaged in bulk in certain containers, polishing agents help reduce the occurrence of sticking between one or more chewable gel units. Suitable polishing agents include pregelatinized starch, citric acid anhydrous, magnesium stearate, and combinations of thereof. It should be understood that other polishing agents and/or polishing agent blends may be used without departing from the spirit of the present invention. Furthermore, it should be understood that the present invention is not limited to chewable gel units having a dusting of polishing agents on an outer surface.

(77) With reference to certain manufacturing processes of the present invention, in some embodiments, the chewable gels are cured after removal from the dosage form forming device. Curing period parameters (e.g., duration, temperature, etc.) are important for producing a chewable gel unit that is physically stable. For example, a curing period that is too long may result in dosage forms that are too hard. Conversely, if the curing period is too short, the resulting dosage forms may be sticky, misshapen, and/or easily deformed. In certain embodiments of the present invention, the chewable gels are cured at room temperature for a duration of about forty-eight hours (cure period). Curing methods having different/additional parameters (e.g., temperature, etc.) may be used without departing from the spirit of the present invention. As discussed above, in certain embodiments of the present invention, the chewable gels may be cured without first being removed from the dosage form forming device.

(78) Additional advantages of the various embodiments of the invention will be apparent to those skilled in the art upon review of the disclosure herein and the working examples below. It will be appreciated that the various embodiments described herein are not necessarily mutually exclusive unless otherwise indicated herein. For example, a feature described or depicted in one embodiment may also be included in other embodiments, but is not necessarily included. Thus, the present invention encompasses a variety of combinations and/or integrations of the specific embodiments described herein.

(79) The present description also uses numerical ranges to quantify certain parameters relating to various embodiments of the invention. It should be understood that when numerical ranges are provided, such ranges are to be construed as providing literal support for claim limitations that only recite the lower value of the range as well as claim limitations that only recite the upper value of the range. For example, a disclosed numerical range of about 10 to about 100 provides literal support for a claim reciting “greater than about 10” (with no upper bounds) and a claim reciting “less than about 100” (with no lower bounds).

(80) The compositions and methods of the appended claims are not limited in scope by the specific compositions, formulations, and methods described herein, which are intended as illustrations of a few aspects of the claims. Any compositions, formulations, and methods that are functionally equivalent are intended to fall within the scope of the claims. Various modifications of the

compositions, formulations, and methods in addition to those shown and described herein are intended to fall within the scope of the appended claims. Further, while only certain representative compositions, formulations, and method steps disclosed herein are specifically described, other combinations of the compositions, formulations, and method steps also are intended to fall within the scope of the appended claims, even if not specifically recited. Thus, a combination of steps, elements, components, or constituents may be explicitly mentioned herein; however, other combinations of steps, elements, components, and constituents are included, even though not explicitly stated.

(81) The term “comprising” and variations thereof as used herein is used synonymously with the term “including” and variations thereof and are open, non-limiting terms. Although the terms “comprising” and “including” have been used herein to describe various embodiments, the terms “consisting essentially of” and “consisting of” can be used in place of “comprising” and “including” to provide for more specific embodiments of the invention and are also disclosed. Other than where noted, all numbers expressing geometries, dimensions, and so forth used in the specification and claims are to be understood at the very least, and not as an attempt to limit the application of the doctrine of equivalents to the scope of the claims, to be construed in light of the number of significant digits and ordinary rounding approaches.

(82) Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of skill in the art to which the disclosed invention belongs. Any publications cited herein and the materials for which they are cited are specifically incorporated by reference.

EXAMPLES

(83) the following Examples set forth preferred therapeutic agents and methods in accordance with the invention, but it is to be understood that these examples are given by way of illustration only, and nothing therein should be taken as a limitation upon the overall scope of the invention.

Example 1

(84) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 1 below. The ingredients corresponding to Example 1 are tabulated in Table 1 with the amount of each ingredient used in the process (i.e., the batch quantity) given in kilograms. Each chewable gel unit formed by the process of Example 1 has a mass of about two thousand four hundred fifty milligrams (2,450 mg). Thirty thousand (30,000) chewable gel units are formed by the process of Example 1; however, as should be understood by those having ordinary skill in the art, the principles of Example 1 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(85) TABLE-US-00001

TABLE 1	Ingredient Name	Batch Quantity
	Bitter blocker powder	0.270
	Carrageenan	1.868
	Corn syrup (liquid glucose)	30.375
	Flavor agent (tutti frutti flavor)	0.075
	HP.beta.CD	1.448
	Maltitol solution	6.300
	Neotame	0.038
	Purified water	26.250
	Sodium chloride	0.375
	Sucralose	0.375
	Sucrose	18.263
	Trisodium citrate	0.300
	Citric acid anhydrous	0.300
	Pregelatinized starch (starch 1500)	1.350

Procedure—Example 1

(86) Step 1: Add about 82.5% of the batch quantity of purified water to a container. Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride under continuous stirring until a clear solution is formed.

(87) Step 2: Add the batch quantity of corn syrup to the solution of Step 1 under continuous stirring, continue stirring while heating the mixture to a temperature in the range of about fifty degrees Celsius (50° C.) to about fifty-five degrees Celsius (55° C.) to form a homogenous mixture.

(88) Step 3: Mix the batch quantities of carrageenan and trisodium citrate, and about 11.0% of the batch quantity of sucrose until a homogenous blend is formed.

- (89) Step 4: Add the blend of Step 3 to the mixture of Step 2 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.
- (90) Step 5: Heat the gel of Step 4 to a temperature in the range of about eighty-five degrees Celsius (85° C.) to about ninety-five degrees Celsius (95° C.) until a thick gel mixture is observed.
- (91) Step 6: Add the batch quantity of maltitol solution and about 89.0% of the batch quantity of sucrose to the gel mixture of Step 5 while heating the mixture to a temperature in the range of about ninety degrees Celsius (90° C.) to about one hundred ten degrees Celsius (110° C.).
- (92) Step 7: Add about 7.6% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.
- (93) Step 8: Combine the solution of Step 7 and the gel mixture of Step 6 under stirring and maintain the temperature of the mixture in the range of about 95° C. to about 110° C. until the total solid content of the mixture raises to about seventy-four percent by weight (74% w/w) or about seventy-four brix (74 brix).
- (94) Step 9: Add about 9.9% of the batch quantity of purified water in a container and add the batch quantity of the flavor agent under stirring until a clear solution is formed.
- (95) Step 10: Combine the solution of Step 9 to the gel mixture of Step 8 under stirring, maintaining a temperature in the range of about 90° C. to about one hundred five degrees Celsius (105° C.), until a gummy mixture is formed.
- (96) Step 11: Prepare a dry mix blend by delumping the batch quantities of pregelatinized starch and citric acid anhydrous using a #40 mesh and mix with a V-blender for approximately about five (5) minutes to form a homogenous blend.
- (97) Step 12: Set-up a gummy depositing line with a hopper and a dosator. Set the hopper, distribution plate, and bottom plate to a temperature in the range of about 85° C. to about one hundred fifteen degrees Celsius (115° C.). Set the cooling chamber to a temperature below fifteen degrees Celsius (15° C.).
- (98) Step 13: Lubricate gummy molds and conveyer belts with mineral oil (further lubricate during process as necessary to reduce sticking). Feed the hopper of a surface coating machine with the polishing blend of Step 11. Transfer the gummy mixture of Step 10 to the hopper of the gummy depositing line and start the molding process. After the molds are filled with the gummy mixture of Step 10, the molds are transferred to the cooling chamber. After cooling, the individual chewable gel units are ejected from the molds onto a conveyor. The individual chewable gel units are conveyed to the surface coating machine where the polishing blend of Step 11 is sprinkled onto the chewable gel units. The excess polishing blend is collected at the bottom of the surface coating machine.
- (99) Step 14: Collect the chewable gel units of Step 13 on curing trays and store for curing at a temperature in the range of about twenty-five degrees Celsius (25° C.) to about thirty-five degrees Celsius (35° C.) for five (5) to seven (7) days.
- (100) Step 15: Transfer the chewable gel units of Step 14 into suitable packaging.

Example 2

(101) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 2 below. The ingredients corresponding to Example 2 are tabulated in Table 2 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 2 the active ingredient is cetirizine HCl. Each chewable gel unit formed in accordance with Example 2 has an active strength of cetirizine HCl of about ten milligrams (10 mg). Each chewable gel unit formed by the process of Example 2 has a mass of about two thousand five hundred fifty milligrams (2,550 mg). Two hundred (200) chewable gel units are formed by the process of Example 2; however, as should be understood by those having ordinary skill in the art, the principles of Example 2 can be used to make more or less chewable gel

units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(102) TABLE-US-00002 TABLE 2 Ingredient Name Batch Quantity Cetirizine HCl 1.992 Bitter blocker powder 1.800 Carrageenan 12.450 Citric acid anhydrous 1.000 Corn syrup (liquid glucose) 207.400 Flavor agent (tutti frutti flavor) 0.250 HP.beta.CD 9.650 Maltitol solution 42.000 Neotame 0.250 Pregelatinized starch (starch 1500) 9.000 Purified water 175.000 Sodium chloride 2.500 Sucralose 2.508 Sucrose 142.200 Trisodium citrate 2.000

Procedure—Example 2

(103) Step 1: Add about 79.2% of the batch quantity of purified water to a container (e.g., manufacturing vessel). Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride under continuous stirring until a clear solution is formed.

(104) Step 2: Add the batch quantity of corn syrup to the solution of Step 1 under continuous stirring, continue stirring while heating the mixture to a temperature in the range of about 50° C. to about 55° C. to form a homogenous mixture.

(105) Step 3: Mix the batch quantities of carrageenan and trisodium citrate, and about 28.1% of the batch quantity of sucrose until a homogenous blend is formed.

(106) Step 4: Add the mixture of Step 3 to the mixture of Step 2 under continuous stirring, maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.

(107) Step 5: Heat the gel of Step 4 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is observed.

(108) Step 6: Add the batch quantity of maltitol solution and about 71.9% of the batch quantity of sucrose to the gel mixture of Step 5 while maintaining a temperature in the range of about 90° C. to about 105° C.

(109) Step 7: Add about 13% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(110) Step 8: Add the batch quantity of cetirizine HCl to the solution of Step 7 under continuous stirring until a clear solution is formed.

(111) Step 9: Combine the solution of Step 8 and the gel mixture of Step 6 under stirring and maintain the temperature of the mixture in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 74% w/w or about 74 brix.

(112) Step 10: Add about 7.8% of the batch quantity of purified water to a container and add the batch quantity of the flavor agent under stirring until a clear solution is formed.

(113) Step 11: Combine the solution of Step 10 to the gel mixture of Step 9 under stirring, maintaining a temperature in the range of about 90° C. to about 105° C., until a gummy mixture is formed.

(114) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about ten (10) to about fifteen (15) minutes and then remove the individual chewable gel units from the mold.

(115) Step 13: Mix the batch quantities of pregelatinized starch and citric acid anhydrous until a homogenous blend is formed.

(116) Step 14: Polish the chewable gel units of Step 12 with the blend of Step 13 for approximately 5 to about 10 minutes to form polished chewable gel units.

(117) Step 15: Store the polished chewable gel units of Step 14 for curing at a temperature in the range of about 25° C. to about 35° C. for 5 to 7 days.

(118) Step 16: Transfer the chewable gel units of Step 15 into suitable packaging.

Example 3

(119) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 3 below. The ingredients corresponding to Example 3 are

tabulated in Table 3 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 3 the active ingredient is cetirizine HCl. Each chewable gel unit formed in accordance with Example 3 has an active strength of cetirizine HCl of about 10 mg. Each chewable gel unit formed by the process of Example 3 has a mass of about 3,272 mg. One hundred fifty (150) chewable gel units are formed by the process of Example 3; however, as should be understood by those having ordinary skill in the art, the principles of Example 3 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(120) TABLE-US-00003 TABLE 3 Ingredient Name Batch Quantity Cetirizine HCl 1.500 Bitter blocker powder 2.273 Carrageenan 14.700 Citric acid anhydrous 0.900 Color agent (FD&C red #40) 0.053 Corn syrup (liquid glucose) 234.750 Flavor agent (strawberry flavor) 0.525 HP.beta.CD 10.500 Magnesium stearate 0.900 Maltitol solution 147.000 Pregelatinized starch (starch 1500) 9.000 Purified water 183.750 Sodium chloride 3.600 Sucralose 2.400 Trisodium citrate 2.700

Procedure—Example 3

(121) Step 1: Add about 65.3% of the batch quantity of purified water to a container (e.g., manufacturing vessel). Slowly add and dissolve the batch quantities of sucralose, bitter blocker powder, and sodium chloride under continuous stirring until a clear solution is formed.

(122) Step 2: Add the batch quantity of corn syrup to the solution of Step 1 under continuous stirring, continue stirring while heating the mixture to a temperature in the range of about 50° C. to about 55° C. to form a homogenous mixture.

(123) Step 3: Mix the batch quantities of carrageenan and trisodium citrate until a homogenous blend is formed.

(124) Step 4: Add the mixture of Step 3 to the mixture of Step 2 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.

(125) Step 5: Heat the gel of Step 4 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is observed.

(126) Step 6: Add the batch quantity of maltitol solution to the gel mixture of Step 5 while maintaining a temperature in the range of about 90° C. to about 105° C.

(127) Step 7: Add about 19.9% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(128) Step 8: Add the batch quantity of cetirizine HCl to the solution of Step 7 under continuous stirring until a clear solution is formed.

(129) Step 9: Combine the solution of Step 8 and the gel mixture of Step 6 under stirring and maintain the temperature of the mixture in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about sixty percent by weight (60% w/w) or about sixty brix (60 brix).

(130) Step 10: Add about 14.8% of the batch quantity of purified water to a container and add the batch quantities of the flavor agent and the color agent under stirring until a clear solution is formed.

(131) Step 11: Combine the solution of Step 10 with the gel mixture of Step 9 under stirring, maintaining a temperature in the range of about 90° C. to about 105° C. until a gummy mixture is formed.

(132) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(133) Step 13: Mix the batch quantities of pregelatinized starch, citric acid anhydrous, and magnesium stearate until a homogenous blend is formed.

(134) Step 14: Polish the chewable gel units of Step 12 with the blend of Step 13 for approximately

5 to about 10 minutes to form polished chewable gel units.

(135) Step 15: Store the chewable gel units of Step 14 for curing at a temperature in the range of about 25° C. to about 35° C. for 5 to 7 days.

(136) Step 16: Transfer the chewable gel units of Step 15 into suitable packaging.

Example 4

(137) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 4 below. The ingredients corresponding to Example 4 are tabulated in Table 4 with the amount of each ingredient used in the process (i.e., the batch quantity) given in kilograms. In Example 4 the active ingredient is diphenhydramine HCl. Each chewable gel unit formed in accordance with Example 4 has an active strength of diphenhydramine HCl of about 12.5 mg. Each chewable gel unit formed by the process of Example 4 has a mass of about 2,500 mg. Thirty thousand (30,000) chewable gel units are formed by the process of Example 4; however, as should be understood by those having ordinary skill in the art, the principles of Example 4 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(138) TABLE-US-00004 TABLE 4 Ingredient Name Batch Quantity Diphenhydramine HCl 0.375 Bitter blocker powder 0.270 Carrageenan 1.875 Citric acid anhydrous 0.150 Corn syrup (liquid glucose) 30.375 Flavor agent (tutti frutti flavor) 0.075 HP.beta.CD 1.448 Maltitol solution 6.300 Neotame 0.038 Pregelatinized starch (starch 1500) 1.350 Purified water 26.250 Sodium chloride 0.375 Sucralose 0.375 Sucrose 18.195 Trisodium citrate 0.300

Procedure—Example 4

(139) Step 1: Add about 82.5% of the batch quantity of purified water to a main manufacturing vessel. Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride under continuous stirring until a clear solution is formed.

(140) Step 2: Add the batch quantity of corn syrup to the solution of Step 1 under continuous stirring, continue stirring while heating the mixture to a temperature in the range of about 50° C. to about 55° C. to form a homogenous mixture.

(141) Step 3: Mix the batch quantities of carrageenan and trisodium citrate, and about 11.0% of the batch quantity of sucrose until a homogenous blend is formed.

(142) Step 4: Add the mixture of Step 3 to the mixture of Step 2 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.

(143) Step 5: Heat the gel of Step 4 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is observed.

(144) Step 6: Add the batch quantity of maltitol solution and about 89.0% of the batch quantity of sucrose to the gel mixture of Step 5, maintaining a temperature in the range of about 90° C. to about 105° C.

(145) Step 7: Add about 7.6% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(146) Step 8: Add the batch quantity of diphenhydramine HCl to the solution of Step 7 under continuous stirring until a clear solution is formed.

(147) Step 9: Combine the solution of Step 8 and the gel mixture of Step 6 under stirring and maintain the temperature of the mixture in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 74% w/w or about 74 brix.

(148) Step 10: Add about 9.9% of the batch quantity of purified water in a container and add the batch quantity of the flavor agent under stirring until a clear solution is formed.

(149) Step 11: Combine the solution of Step 10 and the gel mixture of Step 9 under stirring, maintaining a temperature in the range of about 90° C. to about 105° C. until a gummy mixture is formed.

(150) Step 12: Prepare a dry mix blend by delumping the batch quantities of pregelatinized starch and citric acid anhydrous using a #40 mesh and mix with a V-blender for approximately about five (5) minutes to form a homogenous blend.

(151) Step 13: Set-up a gummy depositing line with a hopper and a dosator. Set the hopper, distribution plate, and bottom plate to a temperature in the range of about 85° C. to about 115° C. Set the cooling chamber to a temperature below 15° C.

(152) Step 14: Lubricate gummy molds and conveyer belts with mineral oil (further lubricate during the process as necessary to reduce sticking). Feed the hopper of a surface coating machine with the polishing blend of Step 12. Transfer the gummy mixture of Step 11 to the hopper of the gummy depositing line and start the molding process. After the molds are filled with the gummy mixture of Step 11, the molds are transferred to the cooling chamber. After cooling, the individual chewable gel units are ejected from the molds onto a conveyor. The individual chewable gel units are conveyed to the surface coating machine where the polishing blend of Step 12 is sprinkled onto the chewable gel units. The excess polishing blend is collected at the bottom of the surface coating machine.

(153) Step 15: Collect the chewable gel units of Step 14 on curing trays and store for curing at a temperature in the range of about 25° C. to about 35° C. for 5 to 7 days.

(154) Step 16: Transfer the chewable gel units of Step 15 into suitable packaging.

Example 5

(155) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 5 below. The ingredients corresponding to Example 5 are tabulated in Table 5 with the amount of each ingredient used in the process (i.e., the batch quantity) given in kilograms. In Example 5 the active ingredient is diphenhydramine HCl. Each chewable gel unit formed in accordance with Example 5 has an active strength of diphenhydramine HCl of about 12.5 mg. Each chewable gel unit formed by the process of Example 5 has a mass of about 2,455 mg. Thirty thousand (30,000) chewable gel units are formed by the process of Example 5; however, as should be understood by those having ordinary skill in the art, the principles of Example 5 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(156) TABLE-US-00005 TABLE 5 Ingredient Name Batch Quantity Diphenhydramine HCl 0.375 Bitter blocker powder 0.270 Carrageenan 1.875 Citric acid anhydrous 0.150 Corn syrup (liquid glucose) 30.375 Flavor agent (tutti frutti flavor) 0.075 HP.beta.CD 1.448 Magnesium stearate 0.150 Maltitol solution 6.300 Neotame 0.038 Pregelatinized starch (starch 1500) 1.350 Purified water 26.250 Sodium chloride 0.375 Sucralose 0.375 Sucrose 18.195 Trisodium citrate 0.300

Procedure—Example 5

(157) Step 1: Add about 82.5% of the batch quantity of purified water to a container (e.g., manufacturing vessel). Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride under continuous stirring until a clear solution is formed.

