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(54) Titre : RENFORCATEURS DU GOUT SUCRE CONTENANT DU REBAUDIOSIDE A OU DU REBAUDIOSIDE D
(54) Title: SWEETNESS ENHANCERS INCLUDING REBAUDIOSIDE A OR D

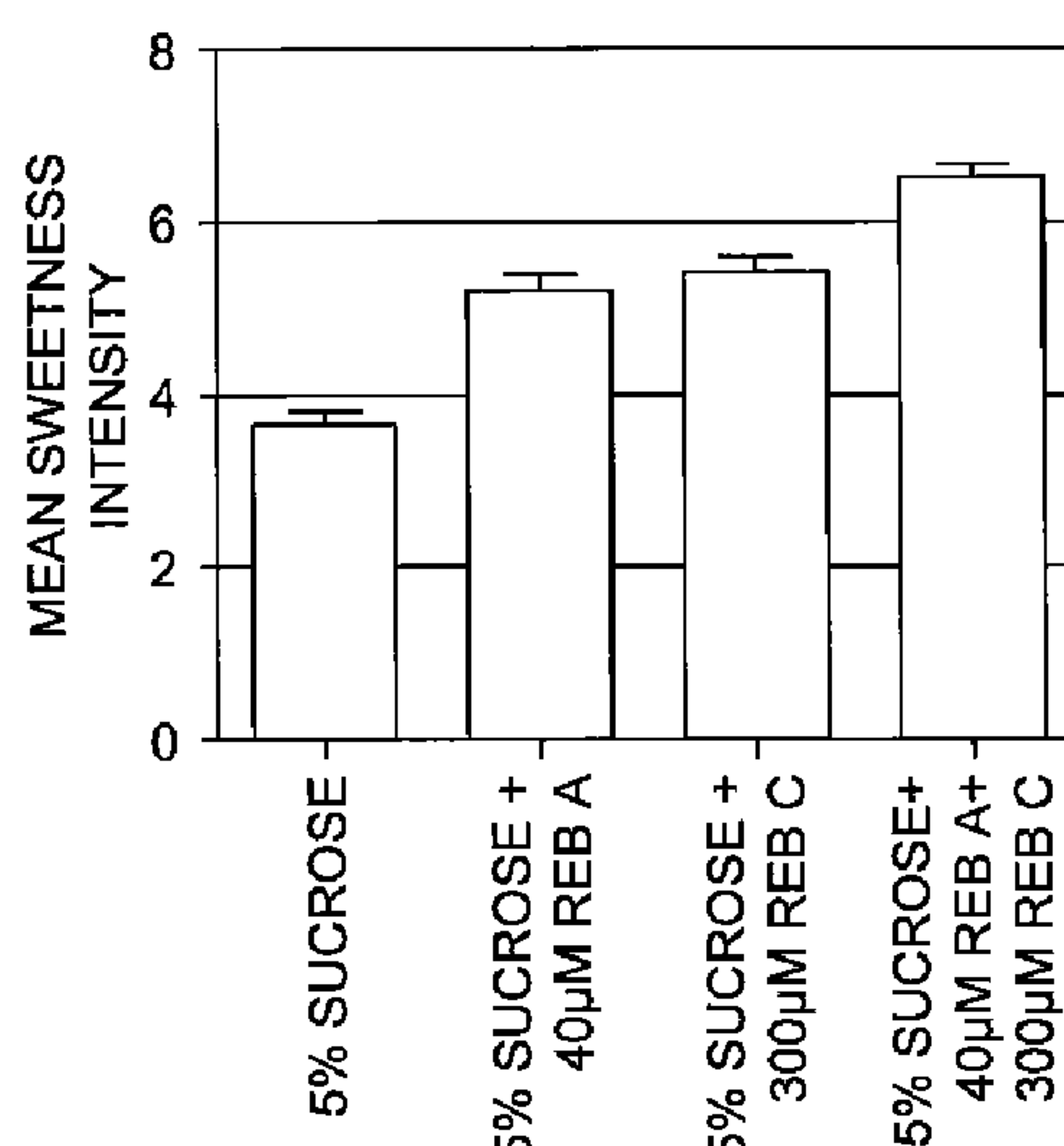
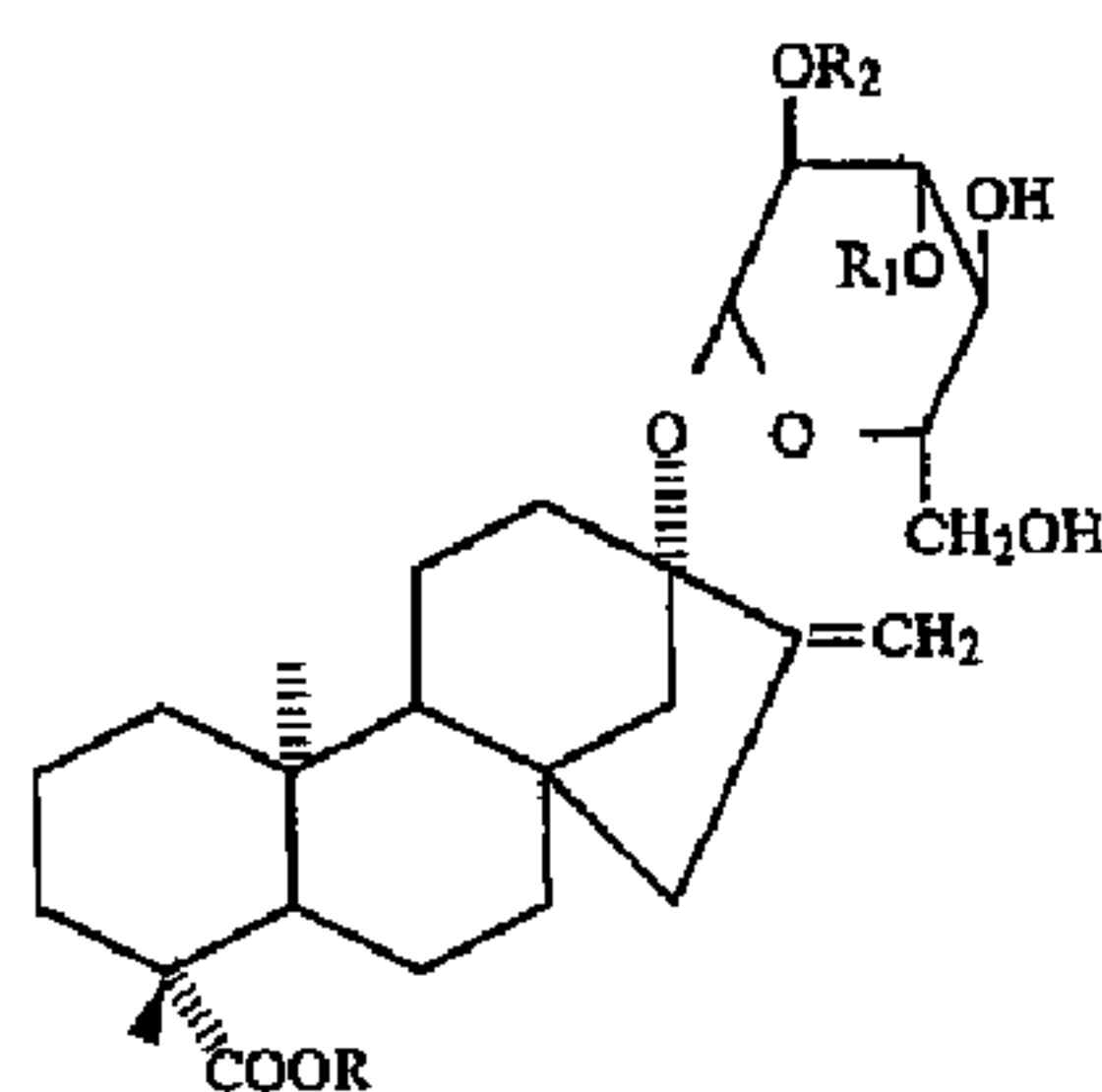


FIG. 11



I

(57) **Abrégé/Abstract:**

The present invention is directed to the use of rebaudioside A or rebaudioside D in combination with one or more compounds of Formula (I), or a stereoisomer thereof, wherein R₂ is rhamnose, and R and R₁ are each independently selected from the group

(57) **Abrégé(suite)/Abstract(continued):**

consisting of hydrogen, glucose, and beta-sophorose, for enhancing the sweet taste of carbohydrate sweeteners, such as sucrose and fructose. The present invention is also directed to consumables which include a combination of a carbohydrate sweetener, rebaudioside A or rebaudioside D, and one or more compounds of Formula (I), or a stereoisomer thereof.

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[Continued on next page]

(54) Title: SWEETNESS ENHANCERS INCLUDING REBAUDIOSIDE A OR D

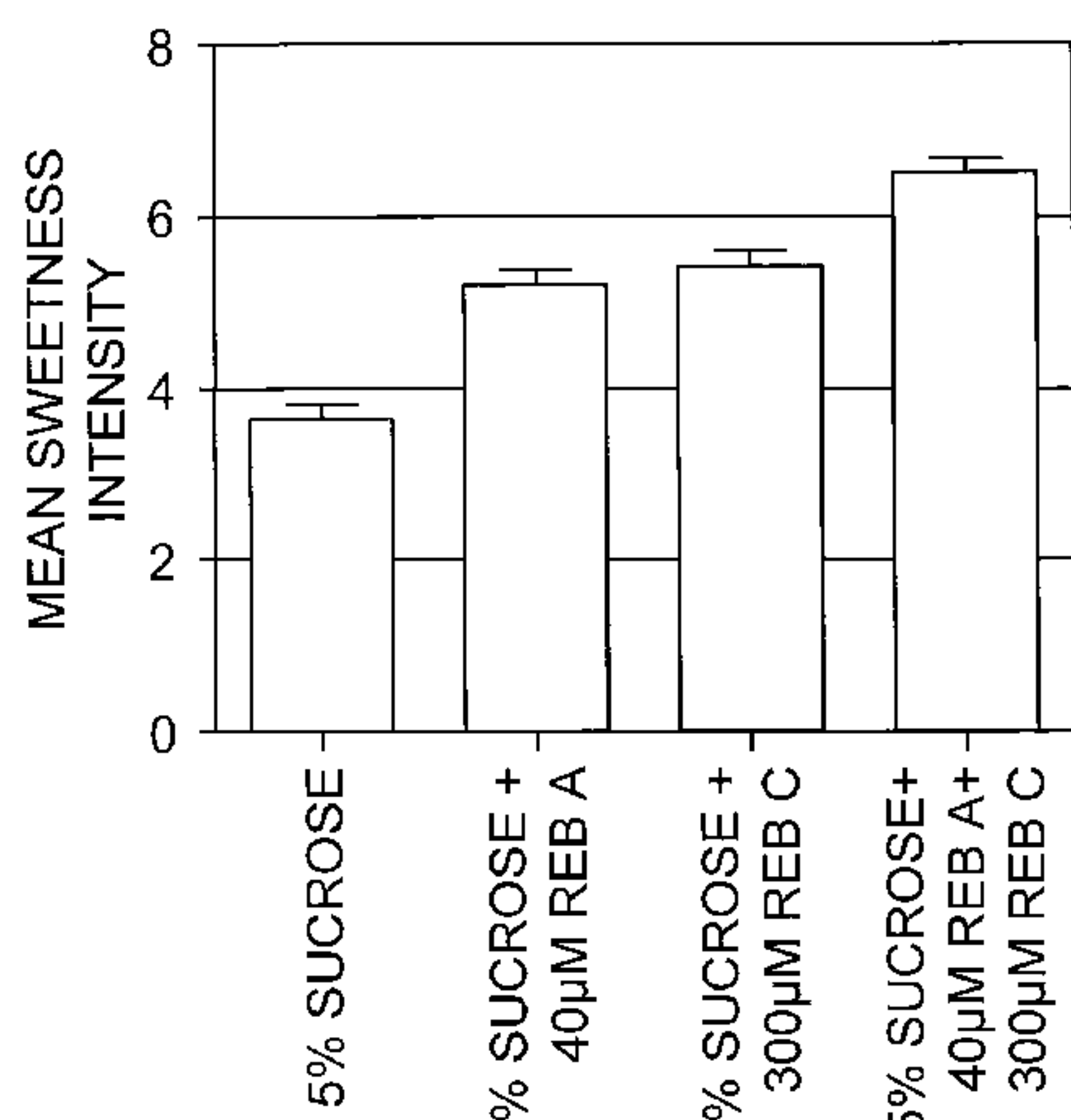
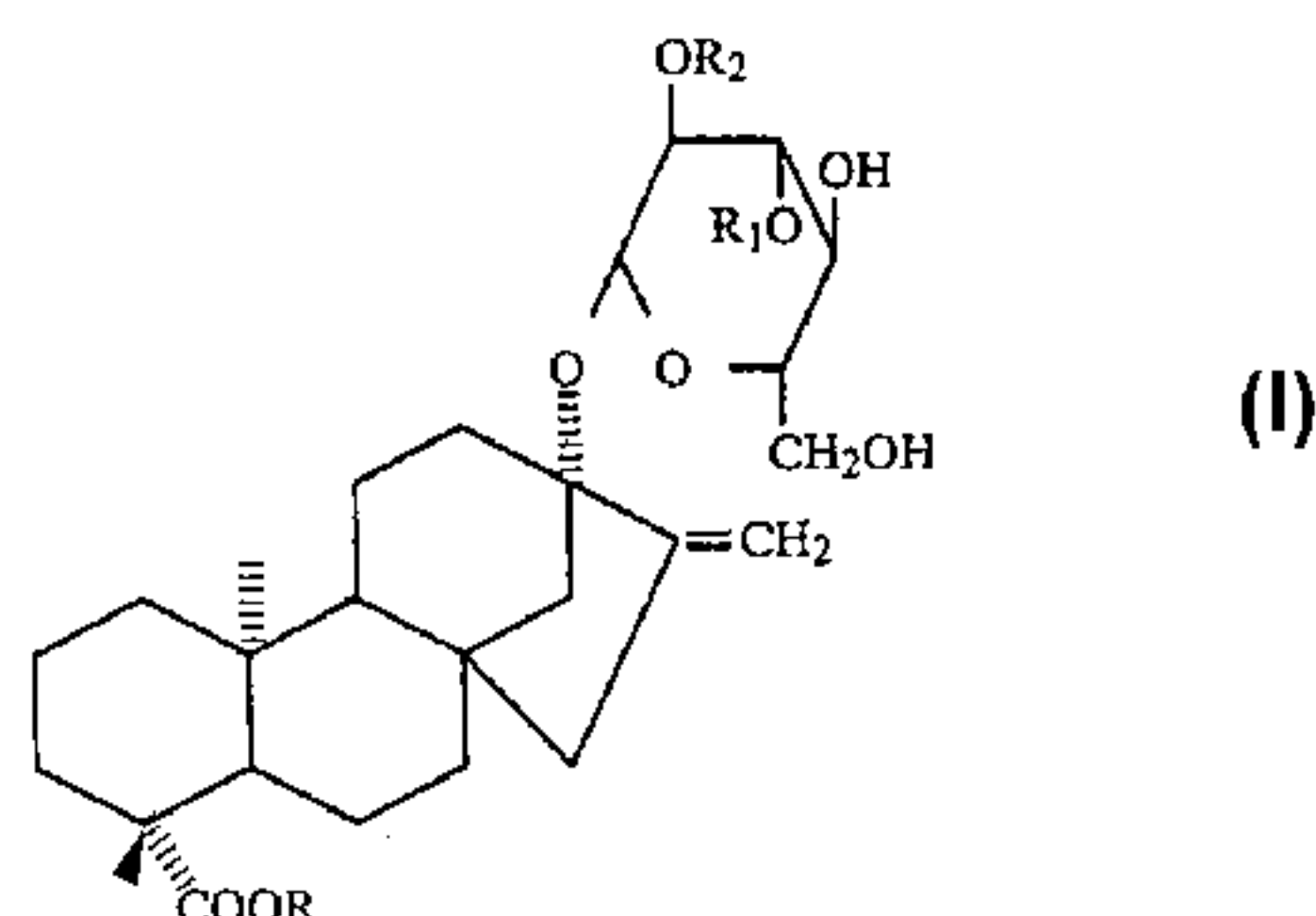


FIG. 11

(57) Abstract: The present invention is directed to the use of rebaudioside A or rebaudioside D in combination with one or more compounds of Formula (I), or a stereoisomer thereof, wherein R₂ is rhamnose, and R and R₁ are each independently selected from the group consisting of hydrogen, glucose, and beta-sophorose, for enhancing the sweet taste of carbohydrate sweeteners, such as sucrose and fructose. The present invention is also directed to consumables which include a combination of a carbohydrate sweetener, rebaudioside A or rebaudioside D, and one or more compounds of Formula (I), or a stereoisomer thereof.

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SWEETNESS ENHANCERS INCLUDING REBAUDIOSIDE A OR D

Introduction

[0001] This application claims benefit of priority to U.S. Provisional Application Serial Nos. 61/240,154, filed September 4, 2009, and 61/296,860, filed January 20, 2010, the contents of which are incorporated herein by reference in their entireties.

Background of the Invention

[0002] The sweet diterpene glycosides of *Stevia* have been characterized, and eight sweet glycosides of steviol have been identified. These glycosides accumulate in *Stevia* leaves where they may attain from 10 to 20% of the leaf weight. On a dry weight basis, a typical profile for the four major glycosides found in the leaves of *Stevia* includes 0.3% dulcoside, 0.6% rebaudioside C, 3.8% rebaudioside A and 9.1% stevioside. Other glycosides identified within *Stevia* include rebaudiosides B, D, and E, and dulcosides A and B. Out of the four major diterpene glycoside sweeteners present in *Stevia* leaves only two (stevioside and rebaudioside A) have physical and sensory properties that are well characterized. Stevioside is known to be 110 to 270 times sweeter than sucrose, rebaudioside A 150 to 320 times sweeter than sucrose, rebaudioside D 200 to 250 times sweeter than sucrose, rebaudioside C 40 to 60 times sweeter than sucrose, and dulcoside A 30 times sweeter than sucrose.

[0003] Of the diterpene glycosides found in *Stevia* extracts, rebaudioside A is known to have the least aftertaste. This aftertaste is described by many as bitter and licorice-like, and is present in all current *Stevia* extracts.

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[0004] Rebaudioside A has been tested in mixtures with other sweeteners, such as fructose, glucose and sucrose, at sweetness intensities equivalent to 3% (w/v-%), 5% (w/v-%) and 7% (w/v-%) sucrose to determine the presence and degree of synergism in these mixtures (Schiffmann et al., *Brain Research Bulletin* 38:105-120 (1995)). According to the results, rebaudioside A appears to have an additive effect in mixtures with fructose and glucose, but a synergistic effect in binary mixtures with sucrose at sweetness intensities equivalent to 3% (w/v-%) sucrose. At sweetness intensities equivalent to 5% (w/v-%) sucrose, rebaudioside A had an additive effect in mixtures with fructose, glucose and sucrose. At sweetness intensities equivalent to 7% (w/v-%) sucrose, rebaudioside A had an additive effect with a mixture with sucrose, but a suppressive effect with mixtures with glucose and fructose. In fact, no sweetener combinations were synergistic at sweetness intensities equivalent to the 7% (w/v-%) sucrose level.

[0005] Rebaudioside A has also been tested in ternary mixtures with other sweeteners, such as sucrose, and artificial sweeteners, such as alitame, neohesperidin dihydrochalcone, aspartame, and Na-cyclamate (Schiffmann et al., *Chem. Senses* 25:131-140 (2000)).

[0006] U.S. Patent No. 4,612,942 mentions that diterpene glycosides can modify or enhance flavor characteristics, such as sweet, when the amount of diterpene glycoside added is less than the sweetness threshold level of the diterpene glycoside in the orally consumable composition. However, no consumable composition for enhancing sweet flavor containing rebaudioside A in combination with rebaudioside C and/or dulcoside A, where the amount of rebaudioside A is less than or equal to the amount of each of rebaudioside C or dulcoside A, is described nor how the sweetness

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intensity of the consumable composition plays a role in the sweetness enhancing effect of a diterpene glycoside. Further, no consumable composition for enhancing sweet flavor containing rebaudioside D in combination with rebaudioside C and/or dulcoside A is described.

[0007] U.S. Patent Application Publication No. 2009/0162484 A1 describes beverage products comprising water and a non-sweetening amount of at least one potent natural sweetener. Examples of such potent natural sweeteners are described to be one or more of the steviosides, rebaudiosides and related compounds suitable for sweetening. The publication does not describe any beverage composition according to the present invention.

[0008] U.S. Patent Application Publication No. 2009/0162487 A1 describes beverage products comprising a non-sweetening amount of rebaudioside A and a sweetening amount of a sweetener other than rebaudioside A. Examples of sweeteners other than rebaudioside A are described to be nutritive natural sweeteners, such as sucrose, glucose, or fructose. However, the publication does not describe any beverage composition according to the present invention.

[0009] A need exists for more potent sweet taste enhancers that can effectively enhance the sweet taste of a carbohydrate sweetener without exhibiting an off-taste, such as a bitter aftertaste. In particular, a need exists in the art for a method of enhancing the sweetness of consumables that are already very sweet, *i.e.*, that have a sweetness intensity equivalent to from about 5% (w/v-%) to about 12% (w/v-%) sucrose solution.

Brief Summary of the Invention

[0010] The present invention is related to the use of at least one of rebaudioside A or rebaudioside D in

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combination with one or more diterpene glycosides of Formula I described below, and especially rebaudioside A in combination with rebaudioside C and/or dulcoside A, and stereoisomers thereof, for enhancing the sweet taste of carbohydrate sweeteners, such as sucrose and fructose. The present invention is also related to the use of rebaudioside D in combination with rebaudioside C and/or dulcoside A, and stereoisomers thereof, for enhancing the sweet taste of carbohydrate sweeteners.

[0011] One aspect of the present invention is to provide a method of enhancing a sweet taste of a carbohydrate sweetener. This method comprises administering to a subject the carbohydrate sweetener and an effective amount of at least one of rebaudioside A or rebaudioside D and one or more compounds having the Formula I, or a stereoisomer thereof, wherein the effective amount provides a sweet taste enhancing effect without exhibiting an off-taste, wherein the amount of rebaudioside A is less than or equal to the amount of each compound of Formula I, or a stereoisomer thereof. In one aspect, the method comprises administering to a subject the carbohydrate sweetener and an effective amount of rebaudioside A and one or more compounds having the Formula I, or a stereoisomer thereof, wherein the effective amount provides a sweet taste enhancing effect without exhibiting an off-taste, wherein the amount of rebaudioside A is less than or equal to the amount of each compound of Formula I, or a stereoisomer thereof. Specifically, in one embodiment, this method comprises administering to a subject the carbohydrate sweetener and an effective amount of rebaudioside A, or a stereoisomer thereof, in combination with an effective amount of rebaudioside C and/or dulcoside A, or stereoisomers thereof, wherein the effective amount

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provides a sweet taste enhancing effect without exhibiting any off-taste, and wherein the amount of rebaudioside A is less than or equal to the amount of each of rebaudioside C or dulcoside A. In one aspect, the method comprises administering to a subject the carbohydrate sweetener and an effective amount of rebaudioside D and one or more compounds having the Formula I, or a stereoisomer thereof, wherein the effective amount provides a sweet taste enhancing effect without exhibiting an off-taste. In one embodiment, this method comprises administering to a subject the carbohydrate sweetener and an effective amount of rebaudioside D, or a stereoisomer thereof, in combination with an effective amount of rebaudioside C and/or dulcoside A, or stereoisomers thereof, wherein the effective amount provides a sweet taste enhancing effect without exhibiting any off-taste. In one embodiment, the amount of rebaudioside D is less than or equal to the amount of each of rebaudioside C or dulcoside A. In one embodiment, the method of the present invention comprises administering to a subject a composition consisting essentially of the carbohydrate sweetener and an effective amount of at least one of rebaudioside A or rebaudioside D and one or more compounds having the Formula I, or a stereoisomer thereof, wherein the effective amount provides a sweet taste enhancing effect without exhibiting an off-taste, wherein the amount of rebaudioside A is less than or equal to the amount of each compound of Formula I, or a stereoisomer thereof. Preferably, the carbohydrate sweetener is sucrose, fructose, or glucose. In one embodiment, the carbohydrate sweetener and the composition comprising at least one of rebaudioside A or rebaudioside D, or a stereoisomer thereof, in combination with rebaudioside C and/or dulcoside A, or stereoisomers

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thereof, are administered in a consumable. The consumable includes, but is not limited to, a food product, a pharmaceutical composition, a dental hygienic composition, a dietary supplement, a nutraceutical, or a cosmetic product.

[0012] In one embodiment, rebaudioside A is present in the consumable of the present invention at a concentration of from about 20 ppm to about 100 ppm (from about 20.7 μM to about 103.5 μM). In one embodiment, rebaudioside D is present in the consumable of the present invention at a concentration of from about 20 ppm to about 100 ppm (from about 18 μM to about 88 μM). In one embodiment, rebaudioside C and/or dulcoside A, or a stereoisomer thereof, are each independently present in the consumable of the present invention at a concentration of from about 100 ppm to about 600 ppm (from about 105 μM to about 630 μM for rebaudioside C; from about 127 μM to about 760 μM for dulcoside A). In one embodiment, rebaudioside C and/or dulcoside A, or a stereoisomer thereof, are each independently present in the consumable at a concentration of from about 150 μM to about 600 μM . In one embodiment, the carbohydrate sweetener is present in the consumable of the present invention at a concentration of from about 20000 ppm to about 100000 ppm. In one embodiment, the sweetness intensity of the consumable is equivalent to about 5-12% (w/v-%) sucrose solution. In one embodiment, the sweetness intensity of the consumable is equivalent to about 5-7% (w/v-%) sucrose solution. In another embodiment, the sweetness intensity of the consumable is equivalent to about 8-12% (w/v-%) sucrose solution. In one embodiment, the sweetness intensity of the consumable is equivalent to about 5% (w/v-%), about 6% (w/v-%), about 7% (w/v-%), or about 8% (w/v-%) sucrose solution. In one embodiment, the

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sweetness intensity of the consumable is equivalent to about 9% (w/v-%), about 10% (w/v-%), about 11% (w/v-%), or about 12% (w/v-%) sucrose solution.

