

PATENT SPECIFICATION

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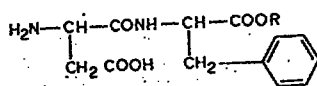


(54) SWEETENING COMPOSITIONS AND METHOD

(71) We, G. D. SEARLE & Co., a corporation organized and existing under the laws of the State of Delaware, United States of America, of P.O. Box 5110, Chicago, Illinois 60680, U.S.A. do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

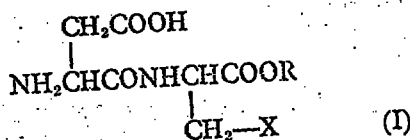
The present invention relates to novel synergistic compositions and their preparation and is an improvement in or modification of our Patent No. 1,152,977.

The specification of the parent describes and claims a sweetening composition comprising a compound of the general formula



wherein R is an alkyl radical containing from 1 to 7 carbon atoms and the stereochemical configuration is DL-DL, L-L DL-L or L-DL and a non-toxic sweetening agent carrier therefor.

The compositions of the present invention contain, as one of the active ingredients, a dipeptide characterized by the following general structural formula



wherein X is a phenyl or hydroxyphenyl radical and R is an alkyl radical containing 1-7 carbon atoms. These compounds are described in pending United Kingdom Application No. 2324/68 (Serial No. 1,206,233) and UK. Patent No. 1,152,977.

It has been discovered that when a dipeptide within the scope of the above structural for-

mula is mixed with a known sweetening agent, e.g., saccharin, cyclamate or sucrose, the sweetening potency of the mixture is enhanced. This synergistic effect is completely unexpected and could not have been predicted from a knowledge of the art. Thus, the mere known fact that the dipeptide, saccharin or another known sweetening agent individually exhibits a sweet taste is neither indicative nor predictive of the synergistic effect (i.e., The composition has a sweetening potency greater than the cumulative effects of the constituents, which is postulated to be a potentiating effect of one agent upon the other.) observed when the dipeptide is combined with a known sweetening agent such as saccharin. (It is to be understood that throughout this application the term "known sweetening agent" is intended to encompass one or more known sweetening agents such as sucrose, saccharin or cyclamate).

A preferred embodiment of this invention is a composition containing saccharin and one of the aforementioned dipeptides of formula (I). An especially preferred embodiment of this invention is the composition containing saccharin and aspartylphenylalanine methyl ester.

A more especially preferred embodiment of this invention is the composition containing saccharin and L - aspartyl - L - phenyl - alanine methyl ester.

The dipeptides which compose one of the active ingredients of the instant compositions have sweetening potencies of from 25 to 150 times that of sucrose. One particularly potent dipeptide is L - aspartyl - L - phenylalanine methyl ester, which has a potency of from 125 to 150 times that of sugar.

The combinations containing a dipeptide of formula (I) and a known sweetening agent can be prepared in a variety of forms suitable for the utilization of sweetening agents. Typical forms which can be employed are: solid forms such as powders, tablets, granules, and dragees; and liquid forms such as solu-

tions, suspensions, syrups, and emulsions, as well as other commonly employed forms particularly suited for combination with edible materials. The term "edible materials" as used herein throughout the specification signifies all non-toxic substances consumable or ingestible by humans or other animals in solid or liquid form. Illustrative of such substances are: foods, including foodstuffs; prepared food items; chewing gum and beverages; food additives, including flavouring and colouring agents as well as flavour enhancers; and proprietary and non-proprietary pharmaceutical preparations.

The instant compositions can be formulated in preparations which can consist of the instant compositions apart or in association with non-toxic sweetening agent carriers i.e., non-toxic substances commonly employed in association with sweetening agents. Such suitable carriers include liquids such as water, ethanol, sorbitol, glycerol, citric acid, corn oil, peanut oil, soybean oil, sesame oil, propylene glycol, corn syrup, maple syrup and liquid paraffin, and solids such as lactose, cellulose, starch, dextrin and other modified starches, calcium phosphate and di- and tri - calcium phosphate. Obviously incompatible for use with these instant compositions would be toxic carriers such as methanol and dimethyl sulphoxide.