(158) Step 2: Add the batch quantity of corn syrup to the solution of Step 1 under continuous stirring while heating the mixture to a temperature in the range of about 50° C. to about 55° C. to form a homogenous mixture.

(159) Step 3: Mix the batch quantities of carrageenan and trisodium citrate, and about 11.0% of the batch quantity of sucrose until a homogenous blend is formed.

(160) Step 4: Add the blend of Step 3 to the mixture of Step 2 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.

(161) Step 5: Heat the gel of Step 4 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is observed.

(162) Step 6: Add the batch quantity of maltitol solution and about 89.0% of the batch quantity of sucrose to the gel mixture of Step 5, maintaining a temperature in the range of about 90° C. to

about 105° C.

(163) Step 7: Add about 7.6% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(164) Step 8: Add the batch quantity of diphenhydramine HCl to the solution of Step 7 under continuous stirring for approximately about twenty (20) minutes or until a clear solution is observed.

(165) Step 9: Combine the solution of Step 8 and the gel mixture of Step 6 under stirring and maintain the temperature of the mixture in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 74% w/w or about 74 brix.

(166) Step 10: Add about 9.9% of the batch quantity of purified water in a container and add the batch quantity of the flavor agent under stirring until a clear solution is formed.

(167) Step 11: Combine the solution of Step 10 and the gel mixture of Step 9 under stirring, maintaining a temperature in the range of about 90° C. to about 105° C. until a gummy mixture is formed.

(168) Step 12: Prepare a dry mix blend by delumping the batch quantities of pregelatinized starch, citric acid anhydrous, and magnesium stearate using a #40 mesh and mix with a V-blender for approximately about five (5) minutes to form a homogenous blend.

(169) Step 13: Set-up a gummy depositing line with a hopper and a dosator. Set the hopper, distribution plate, and bottom plate to a temperature in the range of about 85° C. to about 115° C. Set the cooling chamber to a temperature below 15° C.

(170) Step 14: Lubricate gummy molds and conveyer belts with mineral oil (further lubricate during the process as necessary to reduce sticking). Feed the hopper of a surface coating machine with the polishing blend of Step 12. Transfer the gummy mixture of Step 11 to the hopper of the gummy depositing line and start the molding process. After the molds are filled with the gummy mixture of Step 11, the molds are transferred to the cooling chamber. After cooling, the individual chewable gel units are ejected from the molds onto a conveyor. The individual chewable gel units are conveyed to the surface coating machine where the polishing blend of Step 12 is sprinkled onto the chewable gel units. The excess polishing blend is collected at the bottom of the surface coating machine.

(171) Step 15: Collect the chewable gel units of Step 14 on curing trays and store for curing at a temperature in the range of about 25° C. to about 35° C. for 5 to 7 days.

(172) Step 16: Transfer the chewable gel units of Step 15 into suitable packaging.

Example 6

(173) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 6 below. The ingredients corresponding to Example 6 are tabulated in Table 6 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 6 the active ingredient is diphenhydramine HCl. Each chewable gel unit formed in accordance with Example 6 has an active strength of diphenhydramine HCl of about 25 mg. Each chewable gel unit formed by the process of Example 6 has a mass of about 4,088 mg. Two hundred fifty (250) chewable gel units are formed by the process of Example 6; however, as should be understood by those having ordinary skill in the art, the principles of Example 6 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(174) TABLE-US-00006 TABLE 6

Ingredient Name	Batch Quantity
Diphenhydramine HCl	6.250
Bitter blocker powder	4.250
Carrageenan	25.000
Citric acid anhydrous	2.000
Corn syrup (liquid glucose)	400.000
Flavor agent (tutti frutti flavor)	0.750
HP.beta.CD	25.000
Magnesium stearate	2.000
Maltitol solution	82.500
Neotame	0.250
Pregelatinized starch (starch 1500)	18.000
Purified water	350.000
Sodium chloride	3.250
Sucralose	3.750
Sucrose	245.000
Trisodium citrate	4.000

Procedure—Example 6

- (175) Step 1: Add about 68.6% of the batch quantity of purified water to a main manufacturing vessel. Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride under continuous stirring until a clear solution is formed.
- (176) Step 2: Add the batch quantity of corn syrup to the solution of Step 1 under continuous stirring while heating the mixture to a temperature in the range of about 50° C. to about 55° C. until a homogenous mixture is formed.
- (177) Step 3: Mix the batch quantities of carrageenan and trisodium citrate, and about 32.7% of the batch quantity of sucrose until a homogenous blend is formed.
- (178) Step 4: Add the blend formed in Step 3 to the mixture of Step 2 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.
- (179) Step 5: Heat the gel formed in Step 4 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is formed.
- (180) Step 6: Add the batch quantity of maltitol solution and about 67.3% of the batch quantity of sucrose to the gel mixture formed in Step 5, maintaining the temperature of the mixture in the range of about 90° C. to about 105° C.
- (181) Step 7: Add about 22.9% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.
- (182) Step 8: Add the batch quantity of diphenhydramine HCl to the solution of Step 7 under continuous stirring until a clear solution is formed.
- (183) Step 9: Combine the solution of Step 8 and the gel mixture of Step 6 under stirring and maintain the temperature of the mixture in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 74% w/w or about 74 brix.
- (184) Step 10: Add about 8.5% of the batch quantity of purified water in a container and add the batch quantity of the flavor agent under stirring until a clear solution is formed.
- (185) Step 11: Add the solution formed in Step 10 to the gel mixture of Step 9 under stirring while maintaining a temperature of the mixture in the range of about 90° C. to about 105° C. until a gummy mixture is formed.
- (186) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.
- (187) Step 13: Mix the batch quantities of pregelatinized starch, citric acid anhydrous, and magnesium stearate until a homogenous blend is formed.
- (188) Step 14: Polish the chewable gel units formed in Step 12 with the blend of Step 13 for approximately 5 to about 10 minutes to form polished chewable gel units.
- (189) Step 15: Store the chewable gel units of Step 14 for curing at a temperature in the range of about 25° C. to about 35° C. for 5 to 7 days.
- (190) Step 16: Transfer the chewable gel units of Step 15 into suitable packaging.

Example 7

(191) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 7 below. The ingredients corresponding to Example 7 are tabulated in Table 7 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 7 the active ingredient is loratadine. Each chewable gel unit formed in accordance with Example 7 has an active strength of loratadine of about 10 mg. Each chewable gel unit formed by the process of Example 7 has a mass of about 2,550 mg. One thousand (1,000) chewable gel units are formed by the process of Example 7; however, as should be understood by those having ordinary skill in the art, the principles of Example 7 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(192) TABLE-US-00007 TABLE 7 Ingredient Name Batch Quantity Loratadine 10.000 Bitter blocker powder 9.000 Carrageenan 62.250 Citric acid anhydrous 5.000 Corn syrup (liquid glucose) 993.300 Flavor agent (tutti frutti flavor) 1.250 HP.beta.CD 100.000 Maltitol solution 199.650 Neotame 1.250 Pregelatinized starch (starch 1500) 45.000 Purified water 875.000 Sodium chloride 12.500 Sucralose 12.500 Sucrose 588.300 Trisodium citrate 10.000

Procedure—Example 7

(193) Step 1: Add about 52.9% of the batch quantity of purified water to a container (e.g., manufacturing vessel). Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride under continuous stirring until a clear solution is formed.

(194) Step 2: Add the batch quantity of corn syrup to the solution of Step 1 under continuous stirring while heating the mixture to a temperature in the range of about 50° C. to about 55° C. to form a homogenous mixture.

(195) Step 3: Mix the batch quantities of carrageenan and trisodium citrate, and about 34.0% of the batch quantity of sucrose until a homogenous blend is formed.

(196) Step 4: Add the blend of Step 3 to the mixture of Step 2 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. to form a homogenous gel.

(197) Step 5: Heat the gel formed in Step 4 to a temperature in the range of about 90° C. to about 105° C. to form a thick gel mixture.

(198) Step 6: Add the batch quantity of maltitol solution and about 66.0% of the batch quantity of sucrose to the gel mixture formed in Step 5 while maintaining a temperature of the mixture in the range of about 90° C. to about 105° C.

(199) Step 7: Add about 45.7% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(200) Step 8: Add the batch quantity of loratadine to the solution of Step 7 under continuous stirring until a clear solution is formed and heat the solution to a temperature in the range of about seventy degrees Celsius (70° C.) to about eighty degrees Celsius (80° C.).

(201) Step 9: Add the solution of Step 8 to the gel mixture formed in Step 6 under stirring and maintain the temperature of the mixture in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 74% w/w or about 74 brix.

(202) Step 10: Add about 1.4% of the batch quantity of purified water and the batch quantity of the flavor agent to a container under stirring until a clear solution is formed.

(203) Step 11: Combine the solution of Step 10 and the gel mixture formed in Step 9 under stirring while maintaining a temperature in the range of about 90° C. to about 105° C. until a gummy mixture is formed.

(204) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(205) Step 13: Mix the batch quantities of pregelatinized starch and citric acid anhydrous to form a homogenous blend.

(206) Step 14: Polish the chewable gel units of Step 12 with the blend of Step 13 for approximately 5 to about 10 minutes to form polished chewable gel units.

(207) Step 15: Store the chewable gel units of Step 14 for curing at a temperature in the range of about 25° C. to about 35° C. for 5 to 7 days.

(208) Step 16: Transfer the chewable gel units of Step 15 into suitable packaging.

Example 8

(209) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 8 below. The ingredients corresponding to Example 8 are tabulated in Table 8 with the amount of each ingredient used in the process (i.e., the batch quantity)

given in grams. In Example 8 the active ingredient is loratadine. Each chewable gel unit formed in accordance with Example 8 has an active strength of loratadine of about 10 mg. Each chewable gel unit formed by the process of Example 8 has a mass of about 3,584 mg. One hundred (100) chewable gel units are formed by the process of Example 8; however, as should be understood by those having ordinary skill in the art, the principles of Example 8 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(210) TABLE-US-00008 TABLE 8 Ingredient Name Batch Quantity Loratadine 1.000 Bitter blocker powder 1.515 Carrageenan 10.000 Citric acid anhydrous 0.700 Color agent (FD&C red #40) 0.035 Corn syrup (liquid glucose) 137.500 Flavor agent (orange flavor) 0.350 HP.beta.CD 15.000 Magnesium stearate 0.700 Maltitol solution 106.000 Pregelatinized starch (starch 1500) 7.000 Purified water 125.000 Sucralose 2.100 Trisodium citrate 4.000

Procedure—Example 8

(211) Step 1: Add about 62.4% of the batch quantity of purified water to a main manufacturing vessel. Slowly add and dissolve the batch quantities of sucralose and bitter blocker powder under continuous stirring until a clear solution is formed.

(212) Step 2: Add the batch quantity of corn syrup to the solution of Step 1 under continuous stirring while heating the mixture to a temperature in the range of about 50° C. to about 55° C. until a homogenous mixture is formed.

(213) Step 3: Mix the batch quantities of carrageenan and trisodium citrate until a homogenous blend is formed.

(214) Step 4: Add the blend of Step 3 to the mixture of Step 2 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.

(215) Step 5: Heat the gel formed in Step 4 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is observed.

(216) Step 6: Add the batch quantity of maltitol solution to the gel mixture of Step 5 while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C.

(217) Step 7: Add about 24.0% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(218) Step 8: Add the batch quantity of loratadine to the solution of Step 7 under continuous stirring until a clear solution is formed and heat to a temperature in the range of about 70° C. to about 80° C.

(219) Step 9: Combine the solution of Step 8 and the gel mixture of Step 6 under stirring and maintain the temperature of the mixture in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 74% w/w or about 74 brix.

(220) Step 10: Add about 13.6% of the batch quantity of purified water and the batch quantities of the flavor agent and the color agent to a container under stirring until a clear solution is formed.

(221) Step 11: Add the solution of Step 10 to the gel mixture formed in Step 9 under stirring while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C. until a gummy mixture is formed.

(222) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(223) Step 13: Mix the batch quantities of pregelatinized starch, citric acid anhydrous, and magnesium stearate until a homogenous blend is formed.

(224) Step 14: Polish the chewable gel units of Step 12 with the blend of Step 13 for approximately 5 to about 10 minutes to form polished chewable gel units.

(225) Step 15: Store the chewable gel units formed in Step 14 for curing at a temperature in the

range of about 25° C. to about 35° C. for 5 to 7 days.

(226) Step 16: Transfer the chewable gel units of Step 15 into suitable packaging.

Example 9

(227) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 9 below. The ingredients corresponding to Example 9 are tabulated in Table 9 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 9 the active ingredient is dextromethorphan HBr. Each chewable gel unit formed in accordance with Example 9 has an active strength of dextromethorphan HBr of about 30 mg. Each chewable gel unit formed by the process of Example 9 has a mass of about 3,580 mg. Six hundred (600) chewable gel units are formed by the process of Example 9; however, as should be understood by those having ordinary skill in the art, the principles of Example 9 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(228) TABLE-US-00009

TABLE 9	Ingredient Name	Batch Quantity
	Dextromethorphan HBr	18.972
	Bitter blocker powder	7.500
	Carrageenan	52.800
	Citric acid anhydrous	4.800
	Corn syrup (liquid glucose)	780.000
	Flavor agent (tutti frutti flavor)	1.728
	HP.beta.CD	150.000
	Maltitol solution	168.000
	Neotame	0.600
	Pregelatinized starch (starch 1500)	43.200
	Purified water	720.000
	Sodium chloride	10.800
	Sucralose	9.600
	Sucrose	486.000
	Trisodium citrate	9.000

Procedure—Example 9

(229) Step 1: Add about 72.9% of the batch quantity of purified water to a main manufacturing vessel. Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride under continuous stirring until a clear solution is formed.

(230) Step 2: Add the batch quantity of corn syrup to the solution of Step 1 under continuous stirring while heating the mixture to a temperature in the range of about 50° C. to about 55° C. until a homogenous mixture is formed.

(231) Step 3: Mix the batch quantities of carrageenan and trisodium citrate, and about 34.6% of the batch quantity of sucrose until a homogenous blend is formed.

(232) Step 4: Add the blend of Step 3 to the mixture of Step 2 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.

(233) Step 5: Heat the gel of Step 4 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is observed.

(234) Step 6: Add the batch quantity of maltitol solution and about 65.4% of the batch quantity of sucrose to the gel mixture of Step 5 while maintaining a temperature in the range of about 90° C. to about 105° C.

(235) Step 7: Add about 23.3% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(236) Step 8: Add the batch quantity of dextromethorphan HBr to the solution of Step 7 under continuous stirring until a clear solution is formed.

(237) Step 9: Combine the solution of Step 8 and the gel mixture formed in Step 6 under stirring and maintain the temperature of the mixture in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 74% w/w or about 74 brix.

(238) Step 10: Add about 3.8% of the batch quantity of purified water and the batch quantity of the flavor agent to a container under stirring until a clear solution is formed.

(239) Step 11: Combine the solution of Step 10 and the gel mixture of Step 9 under stirring while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C. until a gummy mixture is formed.

(240) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the

individual chewable gel units from the mold.

(241) Step 13: Mix the batch quantities of pregelatinized starch and citric acid anhydrous until a homogenous blend is formed.

(242) Step 14: Polish the chewable gel units of Step 12 with the blend of Step 13 for approximately 5 to about 10 minutes to form polished chewable gel units.

(243) Step 15: Store the chewable gel units formed in Step 14 for curing at a temperature in the range of about 25° C. to about 35° C. for 5 to 7 days.

(244) Step 16: Transfer the chewable gel units of Step 15 into suitable packaging.

Example 10

(245) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 10 below. The ingredients corresponding to Example 10 are tabulated in Table 10 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 10 the active ingredient is dimenhydrinate. Each chewable gel unit formed in accordance with Example 10 has an active strength of dimenhydrinate of about 25 mg. Each chewable gel unit formed by the process of Example 10 has a mass of about 3,588 mg. Two hundred fifty (250) chewable gel units are formed by the process of Example 10; however, as should be understood by those having ordinary skill in the art, the principles of Example 10 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(246) TABLE-US-00010

Ingredient Name	Batch Quantity
Dimenhydrinate	6.250
Bitter blocker powder	3.250
Carrageenan	21.875
Citric acid anhydrous	2.000
Corn syrup (liquid glucose)	350.000
Flavor agent (tutti frutti flavor)	0.500
HP.beta.CD	87.500
Magnesium stearate	2.000
Maltitol solution	75.000
Neotame	0.250
Pregelatinized starch (starch 1500)	18.000
Purified water	295.000
Sodium chloride	3.750
Sucralose	4.375
Sucrose	155.000
Trisodium citrate	3.500

Procedure—Example 10

(247) Step 1: Add about 59.3% of the batch quantity of purified water to a main manufacturing vessel. Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride under continuous stirring until a clear solution is formed.

(248) Step 2: Add the batch quantity of corn syrup to the solution of Step 1 under continuous stirring while heating the mixture to a temperature in the range of about 50° C. to about 55° C. to form a homogenous mixture.

(249) Step 3: Mix the batch quantities of carrageenan and trisodium citrate, and about 45.2% of the batch quantity of sucrose until a homogenous blend is formed.

(250) Step 4: Add the blend of Step 3 to the mixture of Step 2 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.

(251) Step 5: Heat the gel of Step 4 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is observed.

(252) Step 6: Add the batch quantity of maltitol solution and about 54.8% of the batch quantity of sucrose to the gel mixture of Step 5 while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C.

(253) Step 7: Add about 32.5% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(254) Step 8: Add the batch quantity of dimenhydrinate to the solution of Step 7 under continuous stirring until a clear solution is formed.

(255) Step 9: Combine the solution of Step 8 and the gel mixture of Step 6 under stirring and maintain the temperature of the mixture in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 74% w/w or about 74 brix.

(256) Step 10: Add about 8.2% of the batch quantity of purified water and the batch quantity of the

flavor agent to a container under stirring until a clear solution is formed.

(257) Step 11: Combine the solution of Step 10 and the gel mixture of Step 9 under stirring while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C. until a gummy mixture is formed.

(258) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(259) Step 13: Mix the batch quantities of pregelatinized starch, citric acid anhydrous, and magnesium stearate until a homogenous blend is formed.

(260) Step 14: Polish the chewable gel units of Step 12 with the blend of Step 13 for approximately 5 to about 10 minutes to form polished chewable gel units.

(261) Step 15: Store the chewable gel units of Step 14 for curing at a temperature in the range of about 25° C. to about 35° C. for 5 to 7 days.

(262) Step 16: Transfer the chewable gel units of Step 15 into suitable packaging.