[0013] One aspect of the present invention is to provide a consumable, comprising a carbohydrate sweetener, at least one of rebaudioside A or rebaudioside D, and one or more compounds of Formula I, or a stereoisomer thereof, in an amount effective to enhance the sweet taste of the carbohydrate sweetener without exhibiting an off-taste, wherein the amount of rebaudioside A is less than or equal to the amount of each compound of Formula I, or a stereoisomer thereof. One aspect of the present invention is to provide a consumable, comprising a carbohydrate sweetener, rebaudioside A, and one or more compounds of Formula I, or a stereoisomer thereof, in an amount effective to enhance the sweet taste of the carbohydrate sweetener without exhibiting an off-taste, wherein the amount of rebaudioside A is less than or equal to the amount of each compound of Formula I, or a stereoisomer thereof. In one embodiment of this aspect of the invention, the consumable comprises a carbohydrate sweetener, rebaudioside A and, rebaudioside C and/or dulcoside A, or a stereoisomer thereof, in an amount effective to enhance the sweet taste of the carbohydrate sweetener without exhibiting an off-taste, wherein the amount of rebaudioside A is less than or equal to the amount of each of rebaudioside C or dulcoside A. In one embodiment, the consumable of the present invention contains from about 20 ppm to about 100 ppm (from about 20.7 μ M to about 103.5 μ M) rebaudioside A. One aspect of the present invention is to provide a consumable, comprising a carbohydrate sweetener, rebaudioside D, and one or more compounds of Formula I, or a stereoisomer thereof, in an amount effective to enhance

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the sweet taste of the carbohydrate sweetener without exhibiting an off-taste. In one embodiment, the consumable comprises a carbohydrate sweetener, rebaudioside D and, rebaudioside C and/or dulcoside A, or a stereoisomer thereof, in an amount effective to enhance the sweet taste of the carbohydrate sweetener without exhibiting an off-taste. In one embodiment, the amount of rebaudioside D is less than or equal to the amount of each of rebaudioside C or dulcoside A. In one embodiment, the consumable of the present invention contains from about 20 ppm to about 100 ppm (from about 18 μ M to about 88 μ M) rebaudioside D. In one embodiment, the consumable of the present invention is substantially free of diterpene glycosides other than compounds of Formula I, such as rebaudioside C and dulcoside A, rebaudioside A, and rebaudioside D, and stereoisomers thereof. In one embodiment, the consumable of the present invention comprises a composition consisting essentially of a carbohydrate sweetener, at least one of rebaudioside A or rebaudioside D and, rebaudioside C and/or dulcoside A, or a stereoisomer thereof, in an amount effective to enhance the sweet taste of the carbohydrate sweetener without exhibiting an off-taste. In one embodiment, the amount of rebaudioside A and rebaudioside D in the composition is less than or equal to the amount of each of rebaudioside C or dulcoside A. In one embodiment, the consumable of the present invention contains from about 100 ppm to about 600 ppm rebaudioside C (from about 105 μ M to about 630 μ M) and/or dulcoside A (from about 127 μ M to about 760 μ M), or a stereoisomer thereof. In one embodiment, the consumable of the present invention contains from about 150 μ M to about 600 μ M rebaudioside C and/or dulcoside A, or a stereoisomer thereof. In one embodiment, the consumable of the present invention

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contains from about 20000 ppm to about 100000 ppm of a carbohydrate sweetener. In one embodiment, the consumable has a sweetness intensity equivalent to about 5-12% (w/v-%) sucrose solution. In one embodiment, the consumable has a sweetness intensity equivalent to about 5-7% (w/v-%) sucrose solution. In another embodiment, the consumable has a sweetness intensity equivalent to about 8-12% (w/v-%) sucrose solution. In one embodiment, the sweetness intensity of the consumable of the present invention is equivalent to about 5% (w/v-%), about 6% (w/v-%), about 7% (w/v-%), about 8% (w/v-%), about 9% (w/v-%), about 10% (w/v-%), about 11% (w/v-%), or about 12% (w/v-%) sucrose solution.

[0014] Another aspect of the present invention is to provide a method of decreasing the amount of a carbohydrate sweetener in a consumable, comprising adding at least one of rebaudioside A or rebaudioside D and one or more compounds of Formula I, or a stereoisomer thereof, to the consumable and thereby reducing the amount of the carbohydrate sweetener needed to exhibit a given sweetness. One aspect of the present invention is to provide a method of decreasing the amount of a carbohydrate sweetener in a consumable, comprising adding rebaudioside A and one or more compounds of Formula I, or a stereoisomer thereof, to the consumable and thereby reducing the amount of the carbohydrate sweetener needed to exhibit a given sweetness. In one embodiment, the method of decreasing a carbohydrate sweetener in a consumable comprises adding rebaudioside A and, rebaudioside C and/or dulcoside A, or a stereoisomer thereof, to the consumable and thereby reducing the amount of the carbohydrate sweetener needed to exhibit a given level of sweetness, wherein the amount of rebaudioside A is less than or equal to the amount of each of rebaudioside C

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or dulcoside A. One aspect of the present invention is to provide a method of decreasing the amount of a carbohydrate sweetener in a consumable, comprising adding rebaudioside D and one or more compounds of Formula I, or a stereoisomer thereof, to the consumable and thereby reducing the amount of the carbohydrate sweetener needed to exhibit a given sweetness. In one embodiment, the method of decreasing a carbohydrate sweetener in a consumable comprises adding rebaudioside D and, rebaudioside C and/or dulcoside A, or a stereoisomer thereof, to the consumable and thereby reducing the amount of the carbohydrate sweetener needed to exhibit a given level of sweetness. In one embodiment, the amount of rebaudioside D is less than or equal to the amount of each of rebaudioside C or dulcoside A.

[0015] Another aspect of the invention is to provide a method of enhancing the sweetness of a consumable comprising a carbohydrate sweetener, comprising adding at least one of rebaudioside A or rebaudioside D, and one or more compounds of Formula I, or a stereoisomer thereof, to the consumable in an amount effective to enhance the sweetness of the consumable. One aspect of the invention is to provide a method of enhancing the sweetness of a consumable comprising a carbohydrate sweetener, comprising adding rebaudioside A and one or more compounds of Formula I, or a stereoisomer thereof, to the consumable in an amount effective to enhance the sweetness of the consumable. In one embodiment, rebaudioside A and, rebaudioside C and/or dulcoside A, or a stereoisomer thereof, are added to the consumable in an amount effective to enhance the sweetness of the consumable, wherein the amount of rebaudioside A is less than or equal to the amount of each of rebaudioside C or dulcoside A. One aspect of the invention is to provide a method of enhancing the sweetness

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of a consumable comprising a carbohydrate sweetener, comprising adding rebaudioside D and one or more compounds of Formula I, or a stereoisomer thereof, to the consumable in an amount effective to enhance the sweetness of the consumable. In one embodiment, rebaudioside D and, rebaudioside C and/or dulcoside A, or a stereoisomer thereof, are added to the consumable in an amount effective to enhance the sweetness of the consumable. In one embodiment, the amount of rebaudioside D is less than or equal to the amount of each of rebaudioside C or dulcoside A. In one embodiment, the consumable has a sweetness intensity equivalent to about 5-12% (w/v-%) sucrose solution. In one embodiment, the consumable has a sweetness intensity equivalent to about 5% (w/v-%), about 6% (w/v-%), about 7% (w/v-%), or about 8% (w/v-%) sucrose solution. In one embodiment, the consumable has a sweetness intensity equivalent to about 9% (w/v-%), about 10% (w/v-%), about 11% (w/v-%), or about 12% (w/v-%) sucrose solution. In one embodiment, rebaudioside A is added to the consumable in an amount to obtain a concentration of from about 20 ppm to about 100 ppm (from about 20.7 μM to about 103.5 μM). In one embodiment, rebaudioside D is added to the consumable in an amount to obtain a concentration of from about 20 ppm to about 100 ppm (from about 18 μM to about 88 μM). In one embodiment, rebaudioside C and/or dulcoside A, or a stereoisomer thereof, are each independently added to the consumable in an amount to obtain a concentration of from about 100 ppm to about 600 ppm (from about 105 μM to about 630 μM for rebaudioside C; from about 127 μM to about 760 μM for dulcoside A). In one embodiment, rebaudioside C and/or dulcoside A, or a stereoisomer thereof, are each independently added to the consumable in an amount to

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obtain a concentration of from about 150 μM to about 600 μM .

[0016] Additional embodiments and advantages of the invention will be set forth in part of the description that follows, and will flow from the description, or may be learned by practice of the invention. The embodiments and advantages of the invention will be realized and attained by means of the elements and combinations particularly pointed out in the appended claims.

[0017] It is to be understood that both the foregoing summary and the following detailed description are exemplary and explanatory only and are not restrictive of the invention, as claimed.

Brief Description of the Drawings

[0018] FIG. 1 depicts graphically the results of Example 1 illustrating the sweetness enhancing effect of 300 μM rebaudioside C on 5% (w/v-%) sucrose solution. N = 20 panelists. One-way ANOVA $p < 0.0001$ group effect. (*) indicates significantly different from other groups by Tukey's post-hoc test ($p < 0.05$).

[0019] FIG. 2 depicts graphically the results of Example 2 illustrating the sweetness enhancing effect of 300 μM rebaudioside C on 5% (w/v-%) fructose solution. N = 20 panelists. One-way ANOVA $p < 0.0005$ group effect. (*) indicates significantly different from other groups by Tukey's post-hoc test ($p < 0.05$).

[0020] FIG. 3 depicts graphically the results of Example 4 illustrating the sweetness enhancing effect of 300 μM rebaudioside C on 8% (w/v-%) sucrose solution. N = 20 panelists. One-way ANOVA $p < 0.0001$ group effect. (*) indicates significantly different from other groups by Tukey's post-hoc test ($p < 0.001$).

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[0021] FIG. 4 depicts graphically the results of Example 5 illustrating the sweetness enhancing effect of 150 μ M rebaudioside C on 8% (w/v-%) sucrose solution. N = 20 panelists. One-way ANOVA $p < 0.0001$ group effect. (*) indicates significantly different from other groups by Tukey's post-hoc test ($p < 0.05$).

[0022] FIG. 5 depicts graphically the results of Example 6 illustrating the sweetness enhancing effect of 300 μ M rebaudioside C in iced tea containing 10.39% (w/v-%) high fructose corn syrup (HFCS). N = 20 panelists. One-way ANOVA $p < 0.0001$ group effect. (*) indicates significantly different from other groups by Tukey's post-hoc test ($p < 0.01$).

[0023] FIG. 6 depicts graphically the results of Example 7 illustrating the sweetness enhancing effect of 300 μ M dulcoside A on 8% (w/v-%) sucrose solution. N = 20 panelists. One-way ANOVA $p < 0.0001$ group effect. (*) indicates significantly different from other groups by Tukey's post-hoc test ($p < 0.01$).

[0024] FIG. 7 depicts graphically the results of Example 8 illustrating the sweetness enhancing effect of 300 μ M dulcoside A on 5% (w/v-%) sucrose solution. N = 20 panelists. One-way ANOVA $p < 0.0001$ group effect. (*) indicates significantly different from other groups by Tukey's post-hoc test ($p < 0.001$).

[0025] FIG. 8 depicts graphically the results of Example 9 illustrating the sweetness enhancing effect of 300 μ M rebaudioside C in iced tea containing 8% (w/v-%) sucrose. N = 20 panelists. One-way ANOVA $p < 0.0001$ group effect. (*) indicates significantly different from other groups by Tukey's post-hoc test ($p < 0.01$).

[0026] FIG. 9 depicts graphically the results of Example 10 illustrating the sweetness enhancing effect of 300 μ M

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dulcoside A on 5% (w/v-%) fructose solution. N = 20 panelists. One-way ANOVA $p < 0.0001$ group effect. (*) indicates significantly different from other groups by Tukey's post-hoc test ($p < 0.001$).

[0027] FIG. 10 depicts graphically the results of Example 11 illustrating the taste profiles of 150, 300, and 600 μM rebaudioside C solution and 0.2 mg/ml rebaudioside A solution.

[0028] FIG. 11 depicts graphically the results of Example 12 illustrating the sweetness enhancing effect of 40 μM rebaudioside A and 300 μM rebaudioside C on 5% (w/v-%) sucrose solution separately and in combination compared to the sweetness intensity of 5% (w/v-%) sucrose solution. All pairwise comparisons were significantly different ($p < 0.001$) except 5% sucrose + 40 μM Reb A vs. 5% sucrose + 300 μM Reb C.

[0029] FIG. 12 depicts graphically the results of Example 13 illustrating the sweetness enhancing effect of 40 μM rebaudioside A and 300 μM rebaudioside C on 5% (w/v-%) sucrose solution separately and in combination compared to the sweetness intensity of 7% (w/v-%) sucrose solution. N = 20 panelists. One-way ANOVA $p < 0.0001$ group effect. (*) indicates significantly different from other groups by Tukey's post-hoc test ($p < 0.005$).

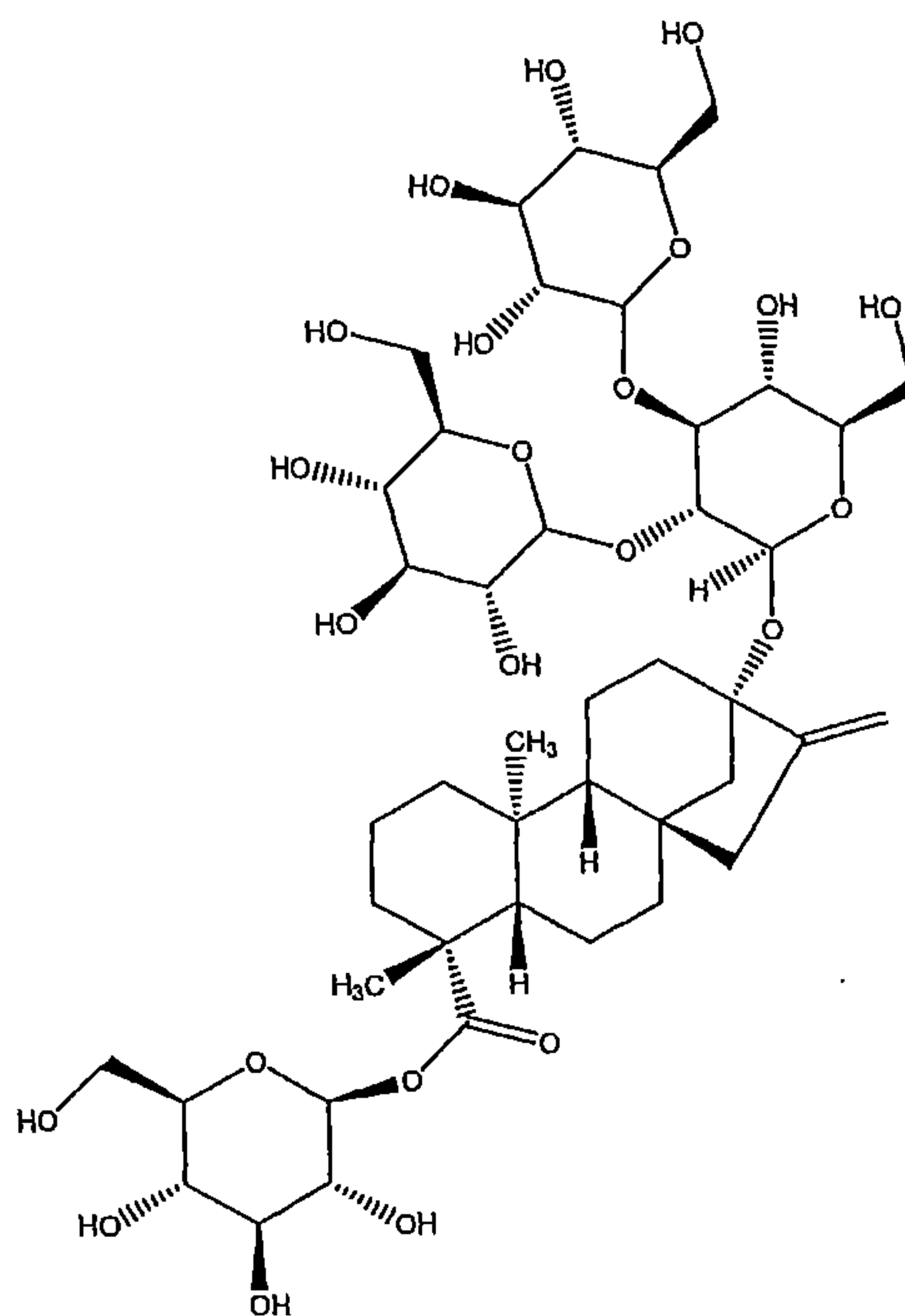
[0030] FIG. 13 depicts graphically the results of Example 14 illustrating the effect of 200 ppm rebaudioside A (RA) on 5% (w/v-%) sucrose solution and the sweetness enhancing effect of 80 ppm rebaudioside A in combination with 190 ppm rebaudioside C (RC) on 5% (w/v-%) sucrose solution compared to the sweetness intensity of 10% (w/v-%) sucrose solution. N = 20 panelists. No significant differences by one-way ANOVA.

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[0031] FIG. 14 depicts graphically the results of Example 15 illustrating the sweetness enhancing effect of 80 ppm rebaudioside D (RD) in combination with 190 ppm rebaudioside C (RC) on 5% (w/v-%) sucrose solution; and 60 ppm rebaudioside D in combination with 210 ppm rebaudioside C on 5% (w/v-%) sucrose solution; and the effect of 400 ppm of rebaudioside D compared to the sweetness intensity of 10% (w/v-%) sucrose solution. N = 20 panelists. One-way ANOVA $p < 0.0001$ group effect. Conditions c and d were significantly different from condition a ($p < 0.001$, Tukey's post-hoc test). Condition b was not significantly different from condition a.

Detailed Description of the Invention

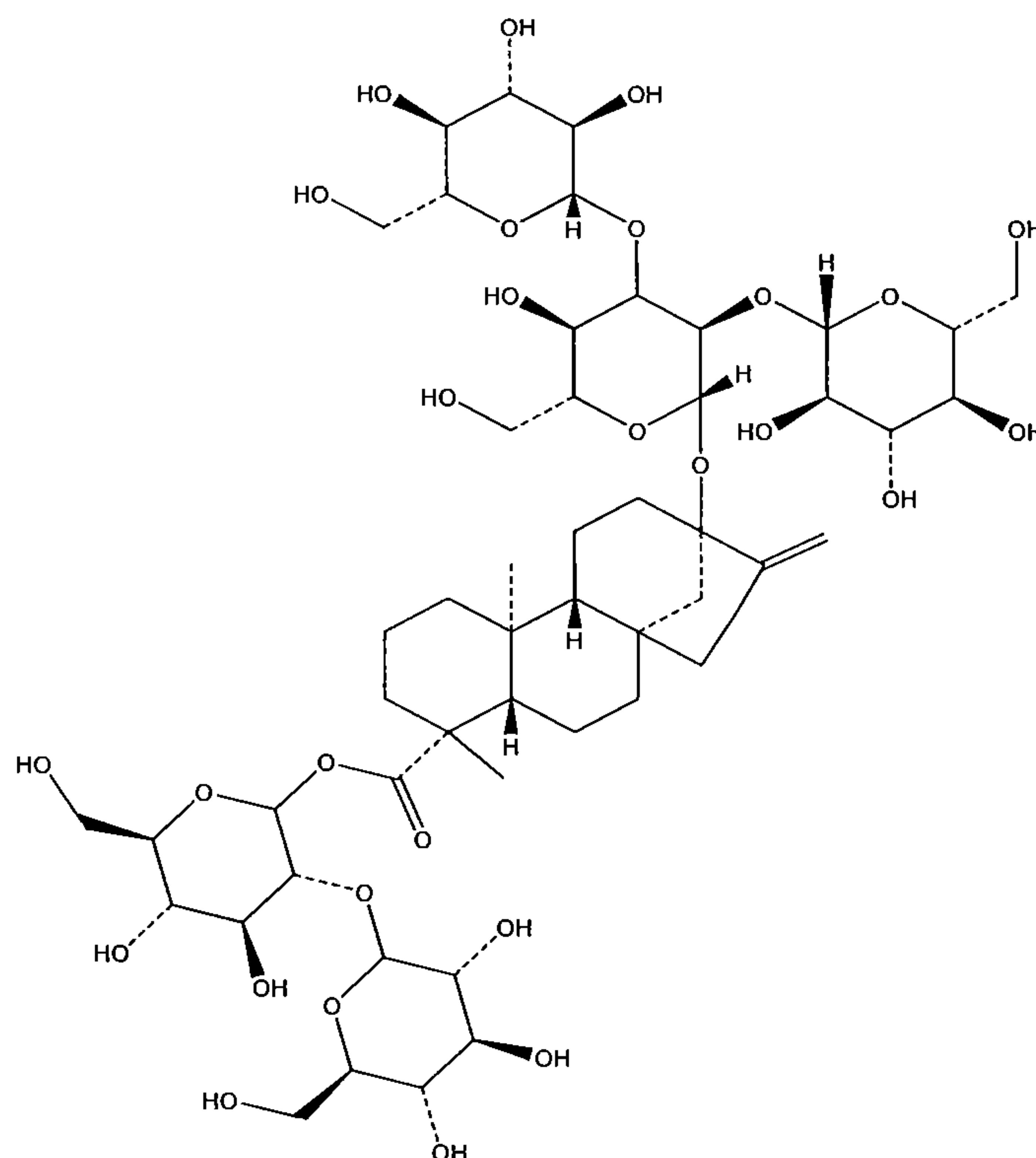
[0032] Rebaudioside A (hereinafter also "Reb A") is a diterpenoid glycoside having the following structure:



[0033] Reb A can be used in a purified or isolated form in the present invention, or as an extract from *Stevia rebaudiana*. Reb A can be isolated as described, for example, in Canadian Patent No. 2278083.

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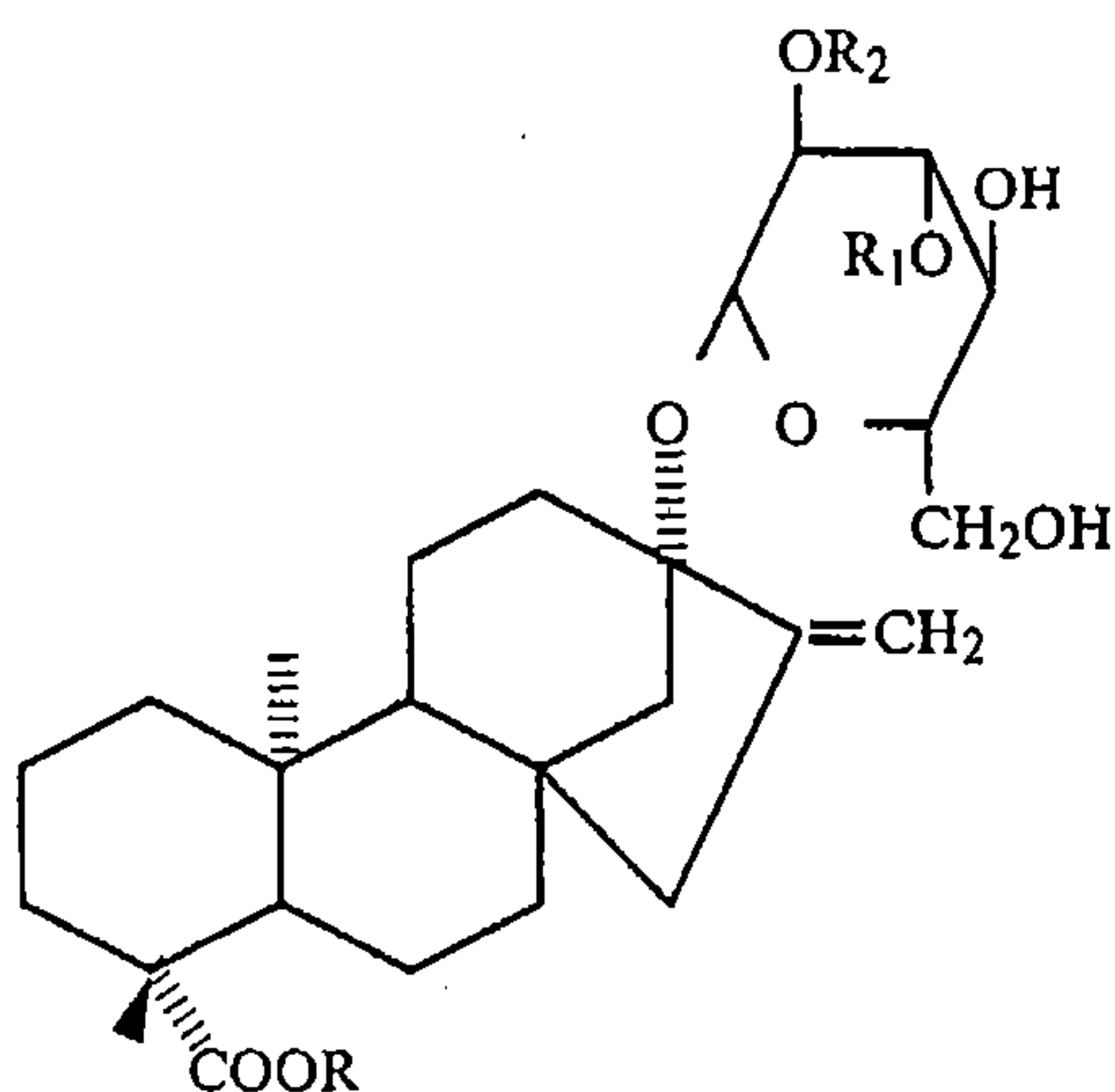
[0034] Rebaudioside D (hereinafter also "Reb D") is a diterpenoid glycoside having the following structure:



[0035] Reb D can be prepared by methods known in the art, such as by isolating from *Stevia rebaudiana* plant material as described in U.S. Patent No. 4,361,697, which is fully incorporated by reference herein in its entirety. Reb D can be used in a purified or isolated form in the present invention.

[0036] The sweetness enhancers of the present invention for use in combination with Reb A and Reb D have the following Formula I:

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I

wherein R_2 is rhamnose, and R and R_1 are each independently selected from the group consisting of hydrogen, glucose, and beta-sophorose, and stereoisomers thereof. In one embodiment, R is glucose. In one embodiment, R_1 is glucose or hydrogen. In one embodiment, the compound of Formula I is rebaudioside C (hereinafter also "Reb C"), wherein R and R_1 both are glucose. In one embodiment, the compound of Formula I is dulcoside A (hereinafter also "Dulc A"), or a stereoisomer thereof, wherein R is glucose and R_1 is hydrogen. Compounds of Formula I can be used in all embodiments of the invention alone or in combination with two or more compounds of Formula I. Compounds of Formula I, including Reb C and Dulc A, can be prepared by methods known in the art, such as by isolating from *Stevia rebaudiana* plant material as described in U.S. Patent No. 4,361,697, which is fully incorporated by reference herein in its entirety. Compounds of Formula I, including Reb C and Dulc A, can be used in a purified or isolated form in the present invention. Alternatively, Reb C and Dulc A can be co-purified. Reb C and Dulc A can be co-purified, for example, by following the procedure described in Canadian Patent No. 2278083. Accordingly, sweet diterpene glycosides are first extracted from *Stevia rebaudiana* and then

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stevioside is separated from the mixture, followed by the separation of rebaudioside A from the mother liquor. Reb C and Dulc A may then be coprecipitated from the remaining filtrate by repeating the procedure used for separating rebaudioside A.

