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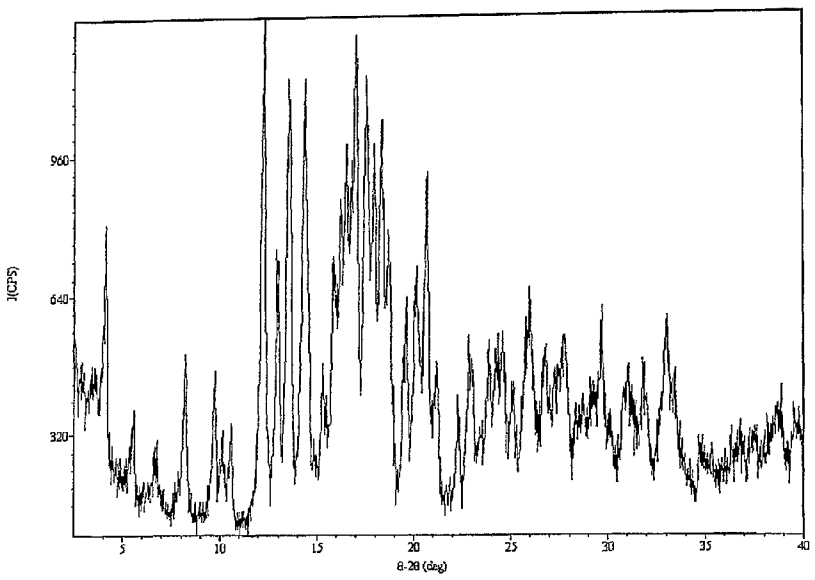
[Continued on next page]

(54) **Title:** PHARMACEUTICAL COMPOSITION WITH HIGH-POTENCY SWEETENER



(57) **Abstract:** The present invention relates generally to pharmaceutical compositions comprising non-caloric or low-caloric high-potency sweeteners and methods for making and using them, in particular, the present invention relates to different pharmaceutical compositions comprising at least one non-caloric or low-caloric natural and/or synthetic high-potency sweetener, at least one sweet taste improving composition, and a pharmaceutically active substance. The present invention also relates to pharmaceutical compositions and methods that can improve the tastes of non-caloric or low-caloric natural and/or synthetic, high- potency sweeteners by imparting a more sugar-like taste or characteristic. In particular, the pharmaceutical compositions and methods provide a more sugar-like temporal profile, including sweetness onset and sweetness linger, and/or a more sugar-like flavor profile.

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PHARMACEUTICAL COMPOSITION WITH HIGH-POTENCY SWEETENER

FIELD OF THE INVENTION

The present invention relates generally to a pharmaceutical composition comprising a high-potency sweetener composition with improved temporal profile and/or flavor profile.

BACKGROUND OF THE INVENTION

Natural caloric sugars, such as sucrose, fructose, and glucose are utilized heavily in beverage, food, pharmaceutical, and oral hygienic/cosmetic industries due to their pleasant taste. In particular, sucrose imparts a desirable taste for consumers. Although sucrose provides superior sweetness characteristics, it is caloric. While calories are necessary for proper bodily functions, there is a need in the market to provide alternative non-caloric or low-caloric sweeteners with sugar-like taste for consumers with sedentary lifestyles or those who are calorie conscious. However, in general, non-caloric or low caloric sweeteners have associated undesirable tastes to consumers such as delayed sweetness onset; lingering sweet aftertaste; bitter taste; metallic taste; astringent taste; cooling taste; licorice-like taste; and/or the like.

For example, the sweet tastes of natural and/or synthetic high-potency sweeteners are slower in onset and longer in duration than the sweet taste produced by sugar and thus change the taste balance of a food composition. Because of these differences, use of a natural high-potency sweetener to replace a bulk sweetener, such as sugar, in a food or beverage, causes an unbalanced temporal profile and/or flavor profile. In addition to the difference in temporal profile, high-potency sweeteners generally exhibit (i) lower maximal response than sugar, (ii) off tastes including bitter, metallic, cooling, astringent, licorice-like taste, etc., and/or (iii) sweetness which diminishes on iterative tasting. It is well known to those skilled in the art of food/beverage formulation that changing the sweetener in a composition requires re-balancing of the flavor and other taste components (e.g., acidulants). If the taste profile of natural and synthetic high-potency sweeteners could be modified to impart specific desired taste characteristics to be more sugar-like, the

type and variety of compositions that may be prepared with that sweetener would be significantly expanded. Accordingly, it would be desirable to selectively modify the taste characteristics of natural and synthetic high-potency sweeteners.

SUMMARY OF THE INVENTION

Generally, this invention addresses the above described need by providing a pharmaceutical composition having improved temporal profile and/or flavor profile and a method for improving the temporal profile and/or flavor profile for pharmaceutical compositions. In particular, this invention improves the temporal profile and/or flavor profile by imparting a more sugar-like temporal profile and/or flavor profile. More particularly, this invention comprises a pharmaceutical composition comprising a pharmaceutically active substance; at least one high-potency sweetener; and at least one sweet taste improving composition.

Objects and advantages of the invention will be set forth in part in the following description, or may be obvious from the description, or may be learned through practice of the invention. Unless otherwise defined, all technical and scientific terms and abbreviations used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention pertains. Although methods and compositions similar or equivalent to those described herein can be used in practice of the present invention, suitable methods and compositions are described without intending that any such methods and compositions limit the invention herein.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a powder x-ray diffraction scan of rebaudioside A polymorph Form 1 on a plot of the scattering intensity versus the scattering angle 2θ in accordance with an embodiment of this invention.

Fig. 2 is a powder x-ray diffraction scan of rebaudioside A polymorph Form 2 on a plot of the scattering intensity versus the scattering angle 2θ in accordance with an embodiment of this invention.

Fig. 3 is a powder x-ray diffraction scan of rebaudioside A polymorph Form 3A on a plot of the scattering intensity versus the scattering angle 2θ in accordance with an embodiment of this invention.

Fig. 4 is a powder x-ray diffraction scan of rebaudioside A polymorph Form 3B on a plot of the scattering intensity versus the scattering angle 2θ in accordance with an embodiment of this invention.

Fig. 5 is a powder-x-ray diffraction scan of rebaudioside A polymorph Form 4 on a plot of the scattering intensity versus the scattering angle 2θ in accordance with an embodiment of this invention.

DETAILED DESCRIPTION OF THE INVENTION

Reference now will be made in detail to the presently proffered embodiments of the invention. Each example is provided by way of explanation of embodiments of the invention, not limitation of the invention. In fact, it will be apparent to those skilled in the art that various modifications and variations can be made in the present invention without departing from the spirit or scope of the invention. For instance, features illustrated or described as part of one embodiment, can be used on another embodiment to yield a still further embodiment. Thus, it is intended that the present invention cover such modifications and variations within the scope of the appended claims and their equivalents.

Generally described, embodiments of the present invention provide pharmaceutical compositions comprising at least one natural and/or synthetic high-potency sweetener, at least one sweet taste improving composition, and a pharmaceutically active substance.

I. Pharmaceutical Compositions

Pharmaceutical compositions generally comprise a pharmaceutically active substance and an excipient material. The excipient material typically includes the at least one natural and/or synthetic high-potency sweetener and the at least one sweet taste improving composition. The pharmaceutical composition may be in the form of a tablet, a capsule, a liquid, an aerosol, a powder, an effervescent tablet or powder, a syrup, an emulsion, a suspension, a solution, or any other form for providing the pharmaceutical composition to a patient. In particular embodiments, the pharmaceutical composition may be in a form for oral administration, buccal administration, sublingual administration, or any other route of administration as known in the art. In oral, buccal, or sublingual administration embodiments of pharmaceutical compositions, the pharmaceutical compositions comprising at least one natural and/or synthetic high-potency sweetener and

at least one sweet taste improving composition can mask a bitter or otherwise undesirable taste of a pharmaceutically active substance or another excipient material.

As referred to herein, "pharmaceutically active substance" means any drug, drug formulation, medication, prophylactic agent, therapeutic agent, or other substance having biological activity. As referred to herein, "excipient material" refers to any inactive substance used as a vehicle for an active ingredient, such as any material to facilitate handling, stability, dispersibility, wettability, and/or release kinetics of a pharmaceutically active substance.

Suitable pharmaceutically active substances for embodiments of this invention include, but are not limited to, medications for the gastrointestinal tract or digestive system, for the cardiovascular system, for the central nervous system, for pain or consciousness, for musculo-skeletal disorders, for the eye, for the ear, nose and oropharynx, for the respiratory system, for endocrine problems, for the reproductive system or urinary system, for contraception, for obstetrics and gynecology, for the skin, for infections and infestations, for immunology, for allergic disorders, for nutrition, for neoplastic disorders, for diagnostics, for euthanasia, or other biological functions or disorders. Examples of suitable pharmaceutically active substances for embodiments of the present invention include, but are not limited to, antacids, reflux suppressants, antiflatulents, antidopaminergics, proton pump inhibitors, cytoprotectants, prostaglandin analogues, laxatives, antispasmodics, antidiarrhoeals, bile acid sequestrants, opioids, beta-receptor blockers, calcium channel blockers, diuretics, cardiac glycosides, antiarrhythmics, nitrates, antianginals, vasoconstrictors, vasodilators, peripheral activators, ACE inhibitors, angiotensin receptor blockers, alpha blockers, anticoagulants, heparin, antiplatelet drugs, fibrinolytics, anti-hemophilic factors, haemostatic drugs, hypolipidaemic agents, statins, hynoptics, anaesthetics, antipsychotics, antidepressants, anti-emetics, anticonvulsants, antiepileptics, anxiolytics, barbiturates, movement disorder drugs, stimulants, benzodiazepines, cyclopyrrolones, dopamine antagonists, antihistamines, cholinergics, anticholinergics, emetics, cannabinoids, analgesics, muscle relaxants, antibiotics, aminoglycosides, anti-virals, anti-fungals, anti-inflammatories, anti-gluacoma drugs, sympathomimetics, steroids, ceruminolytics, bronchodilators, NSAIDS, antitussive, mucolytics, decongestants, corticosteroids, androgens, antiandrogens, gonadotropins, growth hormones, insulin, antidiabetics, thyroid hormones, calcitonin, diphosponates,

vasopressin analogues, alkalizing agents, quinolones, anticholinesterase, sildenafil, oral contraceptives, Hormone Replacement Therapies, bone regulators, follicle stimulating hormones, luteinizings hormones, gamolenic acid, progestogen, dopamine agonist, oestrogen, prostaglandin, gonadorelin, clomiphene, tamoxifen, diethylstilbestrol, antileprotics, antituberculous drugs, antimalarials, anthelmintics, antiprotozoal, antiserums, vaccines, interferons, tonics, vitamins, cytotoxic drugs, sex hormones, aromatase inhibitors, somatostatin inhibitors, or or similar type substances, or combinations thereof. Such components generally are recognized as safe (GRAS) and/or are U.S. Food and Drug Administration (FDA)-approved.

According to particular embodiments of the invention, the pharmaceutically active substance is present in the pharmaceutical composition in widely ranging amounts depending on the particular pharmaceutically active agent being used and its intended applications. An effective dose of any of the herein described pharmaceutically active substances can be readily determined by the use of conventional techniques and by observing results obtained under analogous circumstances. In determining the effective dose, a number of factors are considered including, but not limited to: the species of the patient; its size, age, and general health; the specific disease involved; the degree of involvement or the severity of the disease; the response of the individual patient; the particular pharmaceutically active agent administered; the mode of administration; the bioavailability characteristic of the preparation administered; the dose regimen selected; and the use of concomitant medication. The pharmaceutically active substance is included in the pharmaceutically acceptable carrier, diluent, or excipient in an amount sufficient to deliver to a patient a therapeutic amount of the pharmaceutically active substance in vivo in the absence of serious toxic effects when used in generally acceptable amounts. Thus, suitable amounts can be readily discerned by those skilled in the art.

According to particular embodiments of the present invention, the concentration of pharmaceutically active substance in the pharmaceutical composition will depend on absorption, inactivation, and excretion rates of the drug as well as other factors known to those of skill in the art. It is to be noted that dosage values will also vary with the severity of the condition to be alleviated. It is to be further understood that for any particular subject, specific dosage regimes should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the

administration of the pharmaceutical compositions, and that the dosage ranges set forth herein are exemplary only and are not intended to limit the scope or practice of the claimed composition. The pharmaceutically active substance may be administered at once, or may be divided into a number of smaller doses to be administered at varying intervals of time.

The pharmaceutical composition also may comprise other pharmaceutically acceptable excipient materials in addition to the at least one natural and/or synthetic high-potency sweetener and the at least one sweet taste improving composition. Examples of suitable excipient materials for embodiments of this invention include, but are not limited to, antiadherents, binders (e.g., microcrystalline cellulose, gum tragacanth, or gelatin), coatings, disintegrants, fillers, diluents, softeners, emulsifiers, flavoring agents, coloring agents, adjuvants, lubricants, functional agents (e.g., nutrients), viscosity modifiers, bulking agents, glidiants (e.g., colloidal silicon dioxide) surface active agents, osmotic agents, diluents, or any other non-active ingredient, or combinations thereof. For example, the pharmaceutical compositions of the present invention may include excipient materials selected from the group consisting of calcium carbonate, coloring agents, whiteners, preservatives, and flavors, triacetin, magnesium stearate, sterotes, natural or artificial flavors, essential oils, plant extracts, fruit essences, gelatins, or combinations thereof.

The excipient material of the pharmaceutical composition may optionally include other artificial or natural sweeteners, bulk sweeteners, or combinations thereof. Bulk sweeteners include both caloric and non-caloric compounds. In a particular embodiment, the sweet taste improving composition functions as the bulk sweetener. Non-limiting examples of bulk sweeteners include sucrose, dextrose, maltose, dextrin, dried invert sugar, fructose, high fructose corn syrup, levulose, galactose, corn syrup solids, tagatose, polyols (e.g., sorbitol, mannitol, xylitol, lactitol, erythritol, and maltitol), hydrogenated starch hydrolysates, isomalt, trehalose, and mixtures thereof. In particular embodiments, the bulk sweetener is present in the pharmaceutical composition in widely ranging amounts depending on the degree of sweetness desired. Suitable amounts of both sweeteners would be readily discernable to those skilled in the art.

It is well known to those of ordinary skill in the art that phytonutrients, plant extracts, and herbal compositions may be used in their natural and/or modified form. Modified phytonutrients, plant extracts, and herbal compositions include phytonutrients,

plant extracts, and herbal compositions which have been altered naturally. For example, a modified phytonutrient includes, but is not limited to, phytonutrients which have been fermented, contacted with enzyme, or derivatized or substituted on the phytonutrient. In one embodiment, modified phytonutrients may be used individually or in combination with unmodified phytonutrients. For the sake of brevity, however, in the description of embodiments of this invention, a modified phytonutrient is not described expressly as an alternative to an unmodified phytonutrient, but it should be understood that modified phytonutrients can be substituted for or combined with phytonutrients in any embodiment disclosed herein. The same embodiments would be applicable to plant extracts and other herbal compositions. Plant extracts include extracts from foliage, stems, bark, fruit, seed, and any other plant matter.

A variety of polyphenols also may be included in embodiments of the pharmaceutical composition. In general, polyphenols (also known as "polyphenolics"), are a group of chemical substances found in plants, characterized by the presence of more than one phenol group per molecule. A variety of health benefits may derived from polyphenols, including prevention of cancer, heart disease, and chronic inflammatory disease and improved mental strength and physical strength, for example. Suitable polyphenols for embodiments of this invention, include catechins, proanthocyanidins, procyanidins, anthocyanins, quercerin, rutin, reservatrol, isoflavones, curcumin, punicalagin, ellagitannin, hesperidin, naringin, citrus flavonoids, chlorogenic acid, other similar materials, and combinations thereof.

In particular embodiments, catechins such as, but not limited to, epigallocatechin gallate (EGCG), can inhibit tumor cell growth, reduce lipid, glucose, and/or insulin, act as an anti-inflammatory agent, increase endurance, and/or act as neuroprotection, for example. Suitable sources of catechins for embodiments of this invention include, but are not limited to, green tea, white tea, black tea, oolong tea, chocolate, cocoa, red wine, grape seed, red grape skin, purple grape skin, red grape juice, purple grape juice, berries, pycnogenol, and red apple peel. According to particular embodiments of the present invention, EGCG is present in the pharmaceutical composition in an amount in the range of about 90 mg to about 270 mg per 240 mL serving. In other embodiments, green tea extract is present in the pharmaceutical composition in an amount in the range of about 500 mg to about 600 mg per 240 mL serving.

In some embodiments, proanthocyanidins, procyanidins, or combinations thereof can inhibit tumor cell growth, reduce blood lipid, glucose, and/or insulin, act as an anti-inflammatory agent, increase endurance, and/or act as neuroprotection, for example. Suitable sources of proanthocyanidins and procyanidins for embodiments of this invention include, but are not limited to, red grapes, purple grapes, cocoa, chocolate, grape seeds, red wine, cacao beans, cranberry, apple peel, plum, blueberry, black currants, choke berry, green tea, sorghum, cinnamon, barley, red kidney bean, pinto bean, hops, almonds, hazelnuts, pecans, pistachio, pycnogenol, and colorful berries. According to particular embodiments of the present invention, grape seed extract is present in the pharmaceutical composition in an amount in the range of about 100 mg to about 200 mg per 240 mL serving. In other embodiments, cocoa extract is present in the pharmaceutical composition in an amount in the range of about 400 mg to about 500 mg per 240 mL serving.

In particular embodiments, anthocyanins can inhibit tumor cell growth, can reduce blood lipid, glucose, and/or insulin, act as an anti-inflammatory agent, cause vasodilatory activity, and/or act as neuroprotection, for example. Suitable sources of anthocyanins for embodiments of this invention include, but are not limited to, red berries, blueberries, bilberry, cranberry, raspberry, cherry, pomegranate, strawberry, elderberry, choke berry, red grape skin, purple grape skin, grape seed, red wine, black currant, red currant, cocoa, plum, apple peel, peach, red pear, red cabbage, red onion, red orange, and blackberries. According to particular embodiments of the present invention, blueberry extract is present in the pharmaceutical composition in an amount in the range of about 400 mg to about 500 mg per 240 mL serving.

In some embodiments, quercetin, rutin, or combinations thereof can inhibit tumor cell growth, can reduce blood lipid, glucose, and/or insulin, act as an anti-inflammatory agent, cause vasodilatory activity, and/or act as neuroprotection, for example. Suitable sources of quercetin and rutin for embodiments of this invention include, but are not limited to, red apples, onions, kale, bog whortleberry, lingonberrys, chokeberry, cranberry, blackberry, blueberry, strawberry, raspberry, black currant, green tea, black tea, plum, apricot, parsley, leek, broccoli, chili pepper, berry wine, and ginkgo. According to particular embodiments of the present invention, apple peel extract is present in the pharmaceutical composition in an amount in the range of about 0.5 g to about 1 g per 240 mL serving. In other embodiments, ginkgo extract is present in the pharmaceutical

composition in an amount in the range of about 120 mg to 320 mg about per 240 mL serving.

In some embodiments, resveratrol can inhibit tumor cell growth, can reduce lipid, glucose, and/or insulin, act as an anti-inflammatory agent, prevent heart disease, and/or act as neuroprotection, for example. Suitable sources of resveratrol for embodiments of this invention include, but are not limited to, red grapes, peanuts, cranberry, blueberry, bilberry, mulberry, Japanese Itadori tea, and red wine. According to particular embodiments of the present invention, grape seed extract is present in the pharmaceutical composition in an amount in the range of about 100 mg to 200 mg about per 240 mL serving.

In particular embodiments, isoflavones can inhibit tumor cell growth, reduce lipid, glucose, and/or insulin, act as an anti-inflammatory agent, act as neuroprotection, protect bone, and/or enhance thermogenesis, for example. Suitable sources of isoflavones for embodiments of this invention include, but are not limited to, soy beans, soy products, legumes, alfalfa spouts, chickpeas, peanuts, and red clover. According to particular embodiments of the present invention, isoflavone is present in the pharmaceutical composition in an amount in the range of about 50 mg to about 130 mg per 240 mL serving. In other embodiments, soy protein is present in the pharmaceutical composition in an amount in the range of about 0.1 g to 10 g about per 240 mL serving.

In some embodiments, curcumin can inhibit tumor cell growth, can reduce lipid, glucose, and/or insulin, act as an anti-inflammatory agent, and/or act as neuroprotection, for example. Suitable sources of curcumin for embodiments of this invention include, but are not limited to, turmeric and mustard. According to particular embodiments of the present invention, curcumin is present in the pharmaceutical composition in an amount in the range of about 200 mg to 400 mg about per 240 mL serving. In other embodiments, turmeric extract is present in the pharmaceutical composition in an amount in the range of about 400 mg to about 500 mg per 240 mL serving.

In particular embodiments, punicalagin, ellagitannin, or combinations thereof can inhibit tumor cell growth, reduce lipid, glucose, and/or insulin, act as an anti-inflammatory agent, and/or act as neuroprotection, for example. Suitable sources of punicalagin and ellagitannin for embodiments of this invention include, but are not limited to, pomegranate, raspberry, strawberry, walnut, and oak-aged red wine. According to

particular embodiments of the present invention, pomegranate extract is present in the pharmaceutical composition in an amount in the range of about 400 mg to about 500 mg per 240 mL serving.

In some embodiments, citrus flavonoids, such as hesperidin or naringin, can inhibit tumor cell growth, reduce lipid, glucose, and/or insulin, act as an anti-inflammatory agent, act as neuroprotection, and/or protect bone, for example. Suitable sources of citrus flavonids, such as hesperidin or naringin, for embodiments of this invention include, but are not limited to, oranges, grapefruits, and citrus juices. According to particular embodiments of the present invention, citrus polyphenol is present in the pharmaceutical composition in an amount in the range of about 130 mg to about 260 mg per 240 mL serving.

In particular embodiments, chlorogenic acid can inhibit tumor cell growth, reduce lipid, glucose, and/or insulin, act as an anti-inflammatory agent, and/or act as neuroprotection, for example. Suitable sources of chlorogenic acid for embodiments of this invention include, but are not limited to, green coffee, yerba mate, red wine, grape seed, red grape skin, purple grape skin, red grape juice, purple grape juice, apple juice, cranberry, pomegranate, blueberry, strawberry, sunflower, Echinacea, pycnogenol, and apple peel. According to particular embodiments of the present invention, green coffee extract is present in the pharmaceutical composition in an amount in the range of about 200 mg to about 300 mg per 240 mL serving. According to particular embodiments of the present invention, apple peel extract is present in the pharmaceutical composition in an amount in the range of about 0.5 g to about 1 g per 240 mL serving.

According to particular embodiments of the invention, the excipient material is present in the pharmaceutical composition in widely ranging amounts and suitable amounts of excipient are readily discerned by those skilled in the art

In a particular embodiment, a pharmaceutical composition comprises at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving composition and a pharmaceutically active substance. In a particular embodiment, the at least one natural and/or synthetic high-potency sweetener is present in the pharmaceutical composition in an amount in the range of about 50 ppm to about 3000 ppm of the pharmaceutical composition. In one embodiment, the at least one natural

and/or synthetic high-potency sweetener can present in a tableted pharmaceutical composition in an amount in the range of about 0.1 % to 5 % by weight of the pharmaceutical composition.

II. Sweetener Compositions

As described hereinabove, the pharmaceutical compositions comprise at least one natural and/or synthetic high-potency sweetener and at least one sweet taste improving composition. The combination of the at least one natural and/or synthetic high-potency sweetener and at least one sweet taste improving composition, as used herein, comprises the "sweetener composition." As used herein, a pharmaceutically active substance is synonymous with a "sweetenable composition." In addition, the combination of the sweetener composition and a pharmaceutically active substance comprises a "sweetened composition."

A. Natural High-Potency Sweeteners

Desirably, the sweetener composition comprises at least one natural and/or synthetic high-potency sweetener. As used herein the phrases "natural high-potency sweetener", "NHPS", "NHPS composition", and "natural high-potency sweetener composition" are synonymous. "NHPS" means any sweetener found in nature which may be in raw, extracted, purified, or any other form, singularly or in combination thereof and characteristically have a sweetness potency greater than sucrose, fructose, or glucose, yet have less calories. Non-limiting examples of NHPSs suitable for embodiments of this invention include rebaudioside A, rebaudioside B, rebaudioside C, rebaudioside D, rebaudioside E, rebaudioside F, dulcoside A, dulcoside B, rubusoside, stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, siamenoside, monatin and its salts (monatin SS, RR, RS, SR), curculin, glycyrrhizic acid and its salts, thaumatin, monellin, mabinlin, brazzein, hernandulcin, phyllodulcin, glycyphyllin, phloridzin, trilobatin, baiyunoside, osladin, polypodoside A, pterocaryoside A, pterocaryoside B, mukurozioside, phlomisoside I, periandrin I, abrusoside A, and cyclocarioside I. NHPS also includes modified NHPSs. Modified NHPSs include NHPSs which have been altered naturally. For example, a modified NHPS includes, but is not limited to, NHPSs which have been fermented, contacted with enzyme, or derivatized or substituted on the NHPS. In one embodiment, at least one modified NHPS may be used in combination with at least one NHPS. In another embodiment, at least one modified NHPS may be used without a

NHPS. Thus, modified NHPSs may be substituted for a NHPS or may be used in combination with NHPSs for any of the embodiments described herein. For the sake of brevity, however, in the description of embodiments of this invention, a modified NHPS is not expressly described as an alternative to an unmodified NHPS, but it should be understood that modified NHPSs can be substituted for NHPSs in any embodiment disclosed herein.

In one embodiment, extracts of a NHPS may be used in any purity percentage. In another embodiment, when a NHPS is used as a non-extract, the purity of the NHPS may range for example from about 25% to about 100%. According to other embodiments, the purity of the NHPS may range from about 50% to about 100%; from about 70% to about 100%; from about 80% to about 100%; from about 90% to about 100%; from about 95% to about 100%; from about 95% to about 99.5%; from about 96% to about 100%; from about 97% to about 100%; from about 98% to about 100%; and from about 99% to about 100%.

Purity, as used here, represents the weight percentage of a respective NHPS compound present in a NHPS extract, in raw or purified form. In one embodiment, a steviolglycoside extract comprises a particular steviolglycoside in a particular purity, with the remainder of the stevioglycoside extract comprising a mixture of other steviolglycosides.

To obtain a particularly pure extract of a NHPS, such as rebaudioside A, it may be necessary to purify the crude extract to a substantially pure form. Such methods generally are known to those of ordinary skill in the art.

An exemplary method for purifying a NHPS, such as rebaudioside A, is described in the co-pending patent application no. 60/805,216, entitled "Rebaudioside A Composition and Method for Purifying Rebaudioside A," filed on June 19, 2006, by inventors DuBois, et al., the disclosure of which is incorporated herein by reference in its entirety.

Briefly described, substantially pure rebaudioside A is crystallized in a single step from an aqueous organic solution comprising at least one organic solvent and water in an amount from about 10 % to about 25 % by weight, more particularly from about 15 % to about 20 % by weight. Organic solvents desirably comprise alcohols, acetone, and acetonitile. Non-limiting examples of alcohols include ethanol, methanol, isopranol, 1-

propanol, 1-butanol, 2-butanol, tert-butanol, and isobutanol. Desirably, the at least one organic solvent comprises a mixture of ethanol and methanol present in the aqueous organic solution in a weight ratio ranging from about 20 parts to about 1 part ethanol to 1 part methanol, more desirably from about 3 parts to about 1 part ethanol to 1 part methanol.

Desirably, the weight ratio of the aqueous organic solvent and crude rebaudioside A ranges from about 10 to about 4 parts aqueous organic solvent to 1 part crude rebaudioside A, more particularly from about 5 to about 3 parts aqueous organic solvent to 1 part crude rebaudioside A.

In an exemplary embodiment, the method of purifying rebaudioside A is carried out at approximately room temperature. In another embodiment, the method of purifying rebaudioside A further comprises the step of heating the rebaudioside A solution to a temperature in a range from about 20°C to about 40°C, or in another embodiment to a reflux temperature, for about 0.25 hours to about 8 hours. In another exemplary embodiment, wherein the method for purifying rebaudioside A comprises the step of heating the rebaudioside A solution, the method further comprises the step of cooling the rebaudioside A solution to a temperature in the range from about 4°C to about 25°C for about 0.5 hours to about 24 hours.

According to particular embodiments, the purity of rebaudioside A may range from about 50% to about 100%; from about 70% to about 100%; from about 80% to about 100%; from about 90% to about 100%; from about 95% to about 100%; from about 95% to about 99.5%; about 96% to about 100%; from about 97% to about 100%; from about 98% to about 100%; and from about 99% to about 100%. According to particularly desirable embodiments, upon crystallization of crude rebaudioside A, the substantially pure rebaudioside A composition comprises rebaudioside A in a purity greater than about 95 % by weight up to about 100% by weight on a dry basis. In other exemplary embodiments, substantially pure rebaudioside A comprises purity levels of rebaudioside A greater than about 97 % up to about 100% rebaudioside A by weight on a dry basis, greater than about 98 % up to about 100% by weight on a dry basis, or greater than about 99 % up to about 100% by weight on a dry basis. The rebaudioside A solution during the single crystallization step may be stirred or unstirred.