Example 11

(263) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 11 below. The ingredients corresponding to Example 11 are tabulated in Table 11 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 11 the active ingredient is fexofenadine HCl. Each chewable gel unit formed in accordance with Example 11 has an active strength of fexofenadine HCl of about 30 mg. Each chewable gel unit formed by the process of Example 11 has a mass of about 4,088 mg. One hundred fifty (150) chewable gel units are formed by the process of Example 11; however, as should be understood by those having ordinary skill in the art, the principles of Example 11 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(264) TABLE-US-00011

Ingredient Name	Batch Quantity
Fexofenadine HCl	4.500
Bitter blocker powder	2.400
Carrageenan	16.500
Citric acid anhydrous	1.200
Corn syrup (liquid glucose)	228.900
Flavor agent (cool mint flavor)	0.030
Flavor agent (orange flavor)	0.300
HP.beta.CD	60.000
Magnesium stearate	1.200
Maltitol solution	60.000
Neotame	0.150
Pregelatinized starch (starch 1500)	10.800
Purified water	199.650
Sodium chloride	3.300
Sucralose	3.300
Sucrose	107.250
Trisodium citrate	3.720

Procedure—Example 11

(265) Step 1: Add about 45.1% of the batch quantity of purified water to a main manufacturing vessel. Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride under continuous stirring until a clear solution is formed.

(266) Step 2: Add the batch quantity of corn syrup to the solution of Step 1 under continuous stirring while heating the mixture to a temperature in the range of about 50° C. to about 55° C. to form a homogenous mixture.

(267) Step 3: Mix the batch quantities of carrageenan and trisodium citrate, and about 55.9% of the batch quantity of sucrose until a homogenous blend is formed.

(268) Step 4: Add the blend of Step 3 to the mixture of Step 2 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.

(269) Step 5: Heat the gel of Step 4 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is observed.

(270) Step 6: Add the batch quantity of maltitol solution and about 44.1% of the batch quantity of sucrose to the gel mixture of Step 5 while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C.

(271) Step 7: Add about 42.1% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear

solution is formed.

(272) Step 8: Add the batch quantity of fexofenadine HCl to the solution of Step 7 under continuous stirring until a clear solution is formed.

(273) Step 9: Combine the solution of Step 8 and the gel mixture of Step 6 under stirring and maintain the temperature of the mixture in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 74% w/w or about 74 brix.

(274) Step 10: Add about 12.8% of the batch quantity of purified water and the batch quantities of the flavor agents to a container under stirring until a clear solution is formed.

(275) Step 11: Combine the solution of Step 10 and the gel mixture of Step 9 under stirring while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C. until a gummy mixture is formed.

(276) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(277) Step 13: Mix the batch quantities of pregelatinized starch, citric acid anhydrous, and magnesium stearate until a homogenous blend is formed.

(278) Step 14: Polish the chewable gel units of Step 12 with the blend of Step 13 for approximately 5 to about 10 minutes to form polished chewable gel units.

(279) Step 15: Store the chewable gel units of Step 14 for curing at a temperature in the range of about 25° C. to about 35° C. for 5 to 7 days.

(280) Step 16: Transfer the chewable gel units of Step 15 into suitable packaging.

Example 12

(281) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 12 below. The ingredients corresponding to Example 12 are tabulated in Table 12 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 12 the active ingredient is fexofenadine HCl. Each chewable gel unit formed in accordance with Example 12 has an active strength of fexofenadine HCl of about 60 mg. Each chewable gel unit formed by the process of Example 12 has a mass of about 4,088 mg. One hundred fifty (150) chewable gel units are formed by the process of Example 12; however, as should be understood by those having ordinary skill in the art, the principles of Example 12 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(282) TABLE-US-00012

Ingredient Name	Batch Quantity
Fexofenadine HCl	9.000
Bitter blocker powder	2.400
Carrageenan	16.500
Citric acid anhydrous	1.200
Corn syrup (liquid glucose)	225.000
Flavor agent (cool mint flavor)	0.060
Flavor agent (orange flavor)	0.600
HP.beta.CD	60.000
Magnesium stearate	1.200
Maltitol solution	60.000
Neotame	0.150
Pregelatinized starch (starch 1500)	10.800
Purified water	199.440
Sodium chloride	3.300
Sucralose	3.300
Sucrose	105.000
Trisodium citrate	5.250

Procedure—Example 12

(283) Step 1: Add about 45.1% of the batch quantity of purified water to a main manufacturing vessel. Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride under continuous stirring until a clear solution is formed.

(284) Step 2: Add the batch quantity of corn syrup to the solution of Step 1 under continuous stirring, continue stirring while heating the mixture to a temperature in the range of about 50° C. to about 55° C. to form a homogenous mixture.

(285) Step 3: Mix the batch quantities of carrageenan and trisodium citrate, and about 57.1% of the batch quantity of sucrose until a homogenous blend is formed.

(286) Step 4: Add the blend of Step 3 to the mixture of Step 2 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.

(287) Step 5: Heat the gel of Step 4 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is observed.

(288) Step 6: Add the batch quantity of maltitol solution and about 42.9% of the batch quantity of sucrose to the gel mixture of Step 5 while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C.

(289) Step 7: Add about 45.1% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(290) Step 8: Add the batch quantity of fexofenadine HCl to the solution of Step 7 under continuous stirring until a clear solution is formed.

(291) Step 9: Combine the solution of Step 8 and the gel mixture formed in Step 6 under stirring and maintain the temperature of the mixture in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 74% w/w or about 74 brix.

(292) Step 10: Add about 9.8% of the batch quantity of purified water and the batch quantities of the flavor agents to a container under stirring until a clear solution is formed.

(293) Step 11: Combine the solution of Step 10 and the gel mixture of Step 9 under stirring, maintaining a temperature in the range of about 90° C. to about 105° C. until a gummy mixture is formed.

(294) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(295) Step 13: Mix the batch quantities of pregelatinized starch, citric acid anhydrous, and magnesium stearate until a homogenous blend is formed.

(296) Step 14: Polish the chewable gel units of Step 12 with the blend of Step 13 for approximately 5 to about 10 minutes to form polished chewable gel units.

(297) Step 15: Store the chewable gel units of Step 14 for curing at a temperature in the range of about 25° C. to about 35° C. for 5 to 7 days.

(298) Step 16: Transfer the chewable gel units of Step 15 into suitable packaging.

Example 13

(299) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 13 below. The ingredients corresponding to Example 13 are tabulated in Table 13 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 13 the active ingredient is acetaminophen. Each chewable gel unit formed in accordance with Example 13 has an active strength of acetaminophen of about 160 mg. Each chewable gel unit formed by the process of Example 13 has a mass of about 3,667 mg. Five hundred (500) chewable gel units are formed by the process of Example 13; however, as should be understood by those having ordinary skill in the art, the principles of Example 13 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(300) TABLE-US-00013 TABLE 13 Ingredient Name Batch Quantity Acetaminophen 80.000 Bitter blocker powder 6.653 Carrageenan 46.200 Citric acid anhydrous 3.500 Color agent (FD&C yellow) 0.050 Corn syrup (liquid glucose) 659.644 Flavor agent (cool mint flavor) 0.087 Flavor agent (orange flavor) 0.867 HP.beta.CD 200.000 Maltitol solution 197.378 Neotame 0.578 Pregelatinized starch (starch 1500) 30.000 Purified water 554.750 Sodium chloride 9.240 Sucralose 9.240 Sucrose 297.925 Trisodium citrate 7.390

Procedure—Example 13

(301) Step 1: Add about 51.9% of the batch quantity of purified water to a main manufacturing vessel. Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride under continuous stirring until a clear solution is formed.

(302) Step 2: Add the batch quantity of corn syrup to the solution of Step 1 under continuous

stirring while heating the mixture to a temperature in the range of about 50° C. to about 55° C. to form a homogenous mixture.

(303) Step 3: Mix the batch quantities of carrageenan and trisodium citrate, and about 36.3% of the batch quantity of sucrose until a homogenous blend is formed.

(304) Step 4: Add the blend of Step 3 to the mixture of Step 2 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.

(305) Step 5: Heat the gel of Step 4 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is observed.

(306) Step 6: Add the batch quantity of maltitol solution and about 63.7% of the batch quantity of sucrose to the gel mixture of Step 5 while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C.

(307) Step 7: Add about 46.0% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(308) Step 8: Add the batch quantity of acetaminophen to the solution of Step 7 under continuous stirring until a clear solution is formed and heat to a temperature in the range of about 70° C. to about 80° C.

(309) Step 9: Combine the solution of Step 8 and the gel mixture of Step 6 under stirring and maintain the temperature of the mixture in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 74% w/w or about 74 brix.

(310) Step 10: Add about 2.1% of the batch quantity of purified water and the batch quantities of the flavor agents and the color agent in a container under stirring until a clear solution is formed.

(311) Step 11: Add the solution of Step 10 to the gel mixture formed in Step 9 under stirring while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C. to form a gummy mixture.

(312) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(313) Step 13: Mix the batch quantities of pregelatinized starch and citric acid anhydrous until a homogenous blend is formed.

(314) Step 14: Polish the chewable gel units of Step 12 with the blend of Step 13 for approximately 5 to about 10 minutes to form polished chewable gel units.

(315) Step 15: Store the chewable gel units of Step 14 for curing at a temperature in the range of about 25° C. to about 35° C. for 5 to 7 days.

(316) Step 16: Transfer the chewable gel units of Step 15 into suitable packaging.

Example 14

(317) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 14 below. The ingredients corresponding to Example 14 are tabulated in Table 14 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 14 the active ingredient is guaifenesin. Each chewable gel unit formed in accordance with Example 14 has an active strength of guaifenesin of about 100 mg. Each chewable gel unit formed by the process of Example 14 has a mass of about 4,088 mg. Six hundred (600) chewable gel units are formed by the process of Example 14; however, as should be understood by those having ordinary skill in the art, the principles of Example 14 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(318) TABLE-US-00014
TABLE 14
Ingredient Name Batch Quantity
Guaifenesin 60.000
Bitter blocker powder 11.400
Carrageenan 60.000
Citric acid anhydrous 4.800
Corn syrup (liquid glucose) 720.000
Flavor agent (tutti frutti flavor) 3.000
HP.beta.CD 210.000
Magnesium stearate

4.800 Maltitol solution 240.000 Neotame 0.600 Pregelatinized starch (starch 1500) 43.200 Purified water 840.000 Sodium chloride 7.200 Sucralose 12.000 Sucrose 588.000 Trisodium citrate 7.800
Procedure—Example 14

(319) Step 1: Add about 40.5% of the batch quantity of purified water to a main manufacturing vessel. Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride under continuous stirring until a clear solution is formed.

(320) Step 2: Add the batch quantity of corn syrup to the solution of Step 1 under continuous stirring while heating the mixture to a temperature in the range of about 50° C. to about 55° C. to form a homogenous mixture.

(321) Step 3: Mix the batch quantities of carrageenan and trisodium citrate, and about 32.7% of the batch quantity of sucrose until a homogenous blend is formed.

(322) Step 4: Add the blend of Step 3 to the mixture of Step 2 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.

(323) Step 5: Heat the gel of Step 4 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is observed.

(324) Step 6: Add the batch quantity of maltitol solution and about 67.3% of the batch quantity of sucrose to the gel mixture of Step 5 while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C.

(325) Step 7: Add about 46.4% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(326) Step 8: Add the batch quantity of guaifenesin to the solution of Step 7 under continuous stirring until a clear solution is formed.

(327) Step 9: Combine the solution of Step 8 and the gel mixture formed in Step 6 under stirring and maintain the temperature of the mixture in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 74% w/w or about 74 brix.

(328) Step 10: Add about 13.1% of the batch quantity of purified water and the batch quantity of the flavor agent to a container under stirring until a clear solution is formed.

(329) Step 11: Combine the solution of Step 10 and the gel mixture of Step 9 under stirring while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C. until a gummy mixture is formed.

(330) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(331) Step 13: Mix the batch quantities of pregelatinized starch, citric acid anhydrous, and magnesium stearate until a homogenous blend is formed.

(332) Step 14: Polish the chewable gel units of Step 12 with the blend of Step 13 for approximately 5 to about 10 minutes to form polished chewable gel units.

(333) Step 15: Store the chewable gel units of Step 14 for curing at a temperature in the range of about 25° C. to about 35° C. for 5 to 7 days.

(334) Step 16: Transfer the chewable gel units of Step 15 into suitable packaging.

Example 15

(335) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 15 below. The ingredients corresponding to Example 15 are tabulated in Table 15 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 15 the active ingredient is phenylephrine HCl. Each chewable gel unit formed in accordance with Example 15 has an active strength of phenylephrine HCl of about 10 mg. Each chewable gel unit formed by the process of Example 15 has a mass of about 2,550 mg. Two hundred (200) chewable gel units are formed by the process of Example 15;

however, as should be understood by those having ordinary skill in the art, the principles of Example 15 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(336) TABLE-US-00015 TABLE 15 Batch Ingredient Name Quantity Phenylephrine HCl 2.000 Bitter blocker powder 1.800 Carrageenan 12.400 Citric acid anhydrous 1.000 Corn syrup (liquid glucose) 202.400 Flavor agent (tutti frutti flavor) 0.550 HP.beta.CD 9.600 Maltitol solution 42.000 Neotame 0.250 Pregelatinized starch (starch 1500) 9.000 Purified water 175.000 Sodium chloride 2.500 Sucralose 2.500 Sucrose 122.000 Trisodium citrate 2.000

Procedure—Example 15

(337) Step 1: Add about 57.1% of the batch quantity of purified water to a main manufacturing vessel. Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride under continuous stirring until a clear solution is formed.

(338) Step 2: Add the batch quantity of corn syrup to the solution of Step 1 under continuous stirring while heating the mixture to a temperature in the range of about 50° C. to about 55° C. to form a homogenous mixture.

(339) Step 3: Mix the batch quantities of carrageenan and trisodium citrate, and about 32.8% of the batch quantity of sucrose until a homogenous blend is formed.

(340) Step 4: Add the blend of Step 3 to the mixture of Step 2 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.

(341) Step 5: Heat the gel of Step 4 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is observed.

(342) Step 6: Add the batch quantity of maltitol solution and about 67.2% of the batch quantity of sucrose to the gel mixture of Step 5 while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C.

(343) Step 7: Add about 28.6% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(344) Step 8: Add the batch quantity of phenylephrine HCl to the solution of Step 7 under continuous stirring until a clear solution is formed.

(345) Step 9: Combine the solution of Step 8 and the gel mixture formed in Step 6 under stirring and maintain the temperature of the mixture in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 74% w/w or about 74 brix.

(346) Step 10: Add about 14.3% of the batch quantity of purified water and the batch quantity of the flavor agent to a container under stirring until a clear solution is formed.

(347) Step 11: Combine the solution of Step 10 and the gel mixture formed in Step 9 under stirring while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C. to form a gummy mixture.

(348) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(349) Step 13: Mix the batch quantities of pregelatinized starch and citric acid anhydrous until a homogenous blend is formed.

(350) Step 14: Polish the chewable gel units of Step 12 with the blend of Step 13 for approximately 5 to about 10 minutes to form polished chewable gel units.

(351) Step 15: Store the chewable gel units of Step 14 for curing at a temperature in the range of about 25° C. to about 35° C. for 5 to 7 days.

(352) Step 16: Transfer the chewable gel units of Step 15 into suitable packaging.

Example 16

(353) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 16 below. The ingredients corresponding to Example 16 are tabulated in Table 16 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 16 the active ingredient is acetaminophen. Each chewable gel unit formed in accordance with Example 16 has an active strength of acetaminophen of about 160 mg. Each chewable gel unit formed by the process of Example 16 has a mass of about 4,600 mg. One thousand (1,000) chewable gel units are formed by the process of Example 16; however, as should be understood by those having ordinary skill in the art, the principles of Example 16 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(354) TABLE-US-00016

TABLE 16	Batch	Ingredient	Name	Quantity
		Acetaminophen		161.560
		Bitter blocker powder		26.490
		Carrageenan		130.000
		Color agent (FD&C red #40)		0.010
		Corn syrup (liquid glucose)		1900.000
		Flavor agent (orange flavor)		2.500
		HP.beta.CD		400.000
		Maltitol solution		516.000
		Neotame		1.000
		Pregelatinized starch (starch 1500)		100.000
		Purified water		1640.000
		Sodium chloride		26.000
		Sucralose		26.000
		Sucrose		900.000
		Trisodium citrate		22.000

Procedure—Example 16

(355) Step 1: Add about 97.5% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(356) Step 2: Add the batch quantity of acetaminophen to the solution of Step 1 under continuous stirring until a clear solution is formed and heat to a temperature in the range of about 70° C. to about 80° C.

(357) Step 3: Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride in the solution of Step 2 under continuous stirring until a clear solution is formed.

(358) Step 4: Add the batch quantity of corn syrup to the solution of Step 3 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. to form a homogenous mixture.

(359) Step 5: Mix the batch quantities of carrageenan and trisodium citrate, and about 44.4% of the batch quantity of sucrose until a homogenous blend is formed.

(360) Step 6: Add the blend of Step 5 to the mixture of Step 4 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.

(361) Step 7: Heat the gel of Step 6 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is observed.

(362) Step 8: Add the batch quantity of maltitol solution and about 55.6% of the batch quantity of sucrose to the gel mixture of Step 7 while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C.

(363) Step 9: Maintain the temperature of the gel mixture of Step 8 in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 74% w/w or about 74 brix.

(364) Step 10: Add about 2.5% of the batch quantity of purified water and the batch quantities of the flavor agent and the color agent to a container under stirring until a clear solution is formed.

(365) Step 11: Add the solution of Step 10 to the gel mixture formed in Step 9 under stirring while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C. until a gummy mixture is formed.

(366) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(367) Step 13: Polish the chewable gel units of Step 12 with the batch quantity of pregelatinized starch for approximately 5 to about 10 minutes to form polished chewable gel units.

(368) Step 14: Store the chewable gel units of Step 13 for curing at a temperature in the range of about 25° C. to about 35° C. for 5 to 7 days.

(369) Step 15: Transfer the chewable gel units of Step 14 into suitable packaging.

Example 17

(370) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 17 below. The ingredients corresponding to Example 17 are tabulated in Table 17 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 17 the active ingredient is diphenhydramine HCl. Each chewable gel unit formed in accordance with Example 17 has an active strength of diphenhydramine HCl of about 25 mg. Each chewable gel unit formed by the process of Example 17 has a mass of about 4,090 mg. Eight hundred (800) chewable gel units are formed by the process of Example 17; however, as should be understood by those having ordinary skill in the art, the principles of Example 17 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(371) TABLE-US-00017

TABLE 17	Batch	Ingredient Name	Quantity
		Diphenhydramine HCl	20.000
		Bitter blocker powder	12.000
		Carrageenan	80.000
		Citric acid anhydrous	6.400
		Color agent (FD&C red #40)	0.130
		Corn syrup (liquid glucose)	1280.000
		Flavor agent (strawberry flavor)	8.000
		HP.beta.CD	80.000
		Magnesium stearate	8.000
		Maltitol solution	259.870
		Neotame	0.800
		Pregelatinized starch (starch 1500)	57.600
		Purified water	1120.000
		Sodium chloride	12.000
		Sucralose	11.200
		Sucrose	784.000
		Trisodium citrate	12.000

Procedure—Example 17

(372) Step 1: Add about 17.9% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(373) Step 2: Add the batch quantity of diphenhydramine HCl to the solution of Step 1 under continuous stirring until a clear solution is formed.

(374) Step 3: Add about 77.7% of the batch quantity of purified water to the solution of Step 3 and slowly add the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride thereto under continuous stirring until a clear solution is formed.

(375) Step 4: Add the batch quantity of corn syrup to the solution of Step 3 under continuous stirring while heating the mixture to a temperature in the range of about 50° C. to about 55° C. to form a homogenous mixture.

(376) Step 5: Mix the batch quantities of carrageenan, trisodium citrate, and sucrose until a homogenous blend is formed.

(377) Step 6: Add the blend of Step 5 to the mixture of Step 4 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.

(378) Step 7: Heat the gel of Step 6 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is observed.