[0037] In the embodiments of the present invention, the composition extracted from *Stevia rebaudiana* contains Dulc A and/or Reb C as the major components and rebaudioside A and stevioside as minor components. Preferably, compounds of Formula I, and especially Reb C and Dulc A, to be used in all embodiments of the present invention have less than 10%, preferably less than 5%, and more preferably less than 3% of impurities (*i.e.*, compounds other than those of Formula I) other than water.

[0038] Compounds of Formula I, including Reb C and Dulc A, Reb A, and Reb D may contain one or more asymmetric centers and may thus give rise to enantiomers, diastereomers, and other stereoisomeric forms. The present invention is meant to encompass the uses of all such possible forms, as well as their racemic and resolved forms and mixtures thereof. The individual enantiomers may be separated according to methods known to those of ordinary skill in the art in view of the present disclosure. All tautomers are intended to be encompassed by the present invention as well.

[0039] As used herein, the term "stereoisomers" is a general term for all isomers of individual molecules that differ only in the orientation of their atoms in space. It includes enantiomers and isomers of compounds with more than one chiral center that are not mirror images of one another (diastereomers).

[0040] The term "chiral center" refers to a carbon atom to which four different groups are attached.

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[0041] The terms "enantiomer" and "enantiomeric" refer to a molecule that cannot be superimposed on its mirror image and hence is optically active wherein the enantiomer rotates the plane of polarized light in one direction and its mirror image compound rotates the plane of polarized light in the opposite direction.

[0042] The term "racemic" refers to a mixture of equal parts of enantiomers and which mixture is optically inactive.

[0043] The term "resolution" refers to the separation or concentration or depletion of one of the two enantiomeric forms of a molecule.

[0044] The terms "a" and "an" refer to one or more.

[0045] As used herein, the term "sweetness intensity" refers to the relative strength of sweet sensation as observed or experienced by an individual, e.g., a human, or a degree or amount of sweetness detected by a taster, for example on the scale from 0 (none) to 8 (very strong) (see Example 1) used in sensory evaluations according to the procedure described in *American Society for Testing Materials, Special Technical Publication-434: "Manual on Sensory Testing Methods,"* ASTM International, West Conshohocken, PA (1996).

[0046] As used herein, the phrase "sweet taste enhancing effect" means that the effect of Reb A or Reb D in combination with the compound of Formula I, e.g., Reb C and/or Dulc A, is such that the sensory perception of the sweet flavor is potentiated in a more than additive manner, i.e., synergistically.

[0047] As used herein, the term "off-taste" refers to an amount or degree of taste that is not characteristically or usually found in a consumable. For example, an off-taste is an undesirable taste of a sweetened consumable to the

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consumers, such as, a bitter taste, a licorice-like taste, a metallic taste, an aversive taste, a nasty taste, an astringent taste, a delayed sweetness onset, and a lingering sweet aftertaste, and the like.

[0048] As used herein, the phrase "the detection threshold for its intrinsic sweetness" refers to the concentration of Reb C or Dulc A, or stereoisomers thereof, at which the sweetness of Reb C or Dulc A, or stereoisomers thereof, is perceptible to an individual, e.g., a human.

[0049] As used herein in connection with a measured quantity, "about" refers to the normal variations in that measured quantity, as expected by the skilled artisan making the measurement and exercising a level of care commensurate with the objective of measurement and the precision of the measuring equipment.

[0050] The term "w/v-%" as used herein means the weight of a component (in grams) for every 100 ml of the liquid composition of the present invention.

[0051] The term "ppm" as used herein means the weight of the component (in milligrams) per liter of solution, i.e., $\mu\text{g/ml}$.

[0052] Reb A or Reb D in combination with one or more compounds of Formula I, including Reb C and Dulc A, can be used in consumables, e.g., in food products, pharmaceuticals, dietary supplements, nutraceuticals, dental hygienic compositions, or other products as sweetness enhancers, which retain a desired sweetness but contain lower amounts of a carbohydrate sweetener, such as sucrose, glucose and fructose. In one embodiment, the present invention provides a consumable, comprising an effective amount of a combination of Reb A with Reb C and/or Dulc A, and a carbohydrate sweetener in a reduced amount in order to achieve the same level of sweetness when

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the carbohydrate sweetener is used alone in the traditional amount. In one embodiment, the present invention provides a consumable, comprising an effective amount of a combination of Reb D with Reb C and/or Dulc A, and a carbohydrate sweetener in a reduced amount in order to achieve the same level of sweetness when the carbohydrate sweetener is used alone in the traditional amount. By way of brief example, a common carbonated cola beverage may contain about 20 to 30 grams of sugar (e.g., fructose) and about 100 calories per 8 ounce serving. The present invention enables one to prepare a similar cola beverage with substantially reduced sugar and caloric content with the same level of sweetness. Reb A or Reb D in combination with Reb C and/or Dulc A enhances the sweet taste produced by the reduced sugar content, thereby creating an enhanced sweet taste based on the level of the sugar, without exhibiting any off-taste.

[0053] Suitable carbohydrate sweeteners of the present invention include, but are not limited to, sucrose, fructose, glucose, high fructose corn syrup (containing fructose and glucose), xylose, arabinose, rhamnose, and sugar alcohols, such as erythritol, xylitol, mannitol, sorbitol, or inositol. In one embodiment of the present invention, the carbohydrate sweetener is sucrose, fructose, glucose, high fructose corn syrup, xylose, arabinose or rhamnose, preferably sucrose, fructose, or glucose. In one aspect of this embodiment, the carbohydrate sweetener is sucrose. In another aspect of this embodiment, the carbohydrate sweetener is glucose. In another aspect of this embodiment, the carbohydrate sweetener is fructose. In another embodiment, the carbohydrate sweetener is a sugar alcohol.

[0054] Sucrose, also known as table sugar or saccharose, is a disaccharide of glucose and fructose. Its systematic name

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is α -D-glucopyranosyl-(1 $\rightarrow$ 2)- β -D-fructofuranose. Fructose and glucose are monosaccharide sugars.

[0055] In the present invention, Reb A, Reb D, and one or more compounds of Formula I, or stereoisomers thereof, are used in an amount effective to enhance the sweetness of a carbohydrate sweetener without exhibiting an off-taste. In one embodiment, rebaudioside A is present in an amount less than or equal to each of one or more compounds of Formula I, or a stereoisomer thereof. In one embodiment, Reb A in combination with Reb C and/or Dulc A is used in an amount effective to enhance the sweetness of a carbohydrate sweetener without exhibiting any off-taste, wherein the amount of Reb A is less than or equal to the amount of each of Reb C or Dulc A. Any amount of Reb C and Dulc A, or stereoisomers thereof, that provides the desired degree of sweetness enhancement can be used. In one embodiment, Reb A is used in combination with Reb C in an amount effective to enhance the sweetness of a carbohydrate sweetener without exhibiting an off-taste, wherein Reb A is present in an amount less than or equal to the amount of Reb C. In one embodiment, Reb A is used in combination with Dulc A in an amount effective to enhance the sweetness of a carbohydrate sweetener without exhibiting an off-taste, wherein Reb A is present in an amount less than or equal to the amount of Dulc A. In one embodiment, Reb A is used in combination with both Reb C and Dulc A in an amount effective to enhance the sweetness of a carbohydrate sweetener without exhibiting an off-taste, wherein Reb A is present in an amount less than or equal to the amount of each of Reb C and Dulc A. In one embodiment, Reb A is present in an amount less than the amount of each of Reb C and Dulc A.

[0056] In one embodiment of the present invention, Reb A is used at a concentration of from about 20 ppm to about 100

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ppm (from about 20.7 μM to about 103.5 μM). In one embodiment, Reb A is used at a concentration of from about 20 ppm to about 90 ppm. In one embodiment, Reb A is used at a concentration of from about 20 ppm to about 80 ppm. In one embodiment, Reb A is used at a concentration of from about 30 ppm to about 80 ppm. In one embodiment, Reb A is used at a concentration of from about 40 ppm to about 80 ppm. In one embodiment, Reb A is used at a concentration of from about 60 ppm to about 80 ppm. In one embodiment, Reb A is used at a concentration of about 60 ppm or about 80 ppm. In one embodiment, Reb A is used at a concentration of from about 30 ppm to about 60 ppm. In one embodiment, Reb A is used at a concentration of from about 35 ppm to about 50 ppm. In one embodiment, Reb A is used at a concentration of from about 35 ppm to about 40 ppm. In one embodiment, Reb A is present at a concentration of about 40 μM .

[0057] In one embodiment, rebaudioside D is present in an amount less than or equal to each of one or more compounds of Formula I, or a stereoisomer thereof. In one embodiment, Reb D in combination with Reb C and/or Dulc A is used in an amount effective to enhance the sweetness of a carbohydrate sweetener without exhibiting any off-taste, wherein the amount of Reb D is less than or equal to the amount of each of Reb C or Dulc A. Any amount of Reb C and Dulc A, or stereoisomers thereof, that provides the desired degree of sweetness enhancement can be used. In one embodiment, Reb D is used in combination with Reb C in an amount effective to enhance the sweetness of a carbohydrate sweetener without exhibiting an off-taste, wherein Reb D is present in an amount less than or equal to the amount of Reb C. In one embodiment, Reb D is used in combination with Dulc A in an amount effective to enhance the sweetness of a carbohydrate sweetener without exhibiting an off-taste, wherein Reb D is

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present in an amount less than or equal to the amount of Dulc A. In one embodiment, Reb D is used in combination with both Reb C and Dulc A in an amount effective to enhance the sweetness of a carbohydrate sweetener without exhibiting an off-taste. In one embodiment, Reb D is present in an amount less than or equal to the amount of each of Reb C and Dulc A. In one embodiment, Reb D is present in an amount less than the amount of each of Reb C and Dulc A.

[0058] In one embodiment of the present invention, Reb D is used at a concentration of from about 20 ppm to about 100 ppm (from about 18 μ M to about 88 μ M). In one embodiment, Reb D is used at a concentration of from about 20 ppm to about 90 ppm. In one embodiment, Reb D is used at a concentration of from about 20 ppm to about 80 ppm. In one embodiment, Reb D is used at a concentration of from about 30 ppm to about 80 ppm. In one embodiment, Reb D is used at a concentration of from about 40 ppm to about 80 ppm. In one embodiment, Reb D is used at a concentration of from about 60 ppm to about 80 ppm. In one embodiment, Reb D is used at a concentration of about 60 ppm or about 80 ppm.

[0059] In one embodiment, the concentration at which Reb C and Dulc A are each independently used in the present invention is at, slightly above, or below the detection threshold for its intrinsic sweetness.

[0060] In one embodiment of the present invention, Reb C and Dulc A are each independently used at a concentration of from about 100 ppm to about 600 ppm (from about 105 μ M to about 630 μ M for Reb C; from about 127 μ M to about 760 μ M for Dulc A). In one embodiment, Reb C and Dulc A are each independently used at a concentration of from about 200 ppm to about 500 ppm. In one embodiment, Reb C and Dulc A are each independently used at a concentration of from

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about 250 ppm to about 450 ppm. In one embodiment, Reb C and Dulc A are each independently used at a concentration of from about 250 ppm to about 400 ppm. In one embodiment, Reb C and Dulc A are each independently used at a concentration of about 300 ppm.

[0061] In one embodiment, Reb C and Dulc A are each independently present in the consumable of the present invention at a concentration of from about 150 μM to about 600 μM . In one embodiment, Reb C and Dulc A are each independently present in the consumable of the present invention at a concentration of from about 150 μM to about 350 μM . In one embodiment, Reb C and Dulc A are each independently present in the consumable of the present invention at a concentration of from about 250 μM to about 350 μM . In one embodiment, Reb C and Dulc A are each independently present in the consumable of the present invention at a concentration of from about 350 μM to about 600 μM . In one embodiment, Reb C and Dulc A are each independently present in the consumable of the present invention at a concentration of about 150 μM , about 160 μM , about 170 μM , about 180 μM , about 190 μM , about 200 μM , about 210 μM , about 220 μM , about 230 μM , about 240 μM , about 250 μM , about 260 μM , about 270 μM , about 280 μM , about 290 μM , about 300 μM , about 310 μM , about 320 μM , about 330 μM , about 340 μM , or about 350 μM . In one embodiment, Reb C and Dulc A are each independently present in the consumable of the present invention at a concentration of about 360 μM , about 370 μM , about 380 μM , about 390 μM , about 400 μM , about 410 μM , about 420 μM , about 430 μM , about 440 μM , about 450 μM , about 460 μM , about 470 μM , about 480 μM , about 490 μM , about 500 μM , about 510 μM , about 520 μM , about 530 μM , about 540 μM , about 550 μM , about 560 μM , about 570 μM , about 580 μM ,

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about 590 μM , or about 600 μM . Useful concentrations of Reb C and Dulc A in the consumable of the present invention are about 250 μM or about 300 μM , and specifically about 300 μM . In one embodiment, the ratio of Reb C or Dulc A to the carbohydrate sweetener, especially sucrose, is approximately from 1:150 to 1:200 in a solid consumable. In one embodiment, the consumable of the present invention contains about 0.1 to 0.5 g, preferably about 0.3 g, of Reb C or Dulc A, or a stereoisomer thereof, for every 50 to 100 g of the carbohydrate sweetener. In one embodiment, the consumable of the present invention contains both Reb C and Dulc A, or a stereoisomer thereof, in an amount of about 0.1 to 0.5 g, preferably about 0.3 g, for every 50 to 100 g of the carbohydrate sweetener. In one embodiment, the consumable of the present invention contains about 0.03 to 0.15 g of Reb A for every 50 to 100 g of a carbohydrate sweetener, such as sucrose. In one embodiment, the consumable of the present invention contains about 0.03 to 0.15 g of Reb D for every 50 to 100 g of a carbohydrate sweetener, such as sucrose.

[0062] In one embodiment, Dulc A and Reb C are used together in the consumable of the present invention in concentration ratios of from about 1:4 to about 4:1. In one embodiment, Dulc A and Reb C are used together in a consumable of the present invention in concentration ratios of from about 1:2 to about 2:1, and especially 1:1. In one embodiment, the consumable of the present invention contains 150 μM Dulc A and 600 μM Reb C, 150 μM Dulc A and 450 μM Reb C, 150 μM Dulc A and 300 μM Reb C, 150 μM Dulc A and 150 μM Reb C, 300 μM Dulc A and 150 μM Reb C, 450 μM Dulc A and 150 μM Reb C, 600 μM Dulc A and 150 μM Reb C, 300 μM Dulc A and 300 μM Reb C, 300 μM Dulc A and 600 μM

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Reb C, 600 μ M Dulc A and 300 μ M Reb C, 450 μ M Dulc A and 450 μ M Reb C, or 600 μ M Dulc A and 600 μ M Reb C.

[0063] In one embodiment of the present invention, the carbohydrate sweetener is present in the consumable of the present invention at a concentration of from about 20000 ppm to about 100000 ppm. In one embodiment, the carbohydrate sweetener is present at a concentration of from about 30000 ppm to about 80000 ppm. In one embodiment, the carbohydrate sweetener is present at a concentration of about 50000 ppm. In one embodiment of the present invention, the carbohydrate sweetener is sucrose.

[0064] In one embodiment of the present invention, Reb A and Reb C (or Dulc A) are present in the consumable of the present invention in concentration ratios of from about 1:4 to about 1:10. In one embodiment, Reb A and Reb C are present in the consumable of the present invention in concentration ratios of from about 1:6 to about 1:9. In one embodiment, Reb A and Reb C are present in the consumable of the present invention in concentration ratio of about 1:7.5.

[0065] In one embodiment of the present invention, Reb D and Reb C (or Dulc A) are present in the consumable of the present invention in concentration ratios of from about 1:4 to about 1:10. In one embodiment, Reb D and Reb C are present in the consumable of the present invention in concentration ratios of from about 1:6 to about 1:9. In one embodiment, Reb D and Reb C are present in the consumable of the present invention in concentration ratio of about 1:7.5.

[0066] Compounds of Formula I having rhamnose in the position of R₂, such as Reb C and Dulc A, act synergistically with carbohydrate sweeteners, such as sucrose and fructose, potentiating sweetness intensity even

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at high concentrations of the carbohydrate sweetener. As shown in Examples 1 and 2, Reb C acts synergistically with sucrose and fructose, enhancing the sweetness intensity of 5% (w/v-%) sucrose and 5% (w/v-%) fructose solutions at Reb C concentration of 300 μ M, i.e., at a concentration of Reb C where Reb C itself does not significantly contribute to the overall sweet taste of the mixture. Further, the results of Examples 4 and 5 show the sweetness intensity of 8% (w/v-%) sucrose solution is significantly enhanced at Reb C concentrations of 300 μ M and 150 μ M, respectively. Example 6 shows that Reb C acts synergistically with high fructose corn syrup (HFCS) enhancing the sweetness intensity of an iced tea containing 10.39% (w/v-%) HFCS (equivalent to sweetness intensity of an 8% (w/v-%) sucrose solution at Reb C concentration of 300 μ M. Example 7 shows that Dulc A acts synergistically with sucrose enhancing the sweetness intensity of an 8% (w/v-%) sucrose solution at Dulc A concentration of 300 μ M. Example 8 shows that Dulc A acts synergistically with sucrose enhancing the sweetness intensity of a 5% (w/v-%) sucrose solution at Dulc A concentration of 300 μ M. Example 9 shows that Reb C enhances the sweetness intensity of an iced tea containing 8% (w/v-%) sucrose at Reb C concentration of 300 μ M. Example 10 shows that Dulc A acts synergistically with fructose enhancing the sweetness intensity of a 5% (w/v-%) fructose solution at Dulc A concentration of 300 μ M.

[0067] It has been found that compounds of Formula I, such as Reb C, act synergistically with Reb A in the presence of a carbohydrate sweetener, such as sucrose and fructose, potentiating sweetness intensity even at high concentrations of the carbohydrate sweetener. Example 12 shows that Reb C acts synergistically with Reb A enhancing the sweetness intensity of a 5% (w/v-%) sucrose solution

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containing 40 μ M Reb A at Reb C concentration of 300 μ M. At 5% (w/v-%) sucrose solution, Reb A has only an additive effect on the sweetness intensity (Schiffmann et al., *Brain Research Bulletin* 38:105-120 (1995)). Therefore, it is surprising that Reb C, at a concentration of little or no intrinsic sweetness, potentiates synergistically the additive sweetness enhancing effect of Reb A at a high concentration of a carbohydrate sweetener. Example 13 further shows that the mixture of 5% (w/v-%) sucrose, 40 μ M Reb A and 300 μ M Reb C is substantially sweeter than a 7% (w/v-%) sucrose solution. Example 14 shows that the combination of 80 ppm Reb A and 190 ppm Reb C enhances the sweetness intensity of a 5% (w/v-%) sucrose solution to that of a 10% (w/v-%) sucrose solution. Example 14 also shows that in order to achieve the sweetness intensity of a 10% (w/v-%) sucrose solution, 200 ppm of Reb A must be added to a 5% (w/v-%) sucrose solution.

[0068] It has further been found that compounds of Formula I, such as Reb C, act synergistically with Reb D in the presence of a carbohydrate sweetener, such as sucrose and fructose, potentiating sweetness intensity even at high concentrations of the carbohydrate sweetener. Example 15 shows that Reb C acts synergistically with Reb D enhancing the sweetness intensity of a 5% (w/v-%) sucrose solution containing 80 ppm Reb D at Reb C concentration of 190 ppm. Example 15 also shows that Reb C acts synergistically with Reb D enhancing the sweetness intensity of a 5% (w/v-%) sucrose solution containing 60 ppm Reb D at Reb C concentration of 210 ppm.

[0069] Therefore, at least one of Reb A or Reb D in combination with Reb C and/or Dulc A is especially useful for enhancing the sweetness of a consumable having a sweetness intensity equivalent to about 5-12% (w/v-%)

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sucrose solution. In this aspect of the invention, the consumable is preferably a sweet juice or a soft drink having a sweetness intensity equivalent to about 5-12% (w/v-%) sucrose solution. Reb A or Reb D in combination with Reb C and/or Dulc A can be added to this consumable having a sweetness intensity equivalent to about 5-12% (w/v-%) sucrose solution by admixing it with the consumable or admixing it with a component of the consumable. In one embodiment, Reb A, in combination with Reb C and/or Dulc A, is added to a consumable having a sweetness intensity equivalent to about 5% (w/v-%), about 6% (w/v-%), about 7% (w/v-%), or about 8% (w/v-%) sucrose solution to enhance the sweetness of the consumable. In one embodiment, Reb A, in combination with Reb C and/or Dulc A, is added to a consumable having a sweetness intensity equivalent to about 9% (w/v-%), about 10% (w/v-%), about 11% (w/v-%), or about 12% (w/v-%) sucrose solution to enhance the sweetness of the consumable. In one embodiment, the sweetness intensity of the consumable of the present invention containing Reb A and, Reb C and/or Dulc A, is equivalent to about 5-7% (w/v-%) sucrose solution. In another embodiment, the sweetness intensity of the consumable of the present invention containing Reb A and, Reb C and/or Dulc A, is equivalent to about 8-12% (w/v-%) sucrose solution. In one embodiment, the sweetness intensity of the consumable of the present invention containing Reb A and, Reb C and/or Dulc A, is equivalent to about 5% (w/v-%), about 6% (w/v-%), about 7% (w/v-%), about 8% (w/v-%), about 9% (w/v-%), about 10% (w/v-%), about 11% (w/v-%), or about 12% (w/v-%) sucrose solution.

[0070] In one embodiment, Reb D, in combination with Reb C and/or Dulc A, is added to a consumable having a sweetness intensity equivalent to about 5% (w/v-%), about 6% (w/v-%),

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about 7% (w/v-%), or about 8% (w/v-%) sucrose solution to enhance the sweetness of the consumable. In one embodiment, Reb D, in combination with Reb C and/or Dulc A, is added to a consumable having a sweetness intensity equivalent to about 9% (w/v-%), about 10% (w/v-%), about 11% (w/v-%), or about 12% (w/v-%) sucrose solution to enhance the sweetness of the consumable. In one embodiment, the sweetness intensity of the consumable of the present invention containing Reb D and, Reb C and/or Dulc A, is equivalent to about 5-7% (w/v-%) sucrose solution. In another embodiment, the sweetness intensity of the consumable of the present invention containing Reb D and, Reb C and/or Dulc A, is equivalent to about 8-12% (w/v-%) sucrose solution. In one embodiment, the sweetness intensity of the consumable of the present invention containing Reb D and, Reb C and/or Dulc A, is equivalent to about 5% (w/v-%), about 6% (w/v-%), about 7% (w/v-%), about 8% (w/v-%), about 9% (w/v-%), about 10% (w/v-%), about 11% (w/v-%), or about 12% (w/v-%) sucrose solution.

[0071] Consumables include all food products, dietary supplements, nutraceuticals, pharmaceutical compositions, dental hygienic compositions, and cosmetic products. Also, one or more sweeteners other than carbohydrate sweeteners can be present in the consumables of the present invention, for example, high-intensity sweeteners, such as aspartame, acesulfame potassium, sucralose, and saccharin. The carbohydrate sweetener can be present in the consumable inherently (e.g., in food products containing fruits) or the carbohydrate sweetener is added into the consumable.

[0072] The phrase "food product" as used herein includes, but is not limited to, fruits, vegetables, juices, meat products such as ham, bacon and sausage; egg products, fruit concentrates, gelatins and gelatin-like products such

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as jams, jellies, preserves, and the like; milk products such as ice cream, sour cream, yoghurt, and sherbet; icings, syrups including molasses; corn, wheat, rye, soybean, oat, rice and barley products, cereal products, nut meats and nut products, cakes, cookies, confectionaries such as candies, gums, fruit flavored drops, and chocolates, chewing gum, mints, creams, icing, ice cream, pies and breads, beverages such as coffee, tea, carbonated soft drinks, such as COKE[®] and PEPSI[®], non-carbonated soft drinks, juices and other fruit drinks, sports drinks such as GATORADE[®], coffee, teas, iced teas, cola, alcoholic beverages, such as beers, wines and liquors, and KOOL-AID[®]. Preferably, the food products in which the sweetness of the carbohydrate sweetener is enhanced with Reb A or Reb D in combination with Reb C and/or Dulc A, contains a decreased level of the carbohydrate sweetener. For example, an improved carbonated soft drink can be produced with the same sweetness as the known carbonated soft drink but with a lower sugar content by adding at least one of Reb A or Reb D and, Reb C and/or Dulc A, or stereoisomers thereof.

[0073] Food products also include condiments such as herbs, spices and seasonings, flavor enhancers, such as monosodium glutamate. A food product also includes prepared packaged products, such as dietetic sweeteners, liquid sweeteners, tabletop sweeteners, granulated flavor mixes which upon reconstitution with water provide non-carbonated drinks, instant pudding mixes, instant coffee and tea, coffee whiteners, malted milk mixes, pet foods, livestock feed, tobacco, and materials for baking applications, such as powdered baking mixes for the preparation of breads, cookies, cakes, pancakes, donuts and the like. Food products also include diet or low-calorie food and beverages containing little or no sucrose. Especially

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preferred food products are carbonated beverages containing Reb A or Reb D and, Reb C and/or Dulc A. Other examples of food products envisioned in accordance with the present invention are described below and throughout the specification.

[0074] In another embodiment, the food product is selected from the group consisting of fruits, vegetables, juices, meat products such as ham, bacon and sausage; egg products, fruit concentrates, gelatins and gelatin-like products such as jams, jellies, preserves, and the like; milk products such as ice cream, sour cream, yoghurt, and sherbet; icings, syrups including molasses; corn, wheat, rye, soybean, oat, rice and barley products, cereal products, nut meats and nut products, cakes, cookies, confectionaries such as candies, gums, fruit flavored drops, and chocolates, creams, icing, ice cream, pies and breads.