In an exemplary embodiment, the method of purifying rebaudioside A further comprises the step of seeding (optional step) the rebaudioside A solution at an appropriate temperature with high-purity crystals of rebaudioside A sufficient to promote crystallization of the rebaudioside A to form pure rebaudioside A. An amount of rebaudioside A sufficient to promote crystallization of substantially pure rebaudioside A comprises an amount of rebaudioside A from about 0.0001 % to about 1 % by weight of the rebaudioside A present in the solution, more particularly from about 0.01 % to about 1 % by weight. An appropriate temperature for the step of seeding comprises a temperature in a range from about 18°C to about 35°C.

In another exemplary embodiment, the method of purifying rebaudioside A further comprises the steps of separating and washing the substantially pure rebaudioside A composition. The substantially pure rebaudioside A composition may be separated from the aqueous organic solution by a variety of solid-liquid separation techniques that utilize centrifugal force, that include, without limitation, vertical and horizontal perforated basket centrifuge, solid bowl centrifuge, decanter centrifuge, peeler type centrifuge, pusher type centrifuge, Heinkel type centrifuge, disc stack centrifuge and cyclone separation. Additionally, separation may be enhanced by any of pressure, vacuum, and gravity filtration methods, that include, without limitation, the use of belt, drum, nutsche type, leaf, plate, Rosenmund type, sparkler type, and bag filters and filter press. Operation of the rebaudioside A solid-liquid separation device may be continuous, semi-continuous or in batch mode. The substantially pure rebaudioside A composition also may be washed on the separation device using various aqueous organic solvents and mixtures thereof. The substantially pure rebaudioside A composition can be dried partially or totally on the separation device using any number of gases, including, without limitation, nitrogen and argon, to evaporate residual liquid solvent. The substantially pure rebaudioside A composition may be removed automatically or manually from the separation device using liquids, gases or mechanical means by either dissolving the solid or maintaining the solid form.

In still another exemplary embodiment, the method of purifying rebaudioside A further comprises the step of drying the substantially pure rebaudioside A composition using techniques well known to those skilled in the art, non-limiting examples of which include the use of a rotary vacuum dryer, fluid bed dryer, rotary tunnel dryer, plate dryer,

tray dryer, Nauta type dryer, spray dryer, flash dryer, micron dryer, pan dryer, high and low speed paddle dryer and microwave dryer. In an exemplary embodiment, the step of drying comprises drying the substantially pure rebaudioside A composition using a nitrogen or argon purge to remove the residual solvent at a temperature in a range from about 40°C to about 60°C for about 5 hours to about 100 hours.

In yet another exemplary embodiment, wherein the crude rebaudioside A mixture comprises substantially no rebaudioside D impurity, the method of purifying rebaudioside A further comprises the step of slurrying the composition of substantially pure rebaudioside A with an aqueous organic solvent prior to the step of drying the substantially pure rebaudioside A composition. The slurry is a mixture comprising a solid and an aqueous organic or organic solvent, wherein the solid comprises the substantially pure rebaudioside A composition and is only sparingly soluble in the aqueous organic or organic solvent. In an embodiment, the substantially pure rebaudioside A composition and aqueous organic solvent are present in the slurry in a weight ratio ranging from about 15 parts to 1 part aqueous organic solvent to 1 part substantially pure rebaudioside A composition. In one embodiment, the slurry is maintained at room temperature. In another embodiment, the step of slurrying comprises heating the slurry to a temperature in a range from about 20°C to about 40°C. The substantially pure rebaudioside A composition is slurried for about 0.5 hours to about 24 hours.

In still yet another exemplary embodiment, the method of purifying rebaudioside A further comprises the steps of separating the substantially pure rebaudioside A composition from the aqueous organic or organic solvent of the slurry and washing the substantially pure rebaudioside A composition followed by the step of drying the substantially pure rebaudioside A composition.

If further purification is desired, the method of purifying rebaudioside A described herein may be repeated or the substantially pure rebaudioside A composition may be purified further using an alternative purification method, such as the column chromatography.

It also is contemplated that other NHPSs may be purified using the purification method described herein, requiring only minor experimentation that would be obvious to those of ordinary skill in the art.

The purification of rebaudioside A by crystallization as described above results in the formation of at least four different polymorphs: Form 1: a rebaudioside A hydrate; Form 2: an anhydrous rebaudioside A; Form 3: a rebaudioside A solvate; and Form 4: an amorphous rebaudioside A. The aqueous organic solution and temperature of the purification process influence the resulting polymorphs in the substantially pure rebaudioside A composition. Figures 1-5 are exemplary powder x-ray diffraction (XRPD) scans of polymorphs Form 1 (hydrate), Form 2 (anhydrate), Form 3A (methanol solvate), Form 3B (ethanol solvate), and Form 4 (amorphous), respectively. The material properties of the four rebaudioside A polymorphs are summarized in the following table:

Table 1: Rebaudioside A Polymorphs

	Form 1 Polymorph	**Form 2 Polymorph**	**Form 3 Polymorph**	**Form 4 Polymorph**
Rate of dissolution in H2O at 25°C	Very low (<0.2 %/60 minutes)	Intermediate (<30 %/5 minutes)	High (> 30 % /5 minutes)	High (> 35% /5 minutes)
Alcohol content	< 0.5 %	< 1 %	1-3 %	
Moisture content	> 5 %	< 1 %	< 3 %	6.74 %

The type of polymorph formed is dependent on the composition of the aqueous organic solution, the temperature of the crystallization step, and the temperature during the drying step. Form 1 and Form 3 are formed during the single crystallization step while Form 2 is formed during the drying step after conversion from Form 1 or Form 3.

Low temperatures during the crystallization step, in the range of about 20°C to about 50°C, and a low ratio of water to the organic solvent in the aqueous organic solvent results in the formation of Form 3. High temperatures during the crystallization step, in the range of about 50°C to about 80°C, and a high ratio of water to the organic solvent in the aqueous organic solvent results in the formation of the Form 1. Form 1 can be converted to Form 3 by slurrying in an anhydrous solvent at room temperature (2 -16 hours) or at reflux for approximately (0.5-3 hours). Form 3 can be converted to Form 1 by slurrying the polymorph in water at room temperature for approximately 16 hours or at reflux for approximately 2-3 hours. Form 3 can be converted to the Form 2 during the drying process; however, increasing either the drying temperature above 70°C or the drying time of a substantially pure rebaudioside A composition can result in

decomposition of the rebaudioside A and increase the remaining rebaudioside B impurity in the substantially pure rebaudioside A composition. Form 2 can be converted to Form 1 with the addition of water.

Form 4 may be formed from Form 1, 2, 3, or combinations thereof, using methods well known to those of ordinary skill in the art. Non-limiting examples of such methods include melt-processing, ball milling, crystallization, lyophilization, cryo-grinding, and spray-drying. In a particular embodiment, Form 4 can be prepared from a substantially pure rebaudioside A composition obtained by the purification methods described hereinabove by spray-drying a solution of the substantially pure rebaudioside A composition.

B. Synthetic High-Potency Sweeteners

As used herein, the phrase "synthetic sweetener" refers to any compositions which are not found in nature and characteristically have a sweetness potency greater than sucrose, fructose, or glucose, yet have less calories. Non-limiting examples of synthetic sweeteners suitable for embodiments of this invention include sucralose, potassium acesulfame, aspartame, alitame, saccharin, neohesperidin dihydrochalcone, cyclamate, neotame, N-[N-[3-(3-hydroxy-4-methoxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, N-[N-[3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, salts thereof, and the like.

C. Combinations of Natural and/or Synthetic High-Potency Sweeteners

The NHPS and synthetic sweeteners may be used individually or in combination with other NHPS and/or synthetic sweeteners. For example, the sweetener composition may comprise a single NHPS or a single synthetic sweetener; a single NHPS in combination with a single synthetic sweetener; one or more NHPSs in combination with a single synthetic sweetener; a single NHPS in combination with one or more synthetic sweeteners; or one or more NHPSs in combination with one or more synthetic sweeteners. A plurality of natural and/or synthetic high-potency sweeteners may be used as long as the combined effect does not adversely affect the taste of the sweetener composition.

For example, particular embodiments comprise combinations of NHPSs, such as steviolglycosides. Non-limiting examples of suitable stevioglycosides which may be combined include rebaudioside A, rebaudioside B, rebaudioside C, rebaudioside D,

rebaudioside E, rebaudioside F, dulcoside A, dulcoside B, rubusoside, stevioside, or steviolbioside. According to particularly desirable embodiments of the present invention, the combination of high-potency sweeteners comprises rebaudioside A in combination with rebaudioside B, rebaudioside C, rebaudioside E, rebaudioside F, stevioside, steviolbioside, dulcoside A, or combinations thereof.

Generally, according to a particular embodiment, rebaudioside A is present in the combination of high-potency sweeteners in an amount in the range of about 50 to about 99.5 weight percent of the combination of high-potency sweeteners, more desirably in the range of about 70 to about 90 weight percent, and still more desirably in the range of about 75 to about 85 weight percent.

In another particular embodiment, rebaudioside B is present in the combination of high-potency sweeteners in an amount in the range of about 1 to about 8 weight percent of the combination of high-potency sweeteners, more desirably in the range of about 2 to about 5 weight percent, and still more desirably in the range of about 2 to about 3 weight percent.

In another particular embodiment, rebaudioside C is present in the combination of high-potency sweeteners in an amount in the range of about 1 to about 10 weight percent of the combination of high-potency sweeteners, more desirably in the range of about 3 to about 8 weight percent, and still more desirably in the range of about 4 to about 6 weight percent.

In still another particular embodiment, rebaudioside E is present in the combination of high-potency sweeteners in an amount in the range of about 0.1 to about 4 weight percent of the combination of high-potency sweeteners, more desirably in the range of about 0.1 to about 2 weight percent, and still more desirably in the range of about 0.5 to about 1 weight percent.

In still another particular embodiment, rebaudioside F is present in the combination of high-potency sweeteners in an amount in the range of about 0.1 to about 4 weight percent of the combination of high-potency sweeteners, more desirably in the range of about 0.1 to about 2 weight percent, and still more desirably in the range of about 0.5 to about 1 weight percent.

In still yet another particular embodiment, dulcoside A is present in the combination of high-potency sweeteners in an amount in the range of about 0.1 to about 4 weight percent of the combination of high-potency sweeteners, more desirably in the range of about 0.1 to about 2 weight percent, and still more desirably in the range of about 0.5 to about 1 weight percent.

In yet another particular embodiment, dulcoside B is present in the combination of high-potency sweeteners in an amount in the range of about 0.1 to about 4 weight percent of the combination of high-potency sweeteners, more desirably in the range of about 0.1 to about 2 weight percent, and still more desirably in the range of about 0.5 to about 1 weight percent.

In another particular embodiment, stevioside is present in the combination of high-potency sweeteners in an amount in the range of about 0.5 to about 10 weight percent of the combination of high-potency sweeteners, more desirably in the range of about 1 to about 6 weight percent, and still more desirably in the range of about 1 to about 4 weight percent.

In still another particular embodiment, steviolbioside is present in the combination of high-potency sweeteners in an amount in the range of about 0.1 to about 4 weight percent of the combination of high-potency sweeteners, more desirably in the range of about 0.1 to about 2 weight percent, and still more desirably in the range of about 0.5 to about 1 weight percent.

According to a particularly desirable embodiment, the high-potency sweetener composition comprises a combination of rebaudioside A, stevioside, rebaudioside B, rebaudioside C, and rebaudioside F; wherein rebaudioside A is present in the combination of high-potency sweeteners in an amount in the range of about 75 to about 85 weight percent based on the total weight of the combination of high-potency sweeteners, stevioside is present in an amount in the range of about 1 to about 6 weight percent, rebaudioside B is present in an amount in the range of about 2 to about 5 weight percent, rebaudioside C is present in an amount in the range of about 3 to about 8 weight percent, and rebaudioside F is present in an amount in the range of about 0.1 to about 2 weight percent.

In addition, those of ordinary skill in the art should appreciate that the sweetener composition can be customized to obtain a desired calorie content. For example, a low-caloric or non-caloric NHPS may be combined with a caloric natural sweetener and/or other caloric additives to produce a sweetener composition with a preferred calorie content.

III. Sweet Taste Improving Compositions

The sweetener composition also comprises a sweet taste improving composition, non-limiting examples of which include carbohydrates, polyols, amino acids and their corresponding salts, polyamino acids and their corresponding salts, sugar acids and their corresponding salts, nucleotides, organic acids, inorganic acids, organic salts including organic acid salts and organic base salts, inorganic salts, bitter compounds, flavorants and flavoring ingredients, astringent compounds, proteins or protein hydrolysates, surfactants, emulsifiers, flavonoids, alcohols, polymers, other sweet taste improving taste additives imparting such sugar-like characteristics, and combinations thereof.

In one embodiment, a single sweet taste improving composition may be used in combination with a single natural and/or synthetic high-potency sweetener. In another embodiment of the present invention, a single sweet taste improving composition may be used in combination with one or more natural and/or synthetic high-potency sweeteners. In yet another embodiment, one or more sweet taste improving compositions may be used in combination with a single natural and/or synthetic high-potency sweetener. In a further embodiment, there may be a plurality of sweet taste improving combinations used in combination with one or more natural and/or synthetic high-potency sweeteners.

In a particular embodiment, combinations of at least one natural and/or synthetic high-potency sweetener and at least one sweet taste improving composition suppress, reduce, or eliminate undesirable taste and impart sugar-like characteristics to the sweetener composition. As used herein, the phrase "undesirable taste" includes any taste property which is not imparted by sugars, e.g. glucose, sucrose, fructose, or similar saccharides. Non-limiting examples of undesirable tastes include delayed sweetness onset, lingering sweet aftertaste, metallic taste, bitter taste, cooling sensation taste or menthol-like taste, licorice-like taste, and/or the like.

A. Sweet Taste

In one embodiment, a sweetener composition exhibits a more sugar-like temporal and/or sugar-like flavor profile than a sweetener composition comprising at least one natural and/or synthetic high-potency sweetener, but without a sweet taste improving composition is provided. As used herein, the phrases "sugar-like characteristic," "sugar-like taste," "sugar-like sweet," "sugary," and "sugar-like" are synonymous. Sugar-like characteristics include any characteristic similar to that of sucrose and include, but are not limited to, maximal response, flavor profile, temporal profile, adaptation behavior, mouthfeel, concentration/response function behavior, tastant and flavor/sweet taste interactions, spatial pattern selectivity, and temperature effects. These characteristics are dimensions in which the taste of sucrose is different from the tastes of natural and synthetic high-potency sweeteners. Whether or not a characteristic is more sugar-like is determined by expert sensory panel assessments of sugar and compositions comprising at least one natural and/or synthetic high-potency sweetener, both with and without a sweet taste improving composition. Such assessments quantify similarities of the characteristics of compositions comprising at least one natural and/or synthetic high-potency sweetener, both with and without a sweet taste improving composition, with those comprising sugar. Suitable procedures for determining whether a composition has a more sugar-like taste are well known in the art.

In a particular embodiment, a panel of assessors is used to measure the reduction of sweetness linger. Briefly described, a panel of assessors (generally 8 to 12 individuals) is trained to evaluate sweetness perception and measure sweetness at several time points from when the sample is initially taken into the mouth until 3 minutes after it has been expectorated. Using statistical analysis, the results are compared between samples containing additives and samples that do not contain additives. A decrease in score for a time point measured after the sample has cleared the mouth indicates there has been a reduction in sweetness perception.

The panel of assessors may be trained using procedures well known to those of ordinary skill in the art. In a particular embodiment, the panel of assessors may be trained using the Spectrum™ Descriptive Analysis Method (Meilgaard et al, Sensory Evaluation Techniques, 3rd edition, Chapter 11). Desirably, the focus of training should be the recognition of and the measure of the basic tastes; specifically, sweet. In order to ensure

accuracy and reproducibility of results, each assessor should repeat the measure of the reduction of sweetness linger about three to about five times per sample, taking at least a five minute break between each repetition and/or sample and rinsing well with water to clear the mouth.

Generally, the method of measuring sweetness comprises taking a 10mL sample into the mouth, holding the sample in the mouth for 5 seconds and gently swirling the sample in the mouth, rating the sweetness intensity perceived at 5 seconds, expectorating the sample (without swallowing following expectorating the sample), rinsing with one mouthful of water (e.g., vigorously moving water in mouth as if with mouth wash) and expectorating the rinse water, rating the sweetness intensity perceived immediately upon expectorating the rinse water, waiting 45 seconds and, while wating those 45 seconds, identifying the time of maximum perceived sweetness intensity and rating the sweetness intensity at that time (moving the mouth normally and swallowing as needed), rating the sweetness intensity after another 10 seconds, rating the sweetness intensity after another 60 seconds (cumulative 120 seconds after rinse), and rating the sweetness intensity after still another 60 seconds (cumulative 180 seconds after rinse). Between samples take a 5 minute break, rinsing well with water to clear the mouth.

B. Types of Sweet Taste Improving Compositions

As described hereinabove, sweet taste improving compositions include carbohydrates, polyols, amino acids and their corresponding salts, polyamino acids and their corresponding salts, sugar acids and their corresponding salts, nucleotides, organic acids, inorganic acids, organic salts including organic acid salts and organic base salts, inorganic salts, bitter compounds, flavorants and flavoring ingredients, astringent compounds, proteins or protein hydrolysates, surfactants, emulsifiers, flavonoids, alcohols, polymers, other sweet taste improving taste additives imparting such sugar-like characteristics, and combinations thereof.

As used herein, the term "carbohydrate" generally refers to aldehyde or ketone compounds substituted with multiple hydroxyl groups, of the general formula $(CH_2O)_n$, wherein n is 3-30, as well as their oligomers and polymers. The carbohydrates of the present invention can, in addition, be substituted or deoxygenated at one or more positions. Carbohydrates, as used herein, encompass unmodified carbohydrates, carbohydrate derivatives, substituted carbohydrates, and modified carbohydrates. As used

herein, the phrases "carbohydrate derivatives", "substituted carbohydrate", and "modified carbohydrates" are synonymous. Modified carbohydrate means any carbohydrate wherein at least one atom has been added, removed, substituted, or combinations thereof. Thus, carbohydrate derivatives or substituted carbohydrates include substituted and unsubstituted monosaccharides, disaccharides, oligosaccharides, and polysaccharides. The carbohydrate derivatives or substituted carbohydrates optionally can be deoxygenated at any corresponding C-position, and/or substituted with one or more moieties such as hydrogen, halogen, haloalkyl, carboxyl, acyl, acyloxy, amino, amido, carboxyl derivatives, alkylamino, dialkylamino, arylamino, alkoxy, aryloxy, nitro, cyano, sulfo, mercapto, imino, sulfonyl, sulfenyl, sulfinyl, sulfamoyl, carboalkoxy, carboxamido, phosphonyl, phosphinyl, phosphoryl, phosphino, thioester, thioether, oximino, hydrazino, carbamyl, phospho, phosphonato, or any other viable functional group provided the carbohydrate derivative or substituted carbohydrate functions to improve the sweet taste of the sweetener composition.

Non-limiting examples of carbohydrates in embodiments of this invention include tagatose, trehalose, galactose, rhamnose, cyclodextrin (e.g., α-cyclodextrin, β-cyclodextrin, and γ-cyclodextrin), maltodextrin (including resistant maltodextrins such as Fibersol-2™), dextran, sucrose, glucose, ribulose, fructose, threose, arabinose, xylose, lyxose, allose, altrose, mannose, idose, lactose, maltose, invert sugar, isotrehalose, neotrehalose, palatinose or isomaltulose, erythrose, deoxyribose, gulose, idose, talose, erythrulose, xylulose, psicose, turanose, cellobiose, amylopectin, glucosamine, mannosamine, fucose, glucuronic acid, gluconic acid, glucono-lactone, abequose, galactosamine, beet oligosaccharides, isomalto-oligosaccharides (isomaltose, isomaltotriose, panose and the like), xylo-oligosaccharides (xylotriose, xylobiose and the like), gentio-oligoscaccharides (gentiobiose, gentiotriose, gentiotetraose and the like), sorbose, nigero-oligosaccharides, palatinose oligosaccharides, fructooligosaccharides (kestose, nystose and the like), maltotetraol, maltotriol, malto-oligosaccharides (maltotriose, maltotetraose, maltopentaose, maltohexaose, maltoheptaose and the like), lactulose, melibiose, raffinose, rhamnose, ribose, isomerized liquid sugars such as high fructose corn/starch syrup (e.g., HFCS55, HFCS42, HFCS90), coupling sugars, soybean oligosaccharides, and glucose syrup. Additionally, the carbohydrates as used herein may be in either the D- or L- configuration.

The term "polyol", as used herein, refers to a molecule that contains more than one hydroxyl group. A polyol may be a diol, triol, or a tetraol which contain 2, 3, and 4 hydroxyl groups, respectively. A polyol also may contain more than four hydroxyl groups, such as a pentaol, hexaol, heptaol, or the like, which contain, 5, 6, or 7 hydroxyl groups, respectively. Additionally, a polyol also may be a sugar alcohol, polyhydric alcohol, or polyalcohol which is a reduced form of carbohydrate, wherein the carbonyl group (aldehyde or ketone, reducing sugar) has been reduced to a primary or secondary hydroxyl group.

Non-limiting examples of sweet taste improving polyol additives in embodiments of this invention include erythritol, maltitol, mannitol, sorbitol, lactitol, xylitol, inositol, isomalt, propylene glycol, glycerol (glycerine), threitol, galactitol, palatinose, reduced isomalto-oligosaccharides, reduced xylo-oligosaccharides, reduced gentio-oligosaccharides, reduced maltose syrup, reduced glucose syrup, and sugar alcohols or any other carbohydrates capable of being reduced which do not adversely affect the taste of the sweetener composition.

Suitable sweet taste improving amino acid additives for use in embodiments of this invention include, but are not limited to, aspartic acid, arginine, glycine, glutamic acid, proline, threonine, theanine, cysteine, cystine, alanine, valine, tyrosine, leucine, isoleucine, asparagine, serine, lysine, histidine, ornithine, methionine, carnitine, aminobutyric acid (alpha-, beta-, or gamma- isomers), glutamine, hydroxyproline, taurine, norvaline, sarcosine, and their salt forms such as sodium or potassium salts or acid salts. The sweet taste improving amino acid additives also may be in the D- or L- configuration and in the mono-, di-, or tri- form of the same or different amino acids. Additionally, the amino acids may be α-, β-, γ-, δ-, and ε- isomers if appropriate. Combinations of the foregoing amino acids and their corresponding salts (e.g., sodium, potassium, calcium, magnesium salts or other alkali or alkaline earth metal salts thereof, or acid salts) also are suitable sweet taste improving additives in embodiments of this invention. The amino acids may be natural or synthetic. The amino acids also may be modified. Modified amino acids refers to any amino acid wherein at least one atom has been added, removed, substituted, or combinations thereof (e.g., N-alkyl amino acid, N-acyl amino acid, or N-methyl amino acid). Non-limiting examples of modified amino acids include amino acid derivatives such as trimethyl glycine, N-methyl-glycine, and N-methyl-alanine. As used herein,

amino acids encompass both modified and unmodified amino acids. As used herein, modified amino acid also may encompass peptides and polypeptides (e.g., dipeptides, tripeptides, tetrapeptides, and pentapeptides) such as glutathione and L-alanyl-L-glutamine.

Suitable sweet taste improving polyamino acid additives include poly-L-aspartic acid, poly-L-lysine (e.g., poly-L-α-lysine or poly-L-ε-lysine), poly-L-ornithine (e.g., poly-L-α-ornithine or poly-L-ε-ornithine), poly-L-arginine, other polymeric forms of amino acids, and salt forms thereof (e.g., magnesium, calcium, potassium, or sodium salts such as L-glutamic acid mono sodium salt). The sweet taste improving polyamino acid additives also may be in the D- or L- configuration. Additionally, the polyamino acids may be α-, β-, γ-, δ-, and ε- isomers if appropriate. Combinations of the foregoing polyamino acids and their corresponding salts (e.g., sodium, potassium, calcium, magnesium salts or other alkali or alkaline earth metal salts thereof or acid salts) also are suitable sweet taste improving additives in embodiments of this invention. The polyamino acids described herein also may comprise co-polymers of different amino acids. The polyamino acids may be natural or synthetic. The polyamino acids also may be modified, such that at least one atom has been added, removed, substituted, or combinations thereof (e.g., N-alkyl polyamino acid or N-acyl polyamino acid). As used herein, polyamino acids encompass both modified and unmodified polyamino acids. In accordance with particular embodiments, modified polyamino acids include, but are not limited to polyamino acids of various molecular weights (MW), such as poly-L-α-lysine with a MW of 1,500, MW of 6,000, MW of 25,200, MW of 63,000, MW of 83,000, or MW of 300,000.

Suitable sweet taste improving sugar acid additives for use in embodiments of this invention include, but are not limited to, aldonic, uronic, aldaric, alginic, gluconic, glucuronic, glucaric, galactaric, galacturonic, and their salts (e.g., sodium, potassium, calcium, magnesium salts or other physiologically acceptable salts), and combinations thereof.

Suitable sweet taste improving nucleotide additives for use in embodiments of this invention include, but are not limited to, inosine monophosphate ("IMP"), guanosine monophosphate ("GMP"), adenosine monophosphate ("AMP"), cytosine monophosphate (CMP), uracil monophosphate (UMP), inosine diphosphate, guanosine diphosphate, adenosine diphosphate, cytosine diphosphate, uracil diphosphate, inosine triphosphate,

guanosine triphosphate, adenosine triphosphate, cytosine triphosphate, uracil triphosphate, and their alkali or alkaline earth metal salts, and combinations thereof. The nucleotides described herein also may comprise nucleotide-related additives, such as nucleosides or nucleic acid bases (e.g., guanine, cytosine, adenine, thymine, uracil).

Suitable sweet taste improving organic acid additives include any compound which comprises a –COOH moiety. Suitable sweet taste improving organic acid additives for use in embodiments of this invention include, but are not limited to, C2-C30 carboxylic acids, substituted hydroxyl C1-C30 carboxylic acids, benzoic acid, substituted benzoic acids (e.g. 2,4-dihydroxybenzoic acid), substituted cinnamic acids, hydroxyacids, substituted hydroxybenzoic acids, substituted cyclohexyl carboxylic acids, tannic acid, lactic acid, tartaric acid, citric acid, gluconic acid, glucoheptonic acids, adipic acid, hydroxycitric acid, malic acid, fruitaric acid (a blend of malic, fumaric, and tartaric acids), fumaric acid, maleic acid, succinic acid, chlorogenic acid, salicylic acid, creatine, glucosamine hydrochloride, glucono delta lactone, caffeic acid, bile acids, acetic acid, ascorbic acid, alginic acid, erythorbic acid, polyglutamic acid, and their alkali or alkaline earth metal salt derivatives thereof. In addition, the sweet taste improving organic acid additives also may be in either the D- or L- configuration.

Suitable sweet taste improving organic acid salt additives include, but are not limited to, sodium, calcium, potassium, and magnesium salts of all organic acids, such as salts of citric acid, malic acid, tartaric acid, fumaric acid, lactic acid (e.g., sodium lactate), alginic acid (e.g., sodium alginate), ascorbic acid (e.g., sodium ascorbate), benzoic acid (e.g., sodium benzoate or potassium benzoate), and adipic acid. The examples of the sweet taste improving organic acid salt additives described optionally may be substituted with one or more of the following moiety selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, halo, haloalkyl, carboxyl, acyl, acyloxy, amino, amido, carboxyl derivatives, alkylamino, dialkylamino, arylamino, alkoxy, aryloxy, nitro, cyano, sulfo, thiol, imine, sulfonyl, sulfenyl, sulfinyl, sulfamyl, carboxalkoxy, carboxamido, phosphonyl, phosphinyl, phosphoryl, phosphino, thioester, thioether, anhydride, oximino, hydrazino, carbamyl, phospho, phosphonato, and any other viable functional group, provided the substituted organic acid salt additive functions to improve the sweet taste of the sweetener composition.

Suitable sweet taste improving inorganic acid additives for use in embodiments of this invention include, but are not limited to, phosphoric acid, phosphorous acid, polyphosphoric acid, hydrochloric acid, sulfuric acid, carbonic acid, sodium dihydrogen phosphate, and their corresponding alkali or alkaline earth metal salts thereof (e.g., inositol hexaphosphate Mg/Ca).

Suitable sweet taste improving bitter compound additives for use in embodiments of this invention include, but are not limited to, caffeine, quinine, urea, bitter orange oil, naringin, quassia, and salts thereof.