Examples of specific edible materials which can be sweetened by the addition of a composition containing a compound of formula (I) plus a known sweetening agent, especially saccharin, include: fruits; vegetables; juices; meat products such as ham, bacon and sausage; egg products; fruit concentrates; gelatins and gelatin-like products such as jam, jellies, preserves, milk products such as ice cream, sour cream and sherbet; icings; syrups including molasses; corn, wheat, rye, soybean, oat and rice products such as bread, cereals, pasta and cake mixes; fish and seafood; cheese and cheese products; nut means and nut products; beverages such as coffee, tea, non-carbonated and carbonated soft drinks, beers, wines and other liquors; and confections such as candy and fruit flavoured drops; and condiments such as herbs, spices, seasonings; vinegar and other salad dressings; flavour enhancers such as monosodium glutamate; and chewing gum. Additional illustrations of the types of commercial products in which a composition containing a sweetening agent of formula (I) plus a known sweetening agent, can be used are: prepared packaged products such as dietetic sugar, liquid sweeteners, granulated flavour mixes which upon constitution with water provide non-carbonated drinks, instant pudding mixes, instant coffee and tea, coffee whiteners, malted milk mixes, pet foods, livestock feed, tobacco, dietary supplements, and consumable toiletries such as mouth washes and

tooth paste, as well as other proprietary and non-proprietary pharmaceutical preparations and other products of the food, pharmaceutical, and sundries industries too numerous to mention, for which a demand has been created by the diabetic and dietic-conscious public.

The sweetening potency of saccharin is, depending upon the edible material to which it is added, 500 times that of sucrose. It has been discovered that when saccharin is mixed with one of the aforementioned dipeptides, the sweetening potency is greatly enhanced. The addition of L - aspartyl - L - phenyl - alanine methyl ester, for example, to saccharin raises its potency to 1000.

An example of a suitable tablet containing the instant composition which is adapted for addition to edible materials, e.g., coffee, is

Ingredient	Amount	
A dipeptide of formula (I), e.g., L-aspartyl-L-phenylalanine methyl ester	25 mg.	85
Saccharin	4 mg.	
Mannitol	200 mg.	90
Sorbitol	5 mg.	
Magnesium stearate	1 mg.	

The invention is illustrated by the following examples in which specific illustrations of the synergistic effect resulting from the mixture of the instant dipeptides with a known sweetening agent are given. The concentrations recited in the following formulations are given for the purpose of illustration only and it is recognized that individual taste preferences for degrees of sweetness vary so substantially that well defined limits for usable ranges for concentrations cannot be clearly delineated.

EXAMPLE 1

A non-carbonated imitation strawberry drink is prepared using four different sweetening formulations: A) sucrose alone, B) L - aspartyl - L - phenylalanine methyl ester alone, C) saccharin alone, and D) saccharin and L - aspartyl - L - phenylalanine methyl ester together. The contents for each formulation, amounting to a total volume of 300 millilitres, are shown below:

A. Sucrose alone		115
Sucrose	27 g.	
Dextrose	2.61 g.	
Citric acid	0.15 g.	
Imitation strawberry flavour (Dragoco N1132)	0.12 g.	120
Lactose	1.827 g.	
Water	268 g.	

B. L-aspartyl-L-phenylalanine methyl ester alone

L-aspartyl-L-phenylalanine methyl ester	0.216 g.
Citric acid	0.15 g.
Imitation strawberry flavour (Dragoco N1132)	0.12 g.
Lactose	1.827 g.
Water	299 g.

10 C. Saccharin alone	
Saccharin	0.054 g.
Citric acid	0.15 g.
Lactose	1.827 g.
Imitation strawberry flavour (Dragoco N1132)	0.12 g.
Water	299 g.

D. Saccharin plus L-aspartyl-L-phenylalanine methyl ester

20 L-aspartyl-L-phenylalanine methyl ester	0.108 g.
Citric acid	0.15 g.
Lactose	1.827 g.
Saccharin	0.0165 g.
Imitation strawberry flavour (Dragoco N1132)	0.12 g.

It was determined by a taste panel that each of the above formulations was equivalent in sweetness.

EXAMPLE 2

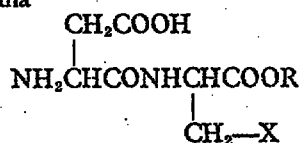
- 30 Approximately 3000 ml. of instant coffee was prepared by dissolving 16.5 g of instant coffee in 3000 ml. of water. 600 ml. Portions of the instant coffee were taken and to each was added one of the following sweetening preparations: E) 24 g. of sucrose, F) 0.16 g. of L - aspartyl - L - phenylalanine methyl ester, G) 0.048 g of saccharin and H) 0.012 g of saccharin with 0.08 g. of L - aspartyl - L - phenylalanine methyl ester.