[0075] In one embodiment, the invention is directed to a method of decreasing the amount of a carbohydrate sweetener in a consumable, such as a food product or a pharmaceutical composition, to exhibit a given level of sweetness, wherein the method comprises reducing the amount of the carbohydrate sweetener and adding at least one of Reb A or Reb D, and one or more compounds of Formula I, or a stereoisomer thereof, to the consumable in an amount effective to maintain the given level of sweetness. In one embodiment, the invention is directed to a method of decreasing the amount of a carbohydrate sweetener in a consumable, such as a food product or a pharmaceutical composition, to exhibit a given level of sweetness, wherein the method comprises reducing the amount of the carbohydrate sweetener and adding Reb A and, Reb C and/or Dulc A, to the consumable in an amount effective to maintain the given level of sweetness of the consumable. In

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one embodiment, the invention is directed to a method of decreasing the amount of a carbohydrate sweetener in a consumable, such as a food product or a pharmaceutical composition, to exhibit a given level of sweetness, wherein the method comprises reducing the amount of the carbohydrate sweetener and adding Reb D and, Reb C and/or Dulc A, to the consumable in an amount effective to maintain the given level of sweetness of the consumable.

[0076] In one embodiment, the food product is a beverage or a drink comprising a carbohydrate sweetener, Reb A, and one or more compounds of Formula I, or a stereoisomer thereof. In one embodiment, the food product is a beverage or a drink comprising a carbohydrate sweetener and Reb A in combination with Reb C and/or Dulc A, or stereoisomers thereof. In one embodiment, the food product is a beverage or a drink comprising a carbohydrate sweetener, Reb D, and one or more compounds of Formula I, or a stereoisomer thereof. In one embodiment, the food product is a beverage or a drink comprising a carbohydrate sweetener and Reb D in combination with Reb C and/or Dulc A, or stereoisomers thereof. Examples of suitable beverages in which having a sweet taste is desired include, but are not limited to coffee, teas, such as black tea, green tea, fermented tea, semi-fermented tea, carbonated soft drinks, such as COKE[®] and PEPSI[®], non-carbonated soft drinks, lemonade, juices and other fruit drinks, sports drinks, such as GATORADE[®], iced teas, cola, alcoholic beverages, such as beers, wines and liquors, and KOOL-AID[®]. In one embodiment, Reb A is present at a concentration from about 20 ppm to about 100 ppm (from about 20.7 μ M to about 103.5 μ M), and Reb C and/or Dulc A are each independently present at a concentration of from about 100 ppm to about 600 ppm (from about 105 μ M to about 630 μ M of Reb C; from about 127 μ M to about 760 μ M of Dulc

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A). In certain embodiments, Reb A is present at a concentration of from about 20 ppm to about 90 ppm. In certain embodiments, Reb A is present at a concentration of from about 20 ppm to about 80 ppm. In one embodiment, Reb A is present at a concentration of from about 30 ppm to about 80 ppm. In one embodiment, Reb A is present at a concentration of from about 40 ppm to about 80 ppm. In one embodiment, Reb A is present at a concentration of from about 60 ppm to about 80 ppm. In one embodiment, Reb A is used at a concentration of about 60 ppm or about 80 ppm. In one embodiment, Reb A is present at a concentration of from about 30 ppm to about 60 ppm. In one embodiment, Reb A is present at a concentration of from about 35 ppm to about 50 ppm. In one embodiment, Reb A is present at a concentration of from about 35 ppm to about 40 ppm. In one embodiment, Reb A is present at a concentration of about 40 μ M. In one embodiment, Reb D is present at a concentration from about 20 ppm to about 100 ppm (from about 18 μ M to about 88 μ M), and Reb C and/or Dulc A are each independently present at a concentration of from about 100 ppm to about 600 ppm (from about 105 μ M to about 630 μ M of Reb C; from about 127 μ M to about 760 μ M of Dulc A). In certain embodiments, Reb D is present at a concentration of from about 20 ppm to about 90 ppm. In one embodiment, Reb D is present at a concentration of from about 20 ppm to about 80 ppm. In one embodiment, Reb D is present at a concentration of from about 30 ppm to about 80 ppm. In one embodiment, Reb D is present at a concentration of from about 40 ppm to about 80 ppm. In one embodiment, Reb D is present at a concentration of from about 60 ppm to about 80 ppm. In one embodiment, Reb D is used at a concentration of about 60 ppm or about 80 ppm. In certain embodiments, Reb C and/or Dulc A are each independently present at a concentration of from about 100

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ppm to about 600 ppm. In one embodiment, Reb C and/or Dulc A are each independently present at a concentration of from about 200 ppm to about 500 ppm. In one embodiment, Reb C and/or Dulc A are each independently present at a concentration of from about 250 ppm to about 450 ppm. In one embodiment, Reb C and/or Dulc A are each independently present at a concentration of about 300 ppm. In one embodiment, Reb C is present at a concentration of from about 105 μM to about 630 μM and/or Dulc A is present at a concentration of from about 127 μM to about 760 μM . In one embodiment, Reb C and/or Dulc A are each independently present at a concentration of from about 150 μM to about 350 μM . In one embodiment, Reb C and/or Dulc A are each independently present at a concentration of from about 250 μM to about 350 μM . In one embodiment, Reb C and/or Dulc A are each independently present at a concentration of from about 350 μM to about 600 μM . In one embodiment, Reb C and/or Dulc A are each independently present in the beverage or drink at a concentration of about 150 μM , about 160 μM , about 170 μM , about 180 μM , about 190 μM , about 200 μM , about 210 μM , about 220 μM , about 230 μM , about 240 μM , about 250 μM , about 260 μM , about 270 μM , about 280 μM , about 290 μM , about 300 μM , about 310 μM , about 320 μM , about 330 μM , about 340 μM , or about 350 μM . In one embodiment, Reb C and/or Dulc A are each independently present in the consumable of the present invention at a concentration of about 360 μM , about 370 μM , about 380 μM , about 390 μM , about 400 μM , about 410 μM , about 420 μM , about 430 μM , about 440 μM , about 450 μM , about 460 μM , about 470 μM , about 480 μM , about 490 μM , about 500 μM , about 510 μM , about 520 μM , about 530 μM , about 540 μM , about 550 μM , about 560 μM , about 570 μM , about 580 μM , about 590 μM , or about 600 μM . Useful concentrations of Reb

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C in the beverage or drink of the present invention is about 250 μM or about 300 μM , and specifically 300 μM . Useful concentrations of Dulc A in the beverage or drink of the present invention is about 250 μM or about 300 μM , and specifically 300 μM . In one embodiment, the beverage or drink comprises one carbohydrate sweetener. In another embodiment, it comprises more than one carbohydrate sweetener. In certain embodiments, the beverage or drink comprises sucrose and corn syrup, or it comprises sucrose and aspartame as sweeteners.

[0077] One embodiment of the invention is directed to a method of enhancing the sweet taste of a cola beverage, such as COKE[®] or PEPSI[®], comprising administering to a subject a cola drink, comprising a carbohydrate sweetener, Reb A and, Reb C and/or Dulc A, wherein Reb A and, Reb C and/or Dulc A, are present in an amount effective to enhance the sweet taste of the carbohydrate sweetener without exhibiting any off-taste, and wherein the amount of Reb A is less than or equal to the amount of each of Reb C and Dulc A. In one embodiment, the invention is directed to a method of enhancing the sweet taste of a cola beverage, comprising administering to a subject a cola drink, comprising a carbohydrate sweetener, Reb D and, Reb C and/or Dulc A, wherein Reb D and, Reb C and/or Dulc A, are present in an amount effective to enhance the sweet taste of the carbohydrate sweetener without exhibiting any off-taste. In one embodiment, the amount of Reb D is less than or equal to the amount of each of Reb C and Dulc A. In a preferred embodiment, the cola beverage contains a reduced amount of sugar but maintains substantially the original level of sweet taste.

[0078] Cola beverages are prepared by mixing cola concentrate with carbonated water. Typically about 50 mL of

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cola concentrate is added per 250 mL of carbonated water. Cola concentrate can be prepared by mixing cola flavor, caramel color, and optionally caffeine with water, one or more carbohydrate sweeteners, Reb A or Reb D, Reb C and/or Dulc A, and one or more acid components, such as phosphoric acid or citric acid.

[0079] A cola flavor refers to either a natural or artificial flavor. Such cola flavors are commercially available. Commercial cola flavors are available, for example, from International Flavor and Fragrances, Dayton, NJ; Artificial #13573011 and Natural #K3559549. Commercial cola flavors are also available from Tastemaker, Cincinnati, OH, and Givaudan Roure, Clifton, NJ

[0080] The acid component refers to an ingredient that contributes sourness to the beverage and is added to balance the flavor profile. Acids include malic acid, citric acid, phosphoric acid or combinations thereof.

[0081] For example, the cola concentrate can prepared by mixing phosphoric acid (75% Rhone-Poulenc), citric acid (anhydrous, ADM, Decatur, IL), caffeine (Mallinckrodt, Paris, KY), caramel Color (DS400, Sethness, Chicago, IL), cola Flavor (SN018976, International Flavors and Fragrances, Dayton, NJ), sucrose, Reb A or Reb D, Reb C and/or Dulc A, and water. The concentrate is blended until all ingredients are dissolved (30-40 minutes) using a magnetic stirring plate. Fifty milliliters of the concentrate are added to 250 mL of carbonated water to complete the preparation of the cola beverage. Fifty milliliters of cola concentrate typically contains from 0.01 to 5 mL of phosphoric acid, preferably about 0.01-1 mL, 0.1 to 100 g of sucrose, preferably about 1-10 g, about 0.03 g to 0.15 g of Reb A, for every 50 to 100 g of sucrose, about 0.1 to about 0.5 g, and preferably about 0.3

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g, of Reb C and/or Dulc A, for every 50 to 100 g of sucrose, about 0.001 g to 0.1 g of citric acid, preferably about 0.005-0.1 g, 0.001 to 1 g of caffeine, preferably about 0.01 to 0.1 g of caffeine, 0.01 to 5 g of caramel flavor, preferably about 0.05 to 1 g, 0.001 to about 10 mL of cola flavor, preferably about 0.01 to about 2 mL. Reb A can be replaced by an equal amount of Reb D in this cola concentrate.

[0082] In certain embodiments, the improved food product, such as the cola beverage, e.g., COKE® or PEPSI®, contains a reduced amount of sugar compared to the prior art cola beverage. The method can be performed such that the amount of sugar required to maintain the desired sweetness of the cola beverage is reduced by at least about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 95%, or from about 60% to about 99%, or alternatively from about 20% to about 50%. Thus, in a more specific embodiment, the cola beverage comprising a carbohydrate sweetener, Reb A or Reb D and, Reb C and/or Dulc A, contains Reb A or Reb D and, Reb C and/or Dulc A, or stereoisomers thereof, in an amount sufficient to reduce the amount of sugar required to maintain the desired sweetness of the beverage by 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 95%, or from about 60% to about 99%, or alternatively from about 30% to about 70%. Of course, in other embodiments, the amount of sugar required may be decreased to differing extents.

[0083] Food products of the present invention also include animal food products, comprising a carbohydrate sweetener and at least one of Reb A or Reb D in combination with Reb C and/or Dulc A, or stereoisomers thereof, in an amount sufficient to enhance the sweet taste of the carbohydrate sweetener without exhibiting any off-taste. Animal food products are well known in the art, see, e.g., U.S. Patent

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No. 6,403,142, and include dog food, cat food, rabbit food, and the like. The animal food product also include food products useful for feeding livestock, such as cattle, bison, pigs, chicken, and the like. In another embodiment, the animal food product of the present invention is a solid hypoallergenic pet food, comprising a component that contains protein or protein fragments wherein all of said component is partially hydrolyzed and further comprises Reb A or Reb D and, Reb C and/or Dulc A, or stereoisomers thereof. In certain embodiments, Reb A, Reb D, and, Reb C and/or Dulc A, are each present in the animal food product in an amount as described above for food products.

[0084] In one embodiment, the consumable is a pharmaceutical composition comprising a carbohydrate sweetener, Reb A, and a compound of Formula I, or a stereoisomer thereof. In one embodiment, the consumable is a pharmaceutical composition comprising a carbohydrate sweetener and Reb A in combination with Reb C and/or Dulc A, or stereoisomers thereof. In one embodiment, the consumable is a pharmaceutical composition comprising a carbohydrate sweetener, Reb D, and a compound of Formula I, or a stereoisomer thereof. In one embodiment, the consumable is a pharmaceutical composition comprising a carbohydrate sweetener and Reb D in combination with Reb C and/or Dulc A, or stereoisomers thereof. Preferred compositions are pharmaceutical compositions comprising Reb A or Reb D and, Reb C and/or Dulc A, or stereoisomers thereof, and one or more pharmaceutically acceptable excipients. These pharmaceutical compositions may be used to formulate pharmaceutical drugs containing one or more active agents that exert a biological effect other than sweetness enhancement. The pharmaceutical composition preferably further comprises one or more active agents that

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exert a biological effect. Such active agents include pharmaceutical and biological agents that have an activity other than taste enhancement. Such active agents are well known in the art. See, e.g., The Physician's Desk Reference. Such compositions can be prepared according to procedures known in the art, for example, as described in Remington's Pharmaceutical Sciences, Mack Publishing Co., Easton, Pa., USA. In one embodiment, such an active agent includes bronchodilators, anorexiant, antihistamines, nutritional supplements, laxatives, analgesics, anesthetics, antacids, H₂-receptor antagonists, anticholinergics, antidiarrheals, demulcents, antitussives, antinauseants, antimicrobials, antibacterials, antifungals, antivirals, expectorants, anti-inflammatory agents, antipyretics, and mixtures thereof. In one embodiment, the active agent is selected from the group consisting of antipyretics and analgesics, e.g., ibuprofen, acetaminophen, or aspirin; laxatives, e.g., phenolphthalein dioctyl sodium sulfosuccinate; appetite depressants, e.g., amphetamines, phenylpropanolamine, phenylpropanolamine hydrochloride, or caffeine; antacids, e.g., calcium carbonate; antiasthmatics, e.g., theophylline; antidiuretics, e.g., diphenoxylate hydrochloride; agents active against flatulence, e.g., simethicone; migraine agents, e.g., ergotamine tartrate; psychopharmacological agents, e.g., haloperidol; spasmolytics or sedatives, e.g., phenobarbital; antihyperkinetics, e.g., methyl dopa or methylphenidate; tranquilizers, e.g., benzodiazepines, hydroxyzine meprobamate or phenothiazines; antihistamines, e.g., astemizole, chlorpheniramine maleate, pyridamine maleate, doxylamine succinate, brompheniramine maleate, phenyltoloxamine citrate, chlorocyclizine hydrochloride, pheniramine maleate, and phenindamine tartrate;

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decongestants, e.g., phenylpropanolamine hydrochloride, phenylephrine hydrochloride, pseudoephedrine hydrochloride, pseudoephedrine sulfate, phenylpropanolamine bitartrate, and ephedrine; beta-receptor blockers, e.g., propranolol; agents for alcohol withdrawal, e.g., disulfiram; antitussives, e.g., benzocaine, dextromethorphan, dextromethorphan hydrobromide, noscapine, carbetapentane citrate, and chlophedianol hydrochloride; fluorine supplements, e.g., sodium fluoride; local antibiotics, e.g., tetracycline or cleocine; corticosteroid supplements, e.g., prednisone or prednisolone; agents against goiter formation, e.g., colchicine or allopurinol; antiepileptics, e.g., phenytoine sodium; agents against dehydration, e.g., electrolyte supplements; antiseptics, e.g., cetylpyridinium chloride; NSAIDs, e.g., acetaminophen, ibuprofen, naproxen, or salts thereof; gastrointestinal active agents, e.g., loperamide and famotidine; various alkaloids, e.g., codeine phosphate, codeine sulfate, or morphine; supplements for trace elements, e.g., sodium chloride, zinc chloride, calcium carbonate, magnesium oxide, and other alkali metal salts and alkali earth metal salts; vitamins; ion-exchange resins, e.g., cholestyramine; cholesterol-depressant and lipid-lowering substances; antiarrhythmics, e.g., N-acetylprocainamide; and expectorants, e.g., guaifenesin.

[0085] Active substances which have a particularly unpleasant taste include antibacterial agents such as ciprofloxacin, ofloxacin, and pefloxacin; antiepileptics such as zonisamide; macrolide antibiotics such as erythromycin; beta-lactam antibiotics such as penicillins and cephalosporins; psychotropic active substances such as chlorpromazine; active substances such as sulpyrine; and agents active against ulcers, such as cimetidine. In another embodiment, the pharmaceutical composition of the

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present invention comprises at least one amino acid selected from the group consisting of glycine, L-alanine, L-arginine, L-aspartic acid, L-cystine, L-glutamic acid, L-glutamine, L-histidine, L-isoleucine, L-leucine, L-lysine, L-methionine, L-ornithine, L-phenylalanine, L-proline, L-serine, L-threonine, L-tryptophan, L-tyrosine, L-valine, creatine, and mixtures thereof.

[0086] The pharmaceutical compositions of the present invention are administered to a subject in any form suitable to achieve their intended purpose. Preferably, however, the composition is one which can be administered buccally or orally. Alternatively, the pharmaceutical composition may be an oral or nasal spray. The subject is any animal, such as a human, although the invention is not intended to be so limited. Other suitable animals include canines, felines, dogs, cats, livestock, horses, cattle, sheep, and the like. A veterinary composition, as used herein, refers to a pharmaceutical composition that suitable for non-human animals. Such veterinary compositions are known in the art.

[0087] In another embodiment, the pharmaceutical composition is a liquid dosage form for oral administration, including pharmaceutically acceptable emulsions, solutions, suspensions, syrups, and elixirs. In addition to the active compounds, the liquid dosage forms may contain inert diluents commonly used in the art such as, for example, water or other solvents, solubilizing agents and emulsifiers such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, dimethyl formamide, oils (in particular, cottonseed, groundnut, corn, germ, olive, castor, and sesame oils), glycerol, tetrahydrofurfuryl alcohol, polyethylene glycols

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and fatty acid esters of sorbitan, and mixtures thereof. Suspensions, in addition to the active compounds, may contain suspending agents as, for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar, and tragacanth, and mixtures thereof.

[0088] The pharmaceutical composition of the present invention can be in the form of a chewable tablet. Chewable tablets are known in the art. See, e.g., U.S. Patent Nos. 4,684,534 and 6,060,078, each of which is incorporated by reference in its entirety. Any kind of medicament may be contained in the chewable tablet, preferably a medicament of bitter taste, natural plant extracts or other organic compounds. More preferably, vitamins such as vitamin A, vitamin B, vitamin B₁, vitamin B₂, vitamin B₆, vitamin C, vitamin E and vitamin K; natural plant extracts such as Sohgunjung-tang extracts, Sipchundaebob-tang extracts and Eleutherococcus senticosus extracts; organic compounds such as dimenhydrinate, meclazine, acetaminophen, aspirin, phenylpropanolamine, and cetylpyridinium chloride; or gastrointestinal agents such as dried aluminum hydroxide gel, domperidone, soluble azulene, L-glutamine and hydrotalcite may be contained in the core.

[0089] The pharmaceutical composition of the present invention can be an orally disintegrating composition. Orally disintegrating tablets are known in the art. See, e.g., U.S. Patent Nos. 6,368,625 and 6,316,029, each of which is hereby incorporated by reference in its entirety.

[0090] The pharmaceutical composition of the present invention can be a nasal composition, comprising a carbohydrate sweetener, Reb A or Reb D and, Reb C and/or Dulc A, or stereoisomers thereof. Nasal sprays are known in the art. See, e.g., U.S. Patent No. 6,187,332. Addition of

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Reb A or Reb D and, Reb C and/or Dulc A, to a nasal spray can reduce the experience of an unpleasant taste associated with the composition of the nasal spray.

[0091] The pharmaceutical composition of the present invention can be a solid dosage form, comprising a carbohydrate sweetener and Reb A or Reb D in combination with Reb C and/or Dulc A, or stereoisomers thereof, and a water and/or saliva activated effervescent granule, such as one having a controllable rate of effervescence. The effervescent composition may further comprise a pharmaceutically active compound. Effervescent pharmaceutical compositions are known in the art. See, e.g., U.S. Patent No. 6,649,186, which is incorporated by reference in its entirety. The effervescent composition can be used in pharmaceutical, veterinary, horticultural, household, food, culinary, pesticidal, agricultural, cosmetic, herbicidal, industrial, cleansing, confectionery and flavoring applications. Formulations incorporating the effervescent composition comprising Reb A or Reb D and, Reb C and/or Dulc A, or stereoisomers thereof, can further include one or more additional adjuvants and/or active ingredients which can be chosen from those known in the art, including flavors, diluents, colors, binders, filler, surfactant, disintegrant, stabilizer, compaction vehicles, and non-effervescent disintegrants.

[0092] The pharmaceutical composition can be a film-shaped or wafer-shaped pharmaceutical composition. Such a film-shaped or wafer-shaped pharmaceutical composition can be configured, for example, as quickly disintegrating administration forms, e.g., administration forms disintegrating within a period of 1 second up to 3 minutes, or as slowly disintegrating administration forms, e.g., administration forms disintegrating within a period of 3 to

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15 minutes. The indicated disintegration times can be set to the above-mentioned ranges by using, for example, matrix-forming polymers which have different disintegrating, or solubility, characteristics. Thus, by mixing the corresponding polymer components, the disintegration time can be adjusted. In addition, disintegrants are known which "draw" water into the matrix and cause the matrix to burst open from within. As a consequence, certain embodiments of the invention include such disintegrants for the purpose of adjusting the disintegration time.

[0093] Suitable are polymers for use in the film-shaped or wafer-shaped pharmaceutical composition include cellulose derivatives, polyvinyl alcohol (e.g. MOWIOL™), polyacrylates, polyvinyl pyrrolidone, cellulose ethers, such as ethyl cellulose, as well as polyvinyl alcohol, polyurethane, polymethacrylates, polymethyl methacrylates and derivatives and copolymerisates of the aforementioned polymers.

[0094] In certain embodiments, the total thickness of the film-shaped or wafer-shaped pharmaceutical composition according to the invention is preferably 5 μm up to 10 mm, preferably 30 μm to 2 mm, and with particular preference 0.1 mm to 1 mm. The pharmaceutical preparations may be round, oval, elliptic, triangular, quadrangular or polygonal shape, but they may also have any rounded shape.

[0095] In one embodiment, the pharmaceutical composition can be a gum base formulation comprising a medicament or agent contained, a carbohydrate sweetener and Reb A or Reb D in combination with Reb C and/or Dulc A, or stereoisomers thereof, in a coating that surrounds the gum base formulation. Preferably, the coating comprises at least 50%

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by weight of the entire product. As the center is chewed, the medicament or agent is released into the saliva. For example, U.S. Patent No. 6,773,716, which is incorporated herein by reference in its entirety, discloses a suitable medicament or agent contained in a coating that surrounds a gum base formulation. It has been found that with respect to certain medicaments or agents that may have an astringent or bitter taste that by adding a sweet taste enhancing agent to the formulation, that a much more palatable formulation, including the medicament, can be provided. In this regard, even though the medicament in, for example, its powder form may be bitter or have an offensive taste, the matrix used as the coating of the present invention, including the enhancing agent, will afford a product having acceptable medicinal properties.

[0096] The pharmaceutical composition of the present invention can be in the form of an aerosol. The aerosol composition may further comprise pharmaceutically active agent. Aerosol compositions are known in the art. See, e.g., U.S. Patent No. 5,011,678, which is hereby incorporated by reference in its entirety. As a nonlimiting example, an aerosol composition according to the present invention may comprise a medically effective amount of a pharmaceutically active substance, one or more carbohydrate sweeteners, Reb A or Reb D and, Reb C and/or Dulc A, or stereoisomers thereof, and a biocompatible propellant, such as a (hydro/fluoro)carbon propellant.

[0097] In one embodiment of the present invention, the pharmaceutical composition is a nutritional composition. Examples of nutritional compositions having an undesirable taste include, but are not necessarily limited to, enteral nutrition products for treatment of nutritional deficit, trauma, surgery, Crohn's disease, renal disease,

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hypertension, obesity and the like, to promote athletic performance, muscle enhancement or general well being or inborn errors of metabolism such as phenylketonuria. In particular, such nutritional formulations may contain one or more amino acids which have a bitter or metallic taste or aftertaste. Such amino acids include, but are not limited to, an essential amino acids selected from the group consisting of L isomers of leucine, isoleucine, histidine, lysine, methionine, phenylalanine, threonine, tryptophan, tyrosine, and valine.

[0098] In one embodiment, the sweet taste of the pharmaceutical composition or nutritional composition of the present invention is being enhanced by Reb A in combination with Reb C and/or Dulc A, or stereoisomers thereof, by at least about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 95%, or from about 60% to about 99%, or alternatively from about 20% to about 50%.

[0099] In one embodiment, the sweet taste of the pharmaceutical composition or nutritional composition of the present invention is being enhanced by Reb D in combination with Reb C and/or Dulc A, or stereoisomers thereof, by at least about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 95%, or from about 60% to about 99%, or alternatively from about 20% to about 50%.

[00100] In one embodiment, the consumable of the present invention is a dental hygienic composition, comprising a carbohydrate sweetener, Reb A, and one or more compounds of Formula I, or a stereoisomer thereof, in an amount sufficient to enhance the sweet taste of the carbohydrate sweetener without exhibiting any off-taste, and wherein the amount of Reb A is less than or equal to the amount of each of Reb C or Dulc A. In one embodiment, the consumable of the present invention is a dental hygienic composition,

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comprising a carbohydrate sweetener and Reb A in combination with Reb C and/or Dulc A, or stereoisomers thereof, in an amount sufficient to enhance the sweet taste of the carbohydrate sweetener without exhibiting any off-taste. In one embodiment, the consumable of the present invention is a dental hygienic composition, comprising a carbohydrate sweetener, Reb D, and one or more compounds of Formula I, or a stereoisomer thereof, in an amount sufficient to enhance the sweet taste of the carbohydrate sweetener without exhibiting any off-taste. In one embodiment, the consumable of the present invention is a dental hygienic composition, comprising a carbohydrate sweetener and Reb D in combination with Reb C and/or Dulc A, or stereoisomers thereof, in an amount sufficient to enhance the sweet taste of the carbohydrate sweetener without exhibiting any off-taste. In one embodiment, the amount of Reb D is less than or equal to the amount of each of Reb C or Dulc A. Dental hygienic compositions are known in the art and include, but are not necessarily limited to, toothpaste, mouthwash, plaque rinse, dental floss, dental pain relievers (such as ANBESOL™), and the like. In one embodiment, the dental hygienic composition comprises one carbohydrate sweetener. In another embodiment, the dental hygienic composition comprises more than one carbohydrate sweetener. In certain embodiments, the dental hygienic composition comprises sucrose and corn syrup, or it comprises sucrose and aspartame.