Suitable sweet taste improving flavorant and flavoring ingredient additives for use in embodiments of this invention include, but are not limited to, vanillin, vanilla extract, mango extract, cinnamon, citrus, coconut, ginger, viridiflorol, almond, menthol (including menthol without mint), grape skin extract, and grape seed extract. "Flavorant" and "flavoring ingredient" are synonymous, and include natural or synthetic substances or combinations thereof. Flavorants also include any other substance which imparts flavor, and may include natural or non-natural (synthetic) substances which are safe for human or animals when used in a generally accepted range. Non-limiting examples of proprietary flavorants include Döhler™ Natural Flavoring Sweetness Enhancer K14323 (Döhler™, Darmstadt, Germany), Symrise™ Natural Flavor Mask for Sweeteners 161453 and 164126 (Symrise, Holzminden™, Germany), Natural Advantage™ Bitterness Blockers 1, 2, 9 and 10 (Natural Advantage™, Freehold, New Jersey, U.S.A.), and Sucramask™ (Creative Research Management, Stockton, California, U.S.A.).

Suitable sweet taste improving polymer additives for use in embodiments of this invention include, but are not limited to, chitosan, pectin, pectic, pectinic, polyuronic, polygalacturonic acid, starch, food hydrocolloid or crude extracts thereof (e.g., gum acacia senegal (Fibergum™), gum acacia seyal, carageenan), poly-L-lysine (e.g., poly-L-α-lysine or poly-L-ε-lysine), poly-L-ornithine (e.g., poly-L-α-ornithine or poly-L-ε-ornithine), polyarginine, polypropylene glycol, polyethylene glycol, poly(ethylene glycol methyl ether), polyaspartic acid, polyglutamic acid, polyethyleneimine, alginic acid, sodium alginate, propylene glycol alginate, sodium hexametaphosphate (SHMP) and its salts, and sodium polyethyleneglycolalginate and other cationic and anionic polymers.

Suitable sweet taste improving protein or protein hydrolysate additives for use in embodiments of this invention include, but are not limited to, bovine serum albumin (BSA), whey protein (including fractions or concentrates thereof such as 90% instant whey protein isolate, 34% whey protein, 50% hydrolyzed whey protein, and 80% whey protein concentrate), soluble rice protein, soy protein, protein isolates, protein hydrolysates, reaction products of protein hydrolysates, glycoproteins, and/or proteoglycans containing amino acids (e.g., glycine, alanine, serine, threonine, asparagine, glutamine, arginine, valine, isoleucine, leucine, norvaline, methionine, proline, tyrosine, hydroxyproline, and the like), collagen (e.g., gelatin), partially hydrolyzed collagen (e.g., hydrolyzed fish collagen), and collagen hydrolysates (e.g., porcine collagen hydrolysate).

Suitable sweet taste improving surfactant additives for use in embodiments of this invention include, but are not limited to, polysorbates (e.g., polyoxyethylene sorbitan monooleate (polysorbate 80), polysorbate 20, polysorbate 60), sodium dodecylbenzenesulfonate, dioctyl sulfosuccinate or dioctyl sulfosuccinate sodium, sodium dodecyl sulfate, cetylpyridinium chloride (hexadecylpyridinium chloride), hexadecyltrimethylammonium bromide, sodium cholate, carbamoyl, choline chloride, sodium glycocholate, sodium taurodeoxycholate, lauric arginate, sodium stearoyl lactylate, sodium taurocholate, lecithins, sucrose oleate esters, sucrose stearate esters, sucrose palmitate esters, sucrose laurate esters, and other emulsifiers, and the like.

Suitable sweet taste improving flavonoid additives for use in embodiments of this invention generally are classified as flavonols, flavones, flavanones, flavan-3-ols, isoflavones, or anthocyanidins. Non-limiting examples of flavonoid additives include catechins (e.g., green tea extracts such as Polyphenon™ 60, Polyphenon™ 30, and Polyphenon™ 25 (Mitsui Norin Co., Ltd., Japan), polyphenols, rutins (e.g., enzyme modified rutin Sanmelin™ AO (San-Ei Gen F.F.I., Inc., Osaka, Japan)), neohesperidin, naringin, neohesperidin dihydrochalcone, and the like.

Suitable sweet taste improving alcohol additives for use in embodiments of this invention include, but are not limited to, ethanol.

Suitable sweet taste improving astringent compound additives include, but are not limited to, tannic acid, europium chloride ($EuCl_3$), gadolinium chloride ($GdCl_3$), terbium chloride ($TbCl_3$), alum, tannic acid, and polyphenols (e.g., tea polyphenols).

Suitable sweet taste improving vitamins include nicotinamide (Vitamin B3) and pyridoxal hydrochloride (Vitamin B6).

The sweet taste improving compositions also may comprise natural and/or synthetic high-potency sweeteners. For example, wherein the sweetener composition comprises at least one NHPS, the at least one sweet taste improving composition may comprise a synthetic high-potency sweetener, non-limiting examples of which include sucralose, potassium acesulfame, aspartame, alitame, saccharin, neohesperidin dihydrochalcone, cyclamate, neotame, N-[N-[3-(3-hydroxy-4-methoxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, N-[N-[3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, salts thereof, and the like.

The sweet taste improving compositions also may be in salt form which may be obtained using standard procedures well known in the art. The term "salt" also refers to complexes that retain the desired chemical activity of the sweet taste improving compositions of the present invention and are safe for human or animal consumption in a generally acceptable range. Alkali metal (for example, sodium or potassium) or alkaline earth metal (for example, calcium or magnesium) salts also can be made. Salts also may include combinations of alkali and alkaline earth metals. Non-limiting examples of such salts are (a) acid addition salts formed with inorganic acids and salts formed with organic acids; (b) base addition salts formed with metal cations such as calcium, bismuth, barium, magnesium, aluminum, copper, cobalt, nickel, cadmium, sodium, potassium, and the like, or with a cation formed from ammonia, N,N-dibenzylethylenediamine, D-glucosamine, tetraethylammonium, or ethylenediamine; or (c) combinations of (a) and (b). Thus, any salt forms which may be derived from the sweet taste improving compositions may be used with the embodiments of the present invention as long as the salts of the sweet taste improving additives do not adversely affect the taste of the sweetener compositions comprising the at least one natural and/or synthetic high-potency sweetener. The salt forms of the additives can be added to the natural and/or synthetic sweetener composition in the same amounts as their acid or base forms.

In particular embodiments, suitable sweet taste improving inorganic salts useful as sweet taste improving additives include, but are not limited to, sodium chloride, potassium chloride, sodium sulfate, potassium citrate, europium chloride ($EuCl_3$), gadolinium chloride ($GdCl_3$), terbium chloride ($TbCl_3$), magnesium sulfate, alum, magnesium chloride, mono-, di-, tri-basic sodium or potassium salts of phosphoric acid (e.g., inorganic phosphates), salts of hydrochloric acid (e.g., inorganic chlorides), sodium carbonate, sodium bisulfate, and sodium bicarbonate. Furthermore, in particular embodiments, suitable organic salts useful as sweet taste improving additives include, but are not limited to, choline chloride, alginic acid sodium salt (sodium alginate), glucoheptonic acid sodium salt, gluconic acid sodium salt (sodium gluconate), gluconic acid potassium salt (potassium gluconate), guanidine HCl, glucosamine HCl, amiloride HCl, monosodium glutamate (MSG), adenosine monophosphate salt, magnesium gluconate, potassium tartrate (monohydrate), and sodium tartrate (dihydrate).

C. Combinations of Sweet Taste Improving Compositions

It has been discovered that combinations of at least one natural and/or synthetic high-potency sweetener and at least one sweet taste improving composition improve the temporal profile and/or flavor profile, including the osmotic taste, to be more sugar-like. One of ordinary skill in the art, with the teachings of the present invention, may arrive at all the possible combinations of natural and/or synthetic high-potency sweeteners and sweet taste improving compositions. For example, non-limiting combinations of the natural and/or synthetic high-potency sweetener and sweet taste improving compositions include:

1. at least one natural and/or synthetic high-potency sweetener and at least one carbohydrate;
2. at least one natural and/or synthetic high-potency sweetener and at least one polyol;
3. at least one natural and/or synthetic high-potency sweetener and at least one amino acid;
4. at least one natural and/or synthetic high-potency sweetener and at least one other sweet taste improving additive;

5. at least one natural and/or synthetic high-potency sweetener, at least one carbohydrate, at least one polyol, at least one amino acid, and at least one other sweet taste improving additive;

6. at least one natural and/or synthetic high-potency sweetener, at least one carbohydrate, and at least one polyol;

7. at least one natural and/or synthetic high-potency sweetener, at least one carbohydrate, and at least one amino acid;

8. at least one natural and/or synthetic high-potency sweetener, at least one carbohydrate, and at least one other sweet taste improving additive;

9. at least one natural and/or synthetic high-potency sweetener, at least one polyol, and at least one amino acid;

10. at least one natural and/or synthetic high-potency sweetener, at least one polyol, and at least one other sweet taste improving additive;

11. at least one natural and/or synthetic high-potency sweetener, at least one amino acid, and at least one other sweet taste improving additive;

12. at least one natural and/or synthetic high-potency sweetener, at least one carbohydrate, at least one polyol, and at least one amino acid;

13. at least one natural and/or synthetic high-potency sweetener, at least one carbohydrate, at least one polyol, and at least one other sweet taste improving additive;

14. at least one natural and/or synthetic high-potency sweetener, at least one polyol, at least one amino acid, and at least one other sweet taste improving additive; and

15. at least one natural and/or synthetic high-potency sweetener, at least one carbohydrate, at least one amino acid, and at least one other sweet taste improving additive.

These fifteen major combinations further may be broken down into further combinations in order to improve the overall taste of the natural and/or synthetic high-potency sweetener or the sweetened compositions comprising the natural and/or synthetic high-potency sweetener.

As explained above, the sweet taste improving composition is selected from the group consisting of polyols, carbohydrates, amino acids, other sweet taste improving additives, and combinations thereof. The other sweet taste improving additives useful in embodiments of this invention are described hereinabove. In one embodiment, a single sweet taste improving composition may be used with a single natural or synthetic high-potency sweetener and a pharmaceutically active substance. In another embodiment of the present invention, a single sweet taste improving composition may be used with one or more natural and/or synthetic high-potency sweeteners and a pharmaceutically active substance. In yet another embodiment, one or more sweet taste improving compositions may be used with a single natural or synthetic high-potency sweetener and a pharmaceutically active substance. In a further embodiment, there may be a plurality of sweet taste improving compositions used in combination with one or more natural and/or synthetic high-potency sweeteners and a pharmaceutically active substance. Thus, non-limiting examples of sweet taste improving composition combinations for embodiments of this invention include:

i. at least one polyol, at least one carbohydrate, at least one amino acid, and at least one other sweet taste improving additive;

ii. at least one polyol, at least one carbohydrate, and at least one other sweet taste improving additive;

iii. at least one polyol and at least one other sweet taste improving additive;

iv. at least one polyol and at least one carbohydrate;

v. at least one carbohydrate and at least one other sweet taste improving additive;

vi. at least one polyol and at least one amino acid;

vii. at least one carbohydrate and at least one amino acid;

viii. at least one amino acid and at least one other sweet taste improving additive.

Other sweet taste improving composition combinations in accordance with embodiments of this invention include:

1. at least one polyol, at least one carbohydrate, and at least one amino acid;

2. at least one polyol, at least one carbohydrate, and at least one polyamino acid;

3. at least one polyol, at least one carbohydrate, and at least one sugar acid;
4. at least one polyol, at least one carbohydrate, and at least one nucleotide;
5. at least one polyol, at least one carbohydrate, and at least one organic acid;
6. at least one polyol, at least one carbohydrate, and at least one inorganic acid;
7. at least one polyol, at least one carbohydrate, and at least one bitter compound;
8. at least one polyol, at least one carbohydrate, and at least one flavorant or flavoring ingredient;
9. at least one polyol, at least one carbohydrate, and at least one polymer;
10. at least one polyol, at least one carbohydrate, and at least one protein or protein hydrolysate or protein or protein hydrolysate with low molecular weight amino acid;
11. at least one polyol, at least one carbohydrate, and at least one surfactant;
12. at least one polyol, at least one carbohydrate, and at least one flavonoid;
13. at least one polyol, at least one carbohydrate, and at least one alcohol;
14. at least one polyol, at least one carbohydrate, and at least one emulsifier;
15. at least one polyol, at least one carbohydrate, and at least one inorganic salt,
16. at least one polyol, at least one carbohydrate, and at least one organic salt,
17. at least one polyol, at least one carbohydrate, and at least one amino acid, and at least one other sweet taste improving additive;
18. at least one polyol, at least one carbohydrate, and at least one polyamino acid, and at least one other sweet taste improving additive;
19. at least one polyol, at least one carbohydrate, and at least one sugar acid, and at least one other sweet taste improving additive;
20. at least one polyol, at least one carbohydrate, and at least one nucleotide, and at least one other sweet taste improving additive;
21. at least one polyol, at least one carbohydrate, and at least one organic acid, and at least one other sweet taste improving additive;
22. at least one polyol, at least one carbohydrate, and at least one inorganic acid, and at least one other sweet taste improving additive;
23. at least one polyol, at least one carbohydrate, and at least one bitter compound, and at least one other sweet taste improving additive;

24. at least one polyol, at least one carbohydrate, and at least one flavorant or flavoring ingredient, and at least one other sweet taste improving additive;

25. at least one polyol, at least one carbohydrate, and at least one polymer, and at least one other sweet taste improving additive;

26. at least one polyol, at least one carbohydrate, and at least one protein or protein hydrolysate, and at least one other sweet taste improving additive;

27. at least one polyol, at least one carbohydrate, and at least one surfactant, and at least one other sweet taste improving additive;

28. at least one polyol, at least one carbohydrate, and at least one flavonoid, and at least one other sweet taste improving additive;

29. at least one polyol, at least one carbohydrate, and at least one alcohol, and at least one other sweet taste improving additive;

30. at least one polyol, at least one carbohydrate, at least one amino acid, and at least one polyamino acid;

31. at least one polyol, at least one carbohydrate, at least one amino acid, at least one polyamino acid, and at least one sugar acid;

32. at least one polyol, at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, and at least one nucleotide;

33. at least one polyol, at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, and at least one organic acid;

34. at least one polyol, at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, and at least one inorganic acid;

35. at least one polyol, at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, and at least one bitter compound;

36. at least one polyol, at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, at least one bitter compound, and at least one polymer;

37. at least one polyol, at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, at least one bitter compound, at least one polymer, and at least one protein or protein hydrolysate;

38. at least one polyol, at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, at least one bitter compound, at least one polymer, at least one protein or protein hydrolysate, and at least one surfactant;

39. at least one polyol, at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, at least one bitter compound, at least one polymer, at least one protein or protein hydrolysate, at least one surfactant, and at least one flavonoid;

40. at least one polyol, at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, at least one bitter compound, at least one polymer, at least one protein or protein hydrolysate, at least one surfactant, at least one flavonoid, and at least one alcohol;

41. at least one polyol, at least one carbohydrate, at least one amino acid, and at least one sugar acid;

42. at least one polyol, at least one carbohydrate, at least one amino acid, and at least one nucleotide;

43. at least one polyol, at least one carbohydrate, at least one amino acid, and at least one organic acid;

44. at least one polyol, at least one carbohydrate, at least one amino acid, and at least one inorganic acid;

45. at least one polyol, at least one carbohydrate, at least one amino acid, and at least one bitter compound;

46. at least one polyol, at least one carbohydrate, at least one amino acid, and at least one polymer;

47. at least one polyol, at least one carbohydrate, at least one amino acid, and at least one protein or protein hydrolysate;

48. at least one polyol, at least one carbohydrate, at least one amino acid, and at least one surfactant;

49. at least one polyol, at least one carbohydrate, at least one amino acid, and at least one flavonoid;

50. at least one polyol, at least one carbohydrate, at least one amino acid, and at least one alcohol;

51. at least one polyol, at least one carbohydrate, at least one polyamino acid, and at least one sugar acid;

52. at least one polyol, at least one carbohydrate, at least one polyamino acid, and at least one nucleotide;

53. at least one polyol, at least one carbohydrate, at least one polyamino acid, and at least one organic acid;

54. at least one polyol, at least one carbohydrate, at least one polyamino acid, and at least one inorganic acid;

55. at least one polyol, at least one carbohydrate, at least one polyamino acid, and at least one bitter compound;

56. at least one polyol, at least one carbohydrate, at least one polyamino acid, and at least one polymer;

57. at least one polyol, at least one carbohydrate, at least one polyamino acid, and at least one protein or protein hydrolysate;

58. at least one polyol, at least one carbohydrate, at least one polyamino acid, and at least one surfactant;

59. at least one polyol, at least one carbohydrate, at least one polyamino acid, and at least one flavonoid;

60. at least one polyol, at least one carbohydrate, at least one polyamino acid, and at least one alcohol;

61. at least one polyol, at least one carbohydrate, at least one sugar acid, and at least one nucleotide;

62. at least one polyol, at least one carbohydrate, at least one sugar acid, and at least one organic acid;

63. at least one polyol, at least one carbohydrate, at least one sugar acid, and at least one inorganic acid;

64. at least one polyol, at least one carbohydrate, at least one sugar acid, and at least one bitter compound;

65. at least one polyol, at least one carbohydrate, at least one sugar acid, and at least one polymer;

66. at least one polyol, at least one carbohydrate, at least one sugar acid, and at least one protein or protein hydrolysate;

67. at least one polyol, at least one carbohydrate, at least one sugar acid, and at least one surfactant;

68. at least one polyol, at least one carbohydrate, at least one sugar acid, and at least one flavonoid;

69. at least one polyol, at least one carbohydrate, at least one sugar acid, and at least one alcohol;

70. at least one polyol, at least one carbohydrate, at least one nucleotide, and at least one organic acid;

71. at least one polyol, at least one carbohydrate, at least one nucleotide, and at least one inorganic acid;

72. at least one polyol, at least one carbohydrate, at least one nucleotide, and at least one bitter compound;

73. at least one polyol, at least one carbohydrate, at least one nucleotide, and at least one polymer;

74. at least one polyol, at least one carbohydrate, at least one nucleotide, and at least one protein or protein hydrolysate;

75. at least one polyol, at least one carbohydrate, at least one nucleotide, and at least one surfactant;

76. at least one polyol, at least one carbohydrate, at least one nucleotide, and at least one flavonoid;

77. at least one polyol, at least one carbohydrate, at least one nucleotide, and at least one alcohol;

78. at least one polyol, at least one carbohydrate, at least one organic acid, and at least one inorganic acid;

79. at least one polyol, at least one carbohydrate, at least one organic acid, and at least one bitter compound;

80. at least one polyol, at least one carbohydrate, at least one organic acid, and at least one polymer;

81. at least one polyol, at least one carbohydrate, at least one organic acid, and at least one protein or protein hydrolysate;

82. at least one polyol, at least one carbohydrate, at least one organic acid, and at least one surfactant;

83. at least one polyol, at least one carbohydrate, at least one organic acid, and at least one flavonoid;

84. at least one polyol, at least one carbohydrate, at least one organic acid, and at least one alcohol;

85. at least one polyol, at least one carbohydrate, at least one inorganic acid, and at least one bitter compound;

86. at least one polyol, at least one carbohydrate, at least one inorganic acid, and at least one polymer;

87. at least one polyol, at least one carbohydrate, at least one inorganic acid, and at least one protein or protein hydrolysate;

88. at least one polyol, at least one carbohydrate, at least one inorganic acid, and at least one surfactant;

89. at least one polyol, at least one carbohydrate, at least one inorganic acid, and at least one flavonoid;

90. at least one polyol, at least one carbohydrate, at least one inorganic acid, and at least one alcohol;

91. at least one polyol, at least one carbohydrate, at least one bitter compound, and at least one polymer;

92. at least one polyol, at least one carbohydrate, at least one bitter compound, and at least one protein or protein hydrolysate;

93. at least one polyol, at least one carbohydrate, at least one bitter compound, and at least one surfactant;

94. at least one polyol, at least one carbohydrate, at least one bitter compound, and at least one flavonoid;

95. at least one polyol, at least one carbohydrate, at least one bitter compound, and at least one alcohol;
96. at least one polyol, at least one carbohydrate, at least one polymer, and at least one protein or protein hydrolysate;
97. at least one polyol, at least one carbohydrate, at least one polymer, and at least one surfactant;
98. at least one polyol, at least one carbohydrate, at least one polymer, and at least one flavonoid;
99. at least one polyol, at least one carbohydrate, at least one polymer, and at least one alcohol;
100. at least one polyol, at least one carbohydrate, at least one protein or protein hydrolysate, and at least one surfactant;
101. at least one polyol, at least one carbohydrate, at least one protein or protein hydrolysate, and at least one flavonoid;
102. at least one polyol, at least one carbohydrate, at least one surfactant, and at least one flavonoid;
103. at least one polyol, at least one carbohydrate, at least one surfactant, and at least one alcohol; and
104. at least one polyol, at least one carbohydrate, at least one flavonoid, and at least one alcohol.

Other sweet taste improving composition combinations in accordance with embodiments of this invention include:

1. at least one polyol and at least one amino acid;
2. at least one polyol and at least one polyamino acid;
3. at least one polyol and at least one sugar acid;
4. at least one polyol and at least one nucleotide;
5. at least one polyol and at least one organic acid;
6. at least one polyol and at least one inorganic acid;
7. at least one polyol and at least one bitter compound;
8. at least one polyol and at least one flavorant or flavoring ingredient;
9. at least one polyol and at least one polymer;

10. at least one polyol and at least one protein or protein hydrolysate;
11. at least one polyol and at least one surfactant;
12. at least one polyol and at least one flavonoid;
13. at least one polyol and at least one alcohol;
14. at least one polyol and at least one emulsifier;
15. at least one polyol and at least one inorganic salt;
16. at least one polyol and at least one organic salt;
17. at least one polyol and at least one protein or protein hydrolysate or mixture of low molecular weight amino acids;
18. at least one polyol, at least one amino acid, and at least one other sweet taste improving additive;
19. at least one polyol, at least one polyamino acid, and at least one other sweet taste improving additive;
20. at least one polyol, at least one sugar acid, and at least one other sweet taste improving additive;
21. at least one polyol, at least one nucleotide, and at least one other sweet taste improving additive;
22. at least one polyol, at least one organic acid, and at least one other sweet taste improving additive;
23. at least one polyol, at least one inorganic acid, and at least one other sweet taste improving additive;
24. at least one polyol, at least one bitter compound, and at least one other sweet taste improving additive;
25. at least one polyol, at least one flavorant or flavoring ingredient, and at least one other sweet taste improving additive;
26. at least one polyol, at least one polymer, and at least one other sweet taste improving additive;
27. at least one polyol, at least one protein or protein hydrolysate, and at least one other sweet taste improving additive;
28. at least one polyol, at least one surfactant, and at least one other sweet taste improving additive;

29. at least one polyol, at least one flavonoid, and at least one other sweet taste improving additive;

30. at least one polyol, at least one alcohol, and at least one other sweet taste improving additive;

31. at least one polyol, at least one amino acid, and at least one polyamino acid;

32. at least one polyol, at least one amino acid, at least one polyamino acid, and at least one sugar acid;

33. at least one polyol, at least one amino acid, at least one polyamino acid, at least one sugar acid, and at least one nucleotide;

34. at least one polyol, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, and at least one organic acid;

35. at least one polyol, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, and at least one inorganic acid;

36. at least one polyol, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, and at least one bitter compound;

37. at least one polyol, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, at least one bitter compound, and at least one polymer;

38. at least one polyol, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, at least one bitter compound, at least one polymer, and at least one protein or protein hydrolysate;

39. at least one polyol, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, at least one bitter compound, at least one polymer, at least one protein or protein hydrolysate, and at least one surfactant;

40. at least one polyol, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, at least one bitter compound, at least one polymer, at least one protein or protein hydrolysate, at least one surfactant, and at least one flavonoid;

41. at least one polyol, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, at least one bitter compound, at least one polymer, at least one protein or protein hydrolysate, at least one surfactant, at least one flavonoid, and at least one alcohol;

42. at least one polyol, at least one amino acid, and at least one sugar acid;

43. at least one polyol, at least one amino acid, and at least one nucleotide;

44. at least one polyol, at least one amino acid, and at least one organic acid;

45. at least one polyol, at least one amino acid, and at least one inorganic acid;

46. at least one polyol, at least one amino acid, and at least one bitter compound;

47. at least one polyol, at least one amino acid, and at least one polymer;

48. at least one polyol, at least one amino acid, and at least one protein or protein hydrolysate;

49. at least one polyol, at least one amino acid, and at least one surfactant;

50. at least one polyol, at least one amino acid, and at least one flavonoid;

51. at least one polyol, at least one amino acid, and at least one alcohol;

52. at least one polyol, at least one polyamino acid, and at least one sugar acid;

53. at least one polyol, at least one polyamino acid, and at least one nucleotide;

54. at least one polyol, at least one polyamino acid, and at least one organic acid;

55. at least one polyol, at least one polyamino acid, and at least one organic salt;

56. at least one polyol, at least one polyamino acid, and at least one inorganic acid;

57. at least one polyol, at least one polyamino acid, and at least one inorganic salt;

58. at least one polyol, at least one polyamino acid, and at least one bitter compound;

59. at least one polyol, at least one polyamino acid, and at least one polymer;

60. at least one polyol, at least one polyamino acid, and at least one protein or protein hydrolysate;

61. at least one polyol, at least one polyamino acid, and at least one surfactant;
62. at least one polyol, at least one polyamino acid, and at least one flavonoid;
63. at least one polyol, at least one polyamino acid, and at least one alcohol;
64. at least one polyol, at least one sugar acid, and at least one nucleotide;
65. at least one polyol, at least one sugar acid, and at least one organic acid;
66. at least one polyol, at least one sugar acid, and at least one inorganic acid;
67. at least one polyol, at least one sugar acid, and at least one bitter compound;
68. at least one polyol, at least one sugar acid, and at least one polymer;
69. at least one polyol, at least one sugar acid, and at least one protein or protein hydrolysate;
70. at least one polyol, at least one sugar acid, and at least one surfactant;
71. at least one polyol, at least one sugar acid, and at least one flavonoid;
72. at least one polyol, at least one sugar acid, and at least one alcohol;
73. at least one polyol, at least one nucleotide, and at least one organic acid;
74. at least one polyol, at least one nucleotide, and at least one inorganic acid;
75. at least one polyol, at least one nucleotide, and at least one bitter compound;
76. at least one polyol, at least one nucleotide, and at least one polymer;
77. at least one polyol, at least one nucleotide, and at least one protein or protein hydrolysate;
78. at least one polyol, at least one nucleotide, and at least one surfactant;
79. at least one polyol, at least one nucleotide, and at least one flavonoid;
80. at least one polyol, at least one nucleotide, and at least one alcohol;
81. at least one polyol, at least one organic acid, and at least one inorganic acid;
82. at least one polyol, at least one organic acid, and at least one bitter compound;
83. at least one polyol, at least one organic acid, and at least one polymer;
84. at least one polyol, at least one organic acid, and at least one protein or protein hydrolysate;
85. at least one polyol, at least one organic acid, and at least one surfactant;
86. at least one polyol, at least one organic acid, and at least one flavonoid;
87. at least one polyol, at least one organic acid, and at least one alcohol;
88. at least one polyol, at least one inorganic acid, and at least one bitter compound;

89. at least one polyol, at least one inorganic acid, and at least one polymer;
90. at least one polyol, at least one inorganic acid, and at least one protein or protein hydrolysate;
91. at least one polyol, at least one inorganic acid, and at least one surfactant;
92. at least one polyol, at least one inorganic acid, and at least one flavonoid;
93. at least one polyol, at least one inorganic acid, and at least one alcohol;
94. at least one polyol, at least one bitter compound, and at least one polymer;
95. at least one polyol, at least one bitter compound, and at least one protein or protein hydrolysate;
96. at least one polyol, at least one bitter compound, and at least one surfactant;
97. at least one polyol, at least one bitter compound, and at least one flavonoid;
98. at least one polyol, at least one bitter compound, and at least one alcohol;
99. at least one polyol, at least one polymer, and at least one protein or protein hydrolysate;
100. at least one polyol, at least one polymer, and at least one surfactant;
101. at least one polyol, at least one polymer, and at least one flavonoid;
102. at least one polyol, at least one polymer, and at least one alcohol;
103. at least one polyol, at least one protein or protein hydrolysate, and at least one surfactant;
104. at least one polyol, at least one protein or protein hydrolysate, and at least one flavonoid;
105. at least one polyol, at least one surfactant, and at least one flavonoid;
106. at least one polyol, at least one surfactant, and at least one alcohol;
107. at least one polyol, at least one flavonoid, and at least one alcohol;
108. at least one sweet taste improving additive and erythritol;
109. at least one sweet taste improving additive and maltitol;
110. at least one sweet taste improving additive and mannitol;
111. at least one sweet taste improving additive and sorbitol;
112. at least one sweet taste improving additive and lactitol;
113. at least one sweet taste improving additive and xylitol;
114. at least one sweet taste improving additive and isomalt;
115. at least one sweet taste improving additive and propylene glycol;

116. at least one sweet taste improving additive and glycerol;

117. at least one sweet taste improving additive and palatinose;

118. at least one sweet taste improving additive and reduced isomalto-oligosaccharides;

119. at least one sweet taste improving additive and reduced xylo-oligosaccharides;

120. at least one sweet taste improving additive and reduced gentio-oligosaccharides;

121. at least one sweet taste improving additive and reduced maltose syrup;

122. at least one sweet taste improving additive and reduced glucose syrup;

123. at least one sweet taste improving additive, erythritol, and at least one other polyol;

124. at least one sweet taste improving additive, maltitol, and at least one other polyol;

125. at least one sweet taste improving additive, mannitol, and at least one other polyol;

126. at least one sweet taste improving additive, sorbitol, and at least one other polyol;

127. at least one sweet taste improving additive, lactitol, and at least one other polyol;

128. at least one sweet taste improving additive, xylitol, and at least one other polyol;

129. at least one sweet taste improving additive, isomalt, and at least one other polyol;

130. at least one sweet taste improving additive, propylene glycol, and at least one other polyol;

131. at least one sweet taste improving additive, glycerol, and at least one other polyol;

132. at least one sweet taste improving additive, palatinose, and at least one other polyol;

133. at least one sweet taste improving additive, reduced isomalto-oligosaccharides, and at least one other polyol;

134. at least one sweet taste improving additive, reduced xylo-oligosaccharides, and at least one other polyol;

135. at least one sweet taste improving additive, reduced gentio-oligosaccharides, and at least one other polyol;

136. at least one sweet taste improving additive, reduced maltose syrup, and at least one other polyol; and

137. at least one sweet taste improving additive, reduced glucose syrup, and at least one other polyol.

