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REVIEW ARTICLE

Potential Source of Low-Calorie Sweeteners from Tropical and Subtropical Plants - A Review

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ABSTRACT

Sweeteners are usually made from the fruit or sap of plants, but can also be made from any other part of the plant, or all of it. Some sweeteners are made from starch, with the use of enzymes. Sweeteners made by animals, especially insects, are put in their own section as they can come from more than one part of plants. The global consumption of herbs as medicine, nutraceuticals, food additives, cosmaceuticals, etc. is increasing rapidly. One of such area of high commercial potential is sweetening properties. Numerous compounds of plant origin are reported to have different degree of sweetness. In the light of limitations of currently marketed synthetic sweeteners as well as drastic reduction of high-calorific sugar consumption especially in developed countries, an area of low-calorie sweetener is gaining tremendous commercial significance. However, in recent past these sweeteners gone through several steps, therefore, before commercialization of these natural sweeteners for both pharmaceutical as well as food industry, it needs to undergo rigorous evaluations. Many other plant-derived compounds are sweet, ranging in structural complexity from sugars and polyhydric alcohols through diterpene and triterpene glycosides to proteins; some of these compounds are intensely sweet, being hundreds or even thousand times sweeter than sucrose, and offer potential for commercial use in dietetic and diabetic foodstuffs. The present review examines the role of ethnobotany in the discovery of sweet-tasting plants, the chemical composition of the sweet compounds, and some description, utilization aspects of these compounds.

KEYWORDS

Plant Metabolites, Low-Calorie Sweeteners, Intense Sweeteners

INTRODUCTION

Plant species with unusual taste properties such as bitterness, sourness or sweetness, and others taste-modifying components, have long been known to man, although their exploitation has been limited. In recent years, the numbers of diabetic and overweight people have greatly increased worldwide. For the prevention of obesity, dental caries or the therapy of diabetes, it is important to limit the ingestion of sugars.

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Together with this trend, there is also an increase in the demand for healthy and natural food products. Therefore, and in order to address this need, there is an intense and ongoing search for alternative sweeteners. Efforts to find additional examples of highly sweet plant constituents have been stimulated both by a public demand for natural flavors, as well as perceived problems with the toxicity, taste quality, stability or price of existing synthetic high-potency sweeteners. At this time in Japan, China, USA, Australia and Europe, some of these natural monosaccharide sweeteners are being consumed. Thus, with the increase in their demand there is a necessity for identification of these nonsacchariferous plant species, as well as the identification of their active sweet principles. This compilation is the account of the non-nutritive intense sweeteners derived from plant metabolites along with various approaches used in discovering new sources[1,2]. This paper also focuses on the chemical composition of the sweet compounds, and some description, utilization aspects.

Sweeteners are the compounds that interact with taste buds that evoke a characteristic response. Sweeteners, therefore, have ability to impart sweet taste by masking the taste of material in which it is added. Sweeteners can be broadly divided into two categories, natural and synthetic (or artificial) sweeteners. Natural sweeteners can be further divided into saccharide and non-saccharide sweeteners. Synthetic sweeteners are further divided into two groups, organic salts and inorganic substituted salts. Although each class has its own merits and demerits, present discussion is confined to the natural non-saccharide intense sweeteners and taste modifying plant metabolites[3]. Ideally, sweeteners should be of low-calorific value, able to mask the taste at lower concentration and it should be free from harmful side effects and suitable for long-term use. It should remain stable at wide range of temperature and pH conditions. It should have quick onset of action and no lingering after taste. Sweetener should be water soluble with high dissolution rate. In addition, it should be non-hygroscopic and should give synergetic effect with other sweeteners. Therefore, in addition to other factors, commercialization of sweetener needs to qualify most of these parameters[2,3].

Types of Sweeteners

Sweetness can be from simple carbohydrates like sucrose, glucose, and fructose, from some amino acids like alanine, glycine, and serine that are mildly sweet, and from high intensity sweeteners that are 100 to 25,000 times sweeter than sucrose. The high intensity sweeteners can be divided into two groups. The first group is the artificial, chemically-synthesized sweeteners. Sucralose, alitame, cyclamate, aspartame, neotame, potassium acesulfame, and saccharin (which was accidentally discovered in 1878), are all examples of commercially available, artificial high intensity sweeteners. The second group is natural high intensity sweeteners extracted from various plant sources. Examples of natural high intensity sweeteners are extracts from *Stevia rebaudiana*, Luo Han Guo, and glycyrrhizin from licorice root. Sweet-tasting proteins from the fruits of African plants are also being commercialized and include thaumatin from *Thaumatococcus daniellii*, monellin from *Dioscoreophyllum cumminsii*, and brazzein from *Pentadiplandra brazzeana*[4]. Lysozyme, from egg whites, is also a sweet-tasting protein. The difference in the density of charged amino acids on the protein surface may result in varying threshold values for the sweet-tasting proteins thereby resulting in differing levels of perceived sweetness[4,5].