[00101] In another embodiment, the consumable of the present invention is a cosmetic product comprising a carbohydrate sweetener, Reb A and one or more compounds of Formula I, or a stereoisomer thereof. In another embodiment, the consumable of the present invention is a cosmetic product comprising a carbohydrate sweetener and Reb A in

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combination with Reb C and/or Dulc A, or stereoisomers thereof. In another embodiment, the consumable of the present invention is a cosmetic product comprising a carbohydrate sweetener, Reb D and one or more compounds of Formula I, or a stereoisomer thereof. In another embodiment, the consumable of the present invention is a cosmetic product comprising a carbohydrate sweetener and Reb D in combination with Reb C and/or Dulc A, or stereoisomers thereof. For example, but not by way of limitation, the cosmetic product can be a face cream, lipstick, lip gloss, and the like. Other suitable compositions of the invention include lip balm, such as CHAPSTICK[®] or BURT'S BEESWAX[®] Lip Balm, further comprising Reb A or Reb D and, Reb C and/or Dulc A, or a stereoisomer thereof.

[00102] The present invention is also directed to various, useful consumables comprising Reb A or Reb D and, Reb C and/or Dulc A, or a stereoisomer thereof, described above.

[00103] In one embodiment, the present invention is directed to a food product comprising a carbohydrate sweetener, Reb A, and one or more compounds of Formula I, or a stereoisomer thereof. In one embodiment, the present invention is directed to a food product comprising a carbohydrate sweetener and Reb A in combination with Reb C and/or Dulc A, or a stereoisomer thereof. In one embodiment, the present invention is directed to a food product comprising a carbohydrate sweetener, Reb D, and one or more compounds of Formula I, or a stereoisomer thereof. In one embodiment, the present invention is directed to a food product comprising a carbohydrate sweetener and Reb D in combination with Reb C and/or Dulc A, or a stereoisomer thereof. In one embodiment, the food product is substantially free of diterpene glycosides other than

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compounds of Formula I, such as rebaudioside C and dulcoside A, rebaudioside A, and rebaudioside D, and stereoisomers thereof. In one embodiment, the food product comprises a composition consisting essentially of a carbohydrate sweetener, at least one of rebaudioside A or rebaudioside D, and rebaudioside C and/or dulcoside A, or stereoisomers thereof. Preferably, the food product is one which exhibits a sweet taste (i.e., inherently contains a carbohydrate sweetener) and/or to which a carbohydrate sweetener has been added. The food product comprises Reb A or Reb D and, Reb C and/or Dulc A, or a stereoisomer thereof, in an amount sufficient to enhance the sweet taste without exhibiting an off-taste, wherein the amount of Reb A is less than or equal to the amount of each of Reb C or Dulc A. In one embodiment, the amount of Reb D is less than or equal to the amount of each of Reb C or Dulc A. Specific carbohydrate sweeteners have been described above. Specific food products in which an enhanced sweet taste is desired include, but are not limited to, cakes, cookies, confectionaries, such as candies, gums and chocolates, creams, icing, ice cream, pies and breads. Specific food products which are beverages include soft drinks, juices and other fruit drinks, sports drinks such as GATORADE[®], coffee, teas, iced teas, cola, alcoholic beverages and KOOL-AID[®].

[00104] In certain aspects, the present invention provides methods and compositions for enabling one to prepare consumable products, such as food and pharmaceutical products, which retain a desired sweetness but contain lower amounts of a carbohydrate sweetener, such as sugar, and in some cases fewer calories.

[00105] The following examples are illustrative, but not limiting, of the compounds, compositions, and methods of

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the present invention. Suitable modifications and adaptations of the variety of conditions and parameters normally encountered in clinical therapy and which are obvious to those skilled in the art in view of this disclosure are within the spirit and scope of the invention.

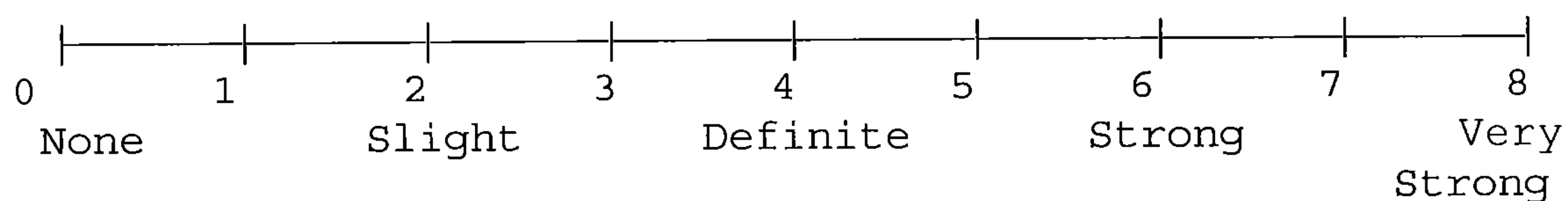
[00106] Reb A, Reb D, Reb C, and Dulc A can be purchased from Chromadex, CA.

Example 1

[00107] The sweetness enhancing effect of 300 μ M Reb C (Chromadex, CA; purity 94.9%; 2.9% impurities other than water) on 5 % (w/v-%) sucrose solution was evaluated in a double-blind controlled test conducted according to the following protocol. Three products were evaluated by trained judges as follows:

- high concentration sucrose (7% w/v)
- low concentration sucrose (5% w/v)
- low concentration sucrose + sweetness enhancer (test compound)

[00108] The products were evaluated using a sequential monadic test protocol. Subjects were given three samples to evaluate. Each subject was directed to swirl the first sample in his or her mouth for 3-5 seconds, expectorate the entire sample into a discard cup, and then assess the sweetness intensity of the sample. The intensity was rated on a score card by marking a numerical value along a scale from 0 to 8 (e.g., 0 = none, 2 = slight, 4 = definite, 8 = very strong). Following the decision regarding the sweetness intensity, subjects were instructed to rinse their mouth with water and spit in the discard cup. Subjects then were given unsalted crackers to cleanse the



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[00111] If any other flavor was present in the sample please describe it. Please rinse your mouth again several times and have some more water and unsalted crackers. You will now have a rest period of 10 minutes before you will be given the next sample.

[00112] The results of this test are presented in FIG. 1. As can be seen from FIG. 1, the judges found that the sweetness of a solution of 5% (w/v-%) sucrose in combination with 300 μ M of Reb C was indistinguishable from that of a 7% (w/v-%) sucrose solution. This is an effect that is equivalent to a standard industry goal for sweetness enhancement.

Example 2

[00113] The sweetness enhancing effect of 300 μ M Reb C on 5% (w/v-%) fructose solution was evaluated in a double-blind controlled test as described in Example 1. The results of this test are presented in FIG. 2. As can be seen from FIG. 2, the judges found that the sweetness of a solution of 5% (w/v-%) fructose in combination with 300 μ M of Reb C was close to that of a 7% (w/v-%) fructose solution.

Example 3

[00114] The taste of a 250 μ M Reb C solution was evaluated by a test group having five (5) subjects as follows (Forced-choice): Subjects were presented with 2 cups, each containing 10 ml of either 250 μ M Reb C water solution or water (room temperature). The contents of the samples were not revealed to the subjects until after the test. Subjects were asked to sip most or all of the 10 ml from the first cup, swish the liquid in their oral cavity, and expectorate into a cup, then rinse their mouths vigorously with water. Soon thereafter, the contents of the second cup were

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sampled in the same manner. Then, subjects were asked to choose the sweeter of the two samples, or if not sweet, to describe the qualitative taste profile of the sample having a detectable taste. All subjects correctly identified the sample containing Reb C and gave the following qualitative taste descriptions:

Subject 1: Metallic, not sweet;
Subject 2: Aversive ("Nasty");
Subject 3: Slight sweet, astringent;
Subject 4: Faintly sweet; and
Subject 5: Slight sweet/licorice.

[00115] The taste of 250 μ M and 300 μ M Reb C solutions were evaluated as follows by another test group having four (4) subjects as follows: 10 ml solutions of 250 and 300 μ M Reb C in water were sampled by four subjects who were asked to report their qualitative taste experience of the solutions. Subjects were aware of the sample contents but had no previous exposure to Reb C nor were they given any verbal suggestion about expected tastes that could influence their report. The subjects have the following qualitative taste descriptions:

Subject 1: Both concentrations bitter and/or licorice;
Subject 2: Both concentrations bitter and/or licorice;
Subject 3: Both concentrations bitter and/or licorice;
and
Subject 4: Both concentrations bitter and/or licorice.

Example 4

[00116] The sweetness enhancing effect of 300 μ M Reb C on 8% (w/v-%) sucrose solution was evaluated in a double-blind controlled test according to the procedure described in Example 1. The results of this test are presented in FIG. 3. As can be seen from FIG. 3, the judges found that the

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sweetness of a solution of 8% (w/v-%) sucrose in combination with 300 μ M of Reb C was close to that of an 11% (w/v-%) sucrose solution.

Example 5

[00117] The sweetness enhancing effect of 150 μ M Reb C on 8% (w/v-%) sucrose solution was evaluated in a double-blind controlled test according to the procedure described in Example 1. The results of this test are presented in FIG. 4. As can be seen from FIG. 4, the judges found that the sweetness of a solution of 8% (w/v-%) sucrose in combination with 150 μ M of Reb C was between that of the 8% (w/v-%) sucrose solution and that of an 11% (w/v-%) sucrose solution. The mean sweetness intensity scores of this test for 8% (w/v-%) sucrose solution, 8% (w/v-%) sucrose solution with 150 μ M Reb C, and 11% (w/v-%) sucrose solution were 5.30, 6.10. and 6.95, respectively.

Example 6

[00118] The sweetness enhancing effect of 300 μ M Reb C (Chromadex, CA; purity 94.9%; 2.9% impurities other than water) in iced tea having 10.39% (w/v-%) high fructose corn syrup (HFCS) (equivalent to the sweetness intensity of an 8% (w/v-%) sucrose solution) was evaluated in a double-blind controlled test conducted according to the following protocol. Three products were evaluated by trained judges as follows:

- high concentration HFCS (14.29% w/v; equivalent to 11% w/v sucrose solution)
- low concentration HFCS (10.39% w/v; equivalent to 8% w/v sucrose solution)

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- low concentration HFCS + sweetness enhancer (test compound)

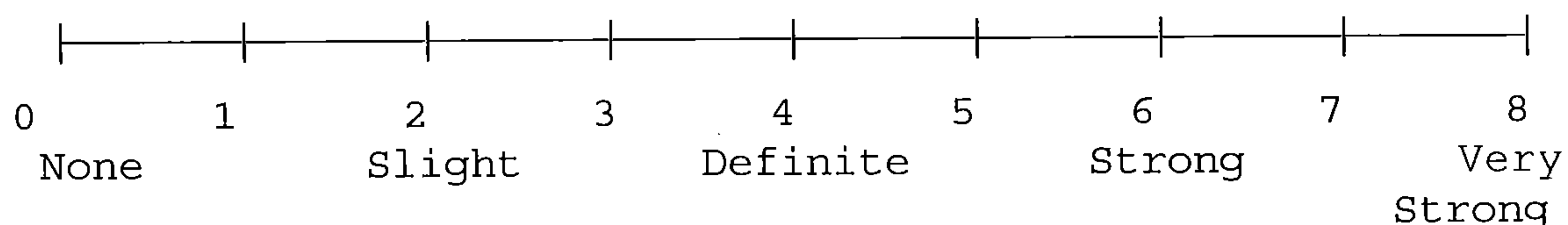
[00119] The products were evaluated using a sequential monadic test protocol. Subjects were given three 10 ml samples to evaluate. Each subject was directed to taste and swallow each sample and then assess the sweetness intensity of the sample. The intensity was rated on a score card by marking a numerical value along a scale from 0 to 8 (e.g., 0 = none, 2 = slight, 4 = definite, 8 = very strong). Following the decision regarding the sweetness intensity, subjects were instructed to vigorously rinse their mouth with water. Subjects then were given unsalted crackers to cleanse the palate. A period of 10 minutes elapsed between presentations of each sample to reduce the potential influence of residual taste effects. A second sample was then presented and evaluated as above and the same procedure was followed until all three products were evaluated. Sample presentation was randomized to avoid order of presentation bias.

[00120] To participate in the sensory panel, judges or subjects were chosen from an expert taste panel. These subjects were screened for taste acuity and were trained in evaluating solutions using the sip and spit protocol and were trained in using a rating ballot. The number of judges who participated in the study was 20. The female subjects were all non-pregnant and all volunteers were of <55 years of age with no history of allergy to sucrose. Judges were asked to execute an informed consent form.

[00121] Specifically, the following instructions were given to the judges: Please take a sip of water. Carefully take the cap off the sample cup placed in front of you. Sip and swallow the sample, then assess the intensity of the sweetness of the sample. Please evaluate the sample for the

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intensity of the sweet flavor and put a vertical mark on the number that best describes the intensity. Rinse your mouth with the water provided and spit into the discard cup. Use crackers provided to cleanse your palate before evaluating the next sample.

SWEETNESS

[00122] If any other flavor was present in the sample please describe it. Please rinse your mouth again several times and have some more water and unsalted crackers. You will now have a rest period of 10 minutes before you will be given the next sample.

[00123] The results of this test are presented in FIG. 5. As can be seen from FIG. 5, the judges found that the sweetness of a solution of 10.39% (w/v-%) HFCS in combination with 300 μ M of Reb C was indistinguishable from that of a 14.29% (w/v-%) HFCS solution (equivalent to the sweetness intensity of an 11% sucrose solution). This is an effect that is equivalent to a standard industry goal for sweetness enhancement.

Example 7

[00124] The sweetness enhancing effect of 300 μ M Dulc A (Chromadex, CA; purity 94%; 3% impurities other than water) on 8% (w/v-%) sucrose solution was evaluated in a double-blind controlled test according to the procedure described in Example 1. The results of this test are presented in FIG. 6. As can be seen from FIG. 6, the judges found that the sweetness of a solution of 8% (w/v-%) sucrose in combination with 300 μ M of Dulc A approached that of an 11%

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(w/v-%) sucrose solution. The mean sweetness intensity scores of this test for 8% (w/v-%) sucrose solution, 8% (w/v-%) sucrose solution with 300 μ M Dulc A, and 11% (w/v-%) sucrose solution were 5.0, 6.3. and 6.7, respectively. No off-tastes were detected.

Example 8

[00125] The sweetness enhancing effect of 300 μ M Dulc A on 5% (w/v-%) sucrose solution was evaluated in a double-blind controlled test according to the procedure described in Example 1. The results of this test are presented in FIG. 7. As can be seen from FIG. 7, the judges found that the sweetness of a solution of 5% (w/v-%) sucrose in combination with 300 μ M of Dulc A achieved that of a 7% (w/v-%) sucrose solution.

Example 9

[00126] The sweetness enhancing effect of 300 μ M Reb C in iced tea having 8% (w/v-%) sucrose was evaluated in a double-blind controlled test as described in Example 6. The results of this test are presented in FIG. 8. As can be seen from FIG. 8, the judges found that the sweetness of a solution of 8% (w/v-%) in combination with 300 μ M Reb C was between that of the 8% (w/v-%) solution and that of an 11% (w/v-%) sucrose solution.

Example 10

[00127] The sweetness enhancing effect of 300 μ M Dulc A on 5% (w/v-%) fructose solution was evaluated in a double-blind controlled test according to the procedure described in Example 1. The results of this test are presented in FIG. 9. As can be seen from FIG. 9, the judges found that the sweetness of a solution of 5% (w/v-%) fructose in

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combination with 300 μ M of Dulc A achieved that of a 7% (w/v-%) fructose solution.

Example 11

[00128] The taste of 150, 300, and 600 μ M Reb C was evaluated by a test group. 10 panelists were trained over a period of a few weeks to provide a quantitative flavor profile of Reb C. Panelists first were trained using standard tastants representing the different taste modalities given in FIG. 10 (i.e., sweet, bitter, salt, sour, and licorice). They then were trained to use the scales when flavors were mixed together. All intensity ratings are on scales ranging from 0 (no taste) to 8 (highest intensity). The intensity rating for sweet is essentially the same as used in Examples 1 and 6. The taste profiles were obtained for 150, 300, and 600 μ M Reb C. Reb A (0.2 mg/ml, a concentration used in some food/beverage applications for sweetening) was also evaluated in the test for comparison. The scale is not linear at the bottom. A rating of 1 is around the threshold for sweetness detection. As can be seen from FIG. 10, Reb C has little or no intrinsic sweetness at the concentrations tested. Also, the unpleasant tastes, bitter and licorice, that also are barely detected, have been undetected when Reb C was combined with sugar.

Example 12

[00129] The sweetness enhancing effect of the combination of 40 μ M Reb A (purity >95%) and 300 μ M Reb C (Chromadex, CA; purity 94.9%; 2.9% impurities other than water) on 5% (w/v-%) sucrose solution was evaluated in a double-blind controlled test conducted according to the following

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protocol. Four products were evaluated by trained judges as follows:

- low concentration sucrose (5% w/v)
- low concentration sucrose + sweetness enhancer 1 (40 μ M Reb A)
- low concentration sucrose + sweetness enhancer 2 (300 μ M Reb C)
- low concentration sucrose + sweetness enhancer 1 + sweetness enhancer 2

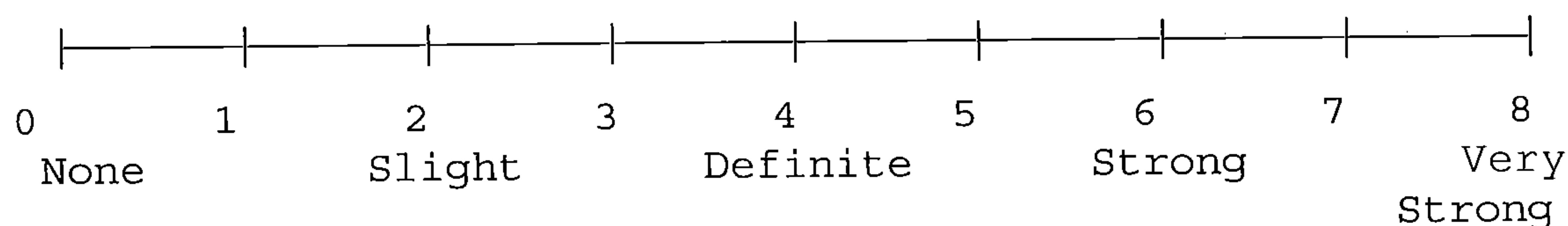
[00130] The products were evaluated using a sequential monadic test protocol. Subjects were given three 10 ml samples to evaluate. Each subject was directed to taste and swallow each sample and then assess the sweetness intensity of the sample. The intensity was rated on a score card by marking a numerical value along a scale from 0 to 8 (e.g., 0 = none, 2 = slight, 4 = definite, 8 = very strong). Following the decision regarding the sweetness intensity, subjects were instructed to vigorously rinse their mouth with water. Subjects then were given unsalted crackers to cleanse the palate. A period of 10 minutes elapsed between presentations of each sample to reduce the potential influence of residual taste effects. A second sample was then presented and evaluated as above and the same procedure was followed until all three products were evaluated. Sample presentation was randomized to avoid order of presentation bias.

[00131] To participate in the sensory panel, judges or subjects were chosen from an expert taste panel. These subjects were screened for taste acuity and were trained in evaluating solutions using the sip and spit protocol and were trained in using a rating ballot. The number of judges who participated in the study was 20. The female

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subjects were all non-pregnant and all volunteers were of <55 years of age with no history of allergy to sucrose. Judges were asked to execute an informed consent form.

[00132] Specifically, the following instructions were given to the judges: Please take a sip of water. Carefully take the cap off the sample cup placed in front of you. Sip and swallow the sample, then assess the intensity of the sweetness of the sample. Please evaluate the sample for the intensity of the sweet flavor and put a vertical mark on the number that best describes the intensity. Rinse your mouth with the water provided and spit into the discard cup. Use crackers provided to cleanse your palate before evaluating the next sample.

SWEETNESS

[00133] If any other flavor was present in the sample please describe it. Please rinse your mouth again several times and have some more water and unsalted crackers. You will now have a rest period of 10 minutes before you will be given the next sample.

[00134] The results of this test are presented in FIG. 11. As can be seen from FIG. 11, the judges found that the sweetness of a solution of 5% (w/v-%) sucrose in combination with 40 μ M Reb A and 300 μ M of Reb C was significantly sweeter than the 40 μ M Reb A and 300 μ M Reb C solutions alone in a 5% (w/v-%) sucrose solution. 300 μ M Reb C enhances synergistically the additive sweet taste enhancing effect of 40 μ M Reb A on 5% (w/v-%) sucrose solution.

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Example 13

[00135] The sweetness enhancing effect of 40 μ M Reb A and 300 μ M Reb C on 5% (w/v-%) sucrose solution was evaluated in a double-blind controlled test according to the procedure described in Example 12. In this test, the sweetness intensities were compared to the mean sweetness intensity of a 7% (w/v-%) sucrose solution instead of a 5% (w/v-%) sucrose solution. The results of this test are presented in FIG. 12. The results show that the mixture of 5% (w/v-%) sucrose, 40 μ M Reb A and 300 μ M Reb C is substantially sweeter than a 7% (w/v-%) sucrose solution.

Example 14

[00136] The sweetness enhancing effect of 80 ppm Reb A and 190 ppm Reb C on 5% (w/v-%) sucrose solution was evaluated in a double-blind controlled test according to the procedure described in Example 12. In this test, the sweetness intensities were compared to the mean sweetness intensity of a 10% (w/v-%) sucrose solution instead of a 5% (w/v-%) sucrose solution. Also, the effect of 200 ppm Reb A on 5% (w/v-%) sucrose solution was evaluated. The results of this test are presented in FIG. 13. The results show that the mixture of 5% (w/v-%) sucrose, 80 ppm Reb A and 190 ppm Reb C is as sweet as a 10% (w/v-%) sucrose solution. The results also show that in order to achieve the sweetness intensity of a 10% (w/v-%) sucrose solution, 200 ppm of Reb A must be added to a 5% (w/v-%) sucrose solution.

Example 15

[00137] The sweetness enhancing effect of the combinations of 80 ppm Reb D (purity >95%) with 190 ppm Reb C and 60 ppm Reb D with 210 ppm Reb C on 5% (w/v-%) sucrose solution

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were evaluated in a double-blind controlled test conducted according to the protocol described in Example 12. Four products were evaluated by trained judges as follows:

- high concentration sucrose (10% w/v)
- low concentration sucrose (5% w/v) + 80 ppm Reb D + 190 ppm Reb C
- low concentration sucrose (5% w/v) + 60 ppm Reb D + 210 ppm Reb C
- 400 ppm Reb D

[00138] The results of this test are presented in FIG. 14. As can be seen from FIG. 14, the judges found that the sweetness of a solution of 5% (w/v-%) sucrose in combination with 80 ppm Reb A and 190 ppm of Reb C achieved that of a 10% (w/v-%) sucrose solution. The sweetness of a solution of 400 ppm of Reb D did not reach the sweetness of a 10% (w/v-%) sucrose solution. The judges also found that the sweetness of a solution of 5% (w/v-%) sucrose in combination with 60 ppm Reb A and 210 ppm of Reb C is significantly different than that of a 10% (w/v-%) sucrose solution, but is close to that of a 400 ppm Reb D solution.

[00139] The following two products were tested earlier according to the protocol described in Example 12:

- low concentration sucrose (5% w/v)
- 200 ppm Reb D

[00140] The judges found that the mean sweetness intensity of both the 5% (w/v-%) sucrose solution and the solution containing 200 ppm of Reb D was about 4.

[00141] The results show that 190 ppm Reb C enhances synergistically the sweet taste enhancing effect of 80 ppm Reb D on 5% (w/v-%) sucrose solution, and that 210 ppm Reb C enhances synergistically the sweet taste enhancing effect of 60 ppm Reb D on 5% (w/v-%) sucrose solution.

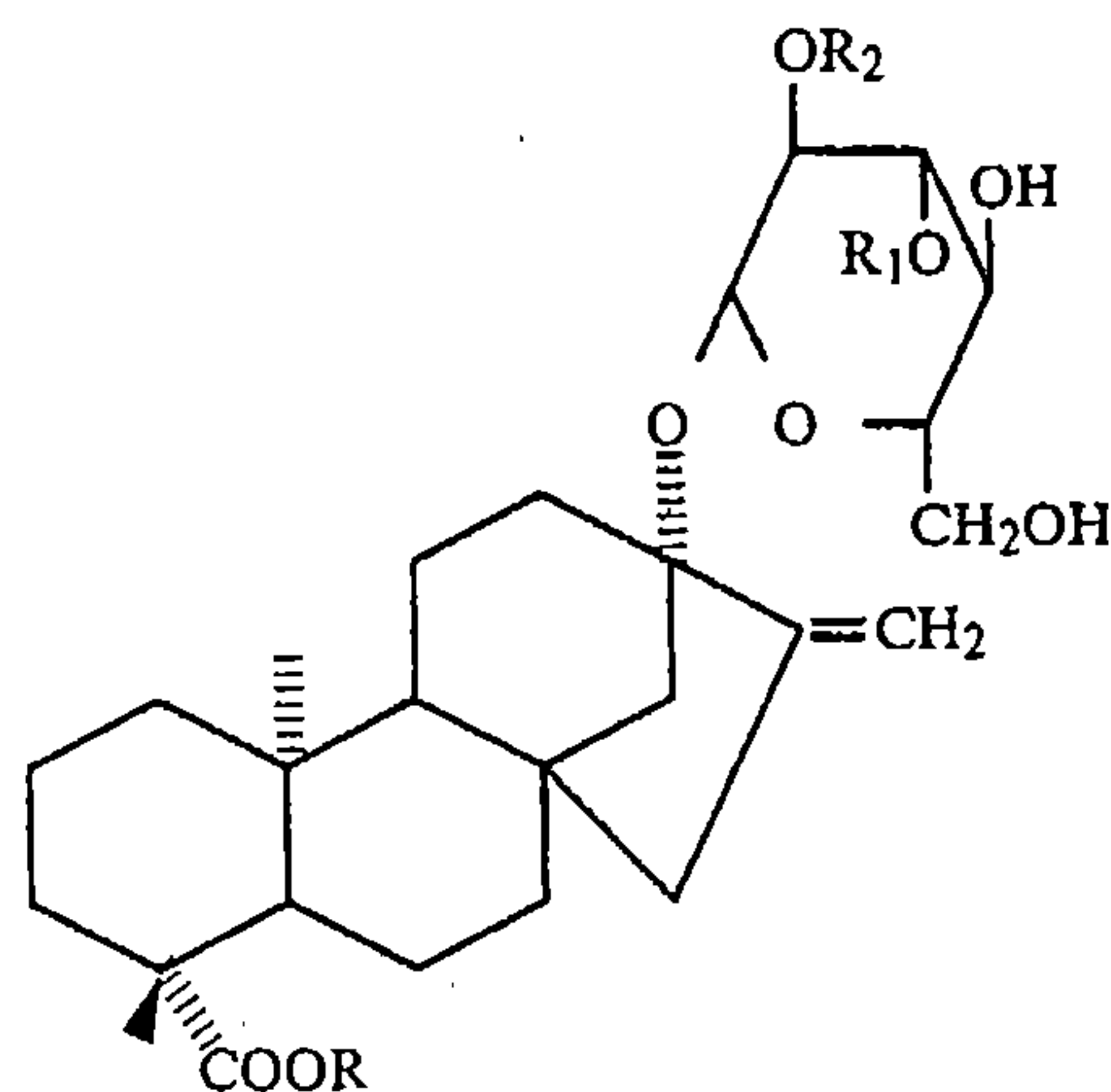
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[00142] Having now fully described this invention, it will be understood by those of ordinary skill in the art that the same can be performed within a wide and equivalent range of conditions, formulations and other parameters without affecting the scope of the invention or any embodiment thereof. All patents, published patent applications, and publications cited herein are fully incorporated by reference herein in their entirety.