Other sweet taste improving composition combinations in accordance with embodiments of this invention include:

1. at least one polyol and tagatose;
2. at least one polyol and trehalose;
3. at least one polyol and galactose;
4. at least one polyol and rhamnose;
5. at least one polyol and dextrin;
6. at least one polyol and cyclodextrin;
7. at least one polyol and α-cyclodextrin, β-cyclodextrin, or γ-cyclodextrin;
8. at least one polyol and maltodextrin;
9. at least one polyol and dextran;
10. at least one polyol and sucrose;
11. at least one polyol and glucose;
12. at least one polyol and fructose;
13. at least one polyol and threose;
14. at least one polyol and arabinose;
15. at least one polyol and xylose;
16. at least one polyol and lyxose;
17. at least one polyol and allose;
18. at least one polyol and altrose;
19. at least one polyol and mannose;
20. at least one polyol and idose;
21. at least one polyol and talose;

22. at least one polyol and lactose;
23. at least one polyol and maltose;
24. at least one polyol and invert sugar;
25. at least one polyol and trehalose;
26. at least one polyol and isotrehalose;
27. at least one polyol and neotrehalose;
28. at least one polyol and palatinose;
29. at least one polyol and galactose;
30. at least one polyol and beet oligosaccharides;
31. at least one polyol and isomalto-oligosaccharides;
32. at least one polyol and isomaltose;
33. at least one polyol and isomaltotriose;
34. at least one polyol and panose;
35. at least one polyol and xylo-oligosaccharides;
36. at least one polyol and xylotriose;
37. at least one polyol and xylobiose;
38. at least one polyol and gentio-oligoscaccharides;
39. at least one polyol and gentiobiose;
40. at least one polyol and gentiotriose;
41. at least one polyol and gentiotetraose;
42. at least one polyol and sorbose;
43. at least one polyol and nigero-oligosaccharides;
44. at least one polyol and palatinose oligosaccharides;
45. at least one polyol and fucose;
46. at least one polyol and fructooligosaccharides;
47. at least one polyol and kestose;
48. at least one polyol and nystose;
49. at least one polyol and maltotetraol;
50. at least one polyol and maltotriol;
51. at least one polyol and malto-oligosaccharides;
52. at least one polyol and maltotriose;
53. at least one polyol and maltotetraose;

54. at least one polyol and maltopentaose;
55. at least one polyol and maltohexaose;
56. at least one polyol and maltoheptaose;
57. at least one polyol and lactulose;
58. at least one polyol and melibiose;
59. at least one polyol and raffinose;
60. at least one polyol and rhamnose;
61. at least one polyol and ribose;
62. at least one polyol and isomerized liquid sugars;
63. at least one polyol and high fructose corn syrup (e.g. HFCS55 and HFCS42) or starch syrup;
64. at least one polyol and coupling sugars;
65. at least one polyol and soybean oligosaccharides;
66. at least one polyol and glucose syrup;
67. at least one polyol, tagatose, and at least one other carbohydrate;
68. at least one polyol, trehalose, and at least one other carbohydrate;
69. at least one polyol, galactose, and at least one other carbohydrate;
70. at least one polyol, rhamnose, and at least one other carbohydrate;
71. at least one polyol, dextrin, and at least one other carbohydrate;
72. at least one polyol, cyclodextrin, and at least one other carbohydrate;
73. at least one polyol, β-cyclodextrin, and at least one other carbohydrate;
74. at least one polyol, maltodextrin, and at least one other carbohydrate;
75. at least one polyol, dextran, and at least one other carbohydrate;
76. at least one polyol, sucrose, and at least one other carbohydrate;
77. at least one polyol, glucose, and at least one other carbohydrate;
78. at least one polyol, fructose, and at least one other carbohydrate;
79. at least one polyol, threose, and at least one other carbohydrate;
80. at least one polyol, arabinose, and at least one other carbohydrate;
81. at least one polyol, xylose, and at least one other carbohydrate;
82. at least one polyol, lyxose, and at least one other carbohydrate;
83. at least one polyol, allose, and at least one other carbohydrate;
84. at least one polyol, altrose, and at least one other carbohydrate;

85. at least one polyol, mannose, and at least one other carbohydrate;
86. at least one polyol, idose, and at least one other carbohydrate;
87. at least one polyol, talose, and at least one other carbohydrate;
88. at least one polyol, lactose, and at least one other carbohydrate;
89. at least one polyol, maltose, and at least one other carbohydrate;
90. at least one polyol, invert sugar, and at least one other carbohydrate;
91. at least one polyol, trehalose, and at least one other carbohydrate;
92. at least one polyol, isotrehalose, and at least one other carbohydrate;
93. at least one polyol, neotrehalose, and at least one other carbohydrate;
94. at least one polyol, palatinose, and at least one other carbohydrate;
95. at least one polyol, galactose, and at least one other carbohydrate;
96. at least one polyol, beet oligosaccharides, and at least one other carbohydrate;
97. at least one polyol, isomalto-oligosaccharides, and at least one other carbohydrate;
98. at least one polyol, isomaltose, and at least one other carbohydrate;
99. at least one polyol, isomaltotriose, and at least one other carbohydrate;
100. at least one polyol, panose, and at least one other carbohydrate;
101. at least one polyol, xylo-oligosaccharides, and at least one other carbohydrate;
102. at least one polyol, xylotriose, and at least one other carbohydrate;
103. at least one polyol, xylobiose, and at least one other carbohydrate;
104. at least one polyol, gentio-oligoscaccharides, and at least one other carbohydrate;
105. at least one polyol, gentiobiose, and at least one other carbohydrate;
106. at least one polyol, gentiotriose, and at least one other carbohydrate;
107. at least one polyol, gentiotetraose, and at least one other carbohydrate;
108. at least one polyol, sorbose, and at least one other carbohydrate;
109. at least one polyol, nigero-oligosaccharides, and at least one other carbohydrate;
110. at least one polyol, palatinose oligosaccharides, and at least one other carbohydrate;
111. at least one polyol, fucose, and at least one other carbohydrate;
112. at least one polyol, fructooligosaccharides, and at least one other carbohydrate;

113. at least one polyol, kestose, and at least one other carbohydrate;
114. at least one polyol, nystose, and at least one other carbohydrate;
115. at least one polyol, maltotetraol, and at least one other carbohydrate;
116. at least one polyol, maltotriol, and at least one other carbohydrate;
117. at least one polyol, malto-oligosaccharides, and at least one other carbohydrate;
118. at least one polyol, maltotriose, and at least one other carbohydrate;
119. at least one polyol, maltotetraose, and at least one other carbohydrate;
120. at least one polyol, maltopentaose, and at least one other carbohydrate;
121. at least one polyol, maltohexaose, and at least one other carbohydrate;
122. at least one polyol, maltoheptaose, and at least one other carbohydrate;
123. at least one polyol, lactulose, and at least one other carbohydrate;
124. at least one polyol, melibiose, and at least one other carbohydrate;
125. at least one polyol, raffinose, and at least one other carbohydrate;
126. at least one polyol, rhamnose, and at least one other carbohydrate;
127. at least one polyol, ribose, and at least one other carbohydrate;
128. at least one polyol, isomerized liquid sugars, and at least one other carbohydrate;
129. at least one polyol, high fructose corn syrup (e.g. HFCS55 and HFCS42) or starch syrup, and at least one other carbohydrate;
130. at least one polyol, coupling sugars, and at least one other carbohydrate;
131. at least one polyol, soybean oligosaccharides, and at least one other carbohydrate;
132. at least one polyol, glucose syrup, and at least one other carbohydrate;
133. at least one carbohydrate and erythritol;
134. at least one carbohydrate and maltitol;
135. at least one carbohydrate and mannitol;
136. at least one carbohydrate and sorbitol;
137. at least one carbohydrate and lactitol;
138. at least one carbohydrate and xylitol;
139. at least one carbohydrate and isomalt;
140. at least one carbohydrate and propylene glycol;
141. at least one carbohydrate and glycerol;

142. at least one carbohydrate and palatinose;
143. at least one carbohydrate and reduced isomalto-oligosaccharides;
144. at least one carbohydrate and reduced xylo-oligosaccharides;
145. at least one carbohydrate and reduced gentio-oligosaccharides;
146. at least one carbohydrate and reduced maltose syrup;
147. at least one carbohydrate and reduced glucose syrup;
148. at least one carbohydrate, erythritol, and at least one other polyol;
149. at least one carbohydrate, maltitol, and at least one other polyol;
150. at least one carbohydrate, mannitol, and at least one other polyol;
151. at least one carbohydrate, sorbitol, and at least one other polyol;
152. at least one carbohydrate, lactitol, and at least one other polyol;
153. at least one carbohydrate, xylitol, and at least one other polyol;
154. at least one carbohydrate, isomalt, and at least one other polyol;
155. at least one carbohydrate, propylene glycol, and at least one other polyol;
156. at least one carbohydrate, glycerol, and at least one other polyol;
157. at least one carbohydrate, palatinose, and at least one other polyol;
158. at least one carbohydrate, reduced isomalto-oligosaccharides, and at least one other polyol;
159. at least one carbohydrate, reduced xylo-oligosaccharides, and at least one other polyol;
160. at least one carbohydrate, reduced gentio-oligosaccharides, and at least one other polyol;
161. at least one carbohydrate, reduced maltose syrup, and at least one other polyol; and
162. at least one carbohydrate, reduced glucose syrup, and at least one other polyol.

Other sweet taste improving composition combinations in accordance with embodiments of this invention include:

1. at least one carbohydrate and at least one amino acid;
2. at least one carbohydrate and at least one polyamino acid;
3. at least one carbohydrate and at least one sugar acid;
4. at least one carbohydrate and at least one nucleotide;

5. at least one carbohydrate and at least one organic acid;
6. at least one carbohydrate and at least one inorganic acid;
7. at least one carbohydrate and at least one bitter compound;
8. at least one carbohydrate and at least one flavorant or flavoring ingredient;
9. at least one carbohydrate and at least one polymer;
10. at least one carbohydrate and at least one protein or protein hydrolysate;
11. at least one carbohydrate and at least one surfactant;
12. at least one carbohydrate and at least one flavonoid;
13. at least one carbohydrate and at least one alcohol;
14. at least one carbohydrate and at least one protein or protein hydrolysate or mixture of low molecular weight amino acids;
15. at least one carbohydrate and at least one emulsifier;
16. at least one carbohydrate and at least one inorganic salt;
17. at least one carbohydrate, at least one amino acid, and at least one other sweet taste improving additive;
18. at least one carbohydrate, at least one polyamino acid, and at least one other sweet taste improving additive;
19. at least one carbohydrate, at least one sugar acid, and at least one other sweet taste improving additive;
20. at least one carbohydrate, at least one nucleotide, and at least one other sweet taste improving additive;
21. at least one carbohydrate, at least one organic acid, and at least one other sweet taste improving additive;
22. at least one carbohydrate, at least one inorganic acid, and at least one other sweet taste improving additive;
23. at least one carbohydrate, at least one bitter compound, and at least one other sweet taste improving additive;
24. at least one carbohydrate, at least one flavorant or flavoring ingredient, and at least one other sweet taste improving additive;
25. at least one carbohydrate, at least one polymer, and at least one other sweet taste improving additive;

26. at least one carbohydrate, at least one protein or protein hydrolysate, and at least one other sweet taste improving additive;

27. at least one carbohydrate, at least one surfactant, and at least one other sweet taste improving additive;

28. at least one carbohydrate, at least one flavonoid, and at least one other sweet taste improving additive;

29. at least one carbohydrate, at least one alcohol, and at least one other sweet taste improving additive;

30. at least one carbohydrate, at least one amino acid, and at least one polyamino acid;

31. at least one carbohydrate, at least one amino acid, at least one polyamino acid, and at least one sugar acid;

32. at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, and at least one nucleotide;

33. at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, and at least one organic acid;

34. at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, and at least one inorganic acid;

35. at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, and at least one bitter compound;

36. at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, at least one bitter compound, and at least one polymer;

37. at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, at least one bitter compound, at least one polymer, and at least one protein or protein hydrolysate;

38. at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, at least one bitter compound, at least one polymer, at least one protein or protein hydrolysate, and at least one surfactant;

39. at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, at least one bitter compound, at least one polymer, at least one protein or protein hydrolysate, at least one surfactant, and at least one flavonoid;

40. at least one carbohydrate, at least one amino acid, at least one polyamino acid, at least one sugar acid, at least one nucleotide, at least one organic acid, at least one inorganic acid, at least one bitter compound, at least one polymer, at least one protein or protein hydrolysate, at least one surfactant, at least one flavonoid, and at least one alcohol;

41. at least one carbohydrate, at least one amino acid, and at least one sugar acid;

42. at least one carbohydrate, at least one amino acid, and at least one nucleotide;

43. at least one carbohydrate, at least one amino acid, and at least one organic acid;

44. at least one carbohydrate, at least one amino acid, and at least one inorganic acid;

45. at least one carbohydrate, at least one amino acid, and at least one bitter compound;

46. at least one carbohydrate, at least one amino acid, and at least one polymer;

47. at least one carbohydrate, at least one amino acid, and at least one protein or protein hydrolysate;

48. at least one carbohydrate, at least one amino acid, and at least one surfactant;

49. at least one carbohydrate, at least one amino acid, and at least one flavonoid;

50. at least one carbohydrate, at least one amino acid, and at least one alcohol;

51. at least one carbohydrate, at least one polyamino acid, and at least one sugar acid;

52. at least one carbohydrate, at least one polyamino acid, and at least one nucleotide;

53. at least one carbohydrate, at least one polyamino acid, and at least one organic acid;

54. at least one carbohydrate, at least one polyamino acid, and at least one inorganic acid;

55. at least one carbohydrate, at least one polyamino acid, and at least one bitter compound;

56. at least one carbohydrate, at least one polyamino acid, and at least one polymer;

57. at least one carbohydrate, at least one polyamino acid, and at least one protein or protein hydrolysate;

58. at least one carbohydrate, at least one polyamino acid, and at least one surfactant;

59. at least one carbohydrate, at least one polyamino acid, and at least one flavonoid;

60. at least one carbohydrate, at least one polyamino acid, and at least one alcohol;

61. at least one carbohydrate, at least one sugar acid, and at least one nucleotide;

62. at least one carbohydrate, at least one sugar acid, and at least one organic acid;

63. at least one carbohydrate, at least one sugar acid, and at least one inorganic acid;

64. at least one carbohydrate, at least one sugar acid, and at least one bitter compound;

65. at least one carbohydrate, at least one sugar acid, and at least one polymer;

66. at least one carbohydrate, at least one sugar acid, and at least one protein or protein hydrolysate;

67. at least one carbohydrate, at least one sugar acid, and at least one surfactant;

68. at least one carbohydrate, at least one sugar acid, and at least one flavonoid;

69. at least one carbohydrate, at least one sugar acid, and at least one alcohol;

70. at least one carbohydrate, at least one nucleotide, and at least one organic acid;

71. at least one carbohydrate, at least one nucleotide, and at least one inorganic acid;

72. at least one carbohydrate, at least one nucleotide, and at least one bitter compound;

73. at least one carbohydrate, at least one nucleotide, and at least one polymer;
74. at least one carbohydrate, at least one nucleotide, and at least one protein or protein hydrolysate;
75. at least one carbohydrate, at least one nucleotide, and at least one surfactant;
76. at least one carbohydrate, at least one nucleotide, and at least one flavonoid;
77. at least one carbohydrate, at least one nucleotide, and at least one alcohol;
78. at least one carbohydrate, at least one organic acid, and at least one inorganic acid;
79. at least one carbohydrate, at least one organic acid, and at least one bitter compound;
80. at least one carbohydrate, at least one organic acid, and at least one polymer;
81. at least one carbohydrate, at least one organic acid, and at least one protein or protein hydrolysate;
82. at least one carbohydrate, at least one organic acid, and at least one surfactant;
83. at least one carbohydrate, at least one organic acid, and at least one flavonoid;
84. at least one carbohydrate, at least one organic acid, and at least one alcohol;
85. at least one carbohydrate, at least one inorganic acid, and at least one bitter compound;
86. at least one carbohydrate, at least one inorganic acid, and at least one polymer;
87. at least one carbohydrate, at least one inorganic acid, and at least one protein or protein hydrolysate;
88. at least one carbohydrate, at least one inorganic acid, and at least one surfactant;
89. at least one carbohydrate, at least one inorganic acid, and at least one flavonoid;
90. at least one carbohydrate, at least one inorganic acid, and at least one alcohol;
91. at least one carbohydrate, at least one bitter compound, and at least one polymer;
92. at least one carbohydrate, at least one bitter compound, and at least one protein or protein hydrolysate;
93. at least one carbohydrate, at least one bitter compound, and at least one surfactant;

94. at least one carbohydrate, at least one bitter compound, and at least one flavonoid;

95. at least one carbohydrate, at least one bitter compound, and at least one alcohol;

96. at least one carbohydrate, at least one polymer, and at least one protein or protein hydrolysate;

97. at least one carbohydrate, at least one polymer, and at least one surfactant;

98. at least one carbohydrate, at least one polymer, and at least one flavonoid;

99. at least one carbohydrate, at least one polymer, and at least one alcohol;

100. at least one carbohydrate, at least one protein or protein hydrolysate, and at least one surfactant;

101. at least one carbohydrate, at least one protein or protein hydrolysate, and at least one flavonoid;

102. at least one carbohydrate, at least one surfactant, and at least one flavonoid;

103. at least one carbohydrate, at least one surfactant, and at least one alcohol;

104. at least one carbohydrate, at least one flavonoid, and at least one alcohol;

105. at least one sweet taste improving additive and D-tagatose;

106. at least one sweet taste improving additive and trehalose;

107. at least one sweet taste improving additive and D-galactose;

108. at least one sweet taste improving additive and rhamnose;

109. at least one sweet taste improving additive and dextrin;

110. at least one sweet taste improving additive and cyclodextrin;

111. at least one sweet taste improving additive and β-cyclodextrin;

112. at least one sweet taste improving additive and maltodextrin;

113. at least one sweet taste improving additive and dextran;

114. at least one sweet taste improving additive and sucrose;

115. at least one sweet taste improving additive and glucose;

116. at least one sweet taste improving additive and fructose;

117. at least one sweet taste improving additive and threose;

118. at least one sweet taste improving additive and arabinose;

119. at least one sweet taste improving additive and xylose;

120. at least one sweet taste improving additive and lyxose;

121. at least one sweet taste improving additive and allose;
122. at least one sweet taste improving additive and altrose;
123. at least one sweet taste improving additive and mannose;
124. at least one sweet taste improving additive and idose;
125. at least one sweet taste improving additive and talose;
126. at least one sweet taste improving additive and lactose;
127. at least one sweet taste improving additive and maltose;
128. at least one sweet taste improving additive and invert sugar;
129. at least one sweet taste improving additive and trehalose;
130. at least one sweet taste improving additive and isotrehalose;
131. at least one sweet taste improving additive and neotrehalose;
132. at least one sweet taste improving additive and palatinose;
133. at least one sweet taste improving additive and galactose;
134. at least one sweet taste improving additive and beet oligosaccharides;
135. at least one sweet taste improving additive and isomalto-oligosaccharides;
136. at least one sweet taste improving additive and isomaltose;
137. at least one sweet taste improving additive and isomaltotriose;
138. at least one sweet taste improving additive and panose;
139. at least one sweet taste improving additive and xylo-oligosaccharides;
140. at least one sweet taste improving additive and xylotriose;
141. at least one sweet taste improving additive and xylobiose;
142. at least one sweet taste improving additive and gentio-oligoscaccharides;
143. at least one sweet taste improving additive and gentiobiose;
144. at least one sweet taste improving additive and gentiotriose;
145. at least one sweet taste improving additive and gentiotetraose;
146. at least one sweet taste improving additive and sorbose;
147. at least one sweet taste improving additive and nigero-oligosaccharides;
148. at least one sweet taste improving additive and palatinose oligosaccharides;
149. at least one sweet taste improving additive and fucose;
150. at least one sweet taste improving additive and fructooligosaccharides;
151. at least one sweet taste improving additive and kestose;
152. at least one sweet taste improving additive and nystose;

153. at least one sweet taste improving additive and maltotetraol;
154. at least one sweet taste improving additive and maltotriol;
155. at least one sweet taste improving additive and malto-oligosaccharides;
156. at least one sweet taste improving additive and maltotriose;
157. at least one sweet taste improving additive and maltotetraose;
158. at least one sweet taste improving additive and maltopentaose;
159. at least one sweet taste improving additive and maltohexaose;
160. at least one sweet taste improving additive and maltoheptaose;
161. at least one sweet taste improving additive and lactulose;
162. at least one sweet taste improving additive and melibiose;
163. at least one sweet taste improving additive and raffinose;
164. at least one sweet taste improving additive and rhamnose;
165. at least one sweet taste improving additive and ribose;
166. at least one sweet taste improving additive and isomerized liquid sugars;
167. at least one sweet taste improving additive and high fructose corn syrup (e.g., HFCS55 and HFCS42) or starch syrup;
168. at least one sweet taste improving additive and coupling sugars;
169. at least one sweet taste improving additive and soybean oligosaccharides;
170. at least one sweet taste improving additive and glucose syrup;
171. at least one sweet taste improving additive, D-tagatose, and at least one other carbohydrate;
172. at least one sweet taste improving additive, trehalose, and at least one other carbohydrate;
173. at least one sweet taste improving additive, D-galactose, and at least one other carbohydrate;
174. at least one sweet taste improving additive, rhamnose, and at least one other carbohydrate;
175. at least one sweet taste improving additive, dextrin, and at least one other carbohydrate;
176. at least one sweet taste improving additive, cyclodextrin, and at least one other carbohydrate;

177. at least one sweet taste improving additive, β-cyclodextrin, and at least one other carbohydrate;

178. at least one sweet taste improving additive, maltodextrin, and at least one other carbohydrate;

179. at least one sweet taste improving additive, dextran, and at least one other carbohydrate;

180. at least one sweet taste improving additive, sucrose, and at least one other carbohydrate;

181. at least one sweet taste improving additive, glucose, and at least one other carbohydrate;

182. at least one sweet taste improving additive, fructose, and at least one other carbohydrate;

183. at least one sweet taste improving additive, threose, and at least one other carbohydrate;

184. at least one sweet taste improving additive, arabinose, and at least one other carbohydrate;

185. at least one sweet taste improving additive, xylose, and at least one other carbohydrate;

186. at least one sweet taste improving additive, lyxose, and at least one other carbohydrate;

187. at least one sweet taste improving additive, allose, and at least one other carbohydrate;

188. at least one sweet taste improving additive, altrose, and at least one other carbohydrate;

189. at least one sweet taste improving additive, mannose, and at least one other carbohydrate;

190. at least one sweet taste improving additive, idose, and at least one other carbohydrate;

191. at least one sweet taste improving additive, talose, and at least one other carbohydrate;

192. at least one sweet taste improving additive, lactose, and at least one other carbohydrate;

193. at least one sweet taste improving additive, maltose, and at least one other carbohydrate;

194. at least one sweet taste improving additive, invert sugar, and at least one other carbohydrate;

195. at least one sweet taste improving additive, trehalose, and at least one other carbohydrate;

196. at least one sweet taste improving additive, isotrehalose, and at least one other carbohydrate;

197. at least one sweet taste improving additive, neotrehalose, and at least one other carbohydrate;

198. at least one sweet taste improving additive, palatinose, and at least one other carbohydrate;

199. at least one sweet taste improving additive, galactose, and at least one other carbohydrate;

200. at least one sweet taste improving additive, beet oligosaccharides, and at least one other carbohydrate;

201. at least one sweet taste improving additive, isomalto-oligosaccharides, and at least one other carbohydrate;

202. at least one sweet taste improving additive, isomaltose, and at least one other carbohydrate;

203. at least one sweet taste improving additive, isomaltotriose, and at least one other carbohydrate;

204. at least one sweet taste improving additive, panose, and at least one other carbohydrate;

205. at least one sweet taste improving additive, xylo-oligosaccharides, and at least one other carbohydrate;

206. at least one sweet taste improving additive, xylotriose, and at least one other carbohydrate;

207. at least one sweet taste improving additive, xylobiose, and at least one other carbohydrate;

208. at least one sweet taste improving additive, gentio-oligoscaccharides, and at least one other carbohydrate;

209. at least one sweet taste improving additive, gentiobiose, and at least one other carbohydrate;

210. at least one sweet taste improving additive, gentiotriose, and at least one other carbohydrate;

211. at least one sweet taste improving additive, gentiotetraose, and at least one other carbohydrate;

212. at least one sweet taste improving additive, sorbose, and at least one other carbohydrate;

213. at least one sweet taste improving additive, nigero-oligosaccharides, and at least one other carbohydrate;

214. at least one sweet taste improving additive, palatinose oligosaccharides, and at least one other carbohydrate;

215. at least one sweet taste improving additive, fucose, and at least one other carbohydrate;

216. at least one sweet taste improving additive, fructooligosaccharides, and at least one other carbohydrate;

217. at least one sweet taste improving additive, kestose, and at least one other carbohydrate;

218. at least one sweet taste improving additive, nystose, and at least one other carbohydrate;

219. at least one sweet taste improving additive, maltotetraol, and at least one other carbohydrate;

220. at least one sweet taste improving additive, maltotriol, and at least one other carbohydrate;

221. at least one sweet taste improving additive, malto-oligosaccharides, and at least one other carbohydrate;

222. at least one sweet taste improving additive, maltotriose, and at least one other carbohydrate;

223. at least one sweet taste improving additive, maltotetraose, and at least one other carbohydrate;

224. at least one sweet taste improving additive, maltopentaose, and at least one other carbohydrate;

225. at least one sweet taste improving additive, maltohexaose, and at least one other carbohydrate;

226. at least one sweet taste improving additive, maltoheptaose, and at least one other carbohydrate;

227. at least one sweet taste improving additive, lactulose, and at least one other carbohydrate;

228. at least one sweet taste improving additive, melibiose, and at least one other carbohydrate;

229. at least one sweet taste improving additive, raffinose, and at least one other carbohydrate;

230. at least one sweet taste improving additive, rhamnose, and at least one other carbohydrate;

231. at least one sweet taste improving additive, ribose, and at least one other carbohydrate;

232. at least one sweet taste improving additive, isomerized liquid sugars, and at least one other carbohydrate;

233. at least one sweet taste improving additive, high fructose corn syrup (e.g. HFCS55 and HFCS42) or starch syrup, and at least one other carbohydrate;

234. at least one sweet taste improving additive, coupling sugars, and at least one other carbohydrate;

235. at least one sweet taste improving additive, soybean oligosaccharides, and at least one other carbohydrate; and

236. at least one sweet taste improving additive, glucose syrup, and at least one other carbohydrate.

In another embodiment, the pharmaceutical composition comprises at least one natural and/or synthetic high-potency sweetener and a pharmaceutically active substance in combination with a plurality of sweet taste improving additives, desirably 3 or more sweet taste improving additives, and even more desirably 4 or more sweet taste improving additives, wherein each sweet taste improving additive is present in an amount such that no one sweet taste improving additive imparts a substantial off taste to the sweetener

composition. In other words, the amounts of the sweet taste improving additives in the sweetener composition are balanced so that no one sweet taste improving additive imparts a substantial off taste to the sweetener composition.