(379) Step 8: Add the batch quantity of maltitol solution to the gel mixture of Step 7 while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C.

(380) Step 9: Maintain the temperature of the gel mixture formed in Step 8 in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 74% w/w or about 74 brix.

(381) Step 10: Add about 4.4% of the batch quantity of purified water and the batch quantities of the flavor agent and the color agent to a container under stirring until a clear solution is formed.

(382) Step 11: Add the solution of Step 10 to the gel mixture formed in Step 9 under stirring while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C. to form a gummy mixture.

(383) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(384) Step 13: Mix the batch quantities of pregelatinized starch, citric acid anhydrous, and magnesium stearate until a homogenous blend is formed.

(385) Step 14: Polish the chewable gel units of Step 12 with the blend of Step 13 for approximately 5 to about 10 minutes to form polished chewable gel units.

(386) Step 15: Collect the chewable gel units of Step 14 on curing trays and store for curing at a temperature in the range of about 25° C. to about 35° C. for 5 to 7 days.

(387) Step 16: Transfer the chewable gel units of Step 15 into suitable packaging.

Example 18

(388) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 18 below. The ingredients corresponding to Example 18 are tabulated in Table 18 with the amount of each ingredient used in the process (i.e., the batch quantity) given in kilograms. In Example 18 the active ingredient is diphenhydramine HCl. Each chewable gel unit formed in accordance with Example 18 has an active strength of diphenhydramine HCl of about 25 mg. Each chewable gel unit formed by the process of Example 18 has a mass of about 3,600 mg. Ninety thousand (90,000) chewable gel units are formed by the process of Example 18; however, as should be understood by those having ordinary skill in the art, the principles of Example 18 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(389) TABLE-US-00018

TABLE 18	Batch Ingredient Name	Quantity
	Diphenhydramine HCl	2.250
	Bitter blocker powder	1.350
	Carrageenan	9.000
	Citric acid anhydrous	1.080
	Color agent (FD&C red #40)	0.009
	Corn syrup (liquid glucose)	144.000
	Flavor agent (tutti frutti flavor)	0.630
	HP.beta.CD	9.000
	Magnesium stearate	1.350
	Maltitol solution	29.240
	Neotame	0.090
	Pregelatinized starch (starch 1500)	9.720
	Purified water	136.000
	Sodium chloride	1.350
	Sucralose	1.260
	Sucrose	88.470
	Trisodium citrate	1.350

Procedure—Example 18

(390) Step 1: Add about 97.8% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(391) Step 2: Add the batch quantity of diphenhydramine HCl to the solution of Step 1 under continuous stirring until a clear solution is formed and heat to a temperature in the range of about sixty degrees Celsius (60° C.) to about 70° C.

(392) Step 3: Slowly add the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride to the solution of Step 2 under continuous stirring until a clear solution is formed.

(393) Step 4: Add the batch quantity of corn syrup to the solution of Step 3 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. to form a homogenous mixture.

(394) Step 5: Mix the batch quantities of carrageenan and trisodium citrate, and about 11.3% of the batch quantity of sucrose until a homogenous blend is formed.

(395) Step 6: Add the blend of Step 5 to the mixture of Step 4 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.

(396) Step 7: Heat the gel of Step 6 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is observed.

(397) Step 8: Add the batch quantity of maltitol solution and about 88.7% of the batch quantity of sucrose to the gel mixture formed in Step 7 while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C.

(398) Step 9: Maintain the temperature of the gel mixture formed in Step 8 in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 74% w/w or about 74 brix.

(399) Step 10: Add about 2.2% of the batch quantity of purified water and the batch quantities of the flavor agent and the color agent to a container under stirring until a clear solution is formed.

(400) Step 11: Add the solution of Step 10 to the gel mixture formed in Step 9 under stirring while maintaining the temperature of the mixture in the range of about 80° C. to about 90° C. until a gummy mixture is formed.

(401) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(402) Step 13: Mix the batch quantities of pregelatinized starch, citric acid anhydrous, and magnesium stearate until a homogenous blend is formed.

(403) Step 14: Polish the chewable gel units of Step 12 with the blend of Step 13 for approximately 5 to about 10 minutes to form polished chewable gel units.

(404) Step 15: Collect the chewable gel units of Step 14 on curing trays and store for curing at a temperature in the range of about 25° C. to about 35° C. for three (3) to five (5) days.

(405) Step 16: Transfer the chewable gel units of Step 15 into suitable packaging.

Example 19

(406) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 19 below. The ingredients corresponding to Example 19 are tabulated in Table 19 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 19 the active ingredient is dimenhydrinate. Each chewable gel unit formed in accordance with Example 19 has an active strength of dimenhydrinate of about 50 mg. Each chewable gel unit formed by the process of Example 19 has a mass of about 4,390 mg. One thousand (1,000) chewable gel units are formed by the process of Example 19; however, as should be understood by those having ordinary skill in the art, the principles of Example 19 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(407) TABLE-US-00019

TABLE 19	Batch Ingredient Name	Quantity
	Dimenhydrinate	50.000
	Bitter blocker powder	23.900
	Carrageenan	130.000
	Citric acid anhydrous	8.000
	Color agent (FD&C yellow #6)	0.100
	Corn syrup (liquid glucose)	1800.000
	Flavor agent (orange flavor)	6.000
	HP.beta.CD	400.000
	Magnesium stearate	10.000
	Maltitol solution	526.000
	Neotame	1.000
	Pregelatinized starch (starch 1500)	72.000
	Purified water	1640.000
	Sodium chloride	26.000
	Sucralose	25.000
	Sucrose	850.000
	Trisodium citrate	22.000

Procedure—Example 19

(408) Step 1: Add about 91.5% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(409) Step 2: Add the batch quantity of dimenhydrinate to the solution of Step 1 under continuous stirring until a clear solution is formed.

(410) Step 3: Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride in the solution of Step 2 under continuous stirring to form a clear solution.

(411) Step 4: Add the batch quantity of corn syrup to the solution of Step 3 under continuous stirring while heating the mixture to a temperature in the range of about 55° C. to about 60° C. to form a homogenous mixture.

(412) Step 5: Mix the batch quantities of carrageenan and trisodium citrate, and about 41.2% of the batch quantity of sucrose until a homogenous blend is formed.

(413) Step 6: Add the blend of Step 5 to the mixture of Step 4 under continuous stirring while

maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.

(414) Step 7: Heat the gel of Step 6 to a temperature in the range of about 90° C. to about 95° C. until a thick gel mixture is formed.

(415) Step 8: Add the batch quantity of maltitol solution and about 58.8% of the batch quantity of sucrose to the gel mixture of Step 7 while maintaining the temperature of the mixture in the range of about 90° C. to about 95° C.

(416) Step 9: Maintain the temperature of the gel mixture formed in Step 8 in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about seventy percent by weight (70% w/w) or about seventy brix (70 brix).

(417) Step 10: Add about 8.5% of the batch quantity of purified water and the batch quantities of the flavor agent and the color agent to a container under stirring until a clear solution is formed.

(418) Step 11: Add the solution of Step 10 to the gel mixture formed in Step 9 under stirring while maintaining the temperature of the mixture in the range of about 80° C. to about 90° C. to form a gummy mixture.

(419) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(420) Step 13: Mix the batch quantities of pregelatinized starch, citric acid anhydrous, and magnesium stearate until a homogenous blend is formed.

(421) Step 14: Polish the chewable gel units of Step 12 with the blend of Step 13 for approximately 5 to about 10 minutes to form polished chewable gel units.

(422) Step 15: Collect the chewable gel units of Step 14 on curing trays and store for curing at a temperature in the range of about 25° C. to about 35° C. for 3 to 5 days.

(423) Step 16: Transfer the chewable gel units of Step 15 into suitable packaging.

Example 20

(424) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 20 below. The ingredients corresponding to Example 20 are tabulated in Table 20 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 20 the active ingredient is dextromethorphan HBr. Each chewable gel unit formed in accordance with Example 20 has an active strength of dextromethorphan HBr of about 15 mg. Each chewable gel unit formed by the process of Example 20 has a mass of about 2,300 mg. One thousand (1,000) chewable gel units are formed by the process of Example 20; however, as should be understood by those having ordinary skill in the art, the principles of Example 20 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(425) TABLE-US-00020

Batch Ingredient	Name	Quantity
Dextromethorphan HBr		15.760
Bitter blocker powder		10.000
Carrageenan		66.000
Color agent (FD&C yellow #5)		0.030
Corn syrup (liquid glucose)		975.000
Flavor agent (sweet grape flavor)		2.000
HP.beta.CD		187.000
Maltitol solution		210.000
Neotame		1.000
Pregelatinized starch (starch 1500)		55.000
Purified water		900.000
Sodium chloride		10.000
Sucralose		12.000
Sucrose		600.210
Trisodium citrate		11.000

Procedure—Example 20

(426) Step 1: Add about 94.4% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(427) Step 2: Add the batch quantity of dextromethorphan HBr to the solution of Step 1 under continuous stirring until a clear solution is formed.

(428) Step 3: Slowly add the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride to the solution of Step 2 under continuous stirring until a clear solution is formed.

- (429) Step 4: Add the batch quantity of corn syrup to the solution of Step 3 under continuous stirring while heating the mixture to a temperature in the range of about 50° C. to about 55° C. until a homogenous mixture is formed.
- (430) Step 5: Mix the batch quantities of carrageenan and trisodium citrate, and about 8.3% of the batch quantity of sucrose until a homogenous blend is formed.
- (431) Step 6: Add the blend of Step 5 to the mixture of Step 4 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 55° C. until a homogenous gel is formed.
- (432) Step 7: Heat the gel of Step 6 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is observed.
- (433) Step 8: Add the batch quantity of maltitol solution and about 91.7% of the batch quantity of sucrose to the gel mixture of Step 7 while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C.
- (434) Step 9: Maintain the temperature of the gel mixture formed in Step 8 in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 70% w/w or about 70 brix.
- (435) Step 10: Add about 5.6% of the batch quantity of purified water and the batch quantities of the flavor agent and the color agent to a container under stirring until a clear solution is formed.
- (436) Step 11: Add the solution of Step 10 to the gel mixture formed in Step 9 under stirring while maintaining the temperature of the mixture in the range of about 90° C. to about 95° C. until a gummy mixture is formed.
- (437) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.
- (438) Step 13: Polish the chewable gel units of Step 12 with the batch quantity of pregelatinized starch for approximately 5 to about 10 minutes to form polished chewable gel units.
- (439) Step 14: Collect the chewable gel units of Step 13 on curing trays and store for curing at a temperature in the range of about 25° C. to about 35° C. for 3 to 5 days.
- (440) Step 15: Transfer the chewable gel units of Step 14 into suitable packaging.

Example 21

(441) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 21 below. The ingredients corresponding to Example 21 are tabulated in Table 21 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 21 the active ingredient is dextromethorphan HBr. Each chewable gel unit formed in accordance with Example 21 has an active strength of dextromethorphan HBr of about 30 mg. Each chewable gel unit formed by the process of Example 21 has a mass of about 4,600 mg. One hundred fifty (150) chewable gel units are formed by the process of Example 21; however, as should be understood by those having ordinary skill in the art, the principles of Example 21 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(442) TABLE-US-00021

Batch Ingredient	Name	Quantity
Dextromethorphan HBr		4.730
Bitter blocker powder		3.660
Carrageenan		18.000
Color agent (FD&C yellow #5)		0.010
Corn syrup (liquid glucose)		283.800
Flavor agent (sweet grape flavor)		0.900
HP.beta.CD		75.000
Maltitol solution		75.000
Neotame		0.150
Pregelatinized starch (starch 1500)		15.000
Purified water		240.000
Sodium chloride		3.750
Sucralose		4.500
Sucrose		150.000
Trisodium citrate		3.000

Procedure—Example 21

(443) Step 1: Add about 91.7% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

- (444) Step 2: Add the batch quantity of dextromethorphan HBr to the solution of Step 1 under continuous stirring until a clear solution is formed.
- (445) Step 3: Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride in the solution of Step 2 under continuous stirring to form a clear solution.
- (446) Step 4: Add the batch quantity of corn syrup to the solution of Step 3 under continuous stirring while heating the mixture to a temperature in the range of about 55° C. to about 60° C. to form a homogenous mixture.
- (447) Step 5: Mix the batch quantities of carrageenan and trisodium citrate, and about 8.3% of the batch quantity of sucrose until a homogenous blend is formed.
- (448) Step 6: Add the blend of Step 5 to the mixture of Step 4 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 60° C. until a homogenous gel is formed.
- (449) Step 7: Heat the gel of Step 6 to a temperature in the range of about 90° C. to about 105° C. until a thick gel mixture is formed.
- (450) Step 8: Add the batch quantity of maltitol solution and about 91.7% of the batch quantity of sucrose to the gel mixture of Step 7 while maintaining the temperature of the mixture in the range of about 90° C. to about 105° C.
- (451) Step 9: Maintain the temperature of the gel mixture formed in Step 8 in the range of about 90° C. to about 105° C. until the total solid content of the mixture raises to about 70% w/w or about 70 brix.
- (452) Step 10: Add about 8.3% of the batch quantity of purified water and the batch quantities of the flavor agent and the color agent to a container under stirring until a clear solution is formed.
- (453) Step 11: Add the solution of Step 10 to the gel mixture formed in Step 9 under stirring while maintaining the temperature of the mixture in the range of about 90° C. to about 95° C. to form a gummy mixture.
- (454) Step 12: Transfer the gummy mixture of Step 11 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.
- (455) Step 13: Polish the chewable gel units of Step 12 with the batch quantity of pregelatinized starch for approximately 5 to about 10 minutes to form polished chewable gel units.
- (456) Step 14: Collect the chewable gel units of Step 13 on curing trays and store for curing at a temperature in the range of about 25° C. to about 35° C. for 3 to 5 days.
- (457) Step 15: Transfer the chewable gel units of Step 14 into suitable packaging.

Example 22

(458) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 22 below. The ingredients corresponding to Example 22 are tabulated in Table 22 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 22 the active ingredient is diphenhydramine HCl. Each chewable gel unit formed in accordance with Example 22 has an active strength of diphenhydramine HCl of about 25 mg. Each chewable gel unit formed by the process of Example 22 has a mass of about 3,600 mg. Two hundred fifty (250) chewable gel units are formed by the process of Example 22; however, as should be understood by those having ordinary skill in the art, the principles of Example 22 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(459) TABLE-US-00022

TABLE 22 Batch Ingredient Name	Quantity
Diphenhydramine HCl	6.250
Bitter blocker powder	3.750
Carrageenan	25.000
Citric acid anhydrous	2.030
Color agent (FD&C red #40)	0.030
Corn syrup (liquid glucose)	400.000
Ethanol	18.750
Flavor agent (tutti frutti flavor)	1.750
HP.beta.CD	50.000
Magnesium stearate	2.030
Maltitol solution	81.230
Mono-diglycerides	

6.250 Neotame 0.250 Pregelatinized starch (starch 1500) 18.450 Purified water 325.000 Sodium chloride 3.750 Sucralose 3.500 Sucrose 245.750 Trisodium citrate 3.750

Procedure—Example 22

(460) Step 1: Add the batch quantities of ethanol and diphenhydramine HCl to a container under continuous stirring while heating the mixture to a temperature in the range of about 70° C. to about 80° C. until a clear solution is formed.

(461) Step 2: Add the batch quantity of mono-diglycerides to the solution of Step 1 under continuous stirring while maintaining the temperature of the mixture in the range of about 70° C. to about 80° C. until a clear solution is formed.

(462) Step 3: Add about 6.2% of the batch quantity of purified water to the solution of Step 3 under continuous stirring while maintaining the temperature of the mixture in the range of about 70° C. to about 80° C. until a clear solution is formed.

(463) Step 4: Add about 87.7% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(464) Step 5: Slowly add the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride to the solution of Step 4 under continuous stirring until a clear solution is formed.

(465) Step 6: Add the batch quantity of corn syrup to the solution of Step 5 under continuous stirring while heating the mixture to a temperature above about 50° C. to form a homogenous mixture.

(466) Step 7: Combine the solution of Step 3 and the mixture of Step 6 under continuous stirring while maintaining the temperature of the mixture above about 70° C. until a homogenous gel is formed.

(467) Step 8: Mix the batch quantities of carrageenan and trisodium citrate, and about 10.2% of the batch quantity of sucrose until a homogenous blend is formed.

(468) Step 9: Add the blend of Step 8 to the gel of Step 7 under continuous stirring while maintaining the temperature of the mixture above seventy-five degrees Celsius (75° C.) until a homogenous gel is formed.

(469) Step 10: Heat the gel of Step 9 to a temperature in the range of about 85° C. to about one hundred degrees Celsius (100° C.) until a thick gel mixture is observed.

(470) Step 11: Add the batch quantity of maltitol solution and about 89.8% of the batch quantity of sucrose to the gel mixture of Step 10 while heating the mixture to a temperature in the range of about 95° C. to about 105° C.

(471) Step 12: Maintain the temperature of the gel mixture formed in Step 11 in the range of about 95° C. to about 105° C. until the total solid content of the mixture raises to about 70% w/w or about 70 brix.

(472) Step 13: Add about 6.1% of the batch quantity of purified water and the batch quantities of the flavor agent and the color agent to a container under stirring until a clear solution is formed.

(473) Step 14: Add the solution of Step 13 to the gel mixture formed in Step 12 under stirring while maintaining the temperature of the mixture in the range of about 80° C. to about 90° C. until a gummy mixture is formed.

(474) Step 15: Transfer the gummy mixture of Step 14 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(475) Step 16: Mix the batch quantities of pregelatinized starch, citric acid anhydrous, and magnesium stearate until a homogenous blend is formed.

(476) Step 17: Polish the chewable gel units of Step 15 with the blend of Step 16 for approximately 5 to about 10 minutes to form polished chewable gel units.

(477) Step 18: Store the polished chewable gel units of Step 17 for curing at a temperature in the range of about 25° C. to about 35° C. for 5 to 7 days.

(478) Step 19: Transfer the cured chewable gel units of Step 18 into suitable packaging.

Example 23

(479) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 23 below. The ingredients corresponding to Example 23 are tabulated in Table 23 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 23 the active ingredient is loratadine. Each chewable gel unit formed in accordance with Example 23 has an active strength of loratadine of about 10 mg. Each chewable gel unit formed by the process of Example 23 has a mass of about 3,700 mg. One thousand (1,000) chewable gel units are formed by the process of Example 23; however, as should be understood by those having ordinary skill in the art, the principles of Example 23 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(480) TABLE-US-00023

TABLE 23	Batch	Ingredient	Name	Quantity
Loratadine	10.000	Bitter		
blocker powder	14.600	Carrageenan	100.000	
Citric acid anhydrous	5.000	Color agent (FD&C yellow #5)	1.000	
Corn syrup (liquid glucose)	1300.000	Ethanol	55.000	
Flavor agent (sweet grape flavor)	3.400	HP.beta.CD	240.000	
Maltitol solution	540.000	Neotame	1.000	
Pregelatinized starch (starch 1500)	80.000	Purified water	1350.000	
Sucralose	20.000	Sucrose	920.000	
Trisodium citrate	40.000			

Procedure—Example 23

(481) Step 1: Add the batch quantities of ethanol and loratadine to a container under continuous stirring until a clear solution is formed.

(482) Step 2: Add about 7.4% of the batch quantity of purified water to the solution of Step 1 under continuous stirring while heating the mixture to a temperature in the range of about 70° C. to about 80° C. until a clear solution is formed.