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What is Claimed is:

1. A method of enhancing a sweet taste of a carbohydrate sweetener, comprising administering to a subject the carbohydrate sweetener, at least one of rebaudioside A or rebaudioside D, and one or more compounds having the Formula I:



I

or a stereoisomer thereof, wherein R_2 is rhamnose, and R and R_1 are each independently selected from the group consisting of hydrogen, glucose, and beta-sophorose, in an amount effective to provide the sweet taste enhancing effect without exhibiting an off-taste, wherein the amount of rebaudioside A or rebaudioside D is less than or equal to the amount of each compound of Formula I.

2. The method of claim 1, wherein the carbohydrate sweetener is sucrose, fructose, glucose, high fructose corn syrup, xylose, arabinose or rhamnose.

3. The method of claim 1, wherein the carbohydrate sweetener is a sugar alcohol.

4. The method of claim 3, wherein the sugar alcohol is erythritol, xylitol, mannitol, sorbitol, or inositol.

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5. The method of any one of claims 1-4, wherein the carbohydrate sweetener and the compound of Formula I, or a stereoisomer thereof, are administered in a consumable.

6. The method of claim 5, wherein the consumable is a food product, a pharmaceutical composition, a dietary supplement, a nutraceutical, a dental hygienic composition or a cosmetic product.

7. The method of claim 6, wherein the food product is a beverage or a drink.

8. The method of any one of claims 1-7, wherein rebaudioside A is present at a concentration of from about 20 ppm to about 100 ppm.

9. The method of any one of claims 1-7, wherein rebaudioside D is present at a concentration of from about 20 ppm to about 100 ppm.

10. The method of any one of claims 1-9, wherein the one or more compounds of Formula I, or a stereoisomer thereof, are each independently present in an amount at, slightly above, or below the detection threshold for its intrinsic sweetness.

11. The method of any one of claims 1-10, wherein the one or more compounds of Formula I, or a stereoisomer thereof, are each independently present at a concentration of from about 100 ppm to about 600 ppm.

12. The method of any one of claims 1-11, wherein the one or more compounds of Formula I is rebaudioside C, or a stereoisomer thereof.

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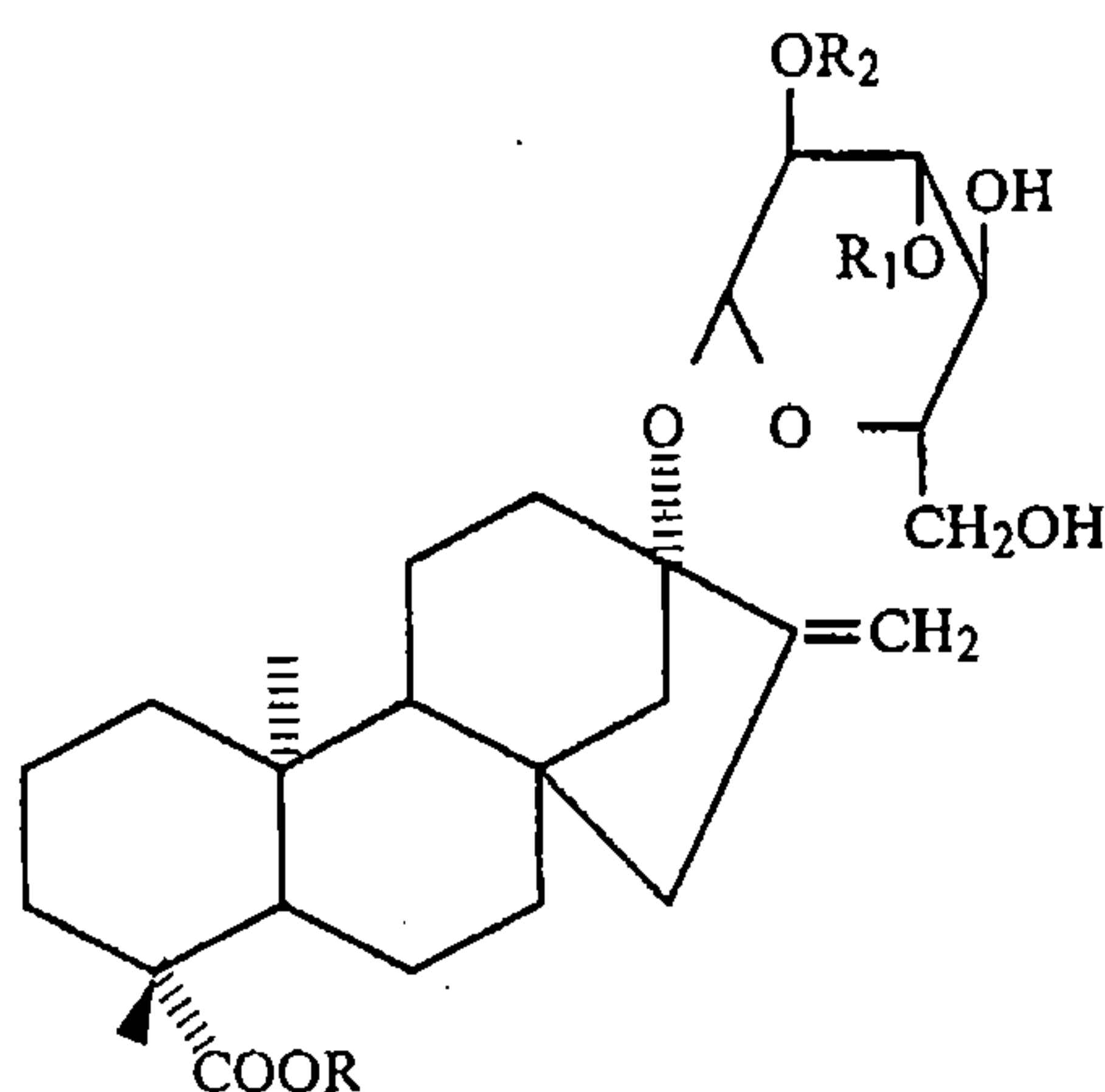
13. The method of any one of claims 1-11, wherein the one or more compounds of Formula I is dulcoside A, or a stereoisomer thereof.

14. The method of claim 12 or 13, wherein rebaudioside C, dulcoside A, or a stereoisomer thereof, is present at a concentration of from about 250 μM to about 350 μM .

15. The method of any one of claims 1-14, wherein the consumable has a sweetness intensity equivalent to about 5-12% (w/v-%) sucrose solution.

16. The method of any one of claims 1-15, wherein the carbohydrate sweetener is present at a concentration of from about 20000 ppm to about 100000 ppm.

17. A consumable, comprising a carbohydrate sweetener, at least one of rebaudioside A or rebaudioside D, and one or more compounds having the Formula I:



I

or a stereoisomer thereof, wherein R₂ is rhamnose, and R and R₁ are each independently selected from the group consisting of hydrogen, glucose, and beta-sophorose, in an amount

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effective to enhance the sweet taste of the carbohydrate sweetener without exhibiting an off-taste, wherein the amount of rebaudioside A or rebaudioside D is less than or equal to the amount of each compound of Formula I.

18. The consumable of claim 17, wherein rebaudioside A is present at a concentration of from about 20 ppm to about 100 ppm.

19. The consumable of claim 17, wherein rebaudioside D is present at a concentration of from about 20 ppm to about 100 ppm.

20. The consumable of any one of claims 17-19, wherein the one or more compounds of Formula I, or a stereoisomer thereof, are each independently present in an amount at, slightly above, or below the detection threshold for its intrinsic sweetness.

21. The consumable of any one of claims 17-20, wherein the one or more compounds of Formula I, or a stereoisomer thereof, are each independently present at a concentration of from about 100 ppm to about 600 ppm.

22. The consumable of any one of claims 17-21, wherein the compound of Formula I is rebaudioside C, or a stereoisomer thereof.

23. The consumable of any one of claims 17-21, wherein the compound of Formula I is dulcoside A, or a stereoisomer thereof.

24. The consumable of claim 22 or 23, wherein rebaudioside C, dulcoside A, or a stereoisomer thereof, is present at a concentration of from about 150 μ M to about 600 μ M.

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25. The consumable of any one of claims 17-24, wherein the consumable has a sweetness intensity equivalent to about 5-12% (w/v-%) sucrose solution.

26. The consumable of any one of claims 17-25, wherein the carbohydrate sweetener is present at a concentration of from about 20000 ppm to about 100000 ppm.

27. The consumable of any one of claims 17-26, wherein the carbohydrate sweetener is sucrose, fructose, glucose, high fructose corn syrup, xylose, arabinose or rhamnose.

28. The consumable of any one of claims 17-26, wherein the carbohydrate sweetener is a sugar alcohol.

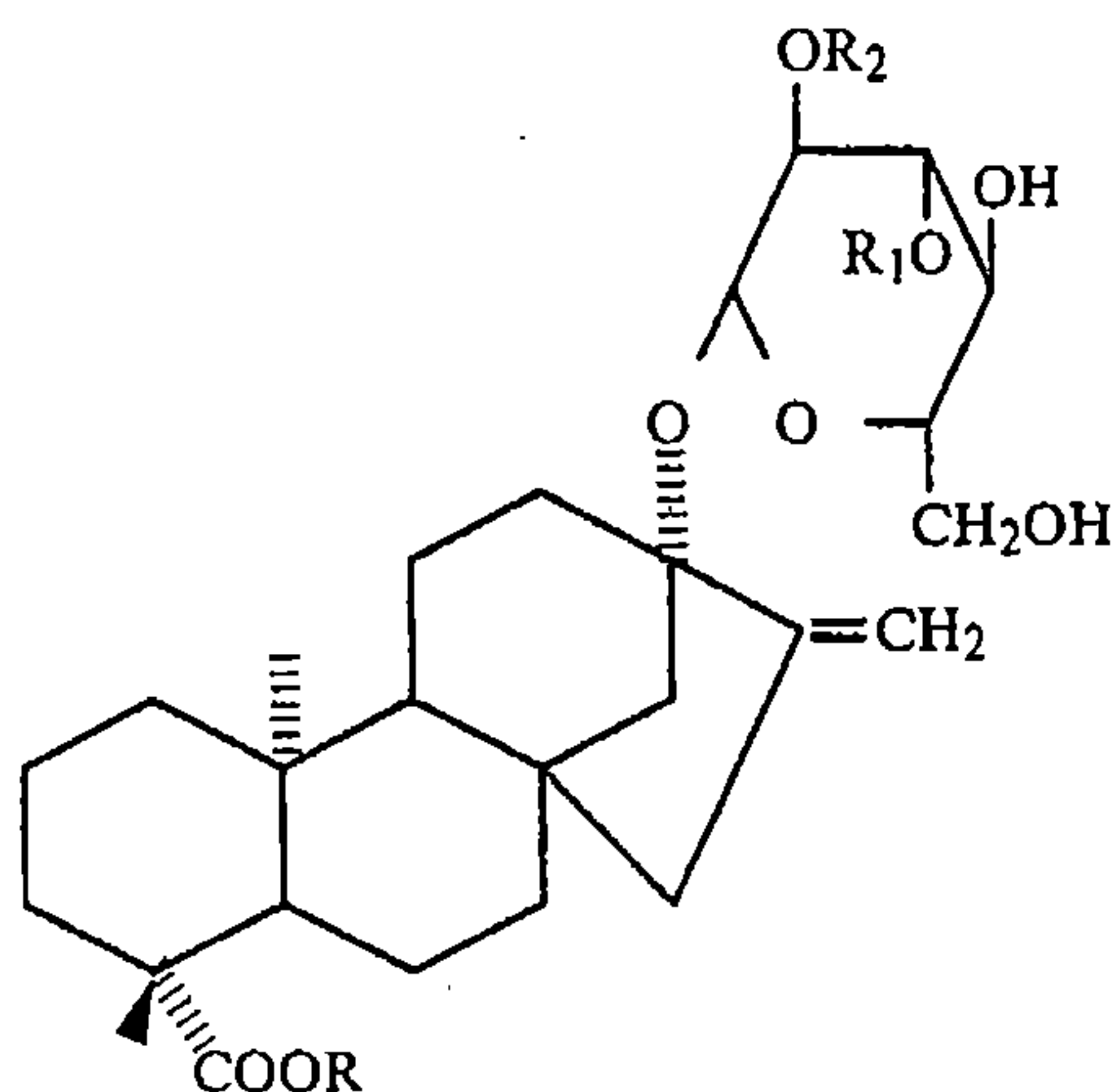
29. The consumable of claim 28, wherein the sugar alcohol is erythritol, xylitol, mannitol, sorbitol, or inositol.

30. The consumable of any one of claims 17-29, wherein the consumable is a food product, pharmaceutical composition, a dietary supplement, a nutraceutical, a dental hygienic composition or a cosmetic product.

31. The consumable of claim 30, wherein the food product is a beverage or a drink.

32. A method of decreasing the amount of a carbohydrate sweetener in a consumable, comprising adding at least one of rebaudioside A or rebaudioside D, and one or more compounds having the Formula I:

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I

or a stereoisomer thereof, wherein R₂ is rhamnose, and R and R₁ are each independently selected from the group consisting of hydrogen, glucose, and beta-sophorose, or a stereoisomer thereof, to the consumable and thereby reducing the amount of the carbohydrate sweetener needed to exhibit a given level of sweetness, wherein the amount of rebaudioside A or rebaudioside D is less than or equal to the amount of each compound of Formula I.

33. The method of 32, wherein the carbohydrate sweetener is sucrose, fructose, glucose, high fructose corn syrup, xylose, arabinose or rhamnose.

34. The method of any one of claims 32, wherein the carbohydrate sweetener is a sugar alcohol.

35. The method of claim 34, wherein the sugar alcohol is erythritol, xylitol, mannitol, sorbitol, or inositol.

36. The method of any one of claims 32-35, wherein the consumable is a food product, a pharmaceutical composition, a dietary supplement, a nutraceutical, a dental hygienic composition or a cosmetic product.

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37. The method of claim 36, wherein the food product is a beverage or a drink.

38. The method of any one of claims 32-37, wherein rebaudioside A is present at a concentration of from about 20 ppm to about 100 ppm.

39. The method of any one of claims 32-37, wherein rebaudioside D is present at a concentration of from about 20 ppm to about 100 ppm.

40. The method of any one of claims 32-39, wherein the one or more compounds of Formula I, or a stereoisomer thereof, are each independently present in an amount at, slightly above, or below the detection threshold for its intrinsic sweetness.

41. The method of any one of claims 32-40, wherein the one or more compounds of Formula I, or a stereoisomer thereof, are each independently present at a concentration of from about 100 ppm to about 600 ppm.

42. The method of any one of claims 32-41, wherein the one or more compounds of Formula I is rebaudioside C, or a stereoisomer thereof.

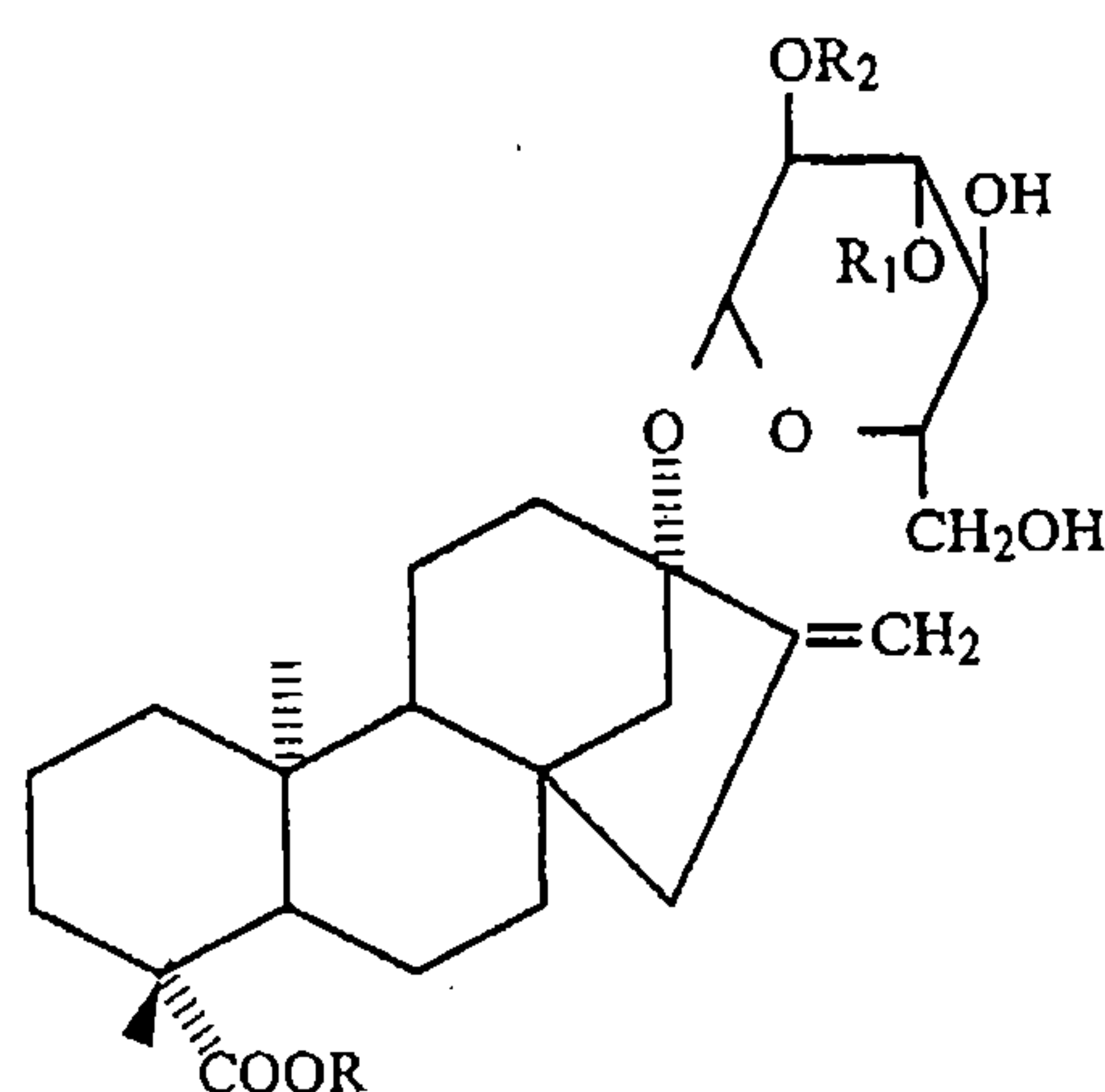
43. The method of any one of claims 32-41, wherein the one or more compounds of Formula I is dulcoside A, or a stereoisomer thereof.

44. The method of claim 42 or 43, wherein rebaudioside C, dulcoside A, or a stereoisomer thereof, is present at a concentration of from about 150 μ M to about 600 μ M.

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45. The method of any one of claims 32-44, wherein the consumable has a sweetness intensity equivalent to about 5-12% (w/v-%) sucrose solution.

46. A method of enhancing the sweetness of a consumable comprising a carbohydrate sweetener, comprising adding at least one of rebaudioside A or rebaudioside D, and one or more compounds having the Formula I:



I

or a stereoisomer thereof, wherein R_2 is rhamnose, and R and R_1 are each independently selected from the group consisting of hydrogen, glucose, and beta-sophorose, to the consumable in an amount effective to enhance the sweetness of the consumable, wherein the amount of rebaudioside A or rebaudioside D is less than or equal to the amount of each compound of Formula I.

47. The method of claim 46, wherein the consumable has a sweetness intensity equivalent to about 5-12% (w/v-%) sucrose solution.

48. The method of any one of claims 46-47, wherein the carbohydrate sweetener is present at a concentration of from about 20000 ppm to about 100000 ppm.

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49. The method of any one of claims 46-48, wherein rebaudioside A is added to the consumable in an amount to obtain a concentration of from about 20 ppm to about 100 ppm.

50. The method of any one of claims 46-48, wherein rebaudioside D is present at a concentration of from about 20 ppm to about 100 ppm.

51. The method of any one of claims 46-50, wherein the one or more compounds of Formula I, or a stereoisomer thereof, are each independently added to the consumable in an amount to obtain a concentration of from about 100 ppm to about 600 ppm.

52. The method of any one of claims 46-51, wherein the one or more compounds of Formula I is rebaudioside C, or a stereoisomer thereof.

53. The method of any one of claims 46-51, wherein the one or more compounds of Formula I is dulcoside A, or a stereoisomer thereof.

54. The method of claim 52 or 53, wherein rebaudioside C, dulcoside A, or a stereoisomer thereof, is added to obtain a concentration of from about 150 μ M to about 600 μ M.

55. The method of any one of claims 46-54, wherein about 0.1 to 0.5 g of rebaudioside C, dulcoside A, or a stereoisomer thereof, is added for every 50 to 100 g of the carbohydrate sweetener, and wherein about 0.03 g to about 0.15 g of rebaudioside A or rebaudioside D is added for every 50 to 100 g of the carbohydrate sweetener.

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56. The method of any one of claims 46-55, wherein the carbohydrate sweetener is sucrose, fructose, glucose, high fructose corn syrup, xylose, arabinose, or rhamnose.

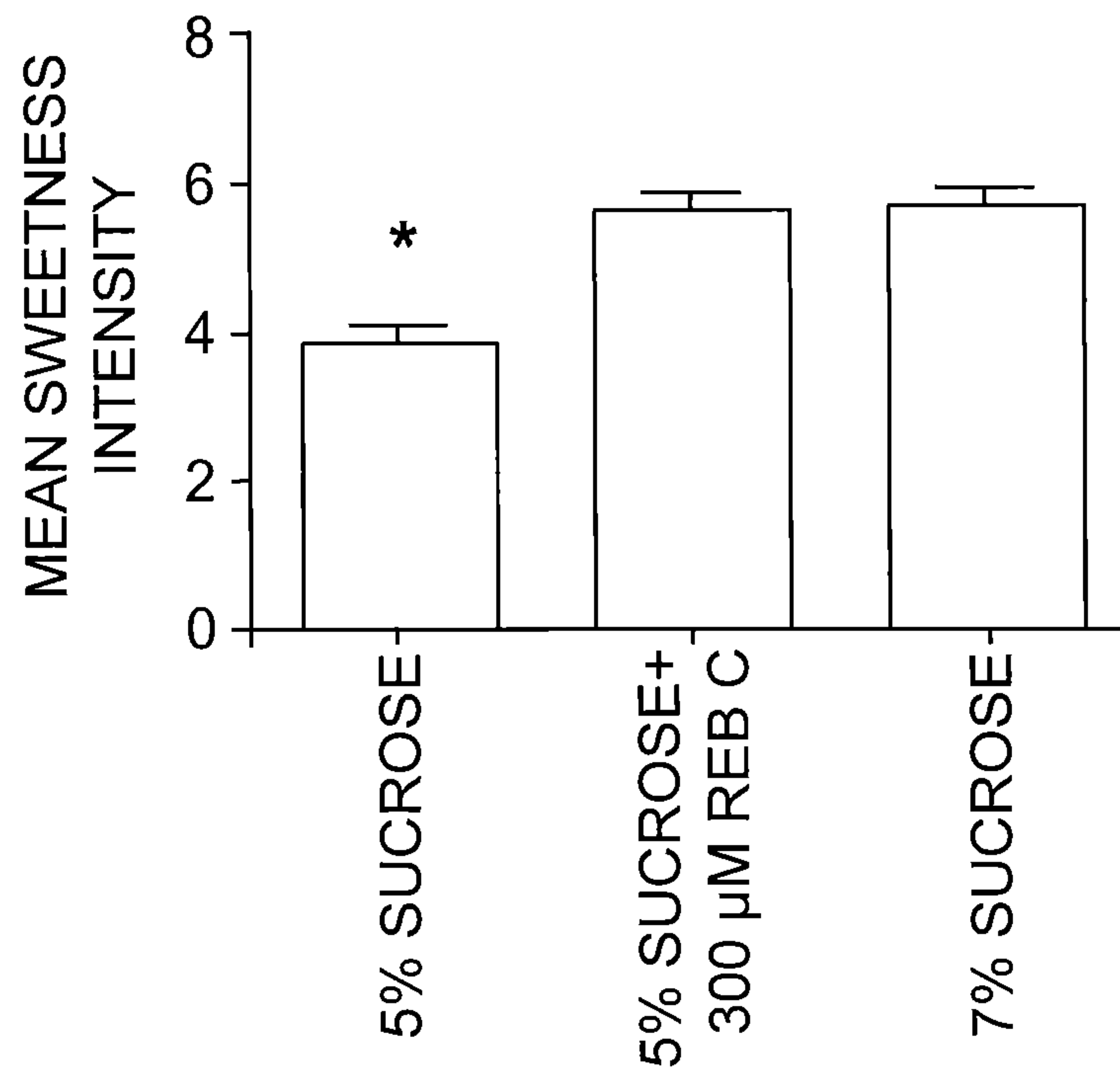
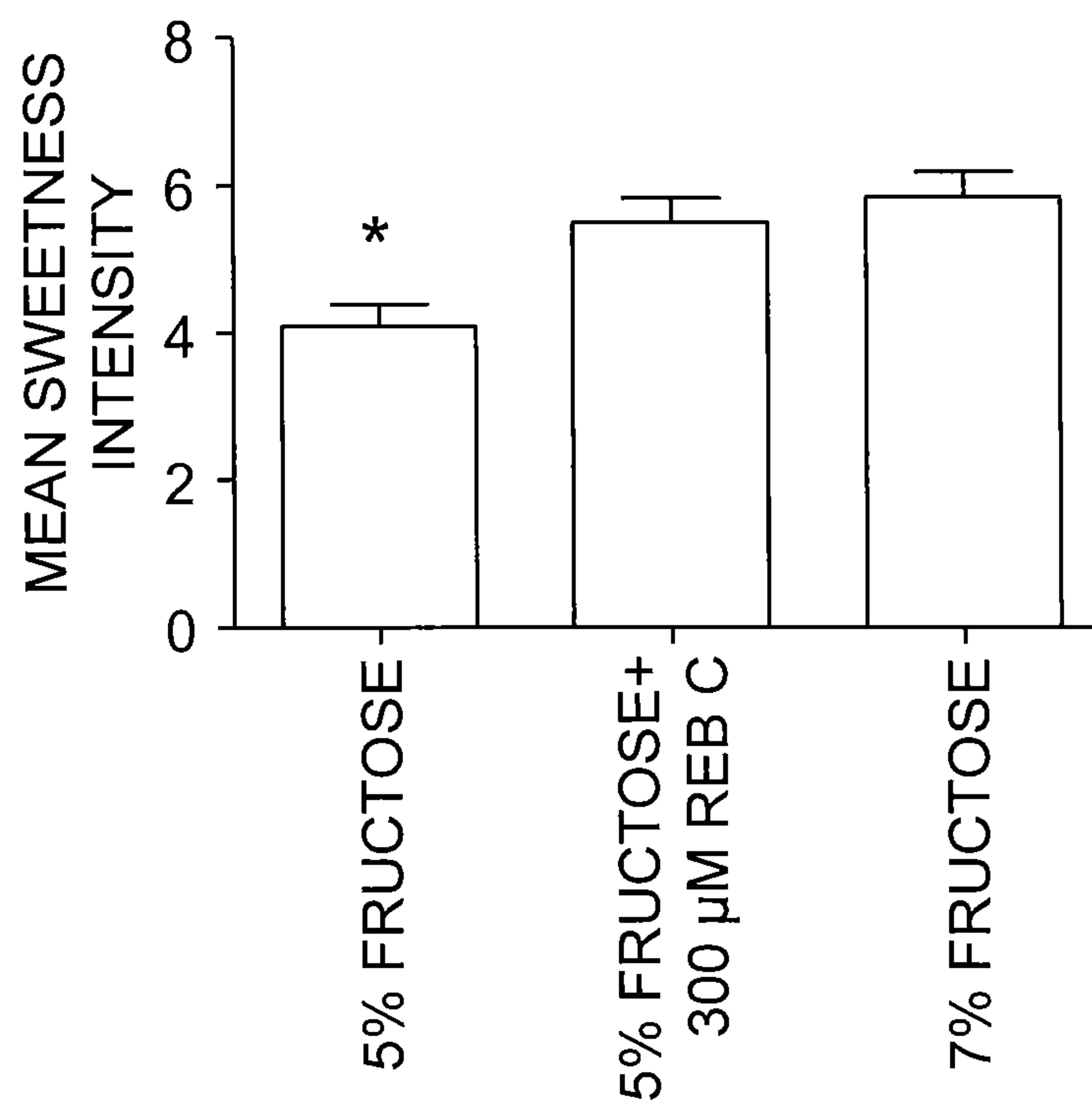
57. The method of any one of claims 46-55, wherein the carbohydrate sweetener is a sugar alcohol.