According to a particular embodiment of this invention, the sweetener composition provided herein comprises at least one sweet taste improving composition in the sweetener composition in an amount effective for the sweetener composition to impart an osmolarity of at least 10 mOsmoles/L to an aqueous solution of the sweetener composition, wherein the at least one natural and/or synthetic high-potency sweetener is present in the aqueous solution in an amount sufficient to impart a maximum sweetness intensity equivalent to that of a 10% aqueous solution of sucrose by weight. As used herein, "mOsmoles/L" refers to milliosmoles per liter. According to another embodiment, the sweetener composition comprises at least one sweet taste improving composition in an amount effective for the sweetener composition to impart an osmolarity of 10 to 500 mOsmoles/L, preferably 25 to 500 mOsmoles/L preferably, more preferably 100 to 500 mOsmoles/L, more preferably 200 to 500 mOsmoles/L, and still more preferably 300 to 500 mOsmoles/L to an aqueous solution of the sweetener composition, wherein the at least one natural and/or synthetic high-potency sweetener is present in the aqueous solution in an amount sufficient to impart a maximum sweetness intensity equivalent to that of a 10% aqueous solution of sucrose by weight. Wherein a plurality of sweet taste improving compositions are combined with at least one natural and/or synthetic high-potency sweetener, the osmolarity imparted is that of the total combination of the plurality of sweet taste improving compositions.

Osmolarity refers to the measure of osmoles of solute per liter of solution, wherein osmole is equal to the number of moles of osmotically active particles in an ideal solution (e.g., a mole of glucose is one osmole), whereas a mole of sodium chloride is two osmoles (one mole of sodium and one mole of chloride). Thus, in order to improve in the quality of taste of the sweetener composition, the osmotically active compounds or the compounds which impart osmolarity must not introduce significant off taste to the formulation.

In one embodiment, suitable sweet taste improving carbohydrate additives for the present invention have a molecular weight less than or equal to 500 and desirably have a molecular weight from 50 to 500. In particular embodiments, suitable carbohydrates with

a molecular weight less than or equal to 500 include, but are not limited to, sucrose, fructose, glucose, maltose, lactose, mannose, galactose, and tagatose. Generally, in accordance with desirable embodiments of this invention, a sweet taste improving carbohydrate additive is present in the sweetener compositions in an amount from about 1,000 to about 100,000 ppm. (Throughout this specification, the term ppm means parts per million by weight or volume. For example, 500 ppm means 500 mg in a liter.) In accordance with other desirable embodiments of this invention, a sweet taste improving carbohydrate additive is present in the sweetened compositions in an amount from about 2,500 to about 10,000 ppm. In another embodiment, suitable sweet taste improving carbohydrate additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, sweet taste improving carbohydrate additives with a molecular weight ranging from about 50 to about 500.

In one embodiment, suitable sweet taste improving polyol additives have a molecular weight less than or equal to 500 and desirably have a molecular weight from 76 to 500. In particular embodiments, suitable sweet taste improving polyol additives with a molecular weight less than or equal to 500 include, but are not limited to, erythritol, glycerol, and propylene glycol. Generally, in accordance with desirable embodiments of this invention, a sweet taste improving polyol additive is present in the sweetener compositions in an amount from about 100 ppm to about 80,000 ppm. In accordance with other desirable embodiments of this invention, a sweet taste improving polyol additive is present in sweetened compositions in an amount from about 400 to about 80,000 ppm. In a sub-embodiment, suitable sweet taste improving polyol additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, sweet taste improving polyol additives with a molecular weight ranging from about 76 to about 500.

In accordance with still other desirable embodiments of this invention, a sweet taste improving polyol additive is present in sweetener compositions in an amount from about 400 to about 80,000 ppm of the total sweetener composition, more particularly from about about 5,000 to about 40,000 ppm, and still more particularly from about 10,000 to about 35,000 ppm. Desirably, the at least one natural and/or synthetic high-potency sweetener and at least one sweet taste improving polyol additive are present in the

sweetener composition in a ratio from about 1:4 to about 1:800, respectively; more particularly from about 1:20 to about 1:600; even more particularly from about 1:50 to about 1:300; and still more particularly from about 1:75 to about 1:150.

Generally, in accordance with another embodiment of this invention, a suitable sweet taste improving alcohol additive is present in the sweetener compositions in an amount from about 625 to about 10,000 ppm. In another embodiment, suitable sweet taste improving alcohol additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, sweet taste improving alcohol additives with a molecular weight ranging from about 46 to about 500. A non-limiting example of sweet taste improving alcohol additive with a molecular weight ranging from about 46 to about 500 includes ethanol.

In one embodiment, suitable sweet taste improving amino acid additives have a molecular weight of less than or equal to 250 and desirably have a molecular weight from 75 to 250. In particular embodiments, suitable sweet taste improving amino acid additives with a molecular weight less than or equal to 250 include, but are not limited to, glycine, alanine, serine, valine, leucine, isoleucine, proline, theanine, and threonine. Preferred sweet taste improving amino acid additives include those which are sweet tasting at high concentrations, but desirably are present in embodiments of this invention at amounts below or above their sweetness taste detection threshold. Even more preferred are mixtures of sweet taste improving amino acid additives at amounts below or above their sweetness taste detection threshold. Generally, in accordance with desirable embodiments of this invention, a sweet taste improving amino acid additive is present in the sweetener compositions in an amount from about 100 ppm to about 25,000 ppm, more particularly from about 1,000 to about 10,000 ppm, and still more particularly from about 2,500 to about 5,000 ppm. In accordance with other desirable embodiments of this invention, a sweet taste improving amino acid additive is present in the sweetened compositions in an amount from about 250 ppm to about 7,500 ppm. In a sub-embodiment, suitable sweet taste improving amino acid additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, sweet taste improving amino acid additives with a molecular weight ranging from about 75 to about 250.

Generally, in accordance with yet another embodiment of this invention, a suitable sweet taste improving amino acid salt additive is present in the sweetener compositions in an amount from about 25 to about 10,000 ppm, more particularly from about 1,000 to about 7,500 ppm, and still more particularly from about 2,500 to about 5,000 ppm. In another embodiment, suitable sweet taste improving amino acid salt additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, sweet taste improving amino acid salt additives with a molecular weight ranging from about 75 to about 300. Non-limiting examples of sweet taste improving amino acid salt additives with a molecular weight ranging from about 75 to about 300 include salts of glycine, alanine, serine, theanine, and threonine.

Generally, in accordance with still another embodiment of this invention, a suitable sweet taste improving protein or protein hydroyslate additive is present in the sweetener compositions in an amount from about 200 to about 10,000 ppm. In another embodiment, suitable sweet taste improving protein or protein hydrolysate additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, sweet taste improving protein or protein hydrolysate additives with a molecular weight ranging from about 75 to about 300. Non-limiting examples of sweet taste improving protein or protein hydrolysate additives with a molecular weight ranging from about 75 to about 300 include proteins or protein hydrolysates containing glycine, alanine, serine, and threonine.

Generally, in accordance with another embodiment of this invention, a suitable sweet taste improving inorganic acid additive is present in the sweetener compositions in an amount from about 25 to about 5,000 ppm. In another embodiment, suitable sweet taste improving inorganic acid additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, phosphoric acid, HCl, and H_2SO_4 and any other inorganic acid additives which are safe for human or animal consumption when used in a generally acceptable range. In a sub-embodiment, suitable sweet taste improving inorganic acid additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, sweet taste improving inorganic acid additives with a molecular weight range from about 36 to about 98.

Generally, in accordance with still another embodiment of this invention, a suitable sweet taste improving inorganic acid salt additive is present in the sweetener compositions in an amount from about 25 to about 5,000 ppm. In another embodiment, suitable sweet taste improving inorganic acid salt additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, salts of inorganic acids, for example sodium, potassium, calcium, and magnesium salts of phosphoric acid, and any other alkali or alkaline earth metal salts of other inorganic acids (e.g., sodium bisulfate) which are safe for human or animal consumption when used in a generally acceptable range. In a sub-embodiment, suitable suitable sweet taste improving inorganic acid salt additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, sweet taste improving inorganic acid salt additives with a molecular weight range from about 58 to about 120.

Generally, in accordance with still another embodiment of this invention, a suitable sweet taste improving organic acid additive is present in the sweetener compositions in an amount from about 10 to about 5,000 ppm. In another embodiment, suitable sweet taste improving organic acid additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, creatine, citric acid, malic acid, succinic acid, hydroxycitric acid, tartaric acid, fumaric acid, gluconic acid, glutaric acid, adipic acid, and any other sweet taste improving organic acid additives which are safe for human or animal consumption when used in a generally acceptable range. In one embodiment, the sweet taste improving organic acid additive comprises a molecular weight range from about 60 to about 208.

Generally, in accordance with still another embodiment of this invention, a suitable sweet taste improving organic acid salt additive is present in the sweetener compositions in an amount from about 20 to about 10,000 ppm. In another embodiment, suitable sweet taste improving organic acid salt additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, salts of sweet taste improving organic acid additives, such as sodium, potassium, calcium, magnesium, and other alkali or alkaline metal salts of citric acid, malic acid, tartaric acid, fumaric acid, gluconic acid, glutaric acid, adipic acid, hydroxycitric acid, succinic acid, and salts of any other sweet taste improving organic acid

additives which are safe for human or animal consumption when used in a generally acceptable range. In one embodiment, the sweet taste improving organic acid salt additive comprises a molecular weight range from about 140 to about 208.

Generally, in accordance with yet another embodiment of this invention, a suitable sweet taste improving organic base salt additive is present in the sweetener compositions in an amount from about 10 to about 5,000 ppm. In another embodiment, suitable sweet taste improving organic base salt additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, inorganic and organic acid salts of organic bases such as glucosamine salts, choline salts, and guanidine salts.

Generally, in accordance with yet another embodiment of this invention, a suitable sweet taste improving astringent additive is present in the sweetener compositions in an amount from about 25 to about 1,000 ppm. In another embodiment, suitable sweet taste improving astringent additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, tannic acid, tea polyphenols, catechins, aluminum sulfate, $AlNa(SO_4)_2$, $AlK(SO_4)_2$ and other forms of alum.

Generally, in accordance with yet another embodiment of this invention, a suitable sweet taste improving nucleotide additive is present in the sweetener compositions in an amount from about 5 to about 1,000 ppm. In another embodiment, suitable sweet taste improving nucleotide additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, adenosine monophosphate.

Generally, in accordance with yet another embodiment of this invention, a suitable sweet taste improving polyamino acid additive is present in the sweetener compositions in an amount from about 30 to about 2,000 ppm. In another embodiment, suitable sweet taste improving polyamino acid additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, poly-L-lysine (e.g., poly-L-α-lysine or poly-L-ε-lysine), poly-L-ornithine (e.g., poly-L-α-ornithine or poly-L-ε-ornithine), and poly-L-arginine.

Generally, in accordance with yet another embodiment of this invention, a suitable sweet taste improving polymer additive is present in the sweetener compositions in an amount from about 30 to about 2,000 ppm. In another embodiment, suitable sweet taste improving polymer additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, chitosan, sodium hexametaphosphate and its salts, pectin, hydrocolloids such as gum acacia senegal, propylene glycol, polyethylene glycol, and poly(ethylene glycol methyl ether).

Generally, in accordance with yet another embodiment of this invention, a suitable sweet taste improving surfactant additive is present in the sweetener compositions in an amount from about 1 to about 5,000 ppm. In another embodiment, suitable sweet taste improving surfactant additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, polysorbates, choline chloride, sodium taurocholate, lecithins, sucrose oleate esters, sucrose stearate esters, sucrose palmitate esters, and sucrlose laurate esters.

Generally, in accordance with yet another embodiment of this invention, a suitable sweet taste improving flavonoid additive is present in the sweetener compositions in an amount from about 0.1 to about 1,000 ppm. In another embodiment, suitable sweet taste improving flavonoid additives for imparting osmolarities ranging from about 10 mOsmoles/L to about 500 mOsmoles/L to a sweetenable composition include, but are not limited to, naringin, catechins, rutins, neohesperidin, and neohesperidin dihydrochalcone.

In a preferred embodiment, non-limiting examples of sweet taste improving compositions enhancing the natural and/or synthetic high-potency sweetener's osmotic taste to be more sugar-like include sweet taste improving carbohydrate additives, sweet taste improving alcohol additives, sweet taste improving polyol additives, sweet taste improving amino acid additives, sweet taste improving amino acid salt additives, sweet taste improving inorganic acid salt additives, sweet taste improving polymer additives, and sweet taste improving protein or protein hydrolysate additives.

In another embodiment, suitable sweet taste improving carbohydrate additives for improving the osmotic taste of the natural and/or synthetic high-potency sweetener to be more sugar-like include, but are not limited to, sweet taste improving carbohydrate additives with a molecular weight ranging from about 50 to about 500. Non-limiting

examples of sweet taste improving carbohydrate additives with a molecular weight ranging from about 50 to about 500 include sucrose, fructose, glucose, maltose, lactose, mannose, galactose, ribose, rhamnose, trehalose, HFCS, and tagatose.

In another embodiment, suitable sweet taste improving polyol additives for improving the osmotic taste of natural and/or synthetic high-potency sweetener to be more sugar-like include, but are not limited to, sweet taste improving polyol additives with a molecular weight ranging from about 76 to about 500. Non-limiting examples of sweet taste improving polyol additives with a molecular weight ranging from about 76 to about 500 include erythritol, glycerol, and propylene glycol. In a sub-embodiment, other suitable sweet taste improving polyol additives include sugar alcohols.

In another embodiment, suitable sweet taste improving alcohol additives for improving the osmotic taste of natural and/or synthetic high-potency sweetener to be more sugar-like include, but are not limited to, sweet taste improving alcohol additives with a molecular weight ranging from about 46 to about 500. A non-limiting example of sweet taste improving alcohol additive with a molecular weight ranging from about 46 to about 500 includes ethanol.

In another embodiment, suitable sweet taste improving amino acid additives for improving the osmotic taste of natural and/or synthetic high-potency sweetener to be more sugar-like include, but are not limited to, sweet taste improving amino acid additives with a molecular weight ranging from about 75 to about 250. Non-limiting examples of sweet taste improving amino acid additives with a molecular weight ranging from about 75 to about 250 include glycine, alanine, serine, leucine, valine, isoleucine, proline, hydroxyproline, glutamine, theanine, and threonine.

In another embodiment, suitable sweet taste improving amino acid salt additives for improving the osmotic taste of natural and/or synthetic high-potency sweetener to be more sugar-like include, but are not limited to, sweet taste improving amino acid salt additives with a molecular weight ranging from about 75 to about 300. Non-limiting examples of sweet taste improving amino acid salt additives with a molecular weight ranging from about 75 to about 300 include salts of glycine, alanine, serine, leucine, valine, isoleucine, proline, hydroxyproline, glutamine, theanine, and threonine.

In another embodiment, suitable sweet taste improving protein or protein hydrolysate additives for improving the osmotic taste of natural and/or synthetic high-potency sweetener to be more sugar-like include, but are not limited to, sweet taste improving protein or protein hydrolysate additives with a molecular weight ranging from about 75 to about 300. Non-limiting examples of sweet taste improving protein or protein hydrolysate additives with a molecular weight ranging from about 75 to about 300 include protein or protein hydrolysates containing glycine, alanine, serine, leucine, valine, isoleucine, proline, and threonine.

In another embodiment, suitable sweet taste improving inorganic acid salt additives for improving the osmotic taste of natural and/or synthetic high-potency sweetener to be more sugar-like include, but are not limited to, sodium chloride, potassium chloride, magnesium chloride, KH_2PO_4 and NaH_2PO_4. Suitable sweet taste improving inorganic acid salt additives for improving the osmotic taste may comprise a molecular weight from about 58 to about 120.

In another embodiment, suitable sweet taste improving bitter additives for improving the osmotic taste of the natural and/or synthetic high-potency sweetener to be more sugar-like include, but are not limited to, caffeine, quinine, urea, quassia, tannic acid, and naringin.

IV. Pharmaceutical Compositions

In one embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving nucleotide additive chosen from inosine monophosphate ("IMP"), guanosine monophosphate ("GMP"), adenosine monophosphate ("AMP"), cytosine monophosphate (CMP), uracil monophosphate (UMP), inosine diphosphate, guanosine diphosphate, adenosine diphosphate, cytosine diphosphate, uracil diphosphate, inosine triphosphate, guanosine triphosphate, adenosine triphosphate, cytosine triphosphate, uracil triphosphate, nucleosides thereof, nucleic acid bases thereof, or salts thereof.

In one embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving carbohydrate additive chosen from tagatose, trehalose, galactose, rhamnose, cyclodextrin (e.g., α-cyclodextrin,

β-cyclodextrin, and γ-cyclodextrin), maltodextrin (including resistant maltodextrins such as Fibersol-2™), dextran, sucrose, glucose, ribulose, fructose, threose, arabinose, xylose, lyxose, allose, altrose, mannose, idose, lactose, maltose, invert sugar, isotrehalose, neotrehalose, palatinose or isomaltulose, erythrose, deoxyribose, gulose, idose, talose, erythrulose, xylulose, psicose, turanose, cellobiose, amylopectin, glucosamine, mannosamine, fucose, glucuronic acid, gluconic acid, glucono-lactone, abequose, galactosamine, beet oligosaccharides, isomalto-oligosaccharides (isomaltose, isomaltotriose, panose and the like), xylo-oligosaccharides (xylotriose, xylobiose and the like), gentio-oligoscaccharides (gentiobiose, gentiotriose, gentiotetraose and the like), sorbose, nigero-oligosaccharides, palatinose oligosaccharides, fucose, fructooligosaccharides (kestose, nystose and the like), maltotetraol, maltotriol, malto-oligosaccharides (maltotriose, maltotetraose, maltopentaose, maltohexaose, maltoheptaose and the like), lactulose, melibiose, raffinose, rhamnose, ribose, isomerized liquid sugars such as high fructose corn/starch syrup (e.g., HFCS55, HFCS42, HFCS90), coupling sugars, soybean oligosaccharides, or glucose syrup.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving polyol additive chosen from erythritol, maltitol, mannitol, sorbitol, lactitol, xylitol, inositol, isomalt, propylene glycol, glycerol (glycerine), threitol, galactitol, palatinose, reduced isomalto-oligosaccharides, reduced xylo-oligosaccharides, reduced gentio-oligosaccharides, reduced maltose syrup, or reduced glucose syrup.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving amino acid additive chosen from aspartic acid, arginine, glycine, glutamic acid, proline, threonine, theanine, cysteine, cystine, alanine, valine, tyrosine, leucine, isoleucine, asparagine, serine, lysine, histidine, ornithine, methionine, carnitine, aminobutyric acid (alpha-, beta-, and gamma-isomers), glutamine, hydroxyproline, taurine, norvaline, sarcosine, or salts thereof.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving polyamino acid additive

chosen from poly-L-aspartic acid, poly-L-lysine (e.g., poly-L-α-lysine or poly-L-ε-lysine), poly-L-ornithine (e.g., poly-L-α-ornithine or poly-L-ε-ornithine), poly-L-arginine, other polymeric forms of amino acids, or salts thereof.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving sugar acid additive chosen from aldonic, uronic, aldaric, alginic, gluconic, glucuronic, glucaric, galactaric, galacturonic, or salts thereof.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving organic acid additive chosen from C2-C30 carboxylic acids, substituted hydroxyl C1-C30 carboxylic acids, benzoic acid, substituted benzoic acids (e.g., 2,4-dihydroxybenzoic acid), substituted cinnamic acids, hydroxyacids, substituted hydroxybenzoic acids, substituted cyclohexyl carboxylic acids, tannic acid, lactic acid, tartaric acid, citric acid, gluconic acid, glucoheptonic acids, glutaric acid, creatine, adipic acid, hydroxycitric acid, malic acid, fruitaric acid, fumaric acid, maleic acid, succinic acid, chlorogenic acid, salicylic acid, caffeic acid, bile acids, acetic acid, ascorbic acid, alginic acid, erythorbic acid, polyglutamic acid, or salts thereof.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving inorganic acid additive chosen from phosphoric acid, phosphorous acid, polyphosphoric acid, hydrochloric acid, sulfuric acid, carbonic acid, sodium dihydrogen phosphate, or salts thereof.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving bitter compound additive chosen from caffeine, quinine, urea, bitter orange oil, naringin, quassia, or salts thereof.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving flavorant additive chosen from vanillin, vanilla extract, mango extract, cinnamon, citrus, coconut, ginger,

viridiflorol, almond, menthol, grape skin extract, or grape seed extract. In another particular embodiment, the at least one sweet taste improving flavorant additive comprises a proprietary sweetener chosen from Döhler™ Natural Flavoring Sweetness Enhancer K14323 (Döhler™, Darmstadt, Germany), Symrise™ Natural Flavor Mask for Sweeteners 161453 or 164126 (Symrise™, Holzminden, Germany), Natural Advantage™ Bitterness Blockers 1, 2, 9 or 10 (Natural Advantage™, Freehold, New Jersey, U.S.A.), or Sucramask™ (Creative Research Management, Stockton, California, U.S.A.)

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving polymer additive chosen from chitosan, pectin, pectic, pectinic, polyuronic, polygalacturonic acid, starch, food hydrocolloid or crude extracts thereof (e.g., gum acacia senegal, gum acacia seyal, carageenan), poly-L-lysine (e.g., poly-L-α-lysine or poly-L-ε-lysine), polyornithine (e.g., poly-L-α-ornithine or poly-ε-ornithine), polypropylene glycol, polyethylene glycol, poly(ethylene glycol methyl ether), polyarginine, polyaspartic acid, polyglutamic acid, polyethyleneimine, alginic acid, sodium alginate, propylene glycol alginate, sodium polyethyleneglycolalginate, sodium hexametaphosphate and its salts, or other cationic and anionic polymers.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving protein hydrolysate additive chosen from bovine serum albumin (BSA), whey protein (including fractions or concentrates thereof such as 90% instant whey protein isolate, 34% whey protein, 50% hydrolyzed whey protein, and 80% whey protein concentrate), soluble rice protein, soy protein, protein isolates, protein hydrolysates, reaction products of protein hydrolysates, glycoproteins, and/or proteoglycans containing amino acids (e.g., glycine, alanine, serine, threonine, theanine, asparagine, glutamine, arginine, valine, isoleucine, leucine, norvaline, methionine, proline, tyrosine, hydroxyproline, or the like).

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving surfactant additive chosen from polysorbates (e.g., polyoxyethylene sorbitan monooleate (polysorbate 80),

polysorbate 20, polysorbate 60), sodium dodecylbenzenesulfonate, dioctyl sulfosuccinate or dioctyl sulfosuccinate sodium, sodium dodecyl sulfate, cetylpyridinium chloride, hexadecyltrimethylammonium bromide, sodium cholate, carbamoyl, choline chloride, sodium glycocholate, sodium taurocholate, sodium taurodeoxycholate, lauric arginate, sodium stearoyl lactylate, lecithins, sucrose oleate esters, sucrose stearate esters, sucrose palmitate esters, sucrose laurate esters, and other emulsifiers, or the like.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving flavonoid additive chosen from catechins, polyphenols, rutins, neohesperidin, naringin, neohesperidin dihydrochalcone, or the like.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with ethanol.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving astringent compound additive chosen from tannic acid, europium chloride ($EuCl_3$), gadolinium chloride ($GdCl_3$), terbium chloride ($TbCl_3$), alum, tannic acid, and polyphenols (e.g., tea polyphenol).

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving inorganic salt additive chosen from sodium chloride, potassium chloride, sodium dihydrogen phosphate, sodium sulfate, potassium citrate, europium chloride ($EuCl_3$), gadolinium chloride ($GdCl_3$), terbium chloride ($TbCl_3$), magnesium sulfate, magnesium phosphate, alum, magnesium chloride, mono-, di-, tri-basic sodium or potassium salts of phosphoric acid, salts of hydrochloric acid, sodium carbonate, sodium bisulfate, or sodium bicarbonate.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving organic salt additive chosen from choline chloride, gluconic acid sodium salt, gluconic acid potassium salt,

guanidine HCl, amiloride HCl, glucosamine HCl, monosodium glutamate (MSG), adenosine monophosphate salt, magnesium gluconate, potassium tartrate, and sodium tartrate.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving nucleotide additive, at least one sweet taste improving carbohydrate additive, and at least one sweet taste improving amino acid additive; wherein the at least one nucleotide additive is chosen from inosine monophosphate ("IMP"), guanosine monophosphate ("GMP"), adenosine monophosphate ("AMP"), cytosine monophosphate (CMP), uracil monophosphate (UMP), inosine diphosphate, guanosine diphosphate, adenosine diphosphate, cytosine diphosphate, uracil diphosphate, inosine triphosphate, guanosine triphosphate, adenosine triphosphate, cytosine triphosphate, uracil triphosphate, nucleosides thereof, nucleic acid bases thereof, or salts thereof; wherein the at least one carbohydrate additive is chosen from tagatose, trehalose, galactose, rhamnose, cyclodextrin (e.g., α-cyclodextrin, β-cyclodextrin, and γ-cyclodextrin), maltodextrin (including resistant maltodextrins such as Fibersol-2™), dextran, sucrose, glucose, ribulose, fructose, threose, arabinose, xylose, lyxose, allose, altrose, mannose, idose, lactose, maltose, invert sugar, isotrehalose, neotrehalose, palatinose or isomaltulose, erythrose, deoxyribose, gulose, idose, talose, erythrulose, xylulose, psicose, turanose, cellobiose, amylopectin, glucosamine, mannosamine, fucose, glucuronic acid, gluconic acid, glucono-lactone, abequose, galactosamine, beet oligosaccharides, isomalto-oligosaccharides (isomaltose, isomaltotriose, panose and the like), xylo-oligosaccharides (xylotriose, xylobiose and the like), gentio-oligoscaccharides (gentiobiose, gentiotriose, gentiotetraose and the like), sorbose, nigero-oligosaccharides, palatinose oligosaccharides, fucose, fructooligosaccharides (kestose, nystose and the like), maltotetraol, maltotriol, malto-oligosaccharides (maltotriose, maltotetraose, maltopentaose, maltohexaose, maltoheptaose and the like), lactulose, melibiose, raffinose, rhamnose, ribose, isomerized liquid sugars such as high fructose corn/starch syrup (e.g., HFCS55, HFCS42, HFCS90), coupling sugars, soybean oligosaccharides, or glucose syrup; and wherein the at least one amino acid additive is chosen from aspartic acid, arginine, glycine, glutamic acid, proline, threonine, theanine, cysteine, cystine, alanine, valine, tyrosine, leucine, isoleucine,