(483) Step 3: Add about 18.5% of the batch quantity of purified water to a container. Slowly add the batch quantities of HP.beta.CD, citric acid anhydrous, and sucralose to the purified water under continuous stirring while heating the mixture to a temperature in the range of about 70° C. to about 80° C. until a clear solution is formed.

(484) Step 4: Combine the solution of Step 2 and the solution of Step 3 under continuous stirring while maintaining the temperature of the mixture in the range of about 70° C. to about 80° C. to evaporate ethanol from the solution.

(485) Step 5: Add about 66.7% of the batch quantity of purified water to a container. Slowly add and dissolve the batch quantities of neotame and bitter blocker powder under continuous stirring until a clear solution is formed.

(486) Step 6: Add the batch quantity of corn syrup to the solution of Step 5 under continuous stirring while heating the mixture to a temperature in the range of about 55° C. to about 60° C. to form a homogenous mixture.

(487) Step 7: Mix the batch quantities of carrageenan and trisodium citrate, and about 34.8% of the batch quantity of sucrose until a homogenous blend is formed.

(488) Step 8: Add the blend of Step 7 to the mixture of Step 6 under continuous stirring while maintaining the temperature of the mixture in the range of about 50° C. to about 60° C. until a homogenous gel is formed.

(489) Step 9: Add the batch quantity of maltitol solution and about 65.2% of the batch quantity of sucrose to the gel of Step 8 and heat to a temperature in the range of about 85° C. to about 95° C.

(490) Step 10: Combine the solution of Step 4 and the gel mixture formed in Step 9 under stirring while heating the mixture to a temperature in the range of about 95° C. to about 105° C. until a thick gel mixture is formed.

(491) Step 11: Add about 7.4% of the batch quantity of purified water and the batch quantities of the flavor agent and the color agent to a container under stirring until a clear solution is formed.

(492) Step 12: Add the solution of Step 11 to the gel mixture of Step 10 under stirring while

maintaining the temperature of the mixture in the range of about 95° C. to about 105° C.

(493) Step 13: Maintain the temperature of the gel mixture formed in Step 12 in the range of about 95° C. to about 105° C. until the total solid content of the mixture raises to about seventy-two percent by weight (72% w/w) or about seventy-two brix (72 brix) to form a gummy mixture.

(494) Step 14: Transfer the gummy mixture of Step 13 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(495) Step 15: Delump the batch quantity of pregelatinized starch using a #40 mesh to form a homogenous powder.

(496) Step 16: Polish the chewable gel units of Step 14 with the powder of Step 15 for approximately 5 to about 10 minutes to form polished chewable gel units.

(497) Step 17: Store the polished chewable gel units of Step 16 for curing at a temperature in the range of about 35° C. to about forty-three degrees Celsius (43° C.) for 3 to 5 days.

(498) Step 18: Transfer the cured chewable gel units of Step 17 into suitable packaging.

Example 24

(499) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 24 below. The ingredients corresponding to Example 24 are tabulated in Table 24, with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 24, the active ingredient is acetaminophen. Each chewable gel unit formed in accordance with Example 24 has an active strength of acetaminophen of about 325 mg. Each chewable gel unit formed by the process of Example 24 has a mass of about 4,600 mg. Two hundred (200) chewable gel units are formed by the process of Example 24; however, as should be understood by those having ordinary skill in the art, the principles of Example 24 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(500) TABLE-US-00024

Batch Ingredient Name	Quantity
Acetaminophen	65.000
Bitter blocker powder	5.300
Carrageenan	26.000
Color agent (FD&C yellow #6)	0.010
Corn syrup (liquid glucose)	346.100
Flavor agent (orange flavor)	1.500
HP.beta.CD	80.000
Maltitol solution	103.200
Neotame	0.200
Polyethylene glycol 400 (PEG 400)	115.000
Povidone (K30)	23.000
Pregelatinized starch (starch 1500)	20.000
Propylene glycol	10.900
Purified water	200.000
Sodium chloride	5.200
Sucralose	5.200
Sucrose	160.000
Trisodium citrate	4.400

Procedure—Example 24

(501) Step 1: Add the batch quantities of polyethylene glycol 400 and propylene glycol to a container under continuous stirring while heating the mixture to a temperature in the range of about 70° C. to about 80° C. until a clear solution is formed.

(502) Step 2: Add the batch quantity of povidone K-30 to the solution of Step 1 under continuous stirring while maintaining the temperature of the mixture in the range of about 70° C. to about 80° C. until a clear solution is formed.

(503) Step 3: Add the batch quantity of acetaminophen to the solution of Step 2 under continuous stirring while maintaining the temperature of the mixture in the range of about 70° C. to about 80° C. until a clear solution is formed.

(504) Step 4: Add about 95.0% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(505) Step 5: Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride in the solution of Step 4 under continuous stirring to form a clear solution.

(506) Step 6: Add the batch quantity of corn syrup to the solution of Step 5 under continuous stirring while heating the mixture to a temperature above about 50° C. to form a homogenous mixture.

(507) Step 7: Combine the solution of Step 3 and the mixture of Step 6 under continuous stirring while heating the mixture to a temperature above about 70° C. until a homogenous mixture is formed.

(508) Step 8: Mix the batch quantities of carrageenan and trisodium citrate, and about 16.3% of the batch quantity of sucrose until a homogenous blend is formed.

(509) Step 9: Combine the blend of Step 8 and the mixture of Step 7 under continuous stirring while heating the mixture to a temperature above 75° C. until a homogenous gel is formed.

(510) Step 10: Heat the gel of Step 9 to a temperature in the range of about 85° C. to about 100° C. until a thick gel mixture is observed.

(511) Step 11: Add the batch quantity of maltitol solution and about 83.7% of the batch quantity of sucrose to the gel mixture of Step 10 while heating the mixture to a temperature in the range of about 95° C. to about 105° C.

(512) Step 12: Maintain the temperature of the gel mixture formed in Step 11 in the range of about 95° C. to about 105° C. until the total solid content of the mixture raises to about eighty percent by weight (80% w/w) or about eighty brix (80 brix).

(513) Step 13: Add about 5.0% of the batch quantity of purified water and the batch quantities of the flavor agent and the color agent to a container under stirring until a clear solution is formed.

(514) Step 14: Add the solution of Step 13 to the gel mixture formed in Step 12 under continuous stirring while maintaining the temperature of the mixture in the range of about 80° C. to about 90° C. to form a gummy mixture.

(515) Step 15: Transfer the gummy mixture of Step 14 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(516) Step 16: Delump the batch quantity of pregelatinized starch using a #40 mesh to form a homogenous powder.

(517) Step 17: Polish the chewable gel units of Step 15 with the powder of Step 16 for approximately 5 to about 10 minutes to form polished chewable gel units.

(518) Step 18: Store the polished chewable gel units of Step 17 on curing trays and store for curing at a temperature in the range of about 25° C. to about 35° C. for 3 to 5 days.

(519) Step 19: Transfer the cured chewable gel units of Step 18 into suitable packaging.

Example 25

(520) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 25 below. The ingredients corresponding to Example 25 are tabulated in Table 25 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 25 the active ingredient is dextromethorphan HBr. Each chewable gel unit formed in accordance with Example 25 has an active strength of dextromethorphan HBr of about 30 mg. Each chewable gel unit formed by the process of Example 25 has a mass of about 4,600 mg. Two hundred (200) chewable gel units are formed by the process of Example 25; however, as should be understood by those having ordinary skill in the art, the principles of Example 25 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(521) TABLE-US-00025

TABLE 25	Batch Ingredient Name	Quantity
6.300	Bitter blocker powder	4.880
	Carrageenan	24.000
	Color agent (FD&C yellow #5)	0.020
	Corn syrup (liquid glucose)	378.400
	Ethanol	11.000
	Flavor agent (sweet grape flavor)	1.200
	HP.beta.CD	100.000
	Maltitol solution	100.000
	Neotame	0.200
	Povidone (K30)	3.000
	Pregelatinized starch (starch 1500)	20.000
	Purified water	309.000
	Sodium chloride	5.000
	Sucralose	6.000
	Sucrose	200.000
	Trisodium citrate	5.000

Procedure—Example 25

(522) Step 1: Add the batch quantities of ethanol and dextromethorphan HBr to a container under

continuous stirring while heating to a temperature in the range of about 70° C. to about 80° C. until a clear solution is formed.

(523) Step 2: Add the batch quantity of povidone K-30 and about 5.0% of the batch quantity of purified water to the solution of Step 1 under continuous stirring while maintaining the temperature of the mixture in the range of about 70° C. to about 80° C. until a clear solution is formed.

(524) Step 3: Add about 88.5% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(525) Step 4: Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride in the solution of Step 3 under continuous stirring to form a clear solution.

(526) Step 5: Add the batch quantity of corn syrup to the solution of Step 4 under continuous stirring while heating the mixture to a temperature above about 50° C. to form a homogenous mixture.

(527) Step 6: Combine the solution of Step 2 and the mixture of Step 5 under continuous stirring while heating the mixture to a temperature above about 70° C. until a homogenous mixture is formed.

(528) Step 7: Mix the batch quantities of carrageenan and trisodium citrate, and about 10.0% of the batch quantity of sucrose until a homogenous blend is formed.

(529) Step 8: Add the blend of Step 7 to the mixture of Step 6 under continuous stirring while maintaining the temperature of the mixture above 75° C. until a homogenous gel is formed.

(530) Step 9: Continue heating the gel of Step 8 to a temperature in the range of about 85° C. to about 100° C. until a thick gel mixture is observed.

(531) Step 10: Add the batch quantity of maltitol solution and about 90.0% of the batch quantity of sucrose to the gel mixture of Step 9 while maintaining the temperature of the mixture in the range of about 95° C. to about 105° C.

(532) Step 11: Maintain the temperature of the gel mixture formed in Step 10 in the range of about 95° C. to about 105° C. until the total solid content of the mixture raises to about 70% w/w or about 70 brix.

(533) Step 12: Add about 6.5% of the batch quantity of purified water and the batch quantities of the flavor agent and the color agent to a container under stirring until a clear solution is formed.

(534) Step 13: Add the solution of Step 12 in the gel mixture formed in Step 11 under stirring while maintaining the temperature of the mixture in the range of about 80° C. to about 90° C. until a gummy mixture is formed.

(535) Step 14: Transfer the gummy mixture of Step 13 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(536) Step 15: Delump the batch quantity of pregelatinized starch using a #40 mesh to form a homogenous powder.

(537) Step 16: Polish the chewable gel units of Step 14 with the powder of Step 15 for approximately 5 to about 10 minutes to form polished chewable gel units.

(538) Step 17: Store the polished chewable gel units of Step 16 for curing at a temperature in the range of about 25° C. to about 35° C. for 3 to 5 days.

(539) Step 18: Transfer the cured chewable gel units of Step 17 into suitable packaging.

Example 26

(540) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 26 below. The ingredients corresponding to Example 26 are tabulated in Table 26 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 26 the active ingredient is acetaminophen. Each chewable gel unit formed in accordance with Example 26 has an active strength of acetaminophen of about 325

mg. Each chewable gel unit formed by the process of Example 26 has a mass of about 4,600 mg. Two hundred (200) chewable gel units are formed by the process of Example 26; however, as should be understood by those having ordinary skill in the art, the principles of Example 26 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(541) TABLE-US-00026

Batch	Ingredient Name	Quantity
	Acetaminophen	65.000
	Bitter blocker powder	5.300
	Carrageenan	26.000
	Color agent (FD&C yellow #6)	0.010
	Corn syrup (liquid glucose)	346.100
	Flavor agent (orange flavor)	1.500
	HP.beta.CD	80.000
	Maltitol solution	103.200
	Neotame	0.200
	Polyethylene glycol 400 (PEG 400)	115.000
	Povidone (K30)	23.000
	Pregelatinized starch (starch 1500)	20.000
	Propylene glycol	10.900
	Purified water	200.000
	Sodium chloride	5.200
	Sucralose	5.200
	Sucrose	160.000
	Trisodium citrate	4.400

Procedure—Example 26

(542) Step 1: Add the batch quantities of polyethylene glycol 400 and propylene glycol to a container under continuous stirring while heating the mixture to a temperature in the range of about 70° C. to about 80° C. until a clear solution is formed.

(543) Step 2: Add the batch quantity of povidone K-30 to the solution of Step 1 under continuous stirring while maintaining the temperature of the mixture in the range of about 70° C. to about 80° C. until a clear solution is formed.

(544) Step 3: Add the batch quantity of acetaminophen to the solution of Step 2 under continuous stirring while maintaining the temperature of the mixture in the range of about 70° C. to about 80° C. until a clear solution is formed.

(545) Step 4: Add about 95.0% of the batch quantity of purified water to the solution of Step 3 and slowly add the batch quantity of HP.beta.CD thereto under continuous stirring until a clear solution is formed.

(546) Step 5: Slowly add the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride to the solution of Step 4 under continuous stirring until a clear solution is formed.

(547) Step 6: Add the batch quantities of corn syrup and maltitol to the solution of Step 5 under continuous stirring while heating the mixture to a temperature above about 50° C. to form a homogenous mixture.

(548) Step 7: Mix the batch quantities of carrageenan and trisodium citrate, and about 16.3% of the batch quantity of sucrose until a homogenous blend is formed.

(549) Step 8: Add the blend of Step 7 to the mixture of Step 6 under continuous stirring while maintaining the temperature of the mixture above 75° C. until a homogenous gel is formed.

(550) Step 9: Heat the gel of Step 8 to a temperature in the range of about 85° C. to about 100° C. until a thick gel mixture is observed.

(551) Step 10: Add about 83.7% of the batch quantity of sucrose to the gel mixture of Step 9 and heat the mixture to a temperature in the range of about 95° C. to about 105° C.

(552) Step 11: Maintain the temperature of the gel mixture formed in Step 10 in the range of about 95° C. to about 105° C. until the total solid content of the mixture raises to about eighty percent by weight (80% w/w) or about eighty brix (80 brix).

(553) Step 12: Add about 5.0% of the batch quantity of purified water and the batch quantities of the flavor agent and the color agent to a container under stirring until a clear solution is formed.

(554) Step 13: Add the solution of Step 12 to the gel mixture formed in Step 11 under stirring while maintaining the temperature of the mixture in the range of about 80° C. to about 90° C. until a gummy mixture is formed.

(555) Step 14: Transfer the gummy mixture of Step 13 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(556) Step 15: Delump the batch quantity of pregelatinized starch using a #40 mesh to form a homogenous powder.

(557) Step 16: Polish the chewable gel units of Step 14 with the powder of Step 15 for approximately 5 to about 10 minutes to form polished chewable gel units.

(558) Step 17: Store the polished chewable gel units of Step 16 for curing at a temperature in the range of about 25° C. to about 35° C. for 3 to 5 days.

(559) Step 18: Transfer the cured chewable gel units of Step 17 into suitable packaging.

Example 27

(560) A process for making chewable gel units in accordance with certain aspects of the present invention is provided in Example 27 below. The ingredients corresponding to Example 27 are tabulated in Table 27 with the amount of each ingredient used in the process (i.e., the batch quantity) given in grams. In Example 27 the active ingredient is diphenhydramine HCl. Each chewable gel unit formed in accordance with Example 27 has an active strength of diphenhydramine HCl of about 25 mg. Each chewable gel unit formed by the process of Example 27 has a mass of about 3,600 mg. One hundred (100) chewable gel units are formed by the process of Example 27; however, as should be understood by those having ordinary skill in the art, the principles of Example 27 can be used to make more or less chewable gel units by proportionally increasing or decreasing the amount of ingredients as necessary to produce the desired quantity of chewable gel units.

(561) TABLE-US-00027

TABLE 27	Batch Ingredient	Name	Quantity
	Diphenhydramine HCl	2.5	
	Bitter blocker powder	1.5	
	Carrageenan	10	
	Citric acid anhydrous	0.8	
	Color agent (FD&C red #40)	0.01	
	Corn syrup (liquid glucose)	160	
	Ethanol	7.5	
	Flavor agent (tutti frutti flavor)	0.7	
	HP.beta.CD	10	
	Magnesium stearate	1	
	Maltitol solution	32.49	
	Neotame	0.1	
	Pregelatinized starch (starch 1500)	7.2	
	Purified water	130	
	Sodium chloride	1.5	
	Sucralose	1.4	
	Sucrose	98.3	
	Trisodium citrate	1.5	

Procedure—Example 27

(562) Step 1: Add the batch quantities of ethanol and diphenhydramine HCl to a container under continuous stirring while heating the mixture to a temperature in the range of about 70° C. to about 80° C. until a clear solution is formed.

(563) Step 2: Add about 6.2% of the batch quantity of purified water to the solution of Step 1 under continuous stirring while maintaining the temperature of the mixture in the range of about 70° C. to about 80° C. until a clear solution is formed.

(564) Step 3: Add about 87.7% of the batch quantity of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring until a clear solution is formed.

(565) Step 4: Slowly add and dissolve the batch quantities of sucralose, neotame, bitter blocker powder, and sodium chloride in the solution of Step 3 under continuous stirring to form a clear solution.

(566) Step 5: Add the batch quantity of corn syrup to the solution of Step 4 under continuous stirring while heating the mixture to a temperature above about 50° C. to form a homogenous mixture.

(567) Step 6: Combine the solution of Step 2 and the mixture of Step 5 under continuous stirring while maintaining the temperature of the mixture above about 70° C. until a homogenous mixture is formed.

(568) Step 7: Mix the batch quantities of carrageenan and trisodium citrate, and about 10.2% of the batch quantity of sucrose until a homogenous blend is formed.

(569) Step 8: Add the blend of Step 7 to the mixture of Step 6 under continuous stirring while heating the mixture to a temperature above 75° C. until a homogenous gel is formed.

(570) Step 9: Continue heating the gel of Step 8 to a temperature in the range of about 85° C. to about 100° C. until a thick gel mixture is observed.

(571) Step 10: Add the batch quantity of maltitol solution and about 89.8% of the batch quantity of sucrose to the gel mixture of Step 9 while heating the mixture to a temperature in the range of about 95° C. to about 105° C.

(572) Step 11: Maintain the temperature of the gel mixture of Step 10 in the range of about 95° C. to about 105° C. until the total solid content of the mixture raises to about 70% w/w or about 70 brix.

(573) Step 12: Add about 6.1% of the batch quantity of purified water and the batch quantities of the flavor agent and the color agent to a container under stirring until a clear solution is formed.

(574) Step 13: Add the solution of Step 12 to the gel mixture of Step 11 under stirring while maintaining a temperature of the mixture in the range of about 80° C. to about 90° C. to form a gummy mixture.

(575) Step 14: Transfer the gummy mixture of Step 13 to a product mold. Allow the gummy mixture to cool at room temperature for about 10 to about 15 minutes and then remove the individual chewable gel units from the mold.

(576) Step 15: Delump the batch quantities of pregelatinized starch, citric acid anhydrous, and magnesium stearate using a #40 mesh to form a homogenous blend.

(577) Step 16: Polish the chewable gel units of Step 14 with the blend of Step 15 for approximately 5 to about 10 minutes to form polished chewable gel units.

(578) Step 17: Store the polished chewable gel units of Step 16 for curing at a temperature in the range of about 25° C. to about 35° C. for 3 to 5 days.

(579) Step 18: Transfer the chewable gel units of Step 17 into suitable packaging.

Example 28

(580) ingredients corresponding to Example 28 are tabulated in Table 28, with the amount of each ingredient given in respective percent-by-weight (% w/w).