58. The method of claim 57, wherein the sugar alcohol is erythritol, xylitol, mannitol, sorbitol, or inositol.

59. The method of any one of claims 46-58, wherein the consumable is a food product, a pharmaceutical composition, a dietary supplement, a nutraceutical, a dental hygienic composition or a cosmetic product.

60. The method of claim 59, wherein the food product is a beverage or a drink.

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*FIG. 1**FIG. 2*

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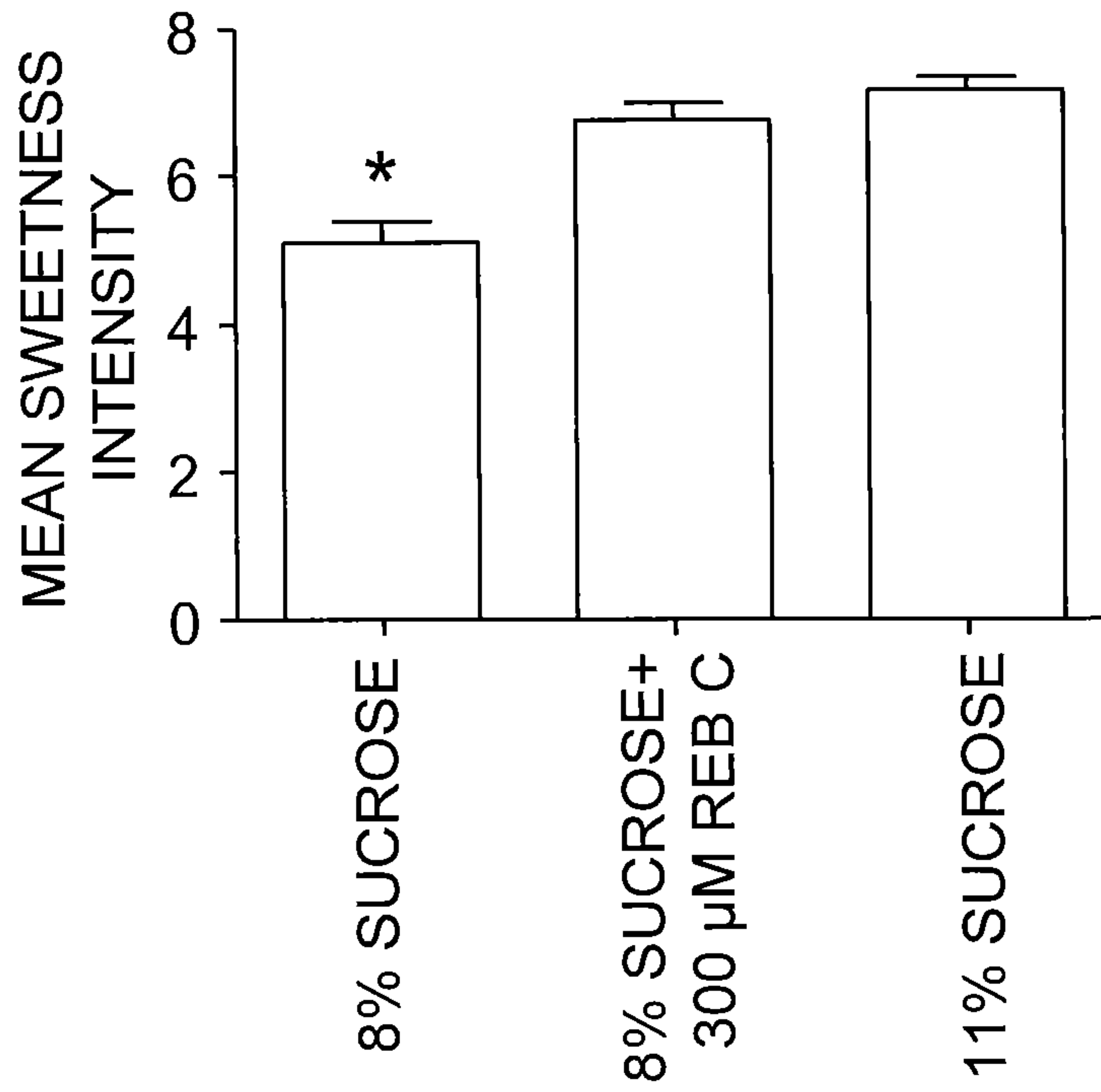


FIG. 3

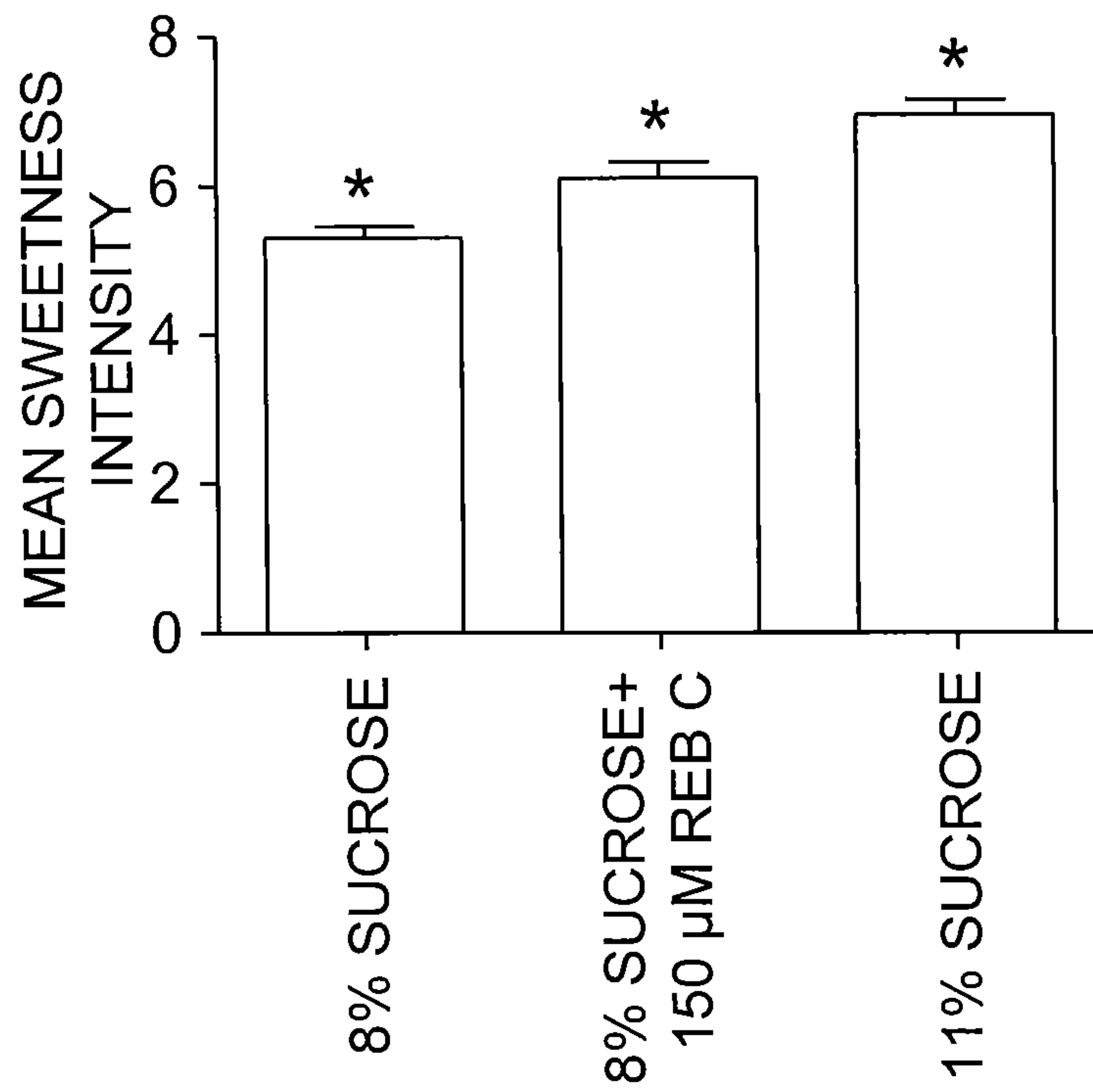
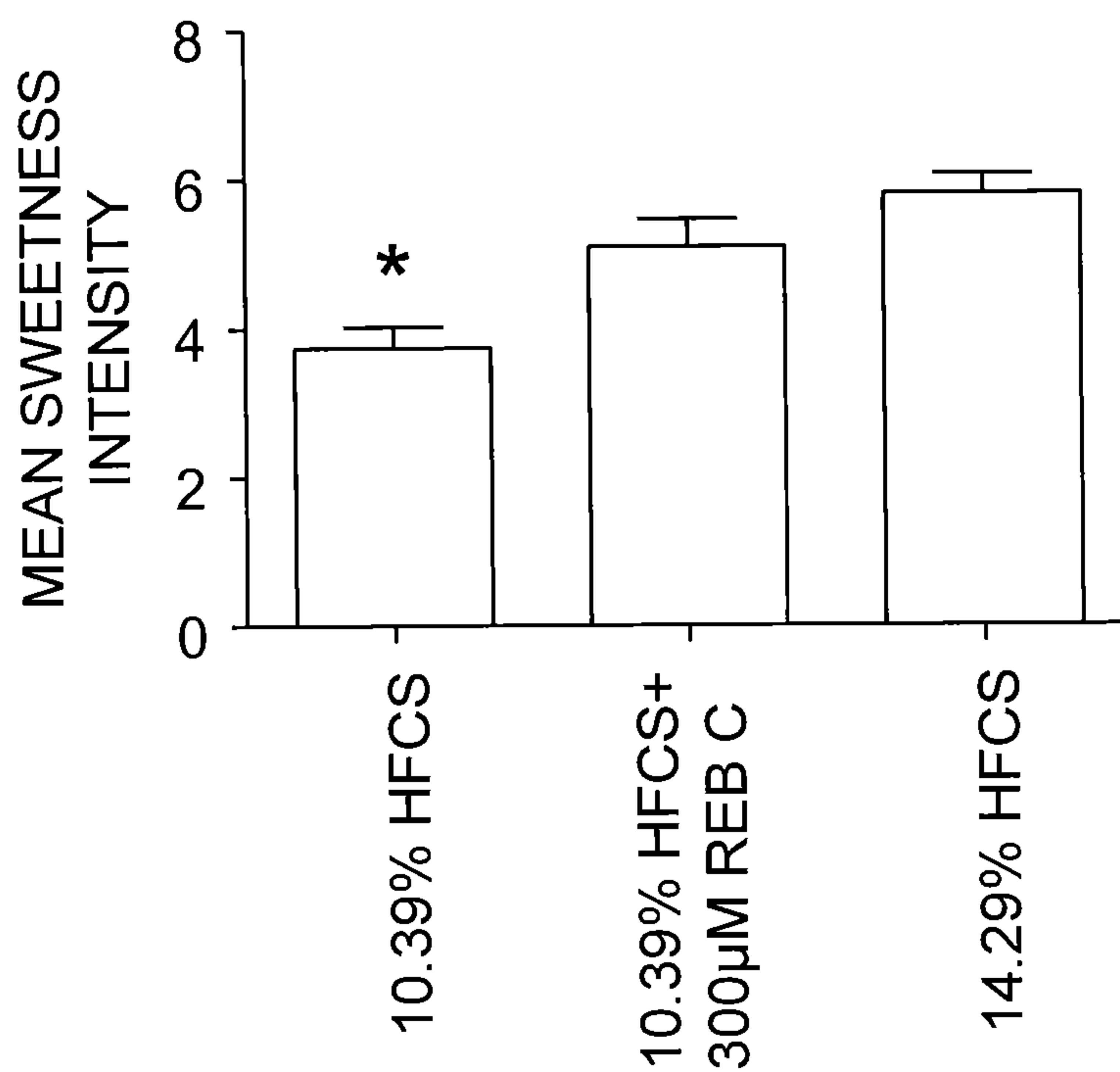
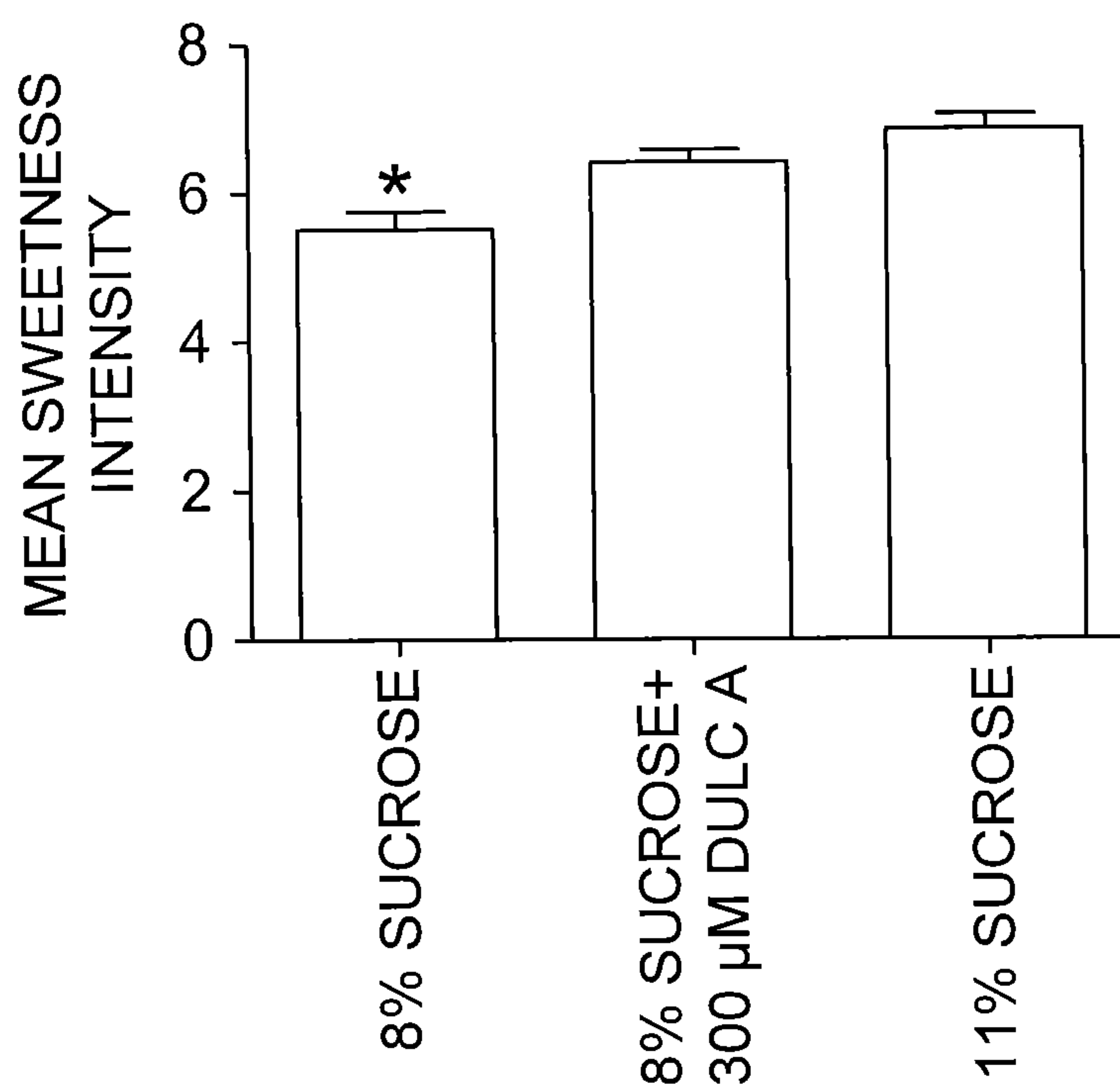


FIG. 4

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*FIG. 5**FIG. 6*

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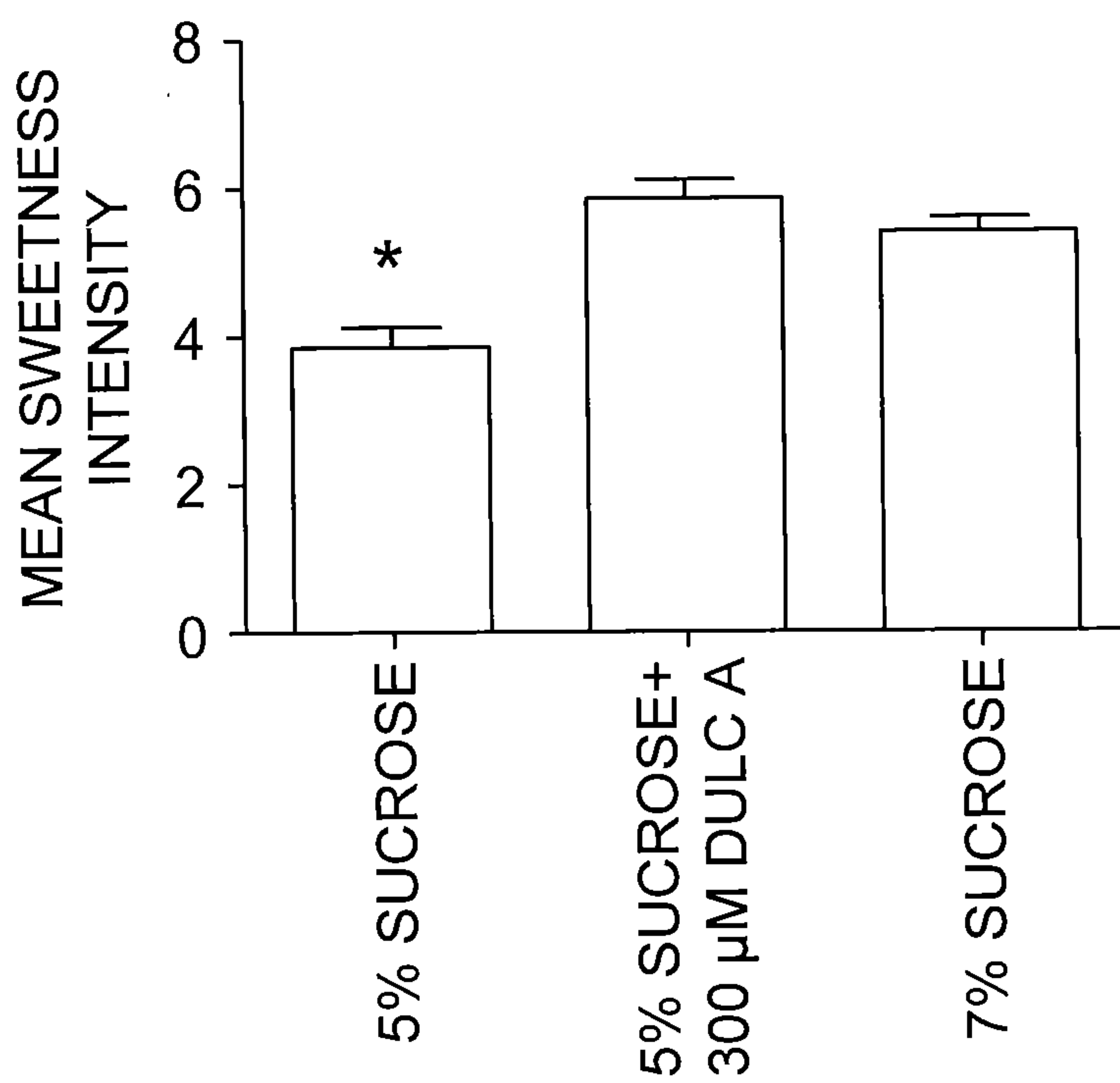