asparagine, serine, lysine, histidine, ornithine, methionine, carnitine, aminobutyric acid (alpha-, beta-, and gamma-isomers), glutamine, hydroxyproline, taurine, norvaline, sarcosine, or salts thereof.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving nucleotide additive and at least one sweet taste improving carbohydrate additive; wherein the at least one nucleotide additive is chosen from inosine monophosphate ("IMP"), guanosine monophosphate ("GMP"), adenosine monophosphate ("AMP"), cytosine monophosphate (CMP), uracil monophosphate (UMP), inosine diphosphate, guanosine diphosphate, adenosine diphosphate, cytosine diphosphate, uracil diphosphate, inosine triphosphate, guanosine triphosphate, adenosine triphosphate, cytosine triphosphate, uracil triphosphate, nucleosides thereof, nucleic acid bases thereof, or salts thereof; and wherein the at least one carbohydrate additive is chosen from tagatose, trehalose, galactose, rhamnose, cyclodextrin (e.g., α-cyclodextrin, β-cyclodextrin, and γ-cyclodextrin), maltodextrin (including resistant maltodextrins such as Fibersol-2™), dextran, sucrose, glucose, ribulose, fructose, threose, arabinose, xylose, lyxose, allose, altrose, mannose, idose, lactose, maltose, invert sugar, isotrehalose, neotrehalose, palatinose or isomaltulose, erythrose, deoxyribose, gulose, idose, talose, erythrulose, xylulose, psicose, turanose, cellobiose, amylopectin, glucosamine, mannosamine, fucose, glucuronic acid, gluconic acid, glucono-lactone, abequose, galactosamine, beet oligosaccharides, isomalto-oligosaccharides (isomaltose, isomaltotriose, panose and the like), xylo-oligosaccharides (xylotriose, xylobiose and the like), gentio-oligoscaccharides (gentiobiose, gentiotriose, genetiotetraose and the like), sorbose, nigero-oligosaccharides, palatinose oligosaccharides, fucose, fructooligosaccharides (kestose, nystose and the like), maltotetraol, maltotriol, malto-oligosaccharides (maltotriose, maltotetraose, maltopentaose, maltohexaose, maltoheptaose and the like), lactulose, melibiose, raffinose, rhamnose, ribose, isomerized liquid sugars such as high fructose corn/starch syrup (e.g., HFCS55, HFCS42, HFCS90), coupling sugars, soybean oligosaccharides, or glucose syrup.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving nucleotide additive and at least one sweet taste improving polyol additive; wherein the at least one nucleotide additive is chosen from inosine monophosphate ("IMP"), guanosine monophosphate ("GMP"), adenosine monophosphate ("AMP"), cytosine monophosphate (CMP), uracil monophosphate (UMP), inosine diphosphate, guanosine diphosphate, adenosine diphosphate, cytosine diphosphate, uracil diphosphate, inosine triphosphate, guanosine triphosphate, adenosine triphosphate, cytosine triphosphate, uracil triphosphate, nucleosides thereof, nucleic acid bases thereof, or salts thereof; and wherein the at least one polyol additive is chosen from erythritol, maltitol, mannitol, sorbitol, lactitol, xylitol, inositol, isomalt, propylene glycol, glycerol (glycerine), threitol, galactitol, palatinose, reduced isomalto-oligosaccharides, reduced xylo-oligosaccharides, reduced gentio-oligosaccharides, reduced maltose syrup, or reduced glucose syrup.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving nucleotide additive and at least one sweet taste improving amino acid; wherein the at least one nucleotide additive is chosen from inosine monophosphate ("IMP"), guanosine monophosphate ("GMP"), adenosine monophosphate ("AMP"), cytosine monophosphate (CMP), uracil monophosphate (UMP), inosine diphosphate, guanosine diphosphate, adenosine diphosphate, cytosine diphosphate, uracil diphosphate, inosine triphosphate, guanosine triphosphate, adenosine triphosphate, cytosine triphosphate, uracil triphosphate, nucleosides thereof, nucleic acid bases thereof, or salts thereof; and wherein the at least one amino acid additive is chosen from aspartic acid, arginine, glycine, glutamic acid, proline, threonine, theanine, cysteine, cystine, alanine, valine, tyrosine, leucine, isoleucine, asparagine, serine, lysine, histidine, ornithine, methionine, carnitine, aminobutyric acid (alpha-, beta-, and gamma-isomers), glutamine, hydroxyproline, taurine, norvaline, sarcosine, or salts thereof.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving carbohydrate additive, at

least one sweet taste improving polyol additive, and at least one sweet taste improving amino acid additive; wherein the at least one carbohydrate additive is chosen from tagatose, trehalose, galactose, rhamnose, cyclodextrin (e.g., α-cyclodextrin, β-cyclodextrin, and γ-cyclodextrin), maltodextrin (including resistant maltodextrins such as Fibersol-2™), dextran, sucrose, glucose, ribulose, fructose, threose, arabinose, xylose, lyxose, allose, altrose, mannose, idose, lactose, maltose, invert sugar, isotrehalose, neotrehalose, palatinose or isomaltulose, erythrose, deoxyribose, gulose, idose, talose, erythrulose, xylulose, psicose, turanose, cellobiose, amylopectin, glucosamine, mannosamine, fucose, glucuronic acid, gluconic acid, glucono-lactone, abequose, galactosamine, beet oligosaccharides, isomalto-oligosaccharides (isomaltose, isomaltotriose, panose and the like), xylo-oligosaccharides (xylotriose, xylobiose and the like), gentio-oligoscaccharides (gentiobiose, gentiotriose, gentiotetraose and the like), sorbose, nigero-oligosaccharides, palatinose oligosaccharides, fucose, fructooligosaccharides (kestose, nystose and the like), maltotetraol, maltotriol, malto-oligosaccharides (maltotriose, maltotetraose, maltopentaose, maltohexaose, maltoheptaose and the like), lactulose, melibiose, raffinose, rhamnose, ribose, isomerized liquid sugars such as high fructose corn/starch syrup (e.g., HFCS55, HFCS42, HFCS90), coupling sugars, soybean oligosaccharides, or glucose syrup; wherein the at least one polyol additive is chosen from erythritol, maltitol, mannitol, sorbitol, lactitol, xylitol, inositol, isomalt, propylene glycol, glycerol (glycerine), threitol, galactitol, palatinose, reduced isomalto-oligosaccharides, reduced xylo-oligosaccharides, reduced gentio-oligosaccharides, reduced maltose syrup, or reduced glucose syrup; and wherein the at least one amino acid additive is chosen from aspartic acid, arginine, glycine, glutamic acid, proline, threonine, theanine, cysteine, cystine, alanine, valine, tyrosine, leucine, isoleucine, asparagine, serine, lysine, histidine, ornithine, methionine, carnitine, aminobutyric acid (alpha-, beta-, and gamma-isomers), glutamine, hydroxyproline, taurine, norvaline, sarcosine, or salts thereof.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving carbohydrate additive and at least one sweet taste improving polyol additive; wherein the at least one carbohydrate additive is chosen from tagatose, trehalose, galactose, rhamnose,

cyclodextrin (e.g., α-cyclodextrin, β-cyclodextrin, and γ-cyclodextrin), maltodextrin (including resistant maltodextrins such as Fibersol-2™), dextran, sucrose, glucose, ribulose, fructose, threose, arabinose, xylose, lyxose, allose, altrose, mannose, idose, lactose, maltose, invert sugar, isotrehalose, neotrehalose, palatinose or isomaltulose, erythrose, deoxyribose, gulose, idose, talose, erythrulose, xylulose, psicose, turanose, cellobiose, amylopectin, glucosamine, mannosamine, fucose, glucuronic acid, gluconic acid, glucono-lactone, abequose, galactosamine, beet oligosaccharides, isomalto-oligosaccharides (isomaltose, isomaltotriose, panose and the like), xylo-oligosaccharides (xylotriose, xylobiose and the like), gentio-oligoscaccharides (gentiobiose, gentiotriose, gentiotetraose and the like), sorbose, nigero-oligosaccharides, palatinose oligosaccharides, fucose, fructooligosaccharides (kestose, nystose and the like), maltotetraol, maltotriol, malto-oligosaccharides (maltotriose, maltotetraose, maltopentaose, maltohexaose, maltoheptaose and the like), lactulose, melibiose, raffinose, rhamnose, ribose, isomerized liquid sugars such as high fructose corn/starch syrup (e.g., HFCS55, HFCS42, HFCS90), coupling sugars, soybean oligosaccharides, or glucose syrup; and wherein the at least one polyol additive is chosen from erythritol, maltitol, mannitol, sorbitol, lactitol, xylitol, inositol, isomalt, propylene glycol, glycerol (glycerine), threitol, galactitol, palatinose, reduced isomalto-oligosaccharides, reduced xylo-oligosaccharides, reduced gentio-oligosaccharides, reduced maltose syrup, or reduced glucose syrup.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving carbohydrate additive and at least one sweet taste improving amino acid additive; wherein the at least one carbohydrate additive is chosen from tagatose, trehalose, galactose, rhamnose, cyclodextrin (e.g., α-cyclodextrin, β-cyclodextrin, and γ-cyclodextrin), maltodextrin (including resistant maltodextrins such as Fibersol-2™), dextran, sucrose, glucose, ribulose, fructose, threose, arabinose, xylose, lyxose, allose, altrose, mannose, idose, lactose, maltose, invert sugar, isotrehalose, neotrehalose, palatinose or isomaltulose, erythrose, deoxyribose, gulose, idose, talose, erythrulose, xylulose, psicose, turanose, cellobiose, amylopectin, glucosamine, mannosamine, fucose, glucuronic acid, gluconic acid, glucono-lactone, abequose, galactosamine, beet oligosaccharides, isomalto-oligosaccharides (isomaltose, isomaltotriose, panose and the like), xylo-oligosaccharides

(xylotriose, xylobiose and the like), gentio-oligoscaccharides (gentiobiose, gentiotriose, gentiotetraose and the like), sorbose, nigero-oligosaccharides, palatinose oligosaccharides, fucose, fructooligosaccharides (kestose, nystose and the like), maltotetraol, maltotriol, malto-oligosaccharides (maltotriose, maltotetraose, maltopentaose, maltohexaose, maltoheptaose and the like), lactulose, melibiose, raffinose, rhamnose, ribose, isomerized liquid sugars such as high fructose corn/starch syrup (e.g., HFCS55, HFCS42, HFCS90), coupling sugars, soybean oligosaccharides, or glucose syrup; and wherein the at least one amino acid additive is chosen from aspartic acid, arginine, glycine, glutamic acid, proline, threonine, theanine, cysteine, cystine, alanine, valine, tyrosine, leucine, isoleucine, asparagine, serine, lysine, histidine, ornithine, methionine, carnitine, aminobutyric acid (alpha-, beta-, and gamma-isomers), glutamine, hydroxyproline, taurine, norvaline, sarcosine, or salts thereof.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving polyol additive and at least one sweet taste improving amino acid additive; wherein the at least one polyol additive is chosen from erythritol, maltitol, mannitol, sorbitol, lactitol, xylitol, inositol, isomalt, propylene glycol, glycerol (glycerin), threitol, galactitol, palatinose, reduced isomalto-oligosaccharides, reduced xylo-oligosaccharides, reduced gentio-oligosaccharides, reduced maltose syrup, or reduced glucose syrup; and wherein the at least one amino acid additive is chosen from aspartic acid, arginine, glycine, glutamic acid, proline, threonine, theanine, cysteine, cystine, alanine, valine, tyrosine, leucine, isoleucine, asparagine, serine, lysine, histidine, ornithine, methionine, carnitine, aminobutyric acid (alpha-, beta-, and gamma-isomers), glutamine, hydroxyproline, taurine, norvaline, sarcosine, or salts thereof.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving polyol additive and at least one sweet taste improving inorganic salt additive; wherein the at least one polyol additive is chosen from erythritol, maltitol, mannitol, sorbitol, lactitol, xylitol, inositol, isomalt, propylene glycol, glycerol (glycerin), threitol, galactitol, palatinose, reduced isomalto-oligosaccharides, reduced xylo-oligosaccharides, reduced gentio-

oligosaccharides, reduced maltose syrup, or reduced glucose syrup; and wherein the at least one inorganic salt additive is chosen from sodium chloride, potassium chloride, sodium dihydrogen phosphate, sodium sulfate, potassium citrate, europium chloride ($EuCl_3$), gadolinium chloride ($GdCl_3$), terbium chloride ($TbCl_3$), magnesium sulfate, alum, magnesium chloride, mono-, di-, tri-basic sodium or potassium salts of phosphoric acid, salts of hydrochloric acid, sodium carbonate, sodium bisulfate, or sodium bicarbonate.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving carbohydrate additive and at least one sweet taste improving inorganic salt additive; wherein the at least one carbohydrate additive is chosen from tagatose, trehalose, galactose, rhamnose, cyclodextrin (e.g., α-cyclodextrin, β-cyclodextrin, and γ-cyclodextrin), maltodextrin (including resistant maltodextrins such as Fibersol-2™), dextran, sucrose, glucose, ribulose, fructose, threose, arabinose, xylose, lyxose, allose, altrose, mannose, idose, lactose, maltose, invert sugar, isotrehalose, neotrehalose, palatinose or isomaltulose, erythrose, deoxyribose, gulose, idose, talose, erythrulose, xylulose, psicose, turanose, cellobiose, amylopectin, glucosamine, mannosamine, fucose, glucuronic acid, gluconic acid, glucono-lactone, abequose, galactosamine, beet oligosaccharides, isomalto-oligosaccharides (isomaltose, isomaltotriose, panose and the like), xylo-oligosaccharides (xylotriose, xylobiose and the like), gentio-oligoscaccharides (gentiobiose, gentiotriose, gentiotetraose and the like), sorbose, nigero-oligosaccharides, palatinose oligosaccharides, fucose, fructooligosaccharides (kestose, nystose and the like), maltotetraol, maltotriol, malto-oligosaccharides (maltotriose, maltotetraose, maltopentaose, maltohexaose, maltoheptaose and the like), lactulose, melibiose, raffinose, rhamnose, ribose, isomerized liquid sugars such as high fructose corn/starch syrup (e.g., HFCS55, HFCS42, HFCS90), coupling sugars, soybean oligosaccharides, or glucose syrup; and wherein the at least one inorganic salt additive is chosen from sodium chloride, potassium chloride, sodium dihydrogen phosphate, sodium sulfate, potassium citrate, europium chloride ($EuCl_3$), gadolinium chloride ($GdCl_3$), terbium chloride ($TbCl_3$), magnesium phosphate, magnesium sulfate, alum, magnesium chloride, mono-, di-, tri-basic sodium or potassium salts of phosphoric acid, salts of hydrochloric acid, sodium carbonate, sodium bisulfate, or sodium bicarbonate.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving carbohydrate additive, at least one sweet taste improving amino acid additive, and at least one sweet taste improving inorganic salt additive; wherein the at least one carbohydrate additive is chosen from tagatose, trehalose, galactose, rhamnose, cyclodextrin (e.g., α-cyclodextrin, β-cyclodextrin, and γ-cyclodextrin), maltodextrin (including resistant maltodextrins such as Fibersol-2™), dextran, sucrose, glucose, ribulose, fructose, threose, arabinose, xylose, lyxose, allose, altrose, mannose, idose, lactose, maltose, invert sugar, isotrehalose, neotrehalose, palatinose or isomaltulose, erythrose, deoxyribose, gulose, idose, talose, erythrulose, xylulose, psicose, turanose, cellobiose, amylopectin, glucosamine, mannosamine, fucose, glucuronic acid, gluconic acid, glucono-lactone, abequose, galactosamine, beet oligosaccharides, isomalto-oligosaccharides (isomaltose, isomaltotriose, panose and the like), xylo-oligosaccharides (xylotriose, xylobiose and the like), gentio-oligoscaccharides (gentiobiose, gentiotriose, gentiotetraose and the like), sorbose, nigero-oligosaccharides, palatinose oligosaccharides, fucose, fructooligosaccharides (kestose, nystose and the like), maltotetraol, maltotriol, malto-oligosaccharides (maltotriose, maltotetraose, maltopentaose, maltohexaose, maltoheptaose and the like), lactulose, melibiose, raffinose, rhamnose, ribose, isomerized liquid sugars such as high fructose corn/starch syrup (e.g., HFCS55, HFCS42, HFCS90), coupling sugars, soybean oligosaccharides, or glucose syrup; wherein the at least one amino acid additive is chosen from aspartic acid, arginine, glycine, glutamic acid, proline, threonine, theanine, cysteine, cystine, alanine, valine, tyrosine, leucine, isoleucine, asparagine, serine, lysine, histidine, ornithine, methionine, carnitine, aminobutyric acid (alpha-, beta-, and gamma-isomers), glutamine, hydroxyproline, taurine, norvaline, sarcosine, or salts thereof; and wherein the at least one inorganic salt additive is chosen from sodium chloride, potassium chloride, sodium sulfate, potassium citrate, europium chloride ($EuCl_3$), gadolinium chloride ($GdCl_3$), terbium chloride ($TbCl_3$), magnesium phosphate, magnesium sulfate, alum, magnesium chloride, mono-, di-, tri-basic sodium or potassium salts of phosphoric acid, salts of hydrochloric acid, sodium carbonate, sodium bisulfate, or sodium bicarbonate.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving polyol additive and at least one sweet taste improving polyamino acid additive; wherein the at least one polyol additive is chosen from erythritol, maltitol, mannitol, sorbitol, lactitol, xylitol, inositol, isomalt, propylene glycol, glycerol (glycerin), threitol, galactitol, palatinose, reduced isomalto-oligosaccharides, reduced xylo-oligosaccharides, reduced gentio-oligosaccharides, reduced maltose syrup, or reduced glucose syrup; and wherein the at least one polyamino acid additive is chosen from poly-L-aspartic acid, poly-L-lysine (e.g., poly-L-α-lysine or poly-L-ε-lysine), poly-L-ornithine (e.g., poly-L-α-ornithine or poly-L-ε-ornithine), poly-L-arginine, and other polymeric forms of amino acids, or salts thereof.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and at least one natural and/or synthetic high-potency sweetener in combination with at least one sweet taste improving protein or protein hydrolysate additive and at least one sweet taste improving inorganic salt additive; wherein the at least one sweet taste improving protein or protein hydrolysate additive is chosen from bovine serum albumin (BSA), whey protein (including fractions or concentrates thereof such as 90% instant whey protein isolate, 34% whey protein, 50% hydrolyzed whey protein, and 80% whey protein concentrate), soluble rice protein, soy protein, protein isolates, protein hydrolysates, reaction products of protein hydrolysates, glycoproteins, and/or proteoglycans containing amino acids (e.g., glycine, alanine, serine, threonine, theanine, asparagine, glutamine, arginine, valine, isoleucine, leucine, norvaline, methionine, proline, tyrosine, hydroxyproline, or the like), collagen (e.g., gelatin), partially hydrolyzed collagen (e.g., hydrolyzed fish collagen), and collagen hydrolysates (e.g., porcine collagen hydrolysate); and wherein the at least one sweet taste improving inorganic salt additive is chosen from sodium chloride, potassium chloride, sodium sulfate, potassium citrate, europium chloride ($EuCl_3$), gadolinium chloride ($GdCl_3$), terbium chloride ($TbCl_3$), magnesium phosphate, magnesium sulfate, alum, magnesium chloride, mono-, di-, tri-basic sodium or potassium salts of phosphoric acid, salts of hydrochloric acid, sodium carbonate, sodium bisulfate, or sodium bicarbonate.

In another embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and rebaudioside A in combination with at least one natural and/or synthetic high-potency sweetener other than rebaudioside-A and at least one sweet taste improving composition.

In another particular embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and rebaudioside A in combination with at least one synthetic high-potency sweetener, wherein the at least one synthetic high-potency sweetener functions as a sweet taste improving composition. Non-limiting examples of suitable sweet taste improving synthetic sweetener additives include sucralose, potassium acesulfame, aspartame, alitame, saccharin, neohesperidin dihydrochalcone, cyclamate, neotame, N-[N-[3-(3-hydroxy-4-methoxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, N-[N-[3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, salts thereof, and the like.

In one embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, cyclamate, saccharin, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving amino acid additive and at least one sweet taste improving polyol additive is provided. In a particular embodiment, the at least one sweet taste improving amino acid additive is present in an amount from about 100 ppm to about 25,000 ppm of the composition, and the at least one sweet taste improving polyol additive is present in an amount from about 400 to about 80,000 ppm of the composition. In a still more particular embodiment, the at least one sweet taste improving amino acid additive is glycine or alanine, and the at least one sweet taste improving polyol additive is erythritol.

In one embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving amino acid additive and

at least one sweet taste improving protein or protein hydrolysate additive is provided. In a particular embodiment, the at least one sweet taste improving amino acid additive is present in an amount from about 100 to about 25,000 ppm of the composition, and the at least one sweet taste improving protein or protein hydrolysate additive is present in an amount from about 200 ppm to about 50,000 ppm of the composition. In a still more particular embodiment, the at least one sweet taste improving amino acid additive is glycine or lysine, and the at least one sweet taste improving protein or protein hydrolysate additive is a protein, a hydrolysate, or a reaction product of a hydrolysate of a protein containing glycine, alanine, serine, leucine, valine, isoleucine, proline, or threonine.

In one embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving protein or protein hydrolysate additive and at least one sweet taste improving polyol additive is provided. In a particular embodiment, the at least one sweet taste improving protein or protein hydrolysate additive is present in an amount from about 200 ppm to about 50,000 ppm of the composition, and at least one sweet taste improving polyol additive is present in an amount from about 400 to about 80,000 ppm of the composition. In a still more particular embodiment, the at least one sweet taste improving protein or protein hydrolysate additive is a protein, a hydrolysate, or a reaction product of a hydrolysate of proteins containing glycine, alanine, serine, leucine, valine, isoleucine, proline, or threonine, and the at least one sweet taste improving polyol additive is erythritol.

In one embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving carbohydrate additive is provided. In a particular embodiment, the at least one sweet taste improving carbohydrate additive is present in an amount from about 1,000 to about 100,000 ppm of the

composition. In a still more particular embodiment, the sweetener composition comprises REBA and glucose, sucrose, HFCS, or D-fructose in an amount from about 10,000 ppm to about 80,000 ppm of the composition.

In one embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving polyol additive is provided. In a particular embodiment, the at least one sweet taste improving polyol additive is present in an amount from about 400 to about 80,000 ppm of the composition. In another particular embodiment, the at least one sweet taste improving polyol additive is present in an amount from about 5,000 to about 60,000 ppm of the composition. Non-limiting examples include a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with propylene glycol, erythritol, or combinations thereof.

In one embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA) (with at least 50 % REBA in a steviol glycoside mixture) in combination with at least one sweet taste improving polyol additive is provided. Desirably, the at least one sweet taste improving polyol additive comprises erythritol. In a particular embodiment of the sweetener composition, rebaudioside A is present in an amount from about 100 to about 3,000 ppm and the erythritol is present in an amount from about 400 to about 80,000 ppm of the total sweetener composition. In another embodiment of the sweetener composition, rebaudioside A is present in an amount from about 100 to about 3,000 ppm and the erythritol is present in an amount from about 5,000 to about 40,000 ppm of the total sweetener composition. In still another embodiment of the sweetener composition, rebaudioside A is present in an amount from about 100 to about 3,000 ppm and the erythritol is present in an amount from about 10,000 to about 35,000 ppm of the total sweetener composition. In another particular embodiment of the sweetener composition, rebaudioside A and erythritol are present in the sweetener composition in a ratio from

about 1:4 to about 1:800, respectively. In yet another particular embodiment of the sweetener composition, rebaudioside A and erythritol are present in the sweetener composition in a ratio from about 1:20 to about 1:600, respectively; more particularly from about 1:50 to about 1:300; and still more particularly from about 1:75 to about 1:150.

In another embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, or curculin, in combination with at least one sweet taste improving synthetic sweetener additive is provided. In a particular embodiment, the pharmaceutical composition comprises a pharmaceutically active substance and a sweetener comprising rebaudioside-A (REBA) in combination with saccharin or acesulfame potassium or other salts in an amount from about 10 ppm to about 100 ppm of the composition.

In one embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving carbohydrate additive and at least one sweet taste improving polyol additive is provided. In a particular embodiment, the at least one sweet taste improving carbohydrate additive is present in an amount from about 1,000 to about 100,000 ppm of the composition and at least one sweet taste improving polyol additive is present in an amount from about 400 to about 80,000 ppm of the composition. Non-limiting examples include a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with tagatose, fructose or sucrose and erythritol.

In one embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving inorganic salt additive is provided. Non-limiting examples include a pharmaceutically active substance and a

sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with NaCl, KCl, $NaHSO_4.H2O$, NaH_2PO_4, $MgSO_4$, $KAl(SO_4)_2$ (alum), magnesium phosphate, magnesium chloride, KCl and KH_2PO_4, or other combinations thereof. A particularly desirable embodiment comprises the a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with a mixture of inorganic salt additives, such as chlorides, phosphates, and sulfates of sodium, magnesium, potassium, and calcium (e.g., sodium chloride and potassium chloride; potassium phosphate and potassium chloride; sodium chloride and sodium phosphate; calcium phosphate and calcium sulfate; magnesium chloride and magnesium phosphate; and calcium phosphate, calcium sulfate, and potassium sulfate).

In a particular embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprises aspartame, acesfulame potassium or other salts, and sucralose in combination with at least one sweet taste improving inorganic salt additive. In a particular embodiment, the at least one sweet taste improving inorganic salt additive is present in an amount in the range of about 25 to about 5,000 ppm of the composition. Non-limiting examples include a pharmaceutically active substance and a sweetener composition comprising aspartame, acesulfame potassium, and sucralose in combination with magnesium chloride; a pharmaceutically active substance and a sweetener composition comprising aspartame, acesulfame potassium, and sucralose in combination with magnesium sulfate; or a pharmaceutically active substance and a sweetener composition comprising aspartame, acesulfame potassium, and sucralose in combination with magnesium sulfate and sodium chloride.

In one embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving organic acid salt additive is provided. Non-limiting examples include a pharmaceutically active substance and a

sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with choline chloride in citrate buffer, D-gluconic acid sodium salt, guanidine HCl, D-glucosamine HCl, amiloride HCl, or combinations thereof.

In one embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving organic acid additive is provided. Non-limiting examples include a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with fumaric acid, malic acid, tartaric acid, citric acid, adipic acid, ascorbic acid, tannic acid, succinic acid, glutaric acid, or combinations thereof.

In one embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving amino acid additive is provided. In a particular embodiment, the at least one sweet taste improving amino acid additive is present in an amount from about 100 to about 25,000 ppm of the composition. Non-limiting examples include a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with glycine, L-alanine, L-serine, L-threonine, β-alanine, aminobutyric acid (alpha-, beta-, or gamma-isomers), L-aspartic acid, L-glutamic acid, L-lysine, glycine and L-alanine mixture, salt derivatives or combinations thereof.

In one embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving surfactant additive is provided. Non-limiting examples include a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with dioctyl sulfosuccinate sodium, cetylpyridinium chloride, hexadecyltrimethylammonium bromide, sucrose oleate, polysorbate 20, polysorbate 80, lecithin, or combinations thereof.

In one embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving polymer additive is provided. Non-limiting examples include a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with cationic polymer such as polyethyleneimine, poly-L-lysine (e.g., poly-L-α-lysine or poly-L-ε-lysine), polyornithine (e.g., poly-L-α-ornithine or poly-ε-ornithine), chitosan, or combinations thereof.

In one embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving polymer additive and at least one sweet taste improving polyol additive is provided. In a particular embodiment, the at least one sweet taste improving polymer additive is present in an amount from about 30 to about 2,000 ppm of the composition, and the at least one sweet taste improving

polyol additive is present in an amount from about 400 to about 80,000 ppm of the composition. Non-limiting examples include a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with a hydrocolloid, such as a gum acacia seyal, and erythritol.

In one embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving protein or protein hydrolysate additive is provided. Non-limiting examples include a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with bovine serum albumin (BSA), whey protein or combinations thereof.

In one embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving amino acid additive and at least one sweet taste improving inorganic acid salt additive is provided. In a particular embodiment, the at least one sweet taste improving amino acid additive is present in an amount from about 100 to about 25,000 ppm of the composition and the at least one sweet taste improving inorganic acid salt additive is present in an amount from about 25 to about 5,000 ppm of the composition. Non-limiting examples include a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with glycine and alum; a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside

IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with glycine and potassium chloride; a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with glycine and sodium chloride; a pharmaceutically active substance and a sweetener composition comprising REBA in combination with glycine, potassium dihydrogen phosphate, and potassium chloride; and rebaudioside-A (REBA), stevia, stevioside, morgroside IV, morgroside V, Lo Han Guo, monatin, curculin, sucralose, saccharin, aspartame, acesulfame potassium or other salts, or neotame, in combination with glycine, sodium chloride, and potassium chloride.

In another embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving carbohydrate additive and at least one sweet taste improving inorganic acid salt additive is provided. In a particular embodiment, the at least one sweet taste improving carbohydrate additive is present in an amount from about 1,000 to about 100,000 ppm of the composition and the at least one sweet taste improving inorganic acid salt additive is present in an amount from about 25 ppm to about 5,000 ppm. Non-limiting examples include a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with fructose, sucrose, or glucose and alum; a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with fructose, sucrose, or glucose and potassium chloride; a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo

Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with fructose, sucrose, or glucose and sodium chloride; a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with fructose, sucrose, or glucose, potassium phosphate, and potassium chloride; and a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with fructose, sucrose, or glucose, sodium chloride, and potassium chloride.

In another embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving bitter additive and at least one sweet taste improving inorganic salt additive is provided. A non-limiting example include a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with urea and sodium chloride.

In another embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving amino acid additive and at least one sweet taste improving polyamino acid additive is provided. In a particular embodiment, the at least one sweet taste improving amino acid additive is present in an amount from about 100 to about 25,000 ppm of the composition and the at least one sweet taste improving polyamino acid additive is present in an amount from

about 30 to about 2,000 ppm of the composition. Non-limiting examples include a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with glycine and poly-α-L-lysine; and a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with glycine and poly-ε-L-lysine.

In another embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving amino acid additive and at least one sweet taste improving organic acid additive is provided. In a particular embodiment, the at least one sweet taste improving amino acid additive is present in an amount from about 100 to about 25,000 ppm of the composition and the at least one sweet taste improving organic acid additive is present in an amount from about 10 to about 5,000 ppm of the composition. A non-limiting example includes a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with glycine and sodium gluconate.

In another embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving amino acid additive and at least one sweet taste improving carbohydrate additive is provided. In a particular embodiment, the at least one sweet taste improving amino acid additive is present in an amount from about 100 to about 25,000 ppm of the composition and the at least one sweet taste improving carbohydrate additive is present in an amount from about

1,000 to about 100,000 ppm of the composition. A non-limiting example includes a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with L-alanine and fructose.