(581) TABLE-US-00028

TABLE 28	Quantity	Ingredient Name	(% w/w)
	2.86	Acetaminophen	
FD&C Red 40	0.1	HP.beta.CD	8.54
Glycerin	4.11	PEG 400	1.23
Strawberry Flavor	0.49	Gelatin	13.55
Light Mineral Oil	0.18	Citric acid	0.8
Maltitol solution	47.96	PVA	0.49
PVP K30	0.49	Dextrose	1.04
Sucralose	0.56	Purified Water	17.58
TOTAL	100		

Procedure—Example 28

(582) STEP I: add about half the quantity of purified water into a container and heat to about sixty-five degrees Celsius (65° C.), then add and dissolve the quantities of acetaminophen and HP.beta.CD under stirring, until clear solution is observed.

(583) STEP II: add the remaining quantity of purified water to a separate container and heat to about eighty-five degrees Celsius (85° C.), then add and dissolve the quantities of PVA and PVP K30 under stirring, until clear solution is observed.

(584) STEP III: combine the mixtures from STEP II and STEP I under continuous stirring. Add and disperse the quantity of gelatin under continuous stirring for at least about ten (10) minutes, maintain temperature at about eighty-five degrees Celsius (85° C.).

(585) STEP IV: add and mix the quantity of Lycasin 80-55 into contents of STEP III. Add and dissolve quantities of dextrose and sucralose with continuous stirring.

(586) STEP V: combine and mix the batch quantities of glycerin, mineral oil, PEG 400, strawberry flavor, and FD&C Red 40 in a separate container.

(587) STEP VI: combine the mixture of STEP V and the mixture of STEP IV. Add and dissolve the quantity of citric acid under continuous stirring until a homogenous solution obtained.

(588) STEP VII: transfer the gummy mixture from STEP VI to a product mold, allow the gummy mixture to stand for about fifteen (15) to about forty-five (45) minutes before removing the gummy dosage forms from the mold.

Example 29

(589) ingredients corresponding to Example 29 are tabulated in Table 29, with the amount of each ingredient given in respective percent-by-weight (% w/w).

(590) TABLE-US-00029

TABLE 29	Quantity	Ingredient Name	(% w/w)	
	0.52	Diphenhydramine		
Hydrochloride	FD&C Red 40	0.1	HP.beta.CD	10
Glycerin	4.11	PEG 400	1.23	
Strawberry Flavor	0.49	Gelatin	12.5	
Mineral Oil	0.18	Citric acid	0.8	
Maltitol solution	49.98	PVA	0.49	
PVP K-30	0.49			

Dextrose 1.04 Sucralose 0.56 Purified Water 17.57 TOTAL 100

Procedure—Example 29

(591) STEP I: add about half of the quantity of purified water to a container and heat to about sixty-five degrees Celsius (65° C.). Add the quantities of diphenhydramine hydrochloride and HP.beta.CD to the purified water under stirring until clear solution is observed.

(592) STEP II: add the remaining batch quantity of purified water into a separate container and heat to about eighty-five degrees Celsius (85° C.). Add and disperse the batch quantities of PVA and PVP K-30 under stirring to until clear solution is observed.

(593) STEP III: combine the contents of STEP II and STEP I under continuous stirring. Add and disperse the batch quantity of gelatin under continuous stirring for approximately ten (10) minutes, maintaining temperature at about eighty-five degrees Celsius (85° C.).

(594) STEP IV: add and mix the batch quantity of maltitol solution into contents of STEP III. Add and dissolve the batch quantities of dextrose and sucralose with continuous stirring.

(595) STEP V: combine and mix batch quantities of glycerin, mineral oil, PEG 400, strawberry flavor, and FD&C Red 40 in a separate container.

(596) STEP VI: combine contents from STEP V and STEP IV. Add and dissolve the batch quantity of citric acid under continuous stirring until a homogenous solution obtained.

(597) STEP VII: transfer the gummy mixture from STEP VI to a product mold, cool to room temperature, and remove the gummy from the mold after cooling for about thirty to forty-five (30-45) minutes.

Example 30

(598) ingredients corresponding to Example 30 are tabulated in Table 30, with the batch quantity amount of each ingredient given grams (g).

(599) TABLE-US-00030

TABLE 30	Ingredient Name	Ingredient Type	Batch Quantity (g)
	Diphenhydramine hydrochloride	active ingredient	514.8
	Sodium chloride	tonicity modifying agent	330
	Trisodium citrate	buffering agent	264
	Bubble gum flavor	flavor	33
	Carrageenan	gelling agent	1650
	HP.beta.CD	complexing agent	1273
	Maltitol solution	non-crystallizing polyol solution	5544
	Bitter blocker powder	taste enhancing agent	238
	Corn syrup	taste enhancing agent/filler	26730
	Neotame	taste enhancing agent	33
	Sucralose	taste enhancing agent	330
	Sugar	taste enhancing agent/filler	15840
	Purified water	water	23100
	TOTAL		75880

(600) Procedure—Example 30: a twelve and one-half milligram (12.5 mg) diphenhydramine hydrochloride translucent gummy pharmaceutical dosage form composition and procedure:

(601) STEP I: add about two thousand grams (2000 g) of purified water to a container. Slowly add the batch quantity of HP.beta.CD to the purified water under continuous stirring for approximately thirty (30) minutes.

(602) STEP II: add the batch quantity of diphenhydramine hydrochloride to the mixture of STEP I under continuous stirring, a clear solution should be observed after approximately fifteen (15) minutes.

(603) STEP III: add about twenty thousand five hundred grams (20500 g) of purified water to a container. Slowly add the batch quantities of sodium chloride, bitter blocker powder, sucralose, and neotame under stirring for approximately fifteen (15) minutes until clear solution observed.

(604) STEP IV: add the batch quantity of corn syrup to the solution of STEP III under stirring for approximately ten (10) minutes and heat to a temperature in the range of about fifty degrees Celsius (50° C.) to about fifty-five degrees Celsius (55° C.).

(605) STEP V: create a dry mix blend by combining the batch quantity of carrageenan, the batch quantity of trisodium citrate, and about two thousand grams (2000 g) sugar and mix for approximately ten (10) minutes.

(606) STEP VI: add the dry mix blend from STEP V to the heated mixture of STEP IV under stirring and heat the mixture a temperature in the range of about fifty degrees Celsius (50° C.) to about fifty-five degrees Celsius (55° C.) under constant stirring.

(607) STEP VII: heat the gummy mixture from STEP VI to about ninety a temperature in the range of about ninety degrees Celsius (90° C.) to about one hundred five degrees Celsius (105° C.), add the batch quantity of maltitol solution and the remaining batch quantity of sugar, and continue heating the mixture to a temperature in the range of about ninety degrees Celsius (90° C.) to about one hundred five degrees Celsius (105° C.) for approximately ninety (90) minutes until the total solid content raises to about seventy-four percent-by-weight (74% w/w) or about seventy-four brix (74 Brix).

(608) STEP VIII: combine the solution of STEP II and the mixture of STEP VII under stirring and maintain a temperature in the range of about ninety degrees Celsius (90° C.) to about one hundred five degrees Celsius (105° C.) until total solid content raises to about seventy-four percent-by-weight (74% w/w) or about seventy-four brix (74 Brix).

(609) STEP IX: add and dissolve the batch quantity of bubble gum flavor to the remaining batch quantity of purified water to a container.

(610) STEP X: combine the solution of STEP IX to mixture of STEP VIII under stirring and maintain a temperature in the range of about ninety-five degrees Celsius (95° C.) to about one hundred five degrees Celsius (105° C.).

(611) STEP XI: transfer the gummy mixture from STEP X to a product mold, cool to room temperature, and remove the gummy from the mold after cooling for about ten (10) to about fifteen (15) minutes.

Example 31

(612) Ingredients corresponding to Example 31 are tabulated in Table 31, with the batch quantity amount of each ingredient given grams (g).

(613) TABLE-US-00031

TABLE 31	Batch Quantity	Ingredient Name (g)
Diphenhydramine hydrochloride	468	
Sodium chloride	300	
Trisodium citrate	240	
Pink color	60	
Bubble gum flavor	60	
Carrageenan	1500	
Maltitol solution	5040	
Bitter blocker	216	
Corn syrup	24300	
Neotame	30	
Sucralose	300	
Sugar	15220	
Purified water	21000	
TOTAL	68734	

(614) Procedure—Example 31: a twelve and one-half milligram (12.5 mg) diphenhydramine hydrochloride translucent chewable pharmaceutical dosage form composition and procedure:

(615) STEP I: add nineteen thousand and five-hundred grams (19,500 g) of purified water to a container. Slowly add the batch quantities of sodium chloride, bitter blocker powder, sucralose, and neotame under stirring for approximately fifteen (15) minutes until clear solution observed.

(616) STEP II: add the batch quantity corn syrup to the solution of STEP I under stirring for approximately ten (10) minutes and heat a temperature in the range of about fifty degrees Celsius (50° C.) to about fifty-five degrees Celsius (55° C.).

(617) STEP III: prepare a dry mix blend by combining the batch quantity of carrageenan, the batch quantity of trisodium citrate, and two thousand grams (2000 g) of sugar and mix for approximately ten (10) minutes.

(618) STEP IV: add the dry mix blend from STEP III to the heated solution of STEP II under stirring.

(619) STEP V: heat the gummy mixture from STEP IV, while stirring to a temperature in the range of about ninety degrees Celsius (90° C.) to about one hundred five degrees Celsius (105° C.).

(620) STEP VI: add the batch quantity of maltitol solution and fifteen thousand two hundred twenty (15,220 g) of sugar to the gummy mixture of STEP V under stirring; and continue heating the gummy mixture to a temperature in the range of about ninety degrees Celsius (90° C.) to about one hundred five degrees Celsius (105° C.) until total solid content raises to about seventy-four percent-by-weight (74% w/w) or about seventy-four brix (74 Brix).

(621) STEP VII: in a container, add and dissolve the batch quantities of diphenhydramine hydrochloride, bubble gum flavor, and pink color in about one thousand five hundred (1500 grams) of purified water.

(622) STEP VIII: combine the mixtures of STEP VI to mixture of STEP VII under stirring and

maintain a temperature in the range of about ninety-five degrees Celsius (95° C.) to about one hundred five degrees Celsius (105° C.).

(623) STEP IX: transfer the gummy mixture from STEP VIII to a product mold, cool to room temperature, and remove the gummy from the mold after cooling for about for about ten (10) to about fifteen (15) minutes.

Example 32

(624) ingredients corresponding to Example 32 are tabulated in Table 32, with the amount of each ingredient given in respective percent-by-weight (% w/w).

(625) TABLE-US-00032

Batch	Quantity	Ingredient	Name (g)
		Acetaminophen	15.00
		Sodium chloride	1.50
		Trisodium citrate	1.20
		FD&C Yellow	0.30
		HP.beta.CD	37.50
		Pineapple flavor	1.50
		Carrageenan	7.50
		Maltitol solution	12.87
		Bitter blocker	1.08
		Corn syrup	121.50
		Neotame	0.15
		Sucralose	1.50
		Sugar	38.17
		Purified water	105.00
		TOTAL	344.77

Procedure—Example 32

(626) STEP I: add purified water to a container; add the batch quantities of HP.beta.CD and acetaminophen under stirring for approximately fifteen (15) minutes.

(627) STEP II: heat the mixture from STEP I to a temperature in the range of about fifty degrees Celsius (50° C.) to about fifty-five degrees Celsius (55° C.) while stirring; clear solution observed after approximately fifteen (15) minutes;

(628) STEP III: add purified water to a container; add the batch quantities of sodium chloride, sucralose, neotame, and bitter blocker under stirring; clear solution observed after approximately fifteen (15) minutes;

(629) STEP IV: add the batch quantity of corn syrup to the solution of STEP III under stirring; a temperature in the range of about fifty degrees Celsius (50° C.) to about fifty-five degrees Celsius (55° C.) while stirring; clear solution observed.

(630) STEP V: prepare a dry mix blend by combining the batch quantity of carrageenan, the batch quantity of trisodium citrate, and 10 grams (10 g) of sugar and mix for approximately ten (10) minutes.

(631) STEP VI: add the dry mix blend from STEP V to the heated solution of STEP IV under constant stirring for approximately twenty (20) minutes;

(632) STEP VII: heat the gummy mixture from STEP VI to a temperature in the range of about ninety degrees Celsius (90° C.) to about ninety-five degrees Celsius (95° C.); add the batch quantity of maltitol solution and the remaining batch quantity of sugar; heat the gummy mixture to and maintain a temperature in the range of about one hundred degrees Celsius (100° C.) to about one hundred five degrees Celsius (105° C.) for approximately ninety (90) minutes until the total solid content raises to seventy-four percent (74% w/w) or about seventy-four brix (74 Brix)

(633) STEP VIII: combine the solution of STEP I and the gummy mixture of STEP VII under stirring; maintain a temperature in the range of about ninety-five degrees Celsius (95° C.) to about one hundred five degrees Celsius (105° C.) until the total solid content is about seventy-four percent-by-weight (74% w/w) or about seventy-four brix (74 Brix).

(634) STEP IX: transfer the gummy mixture from STEP VIII to a product mold, cool to room temperature, and remove the gummy from the mold after cooling for about fifteen (15) to twenty (20) minutes.

(635) The chewable gel units were subjected to several quantitative and qualitative tests. The tests and the findings thereof are discussed and summarized in the paragraphs and tables below. For purposes of Tables D1-D42, the following table headings are to be interpreted as follows: “Ex #” means the Example number whereby the texted chewable gel was formed; “SD” means the duration of time, provided in number of days, that the chewable gel(s) was stored, relative to the curing step provided in the corresponding Example, prior to testing; “ST” means the temperature, provided in degrees Celsius, at which the chewable gel(s) was stored; and “SRH” means the relative humidity, provided in percentage, in which the chewable gel(s) was stored. Other heading

definitions are provided where necessary.

(636) The results of a product characterization analysis performed on the chewable gel units formed in accordance with the Examples provided herein are summarized in Tables D1-D7. Table D1 provides information pertaining to the product characterization analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein shortly after the curing step. In each instance, the chewable gels referenced in Table D1 were translucent.

(637) TABLE-US-00033 TABLE D1 Ex Dimensions # Shape (mm) Color 2 Bear 20 × 12 × 7 Light yellow/brown (L × W × H) 4 Rectangular 18 × 11 × 9.2 Light yellow/brown (L × W × H) 6 Bear 20 × 12 × 7 Light red 6 Rectangular 18 × 11 × 9.2 Light yellow/brown 7 Rectangular 18 × 11 × 9.2 Light yellow/brown 9 Cylindrical 16 × 12.3 Light yellow/brown (L × W) 10 Cylindrical 16 × 12.3 Light yellow/brown 11 Bear 20 × 12 × 7 Light yellow/brown 12 Bear 20 × 12 × 7 Light yellow/brown 13 Cylindrical 16 × 12.3 Orange 14 Cylindrical 16 × 12.3 Light yellow/brown 15 Rectangular 20 × 10 × 13 Light yellow/brown 16 Cylindrical 16.62 × 16.04 Orange 18 Rectangular 20 × 10 × 12 Light red 19 Rectangular 20 × 10 × 14 Orange 20 Rectangular 18 × 10 × 10 Light yellow/green 21 Rectangular 20 × 10 × 15 Light yellow/green 22 Rectangular 20 × 10 × 12 Light red 23 Rectangular 20 × 10 × 13 Light yellow/green 24 Rectangular 20 × 10 × 15 Orange 25 Rectangular 20 × 10 × 15 Light yellow/green 26 Rectangular 20 × 10 × 15 Orange 27 Rectangular 20 × 10 × 12 Light red

(638) Table D2 provides information pertaining to the product characterization analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for thirty (30) days at a temperature of forty degrees Celsius (40° C.) and seventy-five percent (75%). In each instance, the chewable gels referenced in Table D2 were translucent.

(639) TABLE-US-00034 TABLE D2 Ex Dimensions # Shape (mm) Color 4 Rectangular 18 × 11 × 9.2 Light yellow/brown (L × W × H) 7 Rectangular 18 × 11 × 9.2 Light yellow/brown 9 Cylindrical 16 × 12.3 Light yellow/brown (L × W) 10 Cylindrical 16 × 12.3 Light yellow/brown 13 Cylindrical 16 × 12.3 Orange 14 Cylindrical 16 × 12.3 Light yellow/brown 16 Cylindrical 16.60 × 16.02 Orange 18 Rectangular 20 × 10 × 12 Light red 19 Rectangular 20 × 10 × 14 Orange

(640) Table D3 provides information pertaining to the product characterization analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for thirty (30) days at a temperature of 25° C. and a relative humidity of 60%. In each instance, the chewable gels referenced in Table D3 were translucent.

(641) TABLE-US-00035 TABLE D3 Ex Dimensions # Shape (mm) Color 4 Rectangular 18 × 11 × 9.2 Light yellow/brown (L × W × H) 7 Rectangular 18 × 11 × 9.2 Light yellow/brown 13 Cylindrical 16 × 12.3 Orange (L × W)

(642) Table D4 provides information pertaining to the product characterization analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for ninety (90) days at a temperature of 40° C. and a relative humidity of 75%. In each instance, the chewable gels referenced in Table D4 were translucent.

(643) TABLE-US-00036 TABLE D4 Ex Dimensions # Shape (mm) Color 4 Rectangular 18 × 11 × 9.2 Light yellow/brown (L × W × H) 7 Rectangular 18 × 11 × 9.2 Light yellow/brown 9 Cylindrical 16 × 12.3 Light yellow/brown (L × W) 10 Cylindrical 16 × 12.3 Light yellow/brown 13 Cylindrical 16 × 12.3 Orange 14 Cylindrical 16 × 12.3 Light yellow/brown 16 Cylindrical 16.61 × 16.04 Orange 18 Rectangular 20 × 10 × 12 Light red 19 Rectangular 20 × 10 × 14 Orange

(644) Table D5 provides information pertaining to the product characterization analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for ninety (90) days at a temperature of 25° C. and a relative humidity of 60%. In each instance, the chewable gels referenced in Table D5 were translucent.

(645) TABLE-US-00037 TABLE D5 Ex Dimensions # Shape (mm) Color 4 Rectangular 18 × 11 × 9.2 Light yellow/brown (L × W × H) 7 Rectangular 18 × 11 × 9.2 Light yellow/brown 9 Cylindrical 16 × 12.3 Light yellow/brown (L × W) 10 Cylindrical 16 × 12.3 Light yellow/brown 13 Cylindrical

16 × 12.3 Orange 14 Cylindrical 16 × 12.3 Light yellow/brown 16 Cylindrical 16.60 × 16.02

Orange 18 Rectangular 20 × 10 × 12 Light red 19 Rectangular 20 × 10 × 14 Orange

(646) Table D6 provides information pertaining to the product characterization analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for one hundred eighty (180) days at a temperature of 40° C. and a relative humidity of 75%. In each instance, the chewable gels referenced in Table D6 were translucent.

(647) TABLE-US-00038 TABLE D6 Ex Dimensions # Shape (mm) Color 7 Rectangular 18 × 11 × 9.2 Light yellow/brown (L × W × H) 9 Cylindrical 16 × 12.3 Light yellow/brown (L × W) 10 Cylindrical 16 × 12.3 Light yellow/brown 13 Cylindrical 16 × 12.3 Orange 14 Cylindrical 16 × 12.3 Light yellow/brown 16 Cylindrical 16.60 × 16.02 Orange

(648) Table D7 provides information pertaining to the product characterization analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for one hundred eighty (180) days at a temperature of 25° C. and a relative humidity of 60%. In each instance, the chewable gels referenced in Table D7 were translucent.