Approaches to the Discovery of Highly Sweet Molecules from Higher Plants

In the search for new sweeteners, one of the most demanding aspects is to find good candidate sweet-tasting plants, which might contain novel sweet compounds. There is very difficult to predict the occurrence of sweet compounds on a taxonomic basis. For example *Stevia rebaudiana* is well-known for producing the potently sweet glycosides stevioside and rebaudioside A. When the scientists examined organoleptically and phytochemically over 100 herbarium leaf specimens in the genus *Stevia* only one species other than *S. rebaudiana* was found to contain stevioside, namely, *S. phlebophylla.* According to these results I think that prior to phytochemical investigation there must be done detailed ethnobotanical screening in two major ways followed by screening of biological activity of crude extracts[6,7].

Through Field Investigation

One of the most successful ways to locate new sweet plants is to survey local populations, especially in marketplaces. Generally speaking, humans view sweet-tasting plants as safe to consume, while bitter-tasting plants are frequently considered toxic. Other plants may be known as slightly sweet to the indigenous peoples, but are not used as sweeteners due to the low levels of the compounds, or the presence of bitter or bioactive compounds along with the sweet compound. So, some of the plants may not necessarily be identified as distinctly sweet by local people.

Through Literature Sources

Another potential route to identifying candidate sweet plants are ethnobotanical literature sources. There is most likely a general understanding of sweet perception among all human cultures on earth. Therefore, a notation that a plant tastes sweet by a particular indigenous group of people, is frequently validated sometimes by the discovery of new intensely sweet compounds, but more often by the identification of high levels of free sugars. One shortcoming of this type of ethnobotanical screening is that, sweet may also refer to the odour of the plant, which is not related to sweet-taste perception. Another approach involves a search of *Index kewensis*, a source of all of the published scientific names of seed plants, using specific epithets which might be indicative of sweetness and yields a number of new possible lead plants, as well as some well-known sweet plants. For example, a search of the epithet *dulcis*or *dulcificum* (Latin name for sweet)

Assays for Sweetness[8]

Currently, there is no reliable *in vitro* method.

In Vivo Models

In order for humans to taste chromatographic fractions or pure isolates, preliminary safety testing comprised of mouse acute toxicity and bacterial mutagenecity studies must be performed. These tests represent a significant use of time and resources.

Electrophysiological and Behavioural Experiments Using the Mongolian Gerbil

In the electrophysiological assay, a potentially sweet plant extract, fraction, or pure compound is applied to the tongue of an anaesthetized gerbil, and electrophysiological recordings are taken from the chorda typhani nerve, evaluating up to 25 samples with a single gerbil. This is backed by a conditioned-taste aversion assay using gerbils that are trained to avoid sucrose.

The combination of these methods appears to be helpful in selecting extracts of different polarities from plants for the presence or absence of sweet constituents and about 2/3 of the pure compounds tested that were known to be sweet to humans were evaluated as ‘sweet‘ to the gerbil.

While the gerbil is not a perfect model for human sweet taste it does respond well to many “bulk” (i.e., sugars and polyols) and “intense” sweeteners, and the assay is more economic to perform than other *in vivo* options currently available.

Examples of Recently Discovered Natural-Occurring Sweet Compounds

I. Terpenoids and Steroids

Many of these compounds are glycosides containing one or more saccharide units, which results in enhanced water solubility. Among the terpenoids, certain naturally occurring, mono-, sesqui-, di- and triterpenoids, or their derivatives, are known to be intensely sweet. Several of these compounds have commercial application as sucrose substitutes[9].

***Perilla frutescens* (L.) Britton**

Family: Lamiaceae

Synonyms: *Ocimum frutescens* L., *P. ocymoides* L.,

P. nankinensis (Lour.) J. Decaisne

Vernacular names: Perilla, Perilla mint, Chinese basil (En.), Bhanjira (Hindi)

Origin: Mountainous areas of India

Description: Erect, aromatic, annual herb, 0.3-2m tall, green or purplish.

Uses: *volatile oil*– spice, perfumery; *fatty oil*– cooking; *anthocyanins* – for colouring pickled fruits; *medicine* –diaphoretic, anodyne, sedative, diuretic, anti-inflammatory and remedy for cough.

Sweet principle: Perillartine

It is a monoterpenoid constituent of the slightly sweet volatile oil (α -syn-oxime of Perillaldehyde). About 350 times sweeter than sucrose, it is used in Japan for the sweetening of tobacco. The bitter after-taste and low water solubility have restricted its more general use as a sweetener.