In another embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving amino acid additive, at least one sweet taste improving polyol additive, at least one sweet taste improving inorganic salt additive, and at least one sweet taste improving organic acid salt additive is provided. In a particular embodiment, the at least one sweet taste improving amino acid additive is present in an amount from about 100 to about 25,000 ppm of the composition, the at least one sweet taste improving polyol additive is present in an amount from about 400 to about 80,000 ppm of the composition, the at least one sweet taste improving inorganic salt additive is present in an amount from about 25 to about 5,000 ppm of the composition, and the at least one sweet taste improving organic acid salt additive is present in an amount from about 20 to about 10,000 ppm of the composition. A non-limiting example includes a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with erythritol, glycine, KCl, KH_2PO_4, and choline chloride.

In another embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving amino acid additive, at least one sweet taste improving carbohydrate additive, and at least one sweet taste improving polyol additive is provided. In a particular embodiment, the at least one sweet taste improving amino acid additive is present in an amount from about 100 to about

25,000 ppm of the composition, the at least one sweet taste improving carbohydrate additive is present in an amount from about 1,000 to about 100,000 ppm of the composition, and the at least one sweet taste improving polyol additive is present in an amount from about 400 to about 80,000 ppm of the composition. A non-limiting example includes a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with L-alanine, fructose, and erythritol.

In another embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving amino acid additive, at least one sweet taste improving polyol additive, and at least one sweet taste improving inorganic acid salt additive is provided. In a particular embodiment, the at least one sweet taste improving amino acid additive is present in an amount from about 100 to about 25,000 ppm of the composition, the at least one sweet taste improving polyol additive is present in an amount from about 400 to about 80,000 ppm of the composition, and the at least one sweet taste improving inorganic acid salt additive is present in an amount from about 25 to about 5,000 ppm of the composition. A non-limiting example includes a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with erythritol, glycine, KCl, and KH_2PO_4.

In another embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, glycyrrihizin such as mono-ammonium glycyrrhizic acid salt hydrate, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with a sweet taste improving inorganic acid salt additive is

provided. A non-limiting example includes a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, glycyrrihizin such as mono-ammonium glycyrrhizic acid salt hydrate, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with sodium chloride.

In one embodiment, a pharmaceutical composition is provided comprising a pharmaceutically active substance and a sweetener composition comprising rebaudioside-A (REBA), stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, monatin, curculin, glycyrrihizin such as mono-ammonium glycyrrhizic acid salt hydrate, sucralose, saccharin, cyclamate, aspartame, acesulfame potassium or other salts, or neotame, in combination with at least one sweet taste improving polyol additive and at least one sweet taste improving organic acid additive. Desirably, the at least one sweet taste improving polyol additive is present in an amount from about 20,000 to about 50,000 ppm of the composition and the at least one sweet taste improving organic acid additive is present in an amount from about 10 to about 5,000 ppm of the composition. Wherein more than one sweet taste improving organic acid additive is present in the composition, the plurality of sweet taste improving organic acid additives are present in an amount from about 500 to about 2,500 ppm of the composition, more particularly in an amount from about 500 to about 1,500 ppm of the composition. In a particular embodiment, the composition described hereinabove further comprises at least one sweet taste improving inorganic acid additive, at least one sweet taste improving inorganic acid salt additive, at least one sweet taste improving organic acid salt additive, or combinations thereof.

In another embodiment, a pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising REBA in combination with at least one sweet taste improving polyol additive and at least one sweet taste improving organic acid additive is provided. Desirably, the REBA has a purity from about 50 to about 100% by weight of REBA, more desirably from about 80 to about 99.5% by weight REBA, most desirably from about 97 to about 99.5% by weight REBA in a steviolglycoside mixture. In a particular embodiment, the REBA is present in the composition in an amount from about 100 to about 3,000 ppm, more desirably in an amount from about 200 to about 2,000 ppm, and even more desirably in an amount from about 250 to about 750 ppm of the composition. Desirably, the at least one sweet taste

improving polyol additive is present in an amount from about 20,000 to about 50,000 ppm of the composition and the at least one sweet taste improving organic acid additive is present in an amount from about 10 to about 5,000 ppm of the composition. In a particularly desirable embodiment, the at least one sweet taste improving polyol additive is present in an amount from about 30,000 to about 40,000 ppm and the at least one sweet taste improving organic acid additive is present in an amount from about 500 to about 2,500 ppm of the composition. In a particular embodiment, a plurality of sweet taste improving organic acid additives are present in the sweetener composition in an amount from about 500 to about 2,500 ppm of the composition, the plurality of organic acid additives comprising a mixture of lactic acid in an amount from about 40 to about 250 ppm, citric acid in an amount from about 150 to about 460 ppm, malic acid in an amount from about 150 to about 460 ppm, and tartaric acid in an amount from about 150 to about 460 ppm. A non-limiting example includes a pharmaceutically active substance and a sweetener composition comprising REBA in combination with erythritol, lactic acid, citric acid, malic acid, tartaric acid, or combinations thereof. In a particular embodiment, the sweetener composition comprises 34,000 ppm of erythritol, 80 ppm of lactic acid, 310 ppm of citric acid, 310 ppm of malic acid, 310 ppm or tartaric acid, and 550 ppm of REBA. Desirably, the REBA has a purity from about 80 to about 99.5% by weight of REBA, more desirably from about 97 to about 99.5% by weight REBA in a steviolglycoside mixture. The sweetener composition optionally also may include flavorants such as caramel, vanilla, or other such flavorants as described herein, or combinations thereof.

In another embodiment, the pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising REBA in combination with at least one sweet taste improving polyol additive and at least one sweet taste improving organic acid additive described hereinabove further comprises at least one sweet taste improving inorganic acid additive. Desirably, at least one sweet taste improving inorganic acid additive is present in an amount from about 25 to about 5,000 ppm of the composition. Non-limiting examples of sweet taste improving inorganic acid additives include phosphoric acid, benzoic acid, sorbic acid, and combinations thereof.

In yet another embodiment, the dental composition comprising a pharmaceutically active substance and a sweetener composition comprising REBA in combination with at

least one sweet taste improving polyol additive and at least one sweet taste improving organic acid additive described hereinabove further comprises at least one sweet taste improving inorganic acid salt additive and/or at least one sweet taste improving organic acid salt additive. Desirably, the at least one sweet taste improving inorganic acid salt additive is present in an amount from about 25 to about 5,000 ppm of the composition, more desirably in an amount from about 50 to about 250 ppm, most desirably in an amount of about 150 ppm. Desirably, the at least one sweet taste improving organic acid salt additive is present in an amount from about 20 to about 10,000 ppm of the composition, more desirably in an amount from about 50 to about 350 ppm, most desirably in an amount of about 148 ppm. Non-limiting examples include a pharmaceutically active substance and a sweetener composition comprising REBA in combination with erythritol, sodium chloride or magnesium chloride, and lactic acid, citric acid, malic acid, tartaric acid, or combinations thereof; a pharmaceutically active substance and a sweetener composition comprising REBA in combination with erythritol, potassium citrate or sodium citrate, and lactic acid, citric acid, malic acid, tartaric acid, or combinations thereof; or a pharmaceutically active substance and a sweetener composition comprising REBA in combination with erythritol, sodium chloride and sodium citrate, lactic acid, citric acid, malic acid, and tartaric acid, or combinations thereof.

In another embodiment, the pharmaceutical composition comprising a pharmaceutically active substance and a sweetener composition comprising REBA in combination with at least one sweet taste improving polyol additive, at least one sweet taste improving inorganic acid additive, and at least one sweet taste improving organic acid additive described hereinabove further comprises at least one sweet taste improving inorganic acid salt additive and/or at least one sweet taste improving organic acid salt additive. Desirably, the at least one sweet taste improving inorganic acid salt additive is present in an amount from about 25 to about 5,000 ppm of the composition, more desirably in an amount from about 50 to about 250 ppm, most desirably in an amount of about 150 ppm. Desirably, the at least one sweet taste improving organic acid salt additive is present in an amount from about 20 to about 10,000 ppm of the composition, more desirably in an amount from about 50 to about 350 ppm, most desirably in an amount of about 148 ppm. Non-limiting examples include a pharmaceutically active substance and a sweetener composition comprising REBA in combination with erythritol, phosphoric acid,

sodium chloride or magnesium chloride, and lactic acid, citric acid, malic acid, tartaric acid, or combinations thereof; a pharmaceutically active substance and a sweetener composition comprising REBA in combination with erythritol, phosphoric acid, potassium citrate or sodium citrate, and lactic acid, citric acid, malic acid, tartaric acid, or combinations thereof; or a pharmaceutically active substance and a sweetener composition comprising REBA in combination with erythritol, phosphoric acid, sodium chloride and sodium citrate, lactic acid, citric acid, malic acid, and tartaric acid, or combinations thereof.

The desired weight ratio of the natural and/or synthetic high-potency sweetener to sweet taste improving composition(s) in the sweetener composition will depend on the particular natural and/or synthetic high-potency sweetener, and the sweetness and other characteristics desired in the final product. Natural and/or synthetic high-potency sweeteners vary greatly in their potency, ranging from about 30 times more potent than sucrose to about 8,000 times more potent than sucrose on a weight basis. In general, the weight ratio of the natural and/or synthetic high-potency sweetener to sweet taste improving composition may for example range from range between 10,000:1 and 1:10,000; a further non-limiting example may range from about 9,000:1 to about 1:9,000; yet another example may range from about 8,000:1 to about 1:8,000; a further example may range from about 7,000:1 to about 1:7,000; another example may range from about 6,000:1 to about 1:6000; in yet another example may range from about 5,000:1 to about 1:5,000; in yet another example may range from about 4,000:1 to about 1:4,000; in yet another example may range from about 3,000:1 to about 1:3,000; in yet another example may range from about 2,000:1 to about 1:2,000; in yet another example may range from about 1,500:1 to about 1:1,500; in yet another example may range from about 1,000:1 to about 1:1,000; in yet another example may range from about 900:1 to about 1:900; in yet another example may range from about 800:1 to about 1:800; in yet another example may range from about 700:1 to about 1:700; in yet another example may range from about 600:1 to about 1:600; in yet another example may range from about 500:1 to about 1:500; in yet another example may range from about 400:1 to about 1:400; in yet another example may range from about 300:1 to about 1:300; in yet another example may range from about 200:1 to about 1:200; in yet another example may range from about 150:1 to about 1:150; in yet another example may range from about 100:1 to about 1:100; in yet

another example may range from about 90:1 to about 1:90; in yet another example may range from about 80:1 to about 1:80; in yet another example may range from about 70:1 to about 1:70; in yet another example may range from about 60:1 to about 1:60; in yet another example may range from about 50:1 to about 1:50; in yet another example may range from about 40:1 to about 1:40; in yet another example may range from about 30:1 to about 1:30; in yet another example may range from about 20:1 to about 1:20; in yet another example may range from about 15:1 to about 1:15; in yet another example may range from about 10:1 to about 1:10; in yet another example may range from about 9:1 to about 1:9; in yet another example may range from about 8:1 to about 1:8; in yet another example may range from about 7:1 to about 1:7; in yet another example may range from about 6:1 to about 1:6; in yet another example may range from about 5:1 to about 1:5; in yet another example may range from about 4:1 to about 1:4; in yet another example may range from about 3:1 to about 1:3; in yet another example may range from about 2:1 to about 1:2; and in yet another example may be about 1:1; depending on the particular natural and/or synthetic high-potency sweetener selected.

It is contemplated that the combination of at least one natural and/or synthetic high-potency sweetener to at least one sweet taste improving composition may be carried out in any pH range that does not materially or adversely affect the taste of the sweetener composition. A non-limiting example of the pH range may be from about 2 to about 8. A further example includes a pH range from about 2 to about 5.

One of ordinary skill in the art may combine at least one natural and/or synthetic high-potency sweetener, at least one sweet taste improving composition, and sweetenble composition in any manner. For example, at least one natural and/or synthetic high-potency sweetener may be added to the sweetenble composition before the at least one sweet taste improving composition. In another example, at least one natural and/or synthetic high-potency sweetener may be added to the sweetenble composition after the at least one sweet taste improving composition. In yet another example, at least one natural and/or synthetic high-potency sweetener may be added to the sweetenble composition simultaneously with the at least one sweet taste improving composition.

In yet another embodiment, at least one natural and/or synthetic high-potency sweetener may be combined with the at least one sweet taste improving composition prior to being added to a sweetenble composition. For example, the at least one natural and/or

synthetic high-potency sweetener may be in a pure, diluted, or concentrated form as a liquid (e.g., solution), solid (e.g., powder, chunk, pellet, grain, block, crystalline, or the like), suspension, gas state, or combinations thereof may be contacted with the at least one sweet taste improving composition which may be in a pure, diluted, or concentrated form as a liquid (e.g., solution), solid (e.g., powder, chunk, pellet, grain, block, crystalline, or the like), suspension, gas state, or combinations thereof before both are contacted with a sweetenble composition. In yet another embodiment, when there are more than one natural and/or synthetic high-potency sweeteners or more than one sweet taste improving composition in the sweeteneable composition, each component of the sweetenable composition may be added simultaneously, in an alternating pattern, in a random pattern, or any other pattern.

Generally, the amount of natural and/or synthetic high-potency sweetener present in a sweetened composition varies widely depending on the desired sweetness. Those of ordinary skill in the art can readily discern the appropriate amount of sweetener to put in the sweetened composition. In a particular embodiment, the at least one natural and/or synthetic high-potency sweetener is present in the sweetened composition in an amount in the range of about 1 to about 5,000 ppm of the sweetened composition and the at least one sweet taste improving composition is present in the sweetened composition in an amount in the range of about 0.1 to about 100,000 ppm of the sweetened composition.

In accordance with particular embodiments, suitable amounts of natural high-potency sweeteners for sweetened compositions comprise amounts in the range from about 100 ppm to about 3,000 ppm for rebaudioside A; from about 50 ppm to about 3,000 ppm for stevia; from about 50 ppm to about 3,000 ppm for stevioside; from about 50 ppm to about 3,000 ppm for mogroside IV; from about 50 ppm to about 3,000 ppm for mogroside V; from about 50 ppm to about 3,000 ppm for Luo Han Guo sweetener; from about 5 ppm to about 300 ppm for monatin, from about 5 ppm to about 200 ppm for thaumatin; and from about 50 ppm to about 3,000 ppm for mono-ammonium glycyrrhizic acid salt hydrate.

In accordance with particular embodiments, suitable amounts of synthetic high-potency sweeteners for sweetened compositions comprise a range from about 1 ppm to about 60 ppm for alitame; from about 10 ppm to about 600 ppm for aspartame; from about 1 ppm to about 20 ppm for neotame; from about 10 ppm to about 500 ppm for acesulfame

potassium; from about 50 ppm to about 5,000 ppm for cyclamate; from about 10 ppm to about 500 ppm for saccharin; from about 5 ppm to about 250 ppm for sucralose; from about 1 ppm to about 20 ppm for N-[N-[3-(3-hydroxy-4-methoxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester; from about 1 ppm to about 20 ppm for N-[N-[3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester; and from about 1 ppm to about 20 ppm for N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester.

V. Pharmaceutical Composition Formulations and Methods

A variety of functional ingredients, including herbs and nutritional supplements also may be included in the pharmaceutical composition. For example, the pharmaceutical composition may comprise functional ingredients that provide a health benefit beyond basic nutrition, non-limiting examples of which include antioxidants, phytosterols and phytostanols, vitamins (e.g., vitamin D) and minerals (e.g., calcium), glucosamine, saponins, phytoestrogen, dietary fiber, fatty acids (e.g., fish oil), C-reactive protein reducing agents, policosanol, rubisco peptides, autoimmune agents, polyphenols (e.g., catechins, proanthocyanidins, procyanidins, anthocyanins, quercetin, resveratrol, isoflavones, curcumin, punicalagin, ellagitannin, citrus flavonoids such as hesperidin and naringin, and chlorogenic acid), and agents for treating appetite satiation/hydration.

The pharmaceutical compositions embodied herein may be prepared using known techniques. Generally, pharmaceutical compositions may be manufactured by acquiring the pharmaceutically active substance by chemical synthesis, extraction, cell culture or fermentation, recovery from natural sources, or a combination of these processes. The pharmaceutically active substance can then be physically processed by tableting, preparing capsules, preparing solutions, or other pharmaceutical preparation methods which properly dose the pharmaceutically active substance.

For example, in tableting, all the pharamceutically active substances and excipient materials, including the natural and/or synthetic high-potency sweetener and the at least one sweet taste improving composition, should be as dry, powdered, and of uniform grain size as possible. Mixed grain sizes tend to separate out due to operational vibrations, resulting in inconsistent tableting, while any moisture in the system will tend to clog the tableting pathways. Binders, disintegrants, lubricants, and/or coatings may also be used as an excipient in the tablet to be formed from the pharmaceutical composition. The dry

ingredients are then pressed into a tablet having the proper dose of the pharmaceutically active substance.

In another embodiment, the pharmaceutically active substance may be combined with the excipients, including the natural and/or synthetic high-potency sweetener and the at least one sweet taste improving composition, and used to form a solution of a pharmaceutical composition. In some embodiments, the solution could comprise a solvent and a propellant and be used as an aerosol. In other embodiments, the solution could comprise a syrup and be orally introduced into a patient.

Pharmaceutical compositions also may comprise agglomerated components. Not wishing to be bound by any theory, it is believed that physical modifications of the natural and/or synthetic high-potency sweetener by agglomeration may slow its release in pharmaceutical compositions by reducing the solubility or dissolution rate of the natural and/or synthetic high-potency sweetener. Briefly described, agglomerations are prepared by mixing an absorbent with an agglomerating agent in powder form, spraying a solution of the natural and/or synthetic high-potency sweetener onto the powder as mixing continues, removing the powder from the mixer, drying to remove the solvent, and grinding to a desired particle size. Desirably, the absorber comprises a silica and the agglomerating agent comprises a cellulose derivative. Other non-limiting examples of absorbers include silicates, maltodextrin, clays, spongelike beads or microbeads, amorphous sugars, amorphous carbonates and hydroxides, vegetable gums, and other spray dried materials. The agglomerated particles may be added at any point in the pharmaceutical composition processing methods described above.

VI. Examples

The present invention is further illustrated by the following examples, which are not to be construed in any way as imposing limitations upon the scope thereof. On the contrary, it is to be clearly understood that resort may be had to various other embodiments, modifications, and equivalents thereof which, after reading the description therein, may suggest themselves to those skilled in the art without departing from the spirit of the present invention and/or the scope of the appended claims. Unless otherwise specified, %'s are by weight.

Example Set A

Example A1

A pharmaceutical composition comprises a pharmaceutically active substance, at least one high-potency sweetener, and at least one sweet taste improving composition. The pharmaceutically active substance comprises coated ibuprofen gran. The at least one high-potency sweetener comprises rebaudioside A. The at least one sweet taste improving composition comprises erythritol. More specifically the pharmaceutical composition is formed into a tablet having 2.5 mg/tablet of high potency sweetener, 30 mg/tablet of sweet taste improving composition, 3 mg/tablet of FD&C Yellow #6 A1 Lake, 10 mg/tablet of orange flavor, 15 mg/tablet of crospovidone NF, 140.6 mg/tablet of coated ibuprofen granules, 850 mg/tablet of mannitol, and 7.5 mg/tablet of magnesium stearate. The tablet can be made by any method known in the art, including the methods described in U.S. Patent Application Publication No. 2002/0122823, which is hereby incorporated by reference.

Example A2

Cough Lozenges Containing Rebaudioside A

Table 2 provides a prophetic formulation of a cough lozenge that can prepared according to the present invention. Using the formulation in Table 1, a cough lozenge can be prepared by first precooking liquid hydrogenated starch hydroyslate in a precooker to about 245°F, pumped through a cooking unit and cooked to about 295°F (final cool temperature will vary with the type of type of hydrogenated starch hydrolysate). The cooked syrup is then drained into a vacuum chamber to decrease moisture content to 1.5% (finished product moisture will depend on the type of hydrogenated starch hydrolysate and the cook process used). The cooked syrup is mixed with rebaudioside A and the remaining ingredients in an in-line mixer (temperature 265-290°F) and the product tempered on a tempering band, formed into a rope, die cut into desired form, and cooled to room temperature.

Table 2: Formulation for cough lozenges containing Rebaudioside A

Ingredient	Formula Wt. %
Hydrogenated starch hydrolysate	98.075
Corn Oil	0.600
Rebaudioside A	0.015
Menthol	0.170
Eucalyptus Oil	0.140
Erythritol	1.0

Example A3

Antacid Tablets Containing Rebaudioside A

Table 3 provides a prophetic formulation of an antacid tablet that is prepared according to the present invention. The ingredients are blended thoroughly in a mixer. The resulting mix is then pressed to 4-6 kilopound hardness and packaged in airtight containers.

Table 3: Formulation of antacid tablets containing Rebaudioside A

Ingredient	Formula Wt. %
Mannitol	61.7
Calcium Carbonate	34.000
Erythritol	3
Rebaudioside A	0.18
Magnesium Stearate	0.800
Creamy Mint Flavor	0.240
Menthol	0.080

Example A4

Bulk Fiber Laxative Containing Rebaudioside A

Table 4 provides a prophetic formulation of a bulk fiber laxative that can be prepared according to the present invention. The rebaudioside A, erythritol, and a portion of the psyllium husks are blended together, known in the process as Product A. The mannitol is dissolved in distilled water to produce a 10% weight/volume solution, known

in the process as Product B. The bowl of a fluidized bed spray agglomerator is the loaded with the rest of the psyllium husks and Product A. The fluidized bed spray agglomerator is then secured, energized and agglomerated with the mannitol solution marked Product B. The dried agglomerate is then screened and packaged in airtight containers.

Table 4: Formulation of bulk fiber laxative containing Rebaudioside A

Ingredient	Formula Wt. %
Psyllium Seed Husks	94.15975
Mannitol	2.55025
Erythritol	3
Rebaudioside A	0.29

Example A5

Chewable Analgesic Tablets Containing Rebaudioside A

Table 5 provides a prophetic formulation for chewable analgesic tablets that can be prepared according to the present invention. The ingredients are blended in a mixer thoroughly. The resulting mix is pressed to 4-6 kilopound hardness and packaged in airtight containers.

Table 5. Formulation of chewable analgesic tablets containing Rebaudioside A

Ingredient	Formula Wt. %
Mannitol	74.36
Coated Acetaminophen	17.600
Grape Flavor	2.200
Rebaudioside A	0.84
Erythritol	3
Powdered Malic Acid	1.000
Magnesium Stearate	0.500
Stearic Acid	0.500

Example A6

Children's Multi-vitamin Chewable Tablets Containing Rebaudioside A

Table 6 provides a prophetic formulation for children's multi-vitamin chewable tablets that can be prepared according to the present invention. The ingredients are blended thoroughly in a mixer and the resulting mix is then pressed to 4-6 kilopound hardness and packaged in airtight containers.

Table 6: Formulation for children's multi-vitamin chewable tablets containing Rebaudioside A

Ingredient	Formula Wt. %
Mannitol	69.67
Multi-Vitamin Premix	24.380
Grape Flavor	1.300
Rebaudioside A	0.75
Erythritol	3
Powdered Malic Acid	0.500
Magnesium Stearate	0.400

The following Examples B1-B3, C1-C3, D, and E1-E3 illustrate methods of making purified rebaudioside A in accordance with particular embodiments of this invention:

Example Set B

Table 7: Summary of Examples B1-3

	Crude Rebaudioside A (g)	Ethanol (95%)(mL)	Solvent Methanol (99%)(mL)	Water (mL)	Heating T (°C)	Drying T (°C)	Yield (g)	HPLC Purity (wt/wt %)
B1	400	1200	400	320	50	50	130	98.9
B2	100	320	120	50	30-40	60	72	98.3
B3	50	160	60	25	~30	60	27.3	98.2

Example B1

Crude rebaudioside A (77.4% purity) mixture was obtained from a commercial source. The impurities (6.2% stevioside, 5.6% rebaudioside C, 0.6 % rebauiodioside F, 1.0 % other steviolglycosides, 3.0% rebaudioside D, 4.9% rebaudioside B, 0.3% steviolbioside) were identified and quantified using HPLC on dry basis, moisture content 4.7%.

Crude rebaudioside A (400 g), ethanol (95%, 1200 mL), methanol (99%, 400 mL) and water (320 mL) were combined and heated to 50°C for 10 minutes. The clear solution was cooled to 22°C for 16 hours. The white crystals were filtered and washed twice with ethanol (2 x 200 mL, 95%) and dried in a vacuum oven at 50°C for 16-24 hours under reduced pressure (20 mm).

The final composition of substantially pure rebaudioside A (130 g) comprised 98.91% rebaudioside A, 0.06% stevioside, 0.03% rebaudioside C, 0.12% rebaudioside F, 0.13% other steviolglycosides, 0.1% rebaudioside D, 0.49% rebaudioside B and 0.03% steviolbioside, all by weight.

Example B2

Crude rebaudioside A (80.37 %) was obtained from a commercial source. The impurities (6.22% stevioside, 2.28% rebaudioside C, 0.35% Dulcoside, 0.78 % rebaudioside F, 0.72 % other steviolglycosides, 3.33% rebaudioside B, 0.07% steviolbioside) were identified by HPLC on dry basis, moisture content 3.4%.

Crude rebaudioside A (100 g), ethanol (95%, 320 mL), methanol (99%, 120 mL) and water (50 mL) were combined and heated to 30-40°C for 10 minutes. The clear solution was cooled to 22°C for 16 hours. The white crystals were filtered and washed twice with ethanol (2 x 50 mL, 95%). The wet filter cake (88 g) was slurried in ethanol (95%, 1320 mL) for 16 hours, filtered, washed with ethanol (95%, 2 x 100 mL) and dried in a vacuum oven at 60°C for 16-24 hours under reduced pressure (20 mm).

The final composition of substantially pure rebaudioside A (72 g) comprised 98.29% rebaudioside A, 0.03% stevioside, 0.02% rebaudioside C, 0.17% rebaudioside F, 0.06% rebaudioside D and 1.09% rebaudioside B. Steviolbioside was not detected by HPLC.

Example B3

Crude rebaudioside A (80.37%) was obtained from a commercial source. The impurities (6.22% stevioside, 2.28% rebaudioside C, 0.35% Dulcoside, 0.78 % rebaudioside F, 0.72 % other steviolglycosides, 3.33% rebaudioside B, 0.07% steviolbioside) were identified by HPLC on dry basis, moisture content 3.4%.

Crude rebaudioside A (50 g), ethanol (95%, 160 mL), methanol (99%, 60 mL) and water (25 mL) were combined and heated to approximately 30°C for 10 minutes. The clear solution was cooled to 22°C for 16 hours. The white crystals were filtered and washed twice with ethanol (2 x 25 mL, 95%). The wet filter cake (40 g) was slurried in methanol (99%, 600 mL) for 16 hours, filtered, washed with methanol (99%, 2 x 25 mL) and dried in a vacuum oven at 60°C for 16-24 hours under reduced pressure (20 mm).

The final composition of substantially pure rebaudioside A (27.3g) comprised 98.22% rebaudioside A, 0.04% stevioside, 0.04% rebaudioside C, 0.18% rebaudioside F, 0.08% rebaudioside D and 1.03% rebaudioside B. Steviolbioside was not detected by HPLC.

Example Set C

Table 8: Summary of Examples C1-3

		Solvent					
	Crude Rebaudioside A (g)	**Ethanol (95%)(mL)**	**Organic Co-solvent (mL)**	**Water (mL)**	**Wash Solvent**	**Yield (g)**	**HPLC Purity (%)**
C1	5	15	Methanol (6)	3.5	EtOH/MeOH (3:1 v/v)	2.6	>99
C2	5	15	Methanol (5)	4	EtOH/MeOH (3:1 v/v)	2.3	>99
C3	5	16	Methanol (6)	2.5	*EtOH/MeOH (8:3 v/v)	3.2	>98

Example C1

A mixture of crude rebaudioside A (80.37 % purity, 5 g), ethanol (95%, 15 mL), methanol (5 mL) and water (3.5 mL) were combined and heated to reflux for 10 minutes. The clear solution was cooled to 22°C for 16 hours while stirring. The white crystalline product was filtered, washed twice with ethanol:methanol (5.0 mL, 3:1, v/v) mixture and dried in a vacuum oven at 50°C for 16-24 hours under reduced pressure (20 mm) to yield 2.6 g of purified product (>99% by HPLC).

Example C2

A mixture of crude rebaudioside A (80.37 % purity, 5 g), ethanol (95%, 15 mL), methanol (5 mL) and water (4.0 mL) were combined and heated to reflux for 10 minutes. The clear solution was cooled to 22°C for 16 hours while stirring. The white crystalline product was filtered, washed twice with ethanol:methanol (5.0 mL, 3:1, v/v) mixture and dried in a vacuum oven at 50°C for 16-24 hours under reduced pressure (20 mm) to yield 2.3 g of purified product (>99% by HPLC).