(649) TABLE-US-00039 TABLE D7 Ex Dimensions # Shape (mm) Color 7 Rectangular 18 × 11 × 9.2 Light yellow/brown (L × W × H) 9 Cylindrical 16 × 12.3 Light yellow/brown (L × W) 10 Cylindrical 16 × 12.3 Light yellow/brown 13 Cylindrical 16 × 12.3 Orange 14 Cylindrical 16 × 12.3 Light yellow/brown 16 Cylindrical 16.65 × 16.05 Orange 16 Cylindrical 16.60 × 16.00

Orange

(650) A texture analysis was performed using a CT3 Texture Analyzer (Brookfield Engineering) configured as provided in Table D8. Texture parameters derived from the texture analysis are provided in Tables D9-D14, including values for: average hardness cycle 1 (“AHC1”) given in grams; average adhesiveness (“AAd”) given in millijoules; average fracturability with 1% load sensitivity (“AF1”) given in grams; average hardness cycle 2 (“AHC2”) given in grams; average cohesiveness (“ACo”) given in millimeters; average springiness (“ASp”) given in millimeters; average gumminess (“AGu”) given in grams; and average chewiness (“ACh”) given in millijoules. Additional details relating to the foregoing parameters and texture analyzer can be found in the Operating Instructions for the CT3 Texture Analyzer (Manual No. M08-372-F1116), which is incorporated herein by reference in its entirety. It should be understood that the present invention is not limited to parameters measured by a specific instrument and that other instruments may be used without departing from the spirit of the present invention.

(651) TABLE-US-00040 TABLE D8 Target 6.0 mm Hold time 0 sec Trigger load 2 g Test Speed 2.00 mm/sec Return speed 2.0 mm/s Number of cycles 2 Target Type Distance Recovery 0 seconds Same Trigger TRUE Pretest speed 2.00 mm/sec Data rate 20.00 points/sec Probe TA 9 Fixture TA-STF Load Cell 25000 g

(652) Table D9 provides information pertaining to the dissolution analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein shortly after the curing step. Table D9 includes values for: average hardness cycle 1 (“AHC1”) given in grams; average adhesiveness (“AAd”) given in millijoules; average fracturability with 1% load sensitivity (“AF1”) given in grams; and average hardness cycle 2 (“AHC2”) given in grams.

(653) TABLE-US-00041 TABLE D9 Ex # AHC1 AAd AF1 AHC2 4 170 0.2 4 154 6 170 0.2 4 154 9 224 0.3 26 198 13 24.8 0.18 12 17.6 16 88 0.17 8 88 18 170.67 0.43 13.33 130.67 21 91.33 0.13 5.33 79.33 22 131.33 0.17 8.67 98.67 23 144.67 0.23 13.33 109.33 24 156 0.1 14 131.33 25 175.33 0.1 9.33 152.67 26 88 0.17 8 88 26 148.67 0.23 8 122 26 85.33 0.13 4.67 75.33 27 142 0.13 11.33 112

(654) Table D10 provides information pertaining to the dissolution analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for a number of days at a temperature of 40° C. and a relative humidity of 75%. Table D10 includes values for: average hardness cycle 1 (“AHC1”) given in grams; average adhesiveness (“AAd”) given in millijoules; average fracturability with 1% load sensitivity (“AF1”) given in grams; and

average hardness cycle 2 (“AHC2”) given in grams.

(655) TABLE-US-00042 TABLE D10 Ex # SD AHC1 AAd AF1 AHC2 4 30 128 0.1 12 116 7 30 134 0.3 2 122 7 90 150 0.2 10 130 9 30 214 0.1 30 194 16 180 148.67 0.23 8 122

(656) Table D11 provides information pertaining to the dissolution analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for a number of days at a temperature of 25° C. and a relative humidity of 60%. Table D11 includes values for: average hardness cycle 1 (“AHC1”) given in grams; average adhesiveness (“AAd”) given in millijoules; average fracturability with 1% load sensitivity (“AF1”) given in grams; and average hardness cycle 2 (“AHC2”) given in grams.

(657) TABLE-US-00043 TABLE D11 Ex # SD AHC1 AAd AF1 AHC2 4 30 142 0.2 10 108 7 30 414 1.5 414 322 16 180 85.33 0.13 4.67 75.33

(658) Table D12 provides information pertaining to the dissolution analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein shortly after the curing step. Table D12 includes values for: average cohesiveness (“ACo”) given in millimeters; average springiness (“ASp”) given in millimeters; average gumminess (“AGu”) given in grams; and average chewiness (“ACh”) given in millijoules.

(659) TABLE-US-00044 TABLE D12 Ex # ACo ASp AGu ACh 4 0.58 4.47 98 4.3 6 0.58 4.47 98 4.3 9 0.71 5.28 159 8.2 13 0.39 4.91 9.8 0.48 16 0.7 4.35 61.33 2.6 18 0.47 5.01 80.33 3.97 21 0.49 3.81 44.33 1.67 22 0.32 3.59 42.67 1.5 23 0.29 3.55 33.33 1.47 24 0.49 4.63 76 3.47 25 0.54 4.76 94.67 4.47 26 0.7 4.35 61.33 2.6 26 0.45 4.29 67 2.93 26 0.61 5.49 51.67 2.77 27 0.42 4.83 59.67 2.8

(660) Table D13 provides information pertaining to the dissolution analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for a number of days at a temperature of 25° C. and a relative humidity of 60%. Table D13 includes values for: average cohesiveness (“ACo”) given in millimeters; average springiness (“ASp”) given in millimeters; average gumminess (“AGu”) given in grams; and average chewiness (“ACh”) given in millijoules.

(661) TABLE-US-00045 TABLE D13 Ex # SD ACo ASp AGu ACh 4 30 0.46 4.85 65 3.1 7 30 0.51 6.39 210 13.1 16 180 0.61 5.49 51.67 2.77

(662) Table D14 provides information pertaining to the dissolution analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for a number of days at a temperature of 40° C. and a relative humidity of 75%. Table D14 includes values for: average cohesiveness (“ACo”) given in millimeters; average springiness (“ASp”) given in millimeters; average gumminess (“AGu”) given in grams; and average chewiness (“ACh”) given in millijoules.

(663) TABLE-US-00046 TABLE D14 Ex # SD ACo ASp AGu ACh 4 30 0.66 5.24 85 4.4 7 30 0.65 4.12 86 3.5 7 90 0.46 4.6 70 3.1 9 30 0.65 6.69 140 9.2 16 180 0.45 4.29 67 2.93

(664) FIG. 1 illustrates texture analysis load peaks registered at 3-different points and performed using TA9 probe, TA-STF fixture, 25,000-gram load cell, 5-gram trigger load over 6-millimeters, 2-millimeter per second pretest speed, and a data rate of twenty points per second (20 points/second) for the chewable gels formed in accordance with Example 4 after being stored for various durations and under various conditions as indicated in the chart legend.

(665) FIG. 2 illustrates texture analysis load peaks registered at approximately around 3-seconds and 18-seconds performed using TA9 probe, TA-STF fixture, 25,000-gram load cell, 5-gram trigger load over 6-millimeters, 2-millimeter per second pretest speed, and a data rate of twenty points per second (20 points/second) for the chewable gels formed in accordance with Example 6 and stored for 0-days relative to the curing step.

(666) FIG. 3 illustrates texture analysis load peaks registered at 2-different points and performed using TA9 probe, TA-STF fixture, 25,000-gram load cell, 5-gram trigger load over 6-millimeters, 2-millimeter per second pretest speed, and a data rate of twenty points per second (20

points/second) for the chewable gels formed in accordance with Example 7 after being stored for various durations and under various conditions as indicated in the chart legend.

(667) FIG. 4 illustrates texture analysis load peaks registered at 2-different points and performed using TA9 probe, TA-STF fixture, 25,000-gram load cell, 5-gram trigger load over 6-millimeters, 2-millimeter per second pretest speed, and a data rate of twenty points per second (20 points/second) for the chewable gels formed in accordance with Example 9 after being stored for various durations and under various conditions as indicated in the chart legend.

(668) FIG. 5 illustrates texture analysis load peaks registered at 2-different points and performed using TA9 probe, TA-STF fixture, 25,000-gram load cell, 5-gram trigger load over 6-millimeters, 2-millimeter per second pretest speed, and a data rate of twenty points per second (20 points/second) for the chewable gels formed in accordance with Example 16 after being stored for various durations and under various conditions as indicated in the chart legend.

(669) FIG. 6 illustrates texture analysis load peaks registered at approximately 3-seconds and 9-seconds performed using TA9 probe, TA-STF fixture, 25,000-gram load cell, 5-gram trigger load over 6-millimeters, 2-millimeter per second pretest speed, and a data rate of twenty points per second (20 points/second) for the chewable gels formed in accordance with Example 18 and stored for 0-days relative to the curing step.

(670) FIG. 7 illustrates texture analysis load peaks registered at approximately 3-seconds and 9-seconds performed using TA9 probe, TA-STF fixture, 25,000-gram load cell, 5-gram trigger load over 6-millimeters, 2-millimeter per second pretest speed, and a data rate of twenty points per second (20 points/second) for the chewable gels formed in accordance with Example 21 and stored for 0-days relative to the curing step.

(671) FIG. 8 illustrates texture analysis load peaks registered at approximately 3-seconds and 9-seconds performed using TA9 probe, TA-STF fixture, 25,000-gram load cell, 5-gram trigger load over 6-millimeters, 2-millimeter per second pretest speed, and a data rate of twenty points per second (20 points/second) for the chewable gels formed in accordance with Example 22 and stored for 0-days relative to the curing step.

(672) FIG. 9 illustrates texture analysis load peaks registered at approximately 3-seconds and 9-seconds performed using TA9 probe, TA-STF fixture, 25,000-gram load cell, 5-gram trigger load over 6-millimeters, 2-millimeter per second pretest speed, and a data rate of twenty points per second (20 points/second) for the chewable gels formed in accordance with Example 23 and stored for 0-days relative to the curing step.

(673) FIG. 10 illustrates texture analysis load peaks registered at approximately 3-seconds and 9-seconds performed using TA9 probe, TA-STF fixture, 25,000-gram load cell, 5-gram trigger load over 6-millimeters, 2-millimeter per second pretest speed, and a data rate of twenty points per second (20 points/second) for the chewable gels formed in accordance with Example 24 and stored for 0-days relative to the curing step.

(674) FIG. 11 illustrates texture analysis load peaks registered at approximately 3-seconds and 9-seconds performed using TA9 probe, TA-STF fixture, 25,000-gram load cell, 5-gram trigger load over 6-millimeters, 2-millimeter per second pretest speed, and a data rate of twenty points per second (20 points/second) for the chewable gels formed in accordance with Example 25 and stored for 0-days relative to the curing step.

(675) FIG. 12 illustrates texture analysis load peaks registered at approximately 3-seconds and 9-seconds performed using TA9 probe, TA-STF fixture, 25,000-gram load cell, 5-gram trigger load over 6-millimeters, 2-millimeter per second pretest speed, and a data rate of twenty points per second (20 points/second) for the chewable gels formed in accordance with Example 27 and stored for 0-days relative to the curing step.

(676) A pH value determination of the chewable gel units manufactured in accordance with the Examples provided herein was performed in accordance with U.S. Pharmacopeia General Chapter <2> Oral drug products—product quality tests, using a two percent (2%) solution of respective

chewable gel units.

(677) Table D15 provides information pertaining to the pH value determination of the chewable gel units formed in accordance with the corresponding Examples provided therein shortly after the curing step.

(678) TABLE-US-00047 TABLE D15 Ex # SD pH 2 0 4.2 4 0 6.24 6 0 6.24 7 0 5.84 9 0 5.99 10 0 6.75 11 0 5.74 13 0 6.1 14 0 5.97 14 0 6.14 16 0 6.6 17 0 6.03 18 0 6.78 19 0 6.52 20 0 6.94 21 0 6.89

(679) Table D16 provides information pertaining to the pH value determination of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for a number of days at a temperature of 25° C. and a relative humidity of 60%.

(680) TABLE-US-00048 TABLE D16 Ex # SD pH 4 30 6.15 4 90 6.67 7 30 6.07 9 180 8 10 90 6.35 10 180 6.27 13 90 6.38 14 90 6.21 14 180 6.28 16 90 6.84 16 180 6.69 16 180 6.66 17 90 5.98 17 180 5.99 18 90 6.74 19 90 6.28

(681) Table D17 provides information pertaining to the pH value determination of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for a number of days at a temperature of 40° C. and a relative humidity of 75%.

(682) TABLE-US-00049 TABLE D17 Ex # SD pH 4 30 6.31 4 90 6.43 7 30 6.23 9 180 8.2 10 30 6.36 10 90 6.19 10 180 5.99 13 30 6.19 13 90 6.54 14 30 6.31 14 90 5.88 14 180 5.9 16 30 6.64 16 90 6.63 16 180 6.43 17 30 6.09 17 90 6.09 17 180 6.12 18 30 6.7 18 90 6.51 19 30 6.45 19 90 6.6

(683) Table D18 provides information pertaining to the pH value determination of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for a number of days at a temperature of 30° C. and a relative humidity of 65%.

(684) TABLE-US-00050 TABLE D18 Ex # SD pH 4 30 6.33 4 90 6.51 13 30 6.22 13 90 6.4

(685) A loss-on-drying analysis of the chewable gel units manufactured in accordance with the Examples provided herein was performed in accordance with U.S. Pharmacopeia General Chapter <731> Loss on Drying. Table D19 provides information pertaining to the loss-on-drying analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein shortly after the curing step. Table D19 includes values for percentage of mass loss (“LoD”) given in percent and the temperature (in degrees Celsius) at which the chewable gels were heated (“TH”).

(686) TABLE-US-00051 TABLE D19 Ex # SD TH LoD 4 0 95 5.74% 6 0 95 5.74% 7 0 95 6.10% 9 0 95 5.60% 10 0 105 3.60% 11 0 95 13.61% 13 0 95 8.00% 14 0 95 15.78% 16 0 105 11.30% 17 0 105 12.86% 18 0 105 10.50% 19 0 105 9.41% 20 0 105 7.80% 21 0 105 12.20%

(687) Table D20 provides information pertaining to the loss-on-drying analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for a number of days at a temperature of 25° C. and a relative humidity of 60%. Table D20 includes values for percentage of mass loss (“LoD”) given in percent and the temperature (in degrees Celsius) at which the chewable gels were heated (“TH”).

(688) TABLE-US-00052 TABLE D20 Ex # SD TH LoD 4 30 95 9.21% 4 90 95 9.74% 7 30 95 6.30% 9 180 95 8.00% 10 90 105 11.12% 10 180 105 8.80% 13 90 95 12.70% 14 90 95 10.16% 14 180 95 10.40% 16 90 105 12.20% 16 180 105 10.07% 16 180 105 10.51% 17 90 105 9.00% 17 180 105 8.10% 18 90 105 10.15% 19 90 105 8.90%

(689) Table D21 provides information pertaining to the loss-on-drying analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for a number of days at a temperature of 40° C. and a relative humidity of 75%. Table D21 includes values for percentage of mass loss (“LoD”) given in percent and the temperature (in degrees Celsius) at which the chewable gels were heated (“TH”).

(690) TABLE-US-00053 TABLE D21 Ex # SD TH LoD 4 30 95 10.17% 4 90 95 10.59% 7 30 95 6.50% 9 180 95 8.20% 10 30 105 7.40% 10 90 105 10.40% 10 180 105 7.80% 13 30 95 5.58% 13 90 95 10.90% 14 30 95 9.00% 14 90 95 9.56% 14 180 95 10.30% 16 30 105 9.00% 16 90 105 12.00% 16 180 105 10.57% 17 30 105 8.50% 17 90 105 8.90% 17 180 105 9.50% 18

30 105 6.90% 18 90 105 9.94% 19 30 105 9.25% 19 90 105 9.40%

(691) Table D22 provides information pertaining to the loss-on-drying analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for a number of days at a temperature of 30° C. and a relative humidity of 60%. Table D22 includes values for percentage of mass loss (“LoD”) given in percent and the temperature (in degrees Celsius) at which the chewable gels were heated (“TH”).

(692) TABLE-US-00054 TABLE D22 Ex # SD TH LoD 4 30 95 11.57% 4 90 95 9.53% 13 30 95 7.17% 13 90 95 11.60%

(693) An impurity analysis of the chewable gel units manufactured in accordance with the Examples provided herein was performed. Table D23 provides information pertaining to the impurity analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein shortly after the curing step. Table D23 includes values for: assay percentage (“Asy %”); highest impurity percentage (“HIP %”); and percentage of total impurity (“TI %”). As used in Table D23, “ND” means none detected.

(694) TABLE-US-00055 TABLE D23 Ex # Asy % HIP % TI % 2 111.8 ND ND 4 105 0.3 0.55 6 105 0.3 0.55 7 112.4 ND ND 9 108.7 0.06 0.06 9 108.7 0.06 0.06 10 104.2 0.22 0.47 11 102.3 0 0 13 108 0.07 0.07 14 114.8 ND ND 15 97.5 ND ND 16 100.9 ND ND 18 95.2 0.14 0.36 19 100.2 0.09 0.19 20 95.7 — — 21 103.9 — —

(695) Table D24 provides information pertaining to the impurity analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for a number of days at a temperature of 25° C. and a relative humidity of 60%. Table D24 includes values for: assay percentage (“Asy %”); highest impurity percentage (“HIP %”); and percentage of total impurity (“TI %”). As used in Table D24, “ND” means none detected.

(696) TABLE-US-00056 TABLE D24 Ex # SD Asy % HIP % TI % 4 30 100.4 0.33 0.63 4 90 99.8 0.05 0.05 7 30 83.5 ND ND 7 90 102.9 ND ND 7 180 109.9 0.01 0.01 9 90 110.1 ND ND 9 180 104.5 0.06 0.06 10 90 103.4 0.24 0.53 10 180 102 0.22 0.45 13 90 103.9 ND ND 16 90 96.8 0.9 0.01 16 180 100.5 0.0003 0.0004 16 180 100.5 0.0006 0.0007 18 90 97.6 ND 0.45 19 90 98.7 0.19 0.31

(697) Table D25 provides information pertaining to the impurity analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for a number of days at a temperature of 40° C. and a relative humidity of 75%. Table D25 includes values for: assay percentage (“Asy %”); highest impurity percentage (“HIP %”); and percentage of total impurity (“TI %”). As used in Table D25, “ND” means none detected.

(698) TABLE-US-00057 TABLE D25 Ex # SD Asy % HIP % TI % 4 30 96.6 0.44 0.92 4 90 99.2 0.32 0.37 7 30 95.4 ND ND 7 90 115.3 0.03 0.03 7 180 106.8 0.06 0.06 9 30 107.1 0.07 0.07 9 90 119 ND ND 9 180 105.5 0.02 0.02 10 30 99.6 0.29 0.63 10 90 103.9 0.48 0.94 10 180 101.1 0.77 1.2 13 30 105 ND ND 13 90 107 ND ND 13 180 103.2 ND ND 16 30 93.1 ND ND 16 90 97.3 0.09 0.1 16 180 97.8 0.0002 0.0003 18 30 94.9 ND 0.34 18 90 94.2 0.02 0.51 19 30 98.8 0.29 0.42 19 90 97.1 0.55 0.71

(699) Table D26 provides information pertaining to the impurity analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for a number of days at a temperature of 30° C. and a relative humidity of 65%. Table D26 includes values for: assay percentage (“Asy %”); highest impurity percentage (“HIP %”); and percentage of total impurity (“TI %”). As used in Table D26, “ND” means none detected.