- 40 It was determined by a taste panel that each of the latter sweetened coffees has an equivalent sweet taste.

- 45 We are aware of the Artificial Sweeteners in Food Regulations 1969. We do not claim to practice our invention in a manner contrary to law and, subject to the foregoing disclaimer,

WHAT WE CLAIM IS:—

- 50 1. A composition adapted for the sweetening of edible materials which comprises a known sweetening agent and a dipeptide of the formula

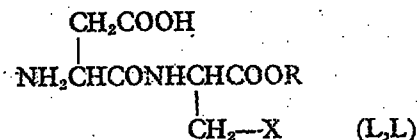


wherein X is a phenyl or hydroxyphenyl

radical and R is an alkyl radical containing 1—7 carbon atoms. 55

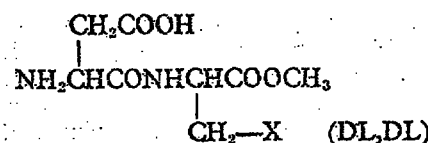
2. A composition as claimed in claim 1 wherein the known sweetening agent is saccharin.

3. A composition as claimed in claim 2 wherein the dipeptide has the general formula 60



wherein X and R are as defined above.

4. A composition as claimed in claim 2 wherein the dipeptide has the general formula 65



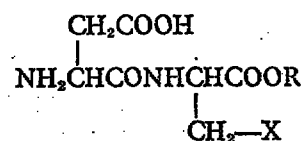
wherein X is as defined above.

5. A composition as claimed in claim 1 which comprises saccharin and L - aspartyl - L - phenylalanine methyl ester. 70

6. A tablet adapted for the sweetening of edible materials which comprises 4 mg. of saccharin and 25 mg. of L - aspartyl - L - phenylalanine methyl ester and optionally a solid non-toxic sweetening agent carrier therefor. 75

7. A composition adapted for the sweetening of edible materials which comprises saccharin and L - aspartyl - L - phenylalanine methyl ester in the ratio of approximately 4 to 25. 80

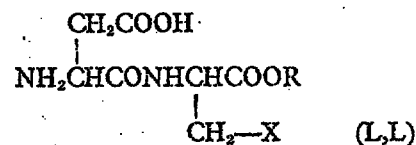
8. A process for the preparation of a composition adapted for the sweetening of edible materials which comprises adding to a known sweetening agent a dipeptide of the formula 85



wherein X is a phenyl or hydroxyphenyl radical and R is an alkyl radical containing 1—7 carbon atoms. 90

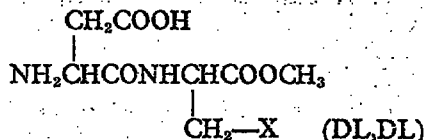
9. A process as claimed in claim 8 wherein the known sweetening agent is saccharin.

10. A process as claimed in claim 9 wherein the dipeptide has the general formula



wherein X and R are as defined above. 95

11. A process as claimed in claim 9 wherein the dipeptide has the general formula



wherein X is as defined above.

5 12. A process as claimed in claim 8 which comprises adding L - aspartyl - L - phenyl - alanine methyl ester to saccharin.

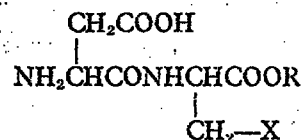
13. A process for the preparation of a tablet adapted for the sweetening of edible materials which comprises adding 25 mg. of L - aspartyl - L - phenylalanine methyl ester to 4 mg. of saccharin optionally combined with a solid non-toxic sweetening agent carrier.

14. A process for the preparation of a composition adapted for the sweetening of edible materials which comprises combining L - aspartyl - L - phenylalanine methyl ester with saccharin in the ratio of approximately 4 to 25.

15. A composition as claimed in claim 1

substantially as described with reference to the Examples.

16. A method for sweetening edible materials which comprises adding thereto a known sweetening agent and a dipeptide of the formula



wherein X and R are as defined above.

17. A method as claimed in claim 16 wherein the known sweetening agent is saccharin.

18. A method as claimed in claim 16 or 17 wherein the dipeptide is L - aspartyl - L - phenylalanine methyl ester.

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