Example C3

A mixture of crude rebaudioside A (80.37 % purity, 5 g), ethanol (95%, 16 mL), methanol (6 mL) and water (2.5 mL) were combined and heated to reflux for 10 minutes. The clear solution was cooled to 22°C for 2 hours. During this time, crystals started to appear. The mixture is stirred at room temperature for 16 hours. The white crystalline product was filtered, washed twice with ethanol:methanol (5.0 mL, 8:3, v/v) mixture and dried in a vacuum oven at 50°C for 16-24 hours under reduced pressure (20 mm) to yield 3.2 g of purified product (>98% by HPLC).

Example D

Table 9: Summary of Example D

		Solvent				
	Crude Rebaudioside A (g)	**Organic Solvent (mL)**	**Water (mL)**	**Wash Solvent**	**Yield (g)**	**HPLC Purity (%)**
D	50	EtOH (160)	40	EtOH	19.8	99.5

A mixture of crude rebaudioside A (80.37 % purity, 50 g), ethanol (95%, 160 mL) and water (40 mL) were combined and heated to reflux for 30 minutes. The mixture was then allowed to cool to ambient temperature for 16-24 hours. The white crystalline product was filtered, washed twice with ethanol (95%, 25 mL), and dried in a vacuum oven at 60°C for 16-24 hours under reduced pressure (20 mm) to yield 19.8 g of purified product (99.5% by HPLC).

Example E

Table 10: Summary of Examples E1-3

	Crude Rebaudioside A (g)	Ethanol (95%)(mL)	Organic Co-solvent (mL)	Water (mL)	Methanol Slurry (mL)	Yield (g)	HPLC Purity (%)
E1	50	160	Methanol (60)	25	200	12.7	>97
E2	50	160	Methanol (60)	25	300	18.6	>97
E3	50	160	Methanol (60)	25	350	22.2	>97

Example E1

A mixture of crude rebaudioside A (41% purity, 50 g), ethanol (95%, 160 mL), methanol (99.8 %, 60 mL) and water (25 mL) were combined by stirring at 22°C. A white product crystallized out in 5-20 hours. The mixture was stirred for additional 48 hours. The white crystalline product was filtered and washed twice with ethanol (95%, 25 mL). The wet cake of white crystalline product then was slurried in methanol (99.8 %, 200 mL) for 16 hours, filtered, washed twice with methanol (99.8 %, 25 mL), and dried in a vacuum oven at 60°C for 16-24 hours under reduced pressure (20 mm) to give 12.7 g of purified product (>97% by HPLC).

Example E2

A mixture of crude rebaudioside A (48% purity, 50 g), ethanol (95%, 160 mL), methanol (99.8 %, 60 mL) and water (25 mL) was combined by stirring at 22°C. The white product crystallized out in 3-6 hours. The mixture was stirred for additional 48 hours. The white crystalline product was filtered and washed twice with ethanol (95%, 25 mL). The wet cake of white crystalline product then was slurried in methanol (99.8 %, 300

mL) for 16 hours, filtered, washed twice with methanol (99.8 %, 25 mL) and dried in a vacuum oven at 60°C for 16-24 hours under reduced pressure (20 mm) to give 18.6 g of purified product (>97% by HPLC).

Example E3

A mixture of crude rebaudioside A (55% purity, 50 g), ethanol (95%, 160 mL), methanol (99.8 %, 60 mL) and water (25 mL) was combined by stirring at 22°C. The white product crystallized out in 15-30 minutes. The mixture was stirred for an additional 48 hours. The white crystalline product was filtered and washed twice with ethanol (95%, 25 mL). The wet cake of white crystalline product was slurried in methanol (99.8 %, 350 mL) for 16 hours, filtered, washed twice with methanol (99.8 %, 25 mL) and dried in a vacuum oven at 60°C for 16-24 hours under reduced pressure (20 mm) to give 22.2 g of purified product (>97% by HPLC).

Example F

A solution of rebaudioside A (>97% pure by HPLC) was prepared in double distilled water (12.5 gm in 50 mL, 25 % concentration) by stirring the mixture at 40°C for 5 minutes. An amorphous rebaudioside A polymorph was formed by immediately using the clear solution for spray drying with the Lab-Plant spray drier SD-04 instrument (Lab-Plant Ltd., West Yorkshire, U.K.). The solution was fed through the feed pump into the nozzle atomizer which atomized it into a spray of droplets with the help of a constant flow of nitrogen / air. Moisture was evaporated from the droplets under controlled temperature conditions (about 90 to about 97°C) and airflow conditions in the drying chamber and resulted in the formation of dry particles. This dry powder (11-12 g, H_2O 6.74 %) was discharged continuously from the drying chamber and was collected in a bottle. The solubility in water at room temperature was determined to be > 35.0 %.

While the invention has been described in detail with respect to specific embodiments thereof, it will be appreciated that those skilled in the art, upon attaining an understanding of the foregoing, may readily conceive of alterations to, variations of, and equivalents to these embodiments. Accordingly, the scope of the present invention should be assessed as that of the appended claims and any equivalents thereof.

We claim:

1. A pharmaceutical composition comprising:

a pharmaceutically active substance;

at least one high-potency sweetener; and

at least one sweet taste improving composition.

2. The pharmaceutical composition of claim 1, wherein the at least one high-potency sweetener comprises a natural high-potency sweetener selected from the group consisting of rebaudioside A, rebaudioside B, rebaudioside C, rebaudioside D, rebaudioside E, rebaudioside F, dulcoside A, dulcoside B, rubusoside, stevia, stevioside, mogroside IV, mogroside V, Luo Han Guo sweetener, siamenoside, monatin and its salts (monatin SS, RR, RS, SR), curculin, glycyrrhizic acid and its salts, thaumatin, monellin, mabinlin, brazzein, hernandulcin, phyllodulcin, glycyphyllin, phloridzin, trilobatin, baiyunoside, osladin, polypodoside A, pterocaryoside A, pterocaryoside B, mukurozioside, phlomisoside I, periandrin I, abrusoside A, cyclocarioside I, and combinations thereof.

3. The pharmaceutical composition of claim 1, wherein the at least one high-potency sweetener comprises a synthetic high-potency sweetener selected from the group consisting of sucralose, acesulfame potassium and other salts, aspartame, alitame, saccharin, neohesperidin dihydrochalcone, cyclamate, neotame, N-[N-[3-(3-hydroxy-4-methoxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, N-[N-[3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, salts thereof, and combinations thereof.

4. The pharmaceutical composition of claim 1, wherein the at least one sweet taste improving composition comprises a first sweet taste improving composition selected from the group consisting of carbohydrates, polyols, amino acids and their corresponding salts, polyamino acids and their corresponding salts, sugar acids and their corresponding salts, organic acids, inorganic acids, organic salts, inorganic salts, bitter compounds, flavorants,

astringent compounds, polymers, proteins or protein hydrolysates, surfactants, emulsifiers, flavonoids, alcohols, and combinations thereof.

5. The pharmaceutical composition of claim 1, wherein the at least one sweet taste improving composition imparts a more sugar-like temporal profile to the pharmaceutical composition than the sweetener would have without the at least one sweet taste improving composition.

6. The pharmaceutical composition of claim 1, further comprising at least one second sweet taste improving composition different from the at least one first sweet taste improving composition and selected from the group consisting of carbohydrates, polyols, amino acids and their corresponding salts, polyamino acids and their corresponding salts, sugar acids and their corresponding salts, organic acids, inorganic acids, organic salts, inorganic salts, bitter compounds, flavorants, astringent compounds, polymers, proteins or protein hydrolysates, surfactants, emulsifiers, flavonoids, alcohols, and combinations thereof.

7. The pharmaceutical composition of claim 6, further comprising at least one third sweet taste improving composition different from the at least one first sweet taste improving composition and the at least one second sweet taste improving composition and selected from the group consisting of carbohydrates, polyols, amino acids and their corresponding salts, polyamino acids and their corresponding salts, sugar acids and their corresponding salts, organic acids, inorganic acids, organic salts, inorganic salts, bitter compounds, flavorants, astringent compounds, polymers, proteins or protein hydrolysates, surfactants, emulsifiers, flavonoids, alcohols, and combinations thereof.

8. The pharmaceutical composition of claim 1, wherein the at least one high-potency sweetener is rebaudioside A, stevioside, stevia, or combinations thereof.

9. The pharmaceutical composition of claim 8, wherein the at least one sweet taste improving composition comprises a polyol.

10. The pharmaceutical composition of claim 9, wherein the at least one polyol comprises erythritol.

11. The pharmaceutical composition of claim 9, wherein the at least one polyol comprises xylitol.

12. The pharmaceutical composition of claim 8, wherein the at least one sweet taste improving composition comprises at least one amino acid.

13. The pharmaceutical composition of claim 12, wherein the at least one amino acid comprises glycine, alanine, proline, hydroxyproline, glutamine, or combinations thereof.

14. The pharmaceutical composition of claim 8, wherein the at least one sweet taste improving composition comprises at least one polyamino acid.

15. The pharmaceutical composition of claim 14, wherein the at least one polyamino acid comprises poly-L-aspartic acid, poly-L-α-lysine, poly-L-ε-lysine, poly-L-α-ornithine, poly-ε-ornithine, poly-L-arginine, salts thereof, or combinations thereof.

16. The pharmaceutical composition of claim 8, wherein the at least one sweet taste improving composition comprises at least one inorganic salt.

17. The pharmaceutical composition of claim 16, wherein the at least one inorganic salt comprises a sodium, potassium, calcium, or magnesium salt.

18. The pharmaceutical composition of claim 16, further comprising at least one inorganic phosphate.

19. The pharmaceutical composition of claim 18, wherein the at least one inorganic phosphate comprises a sodium, potassium, calcium, or magnesium phosphate.

20. The pharmaceutical composition of claim 16, further comprising at least one inorganic chloride.

21. The pharmaceutical composition of claim 20, wherein the at least one inorganic chloride comprises a sodium, potassium, calcium, or magnesium chloride.

22. The pharmaceutical composition of claim 8, wherein the at least one sweet taste improving composition comprises at least one carbohydrate.

23. The pharmaceutical composition of claim 22, wherein the at least one carbohydrate comprises sucrose, high fructose corn syrup, glucose, or sucrose.

24. The pharmaceutical composition of claim 23, wherein the at least one carbohydrate is present in the pharmaceutical composition in an amount from about 10,000 ppm to about 80,000 ppm of the composition.

25. The pharmaceutical composition of claim 8, wherein the at least one sweet taste improving composition comprises at least one synthetic high-potency sweetener.

26. The pharmaceutical composition of claim 25, wherein the at least one synthetic high-potency sweetener comprises sucralose, acesulfame potassium or other salts, aspartame, alitame, saccharin, neohesperidin dihydrochalcone, cyclamate, neotame, N-[N-[3-(3-hydroxy-4-methoxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, N-[N-[3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, salts thereof, and combinations thereof.

27. The pharmaceutical composition of claim 25, wherein the at least one synthetic high-potency sweetener comprises saccharin or acesulfame potassium or other salts.

28. The pharmaceutical composition of claim 27, wherein the at least one synthetic sweetener is present in the pharmaceutical composition in an amount from about 10 ppm to about 100 ppm of the composition.

29. The pharmaceutical composition of claim 8, wherein the rebaudioside A comprises rebaudioside A in a purity greater than about 70 % rebaudioside A by weight on a dry basis.

30. The pharmaceutical composition of claim 8, wherein the rebaudioside A comprises rebaudioside A in a purity greater than about 80 % rebaudioside A by weight on a dry basis.

31. The pharmaceutical composition of claim 8, wherein the rebaudioside A comprises rebaudioside A in a purity greater than about 90 % rebaudioside A by weight on a dry basis.

32. The pharmaceutical composition of claim 8, wherein the rebaudioside A comprises rebaudioside A in a purity greater than about 97 % rebaudioside by weight on a dry basis.

33. The pharmaceutical composition of claim 8, wherein the rebaudioside A comprises rebaudioside A in a purity greater than about 98 % rebaudioside by weight on a dry basis.

34. The pharmaceutical composition of claim 8, wherein the rebaudioside A comprises rebaudioside A in a purity greater than about 99 % rebaudioside by weight on a dry basis.

35. The pharmaceutical composition of claim 1, wherein the pharmaceutically active substance comprises a substance selected from the group consisting of antacids, reflux suppressants, antiflatulents, antidopaminergics, proton pump inhibitors, cytoprotectants, prostaglandin analogues, laxatives, antispasmodics, antidiarrhoeals, bile acid sequestrants, opioids, beta-receptor blockers, calcium channel blockers, diuretics, cardiac glycosides, antiarrhythmics, nitrates, antianginals, vasoconstrictors, vasodilators, peripheral activators, ACE inhibitors, angiotensin receptor blockers, alpha blockers, anticoagulants, heparin, antiplatelet drugs, fibrinolytics, anti-hemophilic factors, haemostatic drugs, hypolipidaemic agents, statins, hynoptics, anaesthetics, antipsychotics, antidepressants, anti-emetics, anticonvulsants, antiepileptics, anxiolytics, barbiturates, movement disorder drugs, stimulants, benzodiazepines, cyclopyrrolones, dopamine antagonists, antihistamines, cholinergics, anticholinergics, emetics, cannabinoids, analgesics, muscle relaxants, antibiotics, aminoglycosides, anti-virals, anti-fungals, anti-inflammatories, anti-gluacoma drugs, sympathomimetics, steroids, ceruminolytics, bronchodilators, NSAIDS, antitussive, mucolytics, decongestants, corticosteroids, androgens, antiandrogens, gonadotropins, growth hormones, insulin, antidiabetics, thyroid hormones, calcitonin, diphosponates, vasopressin analogues, alkalizing agents, quinolones, anticholinesterase, sildenafil, oral contraceptives, Hormone Replacement Therapies, bone regulators, follicle stimulating hormones, luteinizings hormones, gamolenic acid, progestogen, dopamine agonist, oestrogen, prostaglandin, gonadorelin, clomiphene, tamoxifen, diethylstilbestrol,

antileprotics, antituberculous drugs, antimalarials, anthelmintics, antiprotozoal, antiserums, vaccines, interferons, tonics, vitamins, cytotoxic drugs, sex hormones, aromatase inhibitors, somatostatin inhibitors, and combinations thereof.

36. The pharmaceutical composition of claim 1, further comprises an excipient material selected from the group consisting of antiadherents, binders, coatings, disintegrants, fillers, diluents, softeners, emulsifiers, flavoring agents, coloring agents, adjuvants, lubricants, functional agents, viscosity modifiers, bulking agents, glidiants, surface active agents, osmotic agents, diluents, and combinations thereof.

37. The pharmaceutical composition of claim 1, further comprising a bulk sweetener.

38. The pharmaceutical composition of claim 1, wherein the sweet taste improving composition functions as a bulk sweetener.

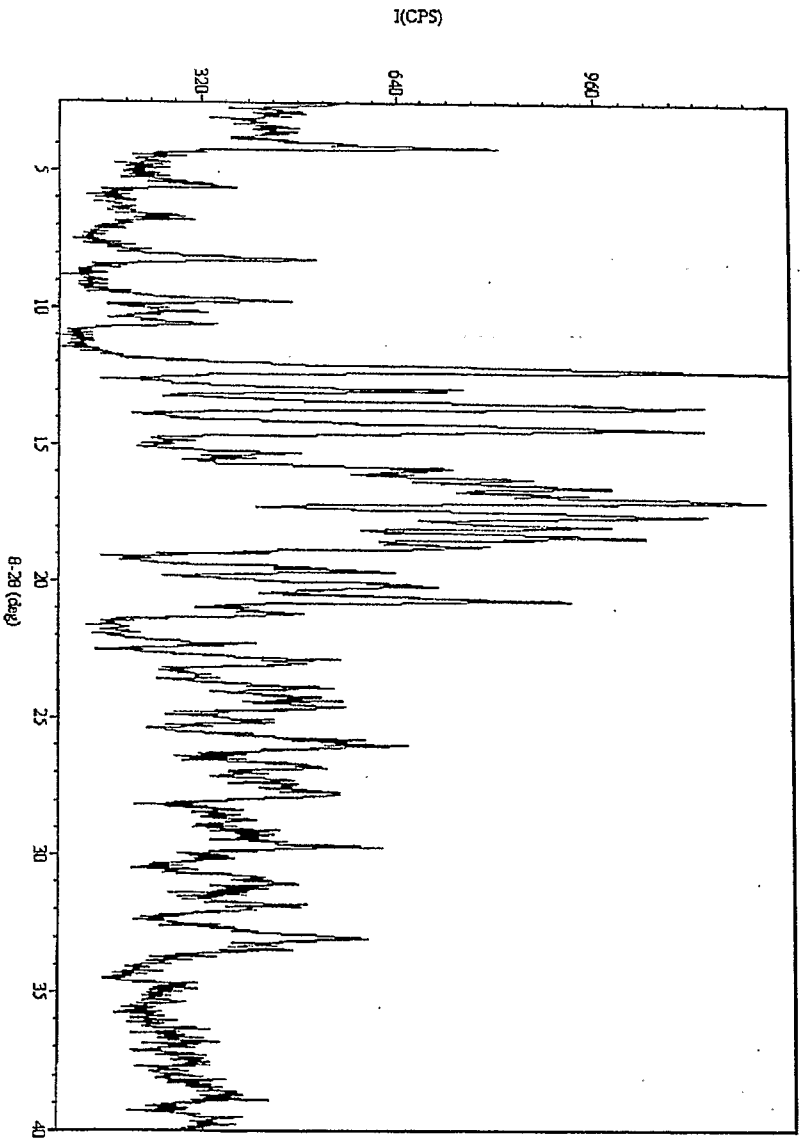

Fig. 1

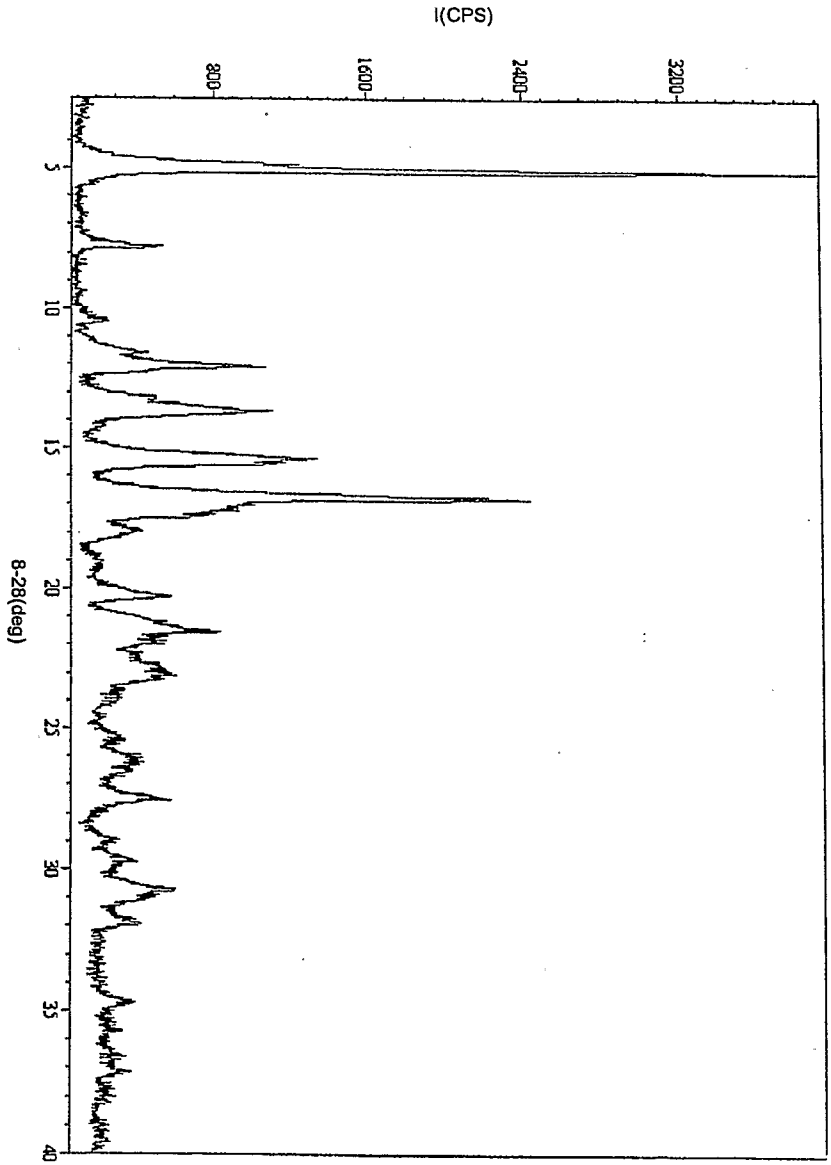

Fig. 2

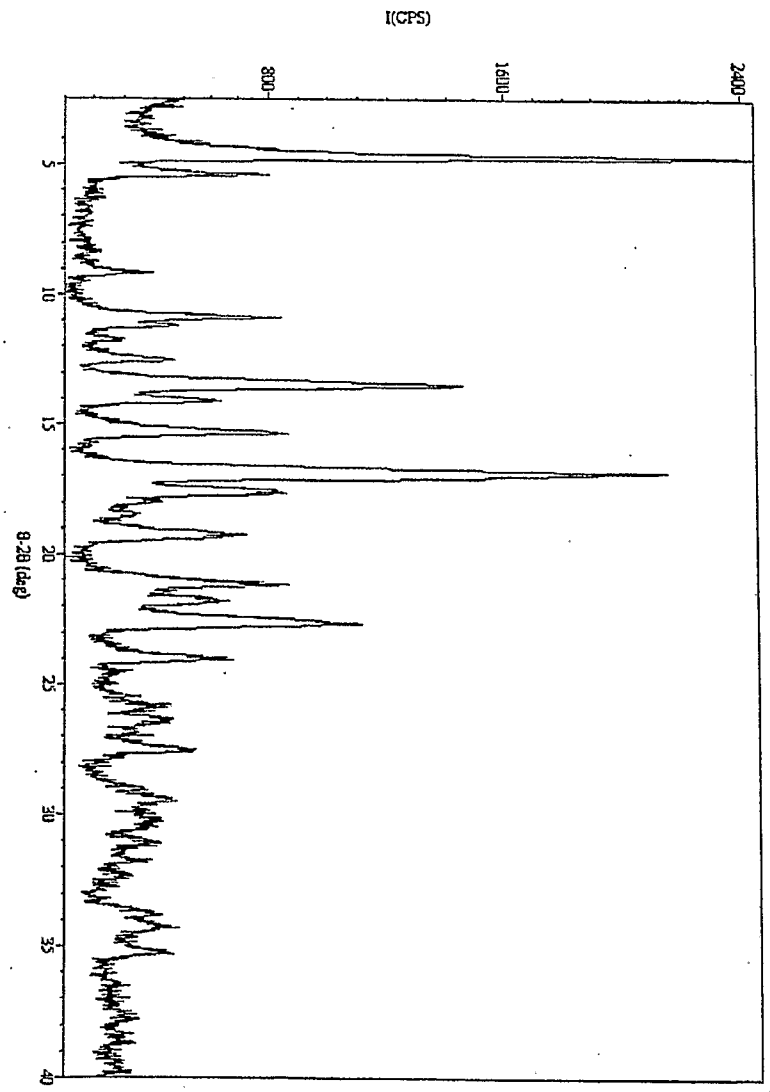

Fig. 3

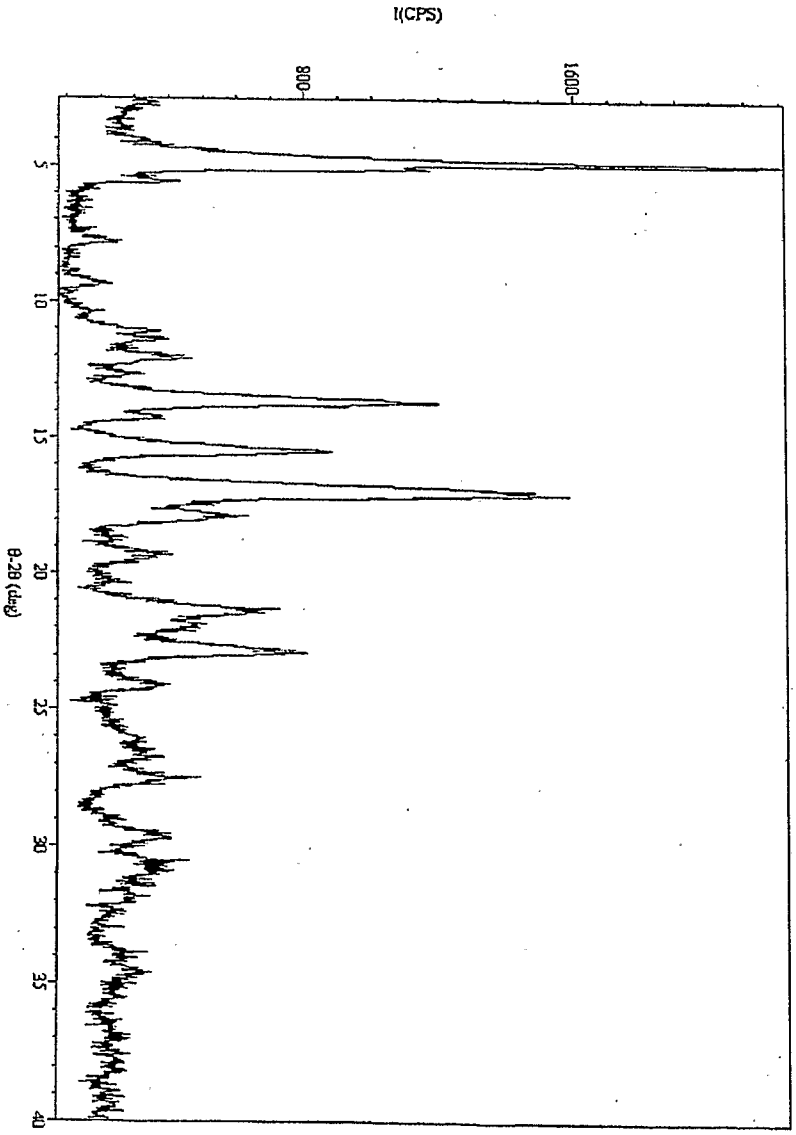

Fig. 4

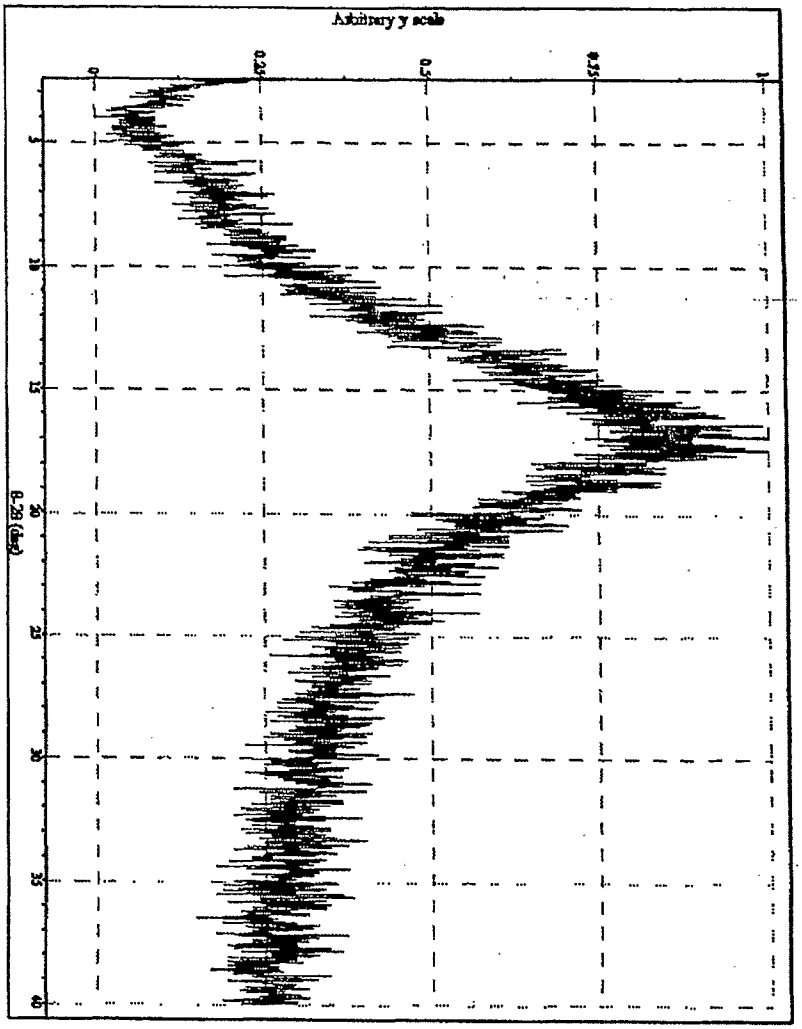

Fig. 5