(700) TABLE-US-00058 TABLE D26 Ex # SD Asy % HIP % TI % 4 30 97.9 0.35 0.68 4 90 101.6 0.08 0.12 13 30 113.2 ND ND 13 90 102.1 ND ND 13 180 104 ND ND

(701) A disintegration analysis of the chewable gel units made in accordance with the Examples provided herein was performed in accordance with U.S. Pharmacopeia General Chapter <701> Disintegration. In each instance, the disintegration analysis was performed using nine hundred milliliters (900 ml) of water at a temperature of about 37° C. (±2° C.) and a sample size of six (6)

chewable gel units. Table D27 provides information pertaining to the disintegration analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein shortly after the curing step. Table D27 includes values for disintegration time (“DT”) provided in minutes.

(702) TABLE-US-00059 TABLE D27 Ex # DT 2 30 4 35 6 35 7 25 9 31 10 35 13 28 14 32 15 35 18 50 22 40 23 35 24 37 25 35 26 37 27 55

(703) A dissolution analysis of the chewable gel units manufactured in accordance with the Examples provided herein was performed in close accordance with U.S. Pharmacopeia General Chapter <711> Dissolution. The analysis parameters of the dissolution analysis are included in Table D28 and include the following: type of apparatus used (“Apparatus”); rotations per minute (“RPM”); dissolution medium (“Medium”); and volume of medium (“MV”) given in milliliters (mL).

(704) TABLE-US-00060 TABLE D28 Ex # Apparatus RPM Medium MV 2 USP Apparatus II 50 Water 900 4 USP Apparatus I 100 Water 500 (10-Mesh) 4 USP Apparatus I 100 Water 500 (10-Mesh) 5 USP Apparatus I 100 Water 500 (10-Mesh) 6 USP Apparatus I 100 Water 500 (10-Mesh) 7 USP Apparatus II 50 0.1 N HCl 500 9 USP Apparatus II 50 Water 900 10 USP Apparatus II 50 Water 900 11 USP Apparatus II 50 0.001 N HCl 900 13 USP Apparatus II 75 Water 900 14 USP Apparatus II 50 Water 900 15 USP Apparatus II 50 SGF w/o P 900 16 USP apparatus II 75 Water 900 17 USP Apparatus II 100 Water 500 18 USP apparatus II 100 citrate buffer (2.2 pH) 1000 19 USP apparatus II 50 Water 900 20 USP apparatus II 50 Water 900 21 USP apparatus II 50 Water 900

(705) Table D29 provides information pertaining to the dissolution analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein shortly after the curing step. Table D29 includes values for: run time (“RT”) provided in minutes; average release percentage (“AR %”); minimum release percentage (“Min-R %”); maximum release percentage (“Max-R %”); and relative standard deviation (“RSD”). In each instance, the sample size used for the dissolution analysis was six (6) chewable gel units, the temperature of the medium was thirty-seven degrees Celsius (37° C.) (±2° C.), and the volume of the medium replenished was ten milliliters (10 ml).

(706) TABLE-US-00061 TABLE D29 Ex # RT AR % Min-R % Max-R % RSD 2 30 100 93 104 3.84 4 30 84 77 90 5.9 4 45 97 90 102 5.14 5 30 97 92 105 4.6 6 30 84 77 90 5.9 6 45 97 90 102 5.14 7 30 83 75 88 5.8 9 30 95 92 102 3.77 9 45 108 104 112 3.04 9 45 108 104 112 3.04 10 30 105 97 110 4.47 10 45 107 101 112 3.64 11 10 50 44 56 8.51 11 30 97 92 102 4.35 13 30 78 70 91 8.92 13 45 97 90 114 8.96 14 45 107 100 112 3.88 15 45 76 69 84 6.76 15 60 93 88 100 4.37 16 45 98 96 101 — 17 30 44 40 48 — 17 45 69 64 73 — 17 60 79 74 84 — 18 45 84 79 87 — 19 30 99 96 103 — 19 45 105 103 105 — 20 45 85 83 88 — 21 30 57 53 61 — 21 45 79 75 82 —

(707) Table D30 provides information pertaining to the dissolution analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for thirty (30) days at a temperature of 40° C. and a relative humidity of 75%. Table D30 includes values for: run time (“RT”) provided in minutes; average release percentage (“AR %”); minimum release percentage (“Min-R %”); maximum release percentage (“Max-R %”); and relative standard deviation (“RSD”). In each instance, the sample size used for the dissolution analysis was six (6) chewable gel units, the temperature of the medium was thirty-seven degrees Celsius (37° C.) (±2° C.), and the volume of the medium replenished was ten milliliters (10 ml).

(708) TABLE-US-00062 TABLE D30 Ex # RT AR % Min-R % Max-R % RSD 4 30 101 95 109 4.57 4 45 103 98 110 3.86 7 30 80 75 88 6.6 9 30 84 71 101 13.95 9 45 99 89 107 7.43 10 30 87 76 95 8.5 10 45 99 93 108 6.16 13 30 83 76 89 6.69 13 45 98 90 104 5.81 14 45 105 102 107 1.85 16 45 92 83 95 — 17 30 58 49 66 — 18 45 86 81 91 — 19 30 73 68 77 — 19 45 93 89 97 —

(709) Table D31 provides information pertaining to the dissolution analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored

for thirty (30) days at a temperature of 25° C. and a relative humidity of 60%. Table D31 includes values for: run time (“RT”) provided in minutes; average release percentage (“AR %”); minimum release percentage (“Min-R %”); maximum release percentage (“Max-R %”); and relative standard deviation (“RSD”). In each instance, the sample size used for the dissolution analysis was six (6) chewable gel units, the temperature of the medium was thirty-seven degrees Celsius (37° C.) ($\pm 2^\circ$ C.), and the volume of the medium replenished was ten milliliters (10 ml).

(710) TABLE-US-00063 TABLE D31 Ex # RT AR % Min-R % Max-R % RSD 4 30 97 90 104 5.31 4 45 103 95 111 6.35 7 30 90 80 94 6.07 13 30 75 67 83 8.37 13 45 91 79 98 7.2

(711) Table D32 provides information pertaining to the dissolution analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for ninety (90) days at a temperature of 40° C. and a relative humidity of 75%. Table D32 includes values for: run time (“RT”) provided in minutes; average release percentage (“AR %”); minimum release percentage (“Min-R %”); maximum release percentage (“Max-R %”); and relative standard deviation (“RSD”). In each instance, the sample size used for the dissolution analysis was six (6) chewable gel units, the temperature of the medium was thirty-seven degrees Celsius (37° C.) ($\pm 2^\circ$ C.), and the volume of the medium replenished was ten milliliters (10 ml).

(712) TABLE-US-00064 TABLE D32 Ex # RT AR % Min-R % Max-R % RSD 4 30 94 86 97 4.14 7 30 92 78 99 8.04 9 30 83 75 102 11.84 9 45 94 85 107 8.99 9 45 94 85 107 8.99 10 30 107 102 110 3.01 10 45 111 106 116 3.92 13 30 104 101 105 1.47 14 45 112 108 118 3.59 16 45 100 94 103 — 17 30 71 65 78 — 17 45 86 81 89 — 17 60 97 93 99 — 18 45 89 82 93 — 19 30 67 65 70 — 19 45 86 84 88 —

(713) Table D33 provides information pertaining to the dissolution analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for ninety (90) days at a temperature of 25° C. and a relative humidity of 60%. Table D33 includes values for: run time (“RT”) provided in minutes; average release percentage (“AR %”); minimum release percentage (“Min-R %”); maximum release percentage (“Max-R %”); and relative standard deviation (“RSD”). In each instance, the sample size used for the dissolution analysis was six (6) chewable gel units, the temperature of the medium was thirty-seven degrees Celsius (37° C.) ($\pm 2^\circ$ C.), and the volume of the medium replenished was ten milliliters (10 ml).

(714) TABLE-US-00065 TABLE D33 Ex # RT AR % Min-R % Max-R % RSD 4 30 92 83 99 5.58 7 30 88 79 94 6.06 9 30 87 82 91 4.91 9 45 98 94 101 2.89 9 45 98 94 101 2.89 10 30 105 95 112 5.71 10 45 107 102 112 3.84 13 30 101 100 104 1.35 14 45 110 105 116 3.95 16 45 101 95 105 — 17 30 63 53 71 — 17 45 82 77 89 — 17 60 95 92 97 — 18 45 83 80 87 — 19 30 64 62 66 — 19 45 85 81 87 —

(715) Table D34 provides information pertaining to the dissolution analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for one hundred eighty (180) days at a temperature of 40° C. and a relative humidity of 75%. Table D34 includes values for: run time (“RT”) provided in minutes; average release percentage (“AR %”); minimum release percentage (“Min-R %”); maximum release percentage (“Max-R %”); and relative standard deviation (“RSD”). In each instance, the sample size used for the dissolution analysis was six (6) chewable gel units, the temperature of the medium was thirty-seven degrees Celsius (37° C.) ($\pm 2^\circ$ C.), and the volume of the medium replenished was ten milliliters (10 ml).

(716) TABLE-US-00066 TABLE D34 Ex # RT AR % Min-R % Max-R % RSD 7 30 96 89 101 5.28 9 30 93 84 99 5.97 9 45 99 94 104 3.9 10 30 112 108 113 1.67 10 45 114 112 115 1.08 13 30 97 82 106 9.37 13 45 99 85 110 9.28 14 45 116 114 123 2.86 16 45 93 90 96 — 17 30 75 63 86 — 17 45 89 82 98 — 17 60 96 93 101 —

(717) Table D35 provides information pertaining to the dissolution analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for one hundred eighty (180) days at a temperature of 25° C. and a relative humidity of 60%. Table D35 includes values for: run time (“RT”) provided in minutes; average release percentage (“AR

%)"; minimum release percentage ("Min-R %"); maximum release percentage ("Max-R %"); and relative standard deviation ("RSD"). In each instance, the sample size used for the dissolution analysis was six (6) chewable gel units, the temperature of the medium was thirty-seven degrees Celsius (37° C.) (±2° C.), and the volume of the medium replenished was ten milliliters (10 ml).
 (718) TABLE-US-00067 TABLE D35 Ex # RT AR % Min-R % Max-R % RSD 7 30 89 84 93 3.68 9 30 92 80 106 9.55 9 45 98 90 109 7.04 10 30 102 100 104 1.36 10 45 103 101 104 1.01 13 30 101 96 106 3.67 13 45 102 96 107 3.58 14 45 114 111 119 2.57 16 45 92 90 94 — 16 45 104 102 105 — 17 30 59 55 61 — 17 45 77 73 80 — 17 60 87 83 90 —

(719) Dissolution profiles corresponding to the chewable gels formed in accordance with Examples 1, 2, 4-7, 9-11, 13, and 14 are provided in FIGS. 13-23, respectively.

(720) A microbiological characterization analysis of the chewable gel units manufactured in accordance with the Examples provided herein was performed in accordance with USP general chapter <1112>. Table D36 provides information pertaining to the microbiological characterization analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein shortly after the curing step. Table D36 includes values for Water Activity (aw).

(721) TABLE-US-00068 TABLE D36 Ex # SD Water Activity (aw) 4 0 0.738 9 0 0.592 9 0 0.592 10 0 0.685 14 0 0.687 16 0 0.68 17 0 0.675 18 0 0.65 19 0 0.66

(722) Table D37 provides information pertaining to the microbiological characterization analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for a number of days at a temperature of 25° C. and a relative humidity of 60%. Table D37 includes values for Water Activity (aw).

(723) TABLE-US-00069 TABLE D37 Ex # SD Water Activity (aw) 4 30 0.6185 4 90 0.644 7 180 0.6468 9 180 0.645 10 90 0.591 10 180 0.6759 13 90 0.729 14 90 0.6768 14 180 0.654 16 90 0.694 16 180 0.6769 16 180 0.6782 17 90 0.661 17 180 0.6459 18 90 0.6504 19 90 0.67

(724) Table D38 provides information pertaining to the microbiological characterization analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for a number of days at a temperature of 40° C. and a relative humidity of 75%. Table D38 includes values for Water Activity (aw).

(725) TABLE-US-00070 TABLE D38 Ex # SD Water Activity (aw) 4 30 0.694 4 90 0.673 6 30 0.644 7 90 0.69 7 180 0.647 9 30 0.591 9 90 0.621 9 180 0.64 10 30 0.574 10 90 0.491 10 180 0.6804 13 30 0.728 14 30 0.6672 14 90 0.6597 14 180 0.643 16 90 0.7181 16 180 0.698 17 30 0.661 17 90 0.659 17 180 0.6039 18 30 0.658 18 90 0.6609 19 30 0.66 19 90 0.67

(726) Table D39 provides information pertaining to the microbiological characterization analysis of the chewable gel units formed in accordance with the corresponding Examples provided therein after being stored for a number of days at a temperature of 30° C. and a relative humidity of 65%. Table D39 includes values for Water Activity (aw).

(727) TABLE-US-00071 TABLE D39 Ex # SD Water Activity (aw) 4 30 0.692 4 90 0.659 13 30 0.718 13 90 0.738

(728) A comparative dissolution analysis was conducted using chewable gels formed in accordance with Example 16 hereof and the marketed product Children's Tylenol® lot number C003XH. The parameters for the comparative dissolution analysis are provided in Table D40 and the results are provided in Table D41, which include the average release percentage ("AR %") and relative standard deviation ("RSD").

(729) TABLE-US-00072 TABLE D40 Apparatus USP apparatus II RPM 75 Media Water Volume 900 ml Temperature 37° C. Run Time 45 minutes

(730) TABLE-US-00073 TABLE D41 Percent Release Sample # Example 16 C003XH 1 101 97 2 96 98 3 98 97 4 98 97 5 99 97 6 97 99 AR % 98 98 RSD 1.75 0.86

(731) A comparative bioavailability study was conducted using the chewable gels formed in accordance with Example 16 hereof and the marketed product Children's Tylenol® Chewables ("CTC"). This bioavailability study was performed on twelve (12) human subjects in a crossover

design for the fasting stage. Pharmacokinetic parameters derived from the comparative bioavailability study are provided in Table D42, including: the maximum serum concentration of the drug (i.e., acetaminophen) achieved in the test area of the body after the drug was administered (“C.sub.Max”); the area under the curve for a given time period, indicating the time-averaged concentration of the drug circulating in the body fluid analyzed (“AUC.sub.T”); the area under the curve from time 0 extrapolated to infinite time (“AUC.sub.INF”); the amount of time required to achieve maximum drug concentration in plasma (“T.sub.Max”); the elimination rate constant indicating the rate at which drug fraction is eliminated per unit time at the drug elimination phase (“K.sub.el”); and the half life of the drug—the amount of time required to achieve half the maximum drug concentration in plasma (“T.sub.Half”). The “T/R Ratio” provided in Table D42 is the ratio of the “Geometric Mean” of Example 16 for a respective parameter to the “Geometric Mean” of CTC for the corresponding parameter. A plot comparing the mean serum concentration of acetaminophen over a 24-hour period of chewable gels formed in accordance with Example 16 to that of the reference (i.e., CTC) is provided in the chart of FIG. 24.

(732) TABLE-US-00074 TABLE D42 Geometric Mean Geometric T/R Parameter Unit Example 16 Mean CTC Ratio C.sub.Max ng/ml 3480.6726 3261.2333 106.73% AUC.sub.T hr*ng/mL 9794.9982 9375.0118 104.48% AUC.sub.INF hr*ng/mL 10020.6797 9636.5146 103.99% T.sub.Max hr 0.43 0.485 — K.sub.el 1/hr 0.156 0.129 — T.sub.Half hr 4.435 5.355 —

(733) The invention is capable of considerable modification, alteration, and equivalents in form and function, as will occur to those ordinarily skilled in the pertinent arts having the benefit of this disclosure.

(734) While the present invention has been described for what are presently considered the preferred embodiments, the invention is not so limited. To the contrary, the invention is intended to cover various modifications and equivalent arrangements included within the spirit and scope of the description provided above.

Claims

1. A process for manufacture of a translucent chewable gel that is pharmaceutically suitable for oral administration comprising the steps of: (a) preparing a mixture comprising water, a tonicity modifying agent, at least one taste enhancing agent, carrageenan, a buffering agent, a sugar, a non-crystallizing polyol solution, a functional/active ingredient, and a complexing agent; wherein said mixture has a pH of at least 5, (b) heating said mixture to a temperature in the range of about 90° C. to about 105° C. until the heated mixture has a total solid content in the range of about 65 brix to about 75 brix to form a gummy mixture; and (c) transferring the gummy mixture to a forming device, allowing the gummy mixture to cool in the forming device to form said chewable gel, and removing the chewable gel from the forming device after a period of time of less than 30-minutes.
2. The process as claimed in claim 1, wherein said a tonicity modifying agent comprises sodium chloride.
3. The process as claimed in claim 1, said taste enhancing agent being selected from the group consisting of corn syrup, bitter blocker powder, neotame, sucralose, and combinations thereof.
4. The process as claimed in claim 1, wherein said buffering agent comprises trisodium citrate.
5. The process as claimed in claim 1, wherein said non-crystallizing polyol solution comprises maltitol solution.
6. The process as claimed in claim 1, wherein said complexing agent comprises hydroxypropyl-beta cyclodextrin.
7. The process as claimed in claim 1, said functional/active ingredient comprises one or more active pharmaceutical ingredients.
8. The process as claimed in claim 7, said one or more active pharmaceutical ingredients being selected from the group consisting of acetaminophen, aspirin, azithromycin dihydrate, cetirizine

hydrochloride, dextromethorphan hydrobromide, dimenhydrinate, diphenhydramine hydrochloride, fexofenadine hydrochloride, guaifenesin, ibuprofen, loratadine, methylphenidate hydrochloride, phenylephrine hydrochloride, and combinations thereof.

9. The process as claimed in claim 1, wherein said chewable gel has an active ingredient concentration in the range of about 0.001% weight-by-weight to about 5% weight-by-weight.

10. The process as claimed in claim 1, wherein said mixture includes a flavor agent.

11. The process as claimed in claim 1, wherein said mixture includes a sugar.

12. The process as claimed in claim 1, said water comprising a first water portion and a second water portion, step (a) including the steps of: combining said functional/active ingredient, said complexing agent, and the first water portion to form solution-1; and combining solution-1 with said tonicity modifying agent, said at least one taste enhancing agent, said carrageenan, said buffering agent, said sugar, said non-crystallizing polyol solution, and the second water portion to form said mixture.

13. The process as claimed in claim 12, step (a) including the steps of: combining said tonicity modifying agent, said at least one taste enhancing agent, and said second portion of said water to form solution-2; and combining solution-2 with said solution-1, said carrageenan, said buffering agent, said sugar, said non-crystallizing polyol solution to form said mixture.

14. The process as claimed in claim 12, step (a) including the steps of: combining said tonicity modifying agent, said at least one taste enhancing agent, and said second portion of said water to form solution-2; and combining solution-2 with said solution-1, said carrageenan, said buffering agent, said sugar, said non-crystallizing polyol solution to form said mixture.

15. The process as claimed in claim 12, step (a) including the steps of: preparing a dry mixture with said carrageenan, said buffering agent, said sugar; and combining the dry mixture with said solution-1, said tonicity modifying agent, said at least one taste enhancing agent, said non-crystallizing polyol solution, and the second portion of said water to form said mixture.