FIG. 7

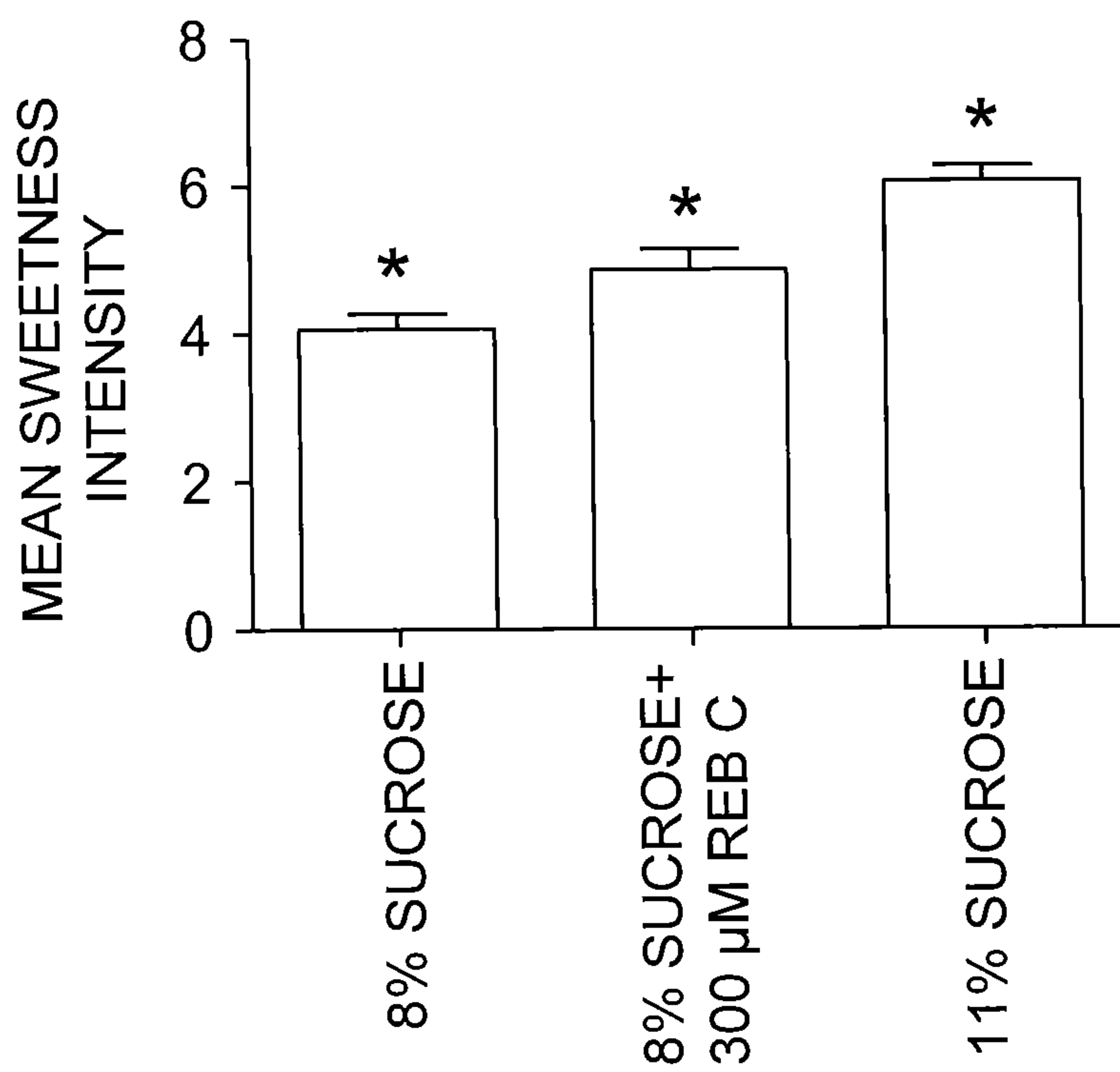
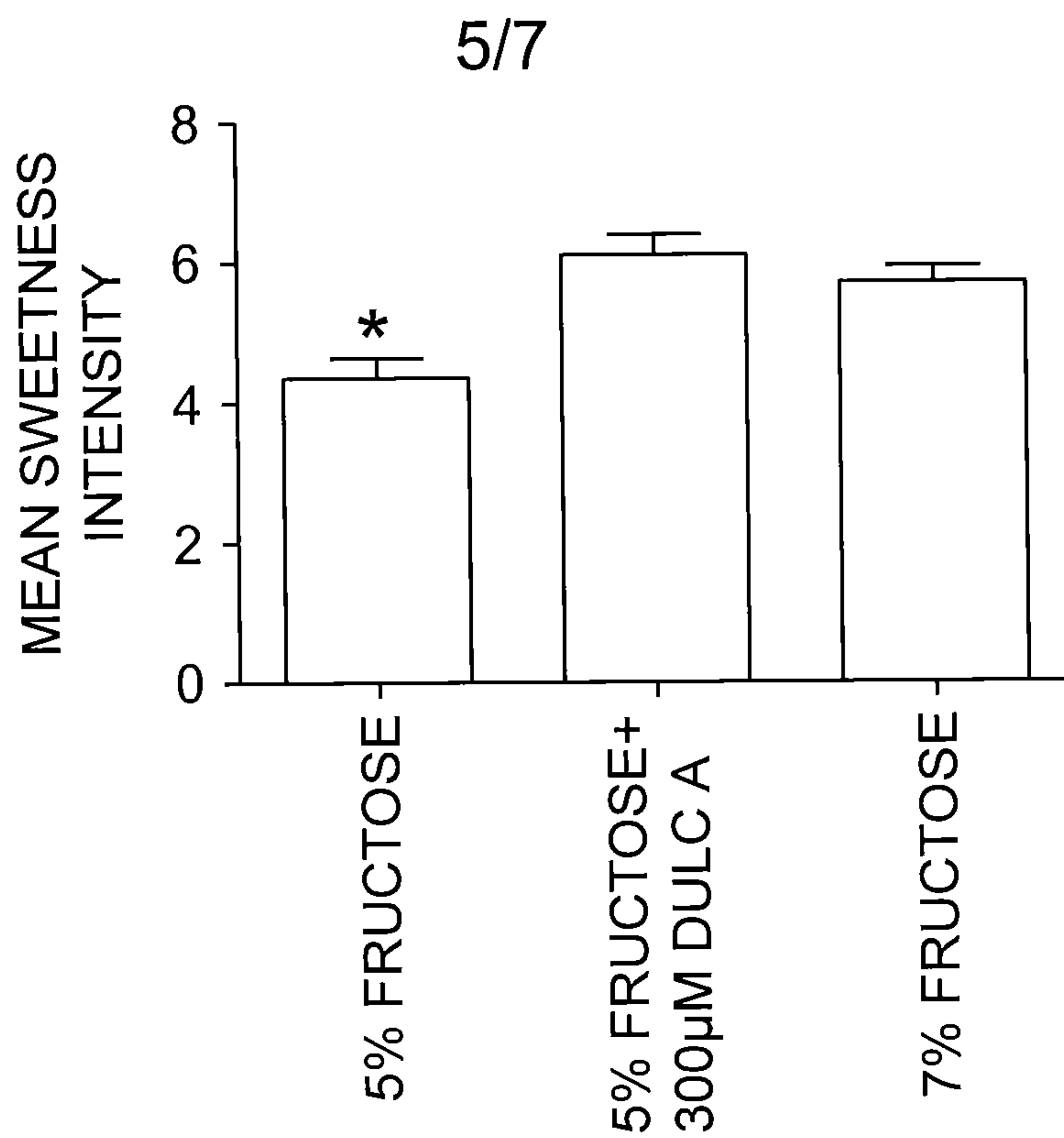
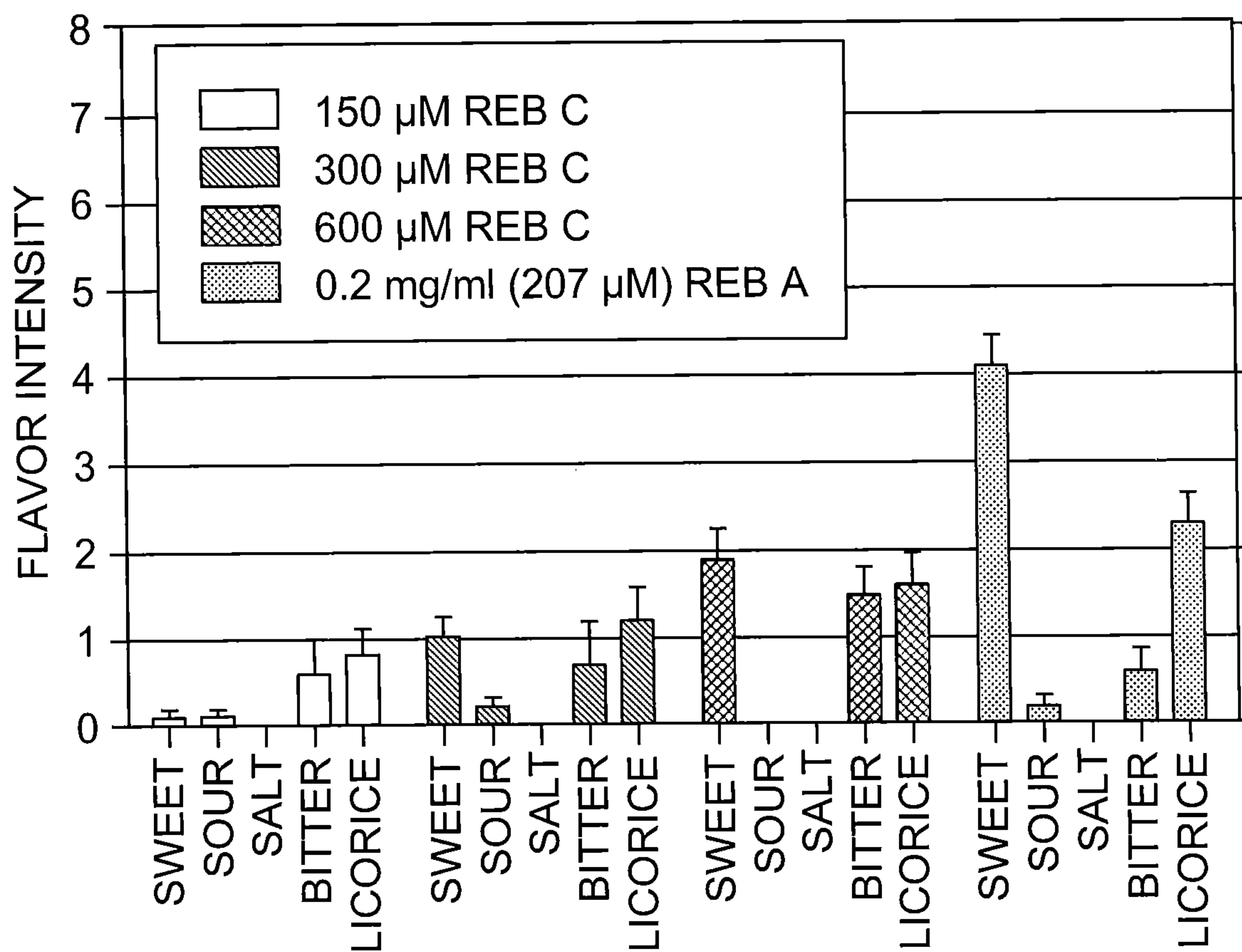
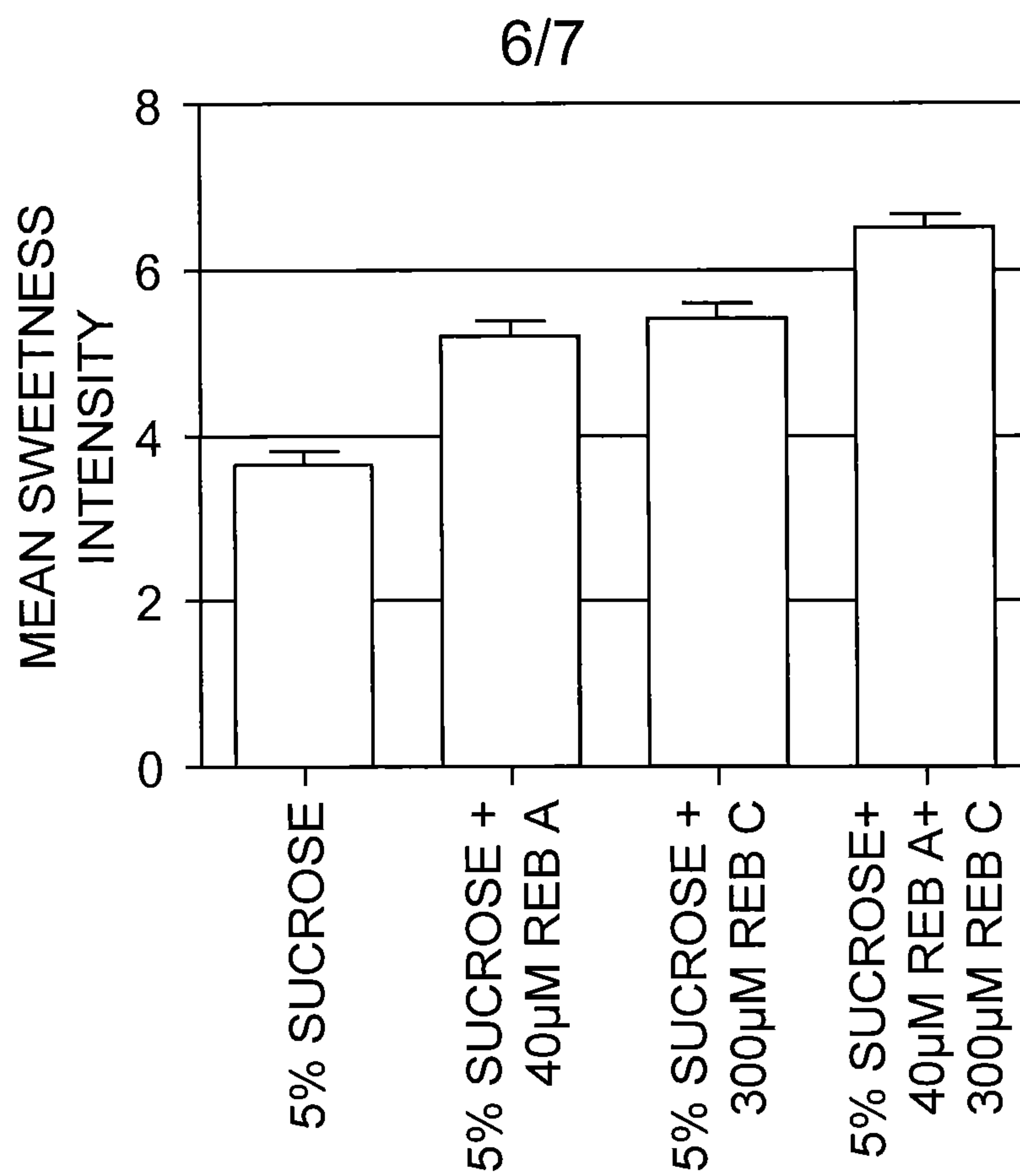
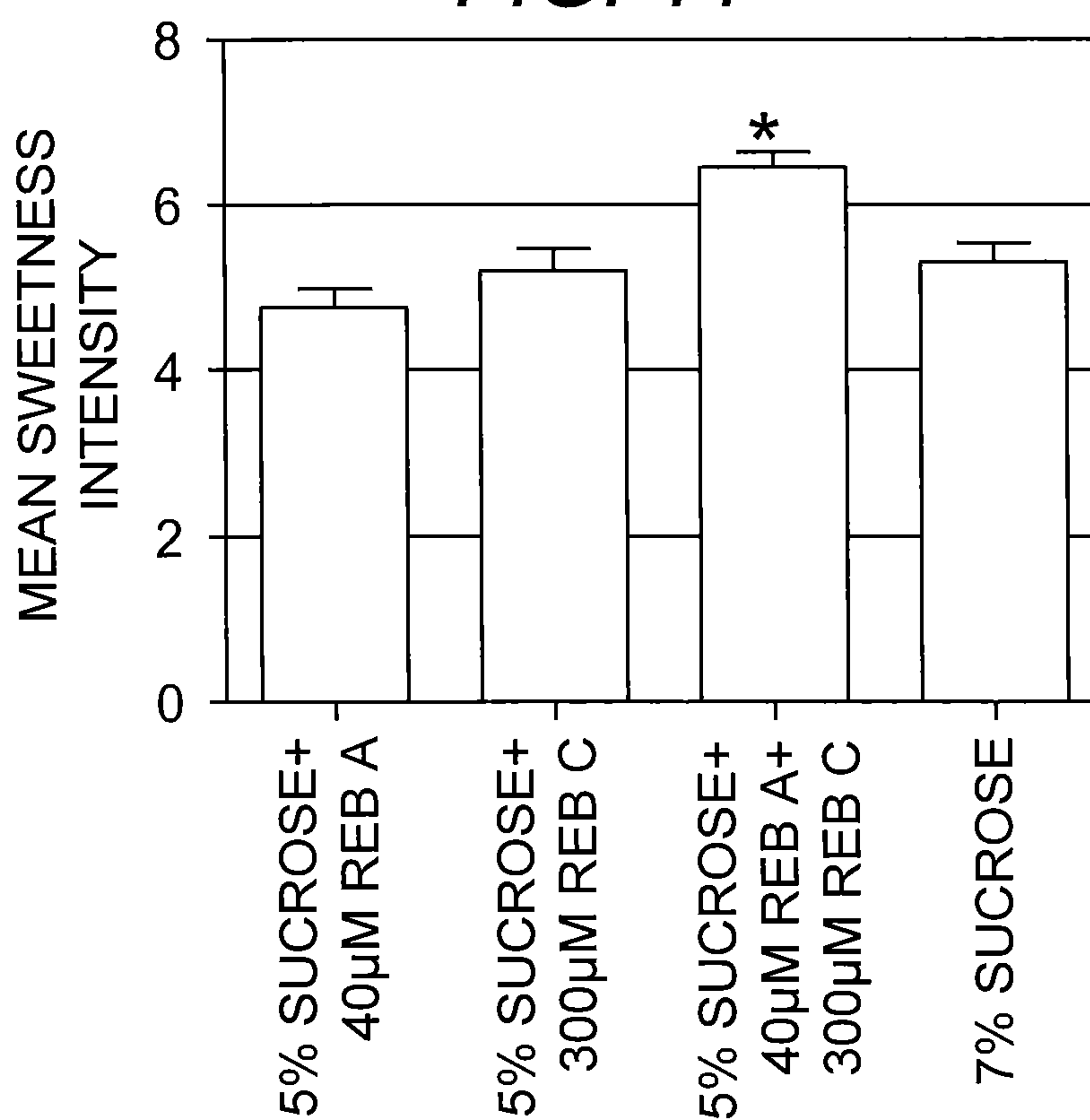
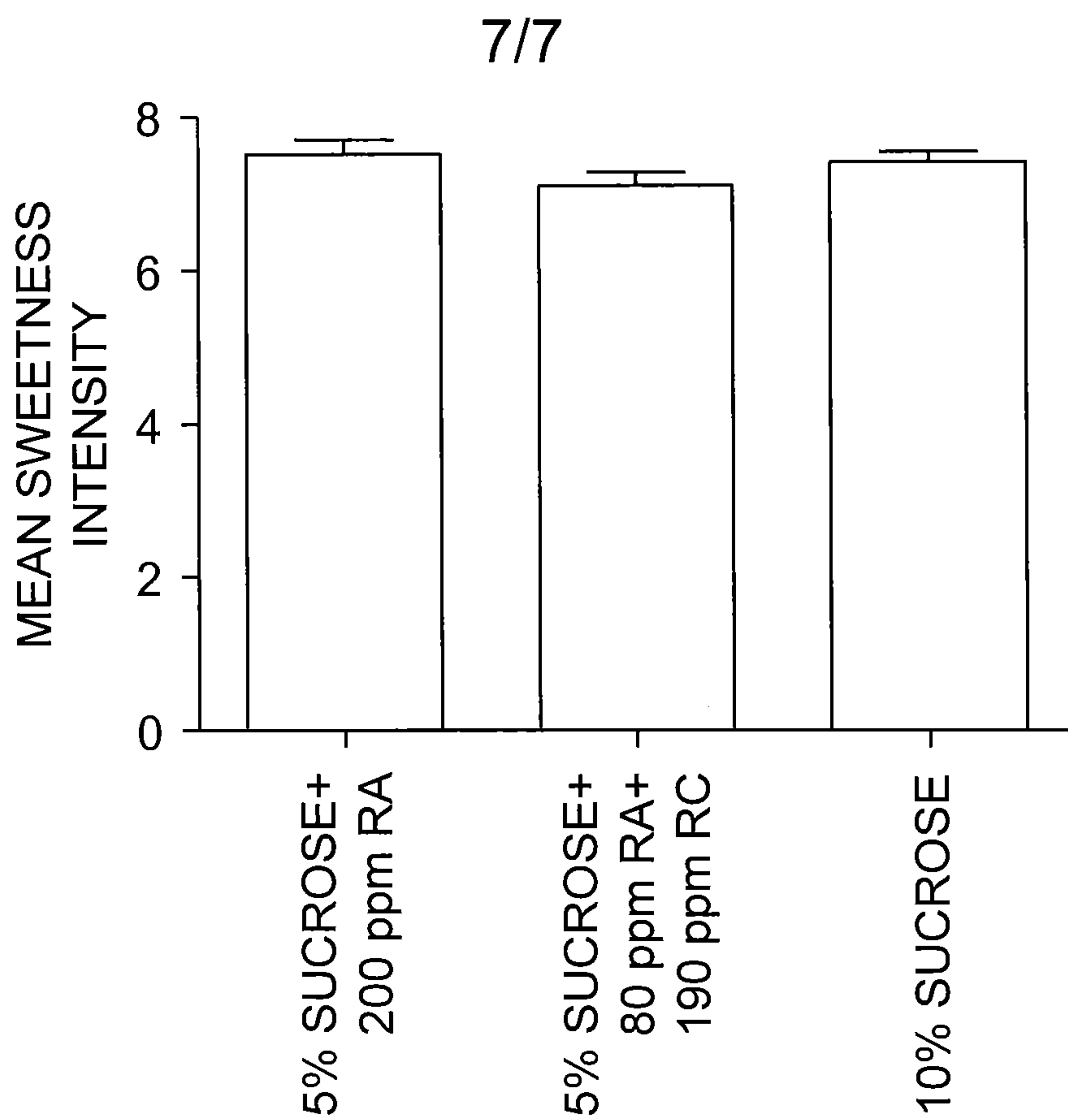
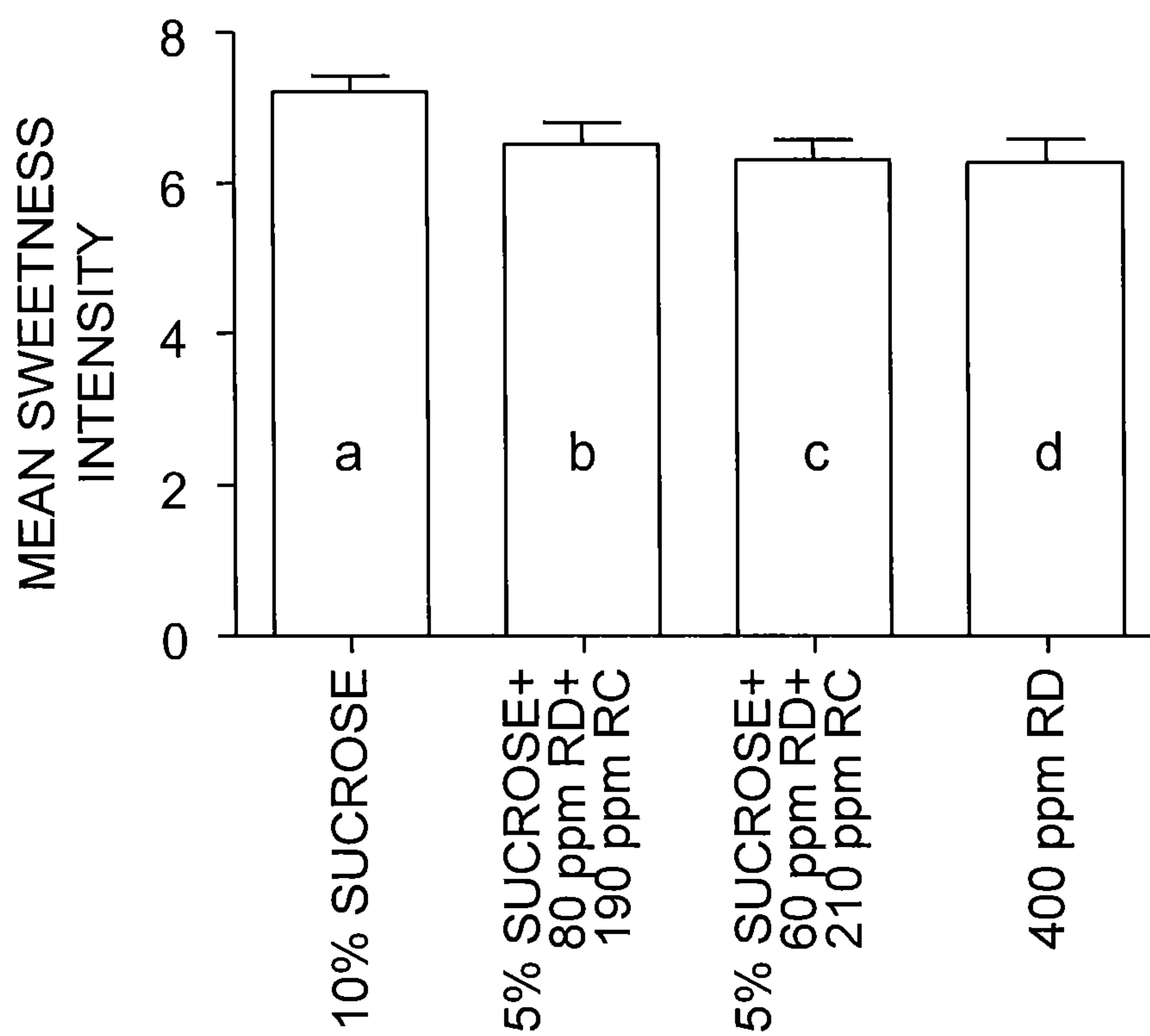


FIG. 8

**FIG. 9****FIG. 10**

**FIG. 11****FIG. 12**

**FIG. 13****FIG. 14**

MEAN SWEETNESS
INTENSITY

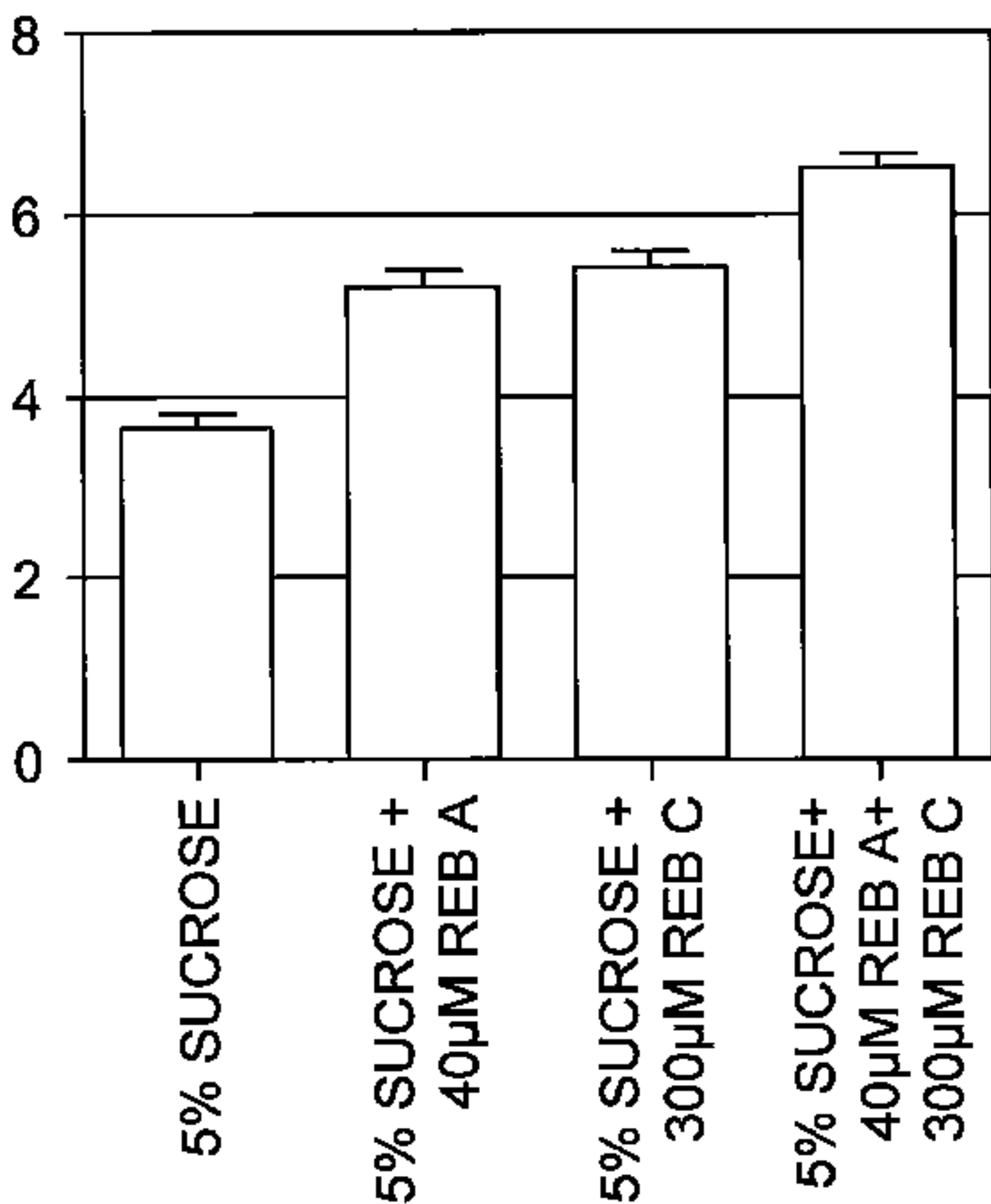


FIG. 11