***Lippia dulcis* Trevir**

Family: Verbenaceae

Synonyms: *Phylla scaberrima* (Juss. ex Pers.) Moldenke.

Vernacular names: Mexican lippia, Sweet lippia.

Origin: Central America

Description: Fast growing, low perennial creeper (up to 30 cm) with small white flowers.

Uses: *medicine* - for coughs, colds, bronchitis, asthma, and colic.

Sweet principle: Hernandulcin

Bisabolane sesquiterpenoid from the aerial parts of the plant. Present in the amount of 0.04 – 0.15% w/w dry weight. Despite being about 1,000 times sweeter than sucrose, naturally occurring Hernandulcin is somewhat thermolabile and has an unpleasant aftertaste and some inherent bitterness (due to presence of camphor), which could restrict its potential sweetening applications

***Stevia rebaudiana* Bertoni**

Family: Asteraceae

Synonyms: *Eupatorium rebaudianum* Bertoni

Vernacular names: Stevia, Sweet herb of Paraguay, Honey-yerba (En.)

Origin: Cierra Amambay in North Eastern Paraguay

Description: A slender, erect, perennial herb 50-100 cm tall in natural stands and up to 120 cm under cultivation.

Uses: natural low-calorie sweetener; *medicine*– treatment of diabetes, obesity and could lower blood pressure; *cosmetic products*

Sweet principle: Stevioside

• Sweet *ent*-kaurene glycoside

• Stevioside – the most abundant sweet constituent of this plant (9%). It is stable over the pH range 3-9 for 1 hour at 100°C. Over 90% pure stevioside also exhibit a persistent aftertaste along with some bitterness. The sweetness intensity: 150-300 times sweeter than sucrose. Acute toxicity: LD_{50}= 8.2 g/kg.

Glycyrrhiza glabraL

Family: Fabaceae

Synonym: *Glycyrrhiza glabra*L. var. glabra

Vernacular names: Common licorice, licorice (En.)

Origin: Mediterranean region

Description: Perennial herb up to 1.8 m tall, has dark green leaflets, yellow, blue, or violet flowers, and sweet-flavoured rhizomes.

Uses: natural sweetener in food and pharmaceutical industry; *medicine* demulcent, diuretic, emollient, expectorant, laxative, pectoral, and stomachic agent.

Sweet principle: Glycyrrhizin

Oleanane-type triterpenoid saponin Occurs in the roots in high yields (6-14% 50-100 times sweeter than sucrose, it has a very slow onset of taste and a long aftertaste. Ammoniated glycyrrhizin is 50 times sweeter than sucrose and is considered GRAS (generally regarded as safe) by US Food and Drug Administration for use as a flavouring compound.

***Momordica grosvenori* Swingle**

Family: Cucurbitaceae

Synonym: *Siraitia grosvenorii* (Swingle), *Thladiantha grosvenorii* (Swingle) C. Jeffrey

Vernacular names: Arhat fruit, longevity fruit (En.), luo han guo (Chinese)

Origin: Southern China

Description: Perennial, dioecious, herbaceous climbing vine, 2–5 m. in length. Roots tuberous, fusiform when young, finally subglobose, 10–15 cm in diameter.

Uses: Low calorie sweetening agent in other juices or drinks, or it can be made into a desirable beverage itself. Dried fruit used often in Cantonese soups.

Sweet principle: Mogroside IV and V

• Cucurbitane-type triterpenoid glycosides

• In aqueous extracts of the fruits

• Mogroside V – more abundant and more water soluble; it occurs in yields of greater than 1% of dried fruits 250 times sweeter than sucrose

***Abrus precatorius* L.**

Family: Fabaceae

Vernacular names: Indian licorice, jequirity bean, crab's eye (En.), Akar saga (Malaysia)

Origin: Tropical Asia

Description: A woody climber up to 6-9 m long, stem 1.5 cm in diameter, leaves with 16-34 oblong or ovate leaflets; flowers in dense robust clusters; fruit oblong 1-7 seeded pod; seeds ovoid scarlet with area around hilum black.

Uses: *Medicinal*– treatment of conjuctivitis, aphta and asthma, leaves – natural sweetener; seeds are used in Ornamentals.

Sweet principle : Abrusosides A-D

• Sweet-tasting cycloartane-type triterpene glycosides

• Abrusosides A-D were rated as being, respectively, 30, 100, 50 and 75 times sweeter than 2% sucrose and exhibit a pleasant sweet taste without any bitterness but they have delayed onset of sweet taste

• Yield < 1% in dry leaves

II. Dihydroisocoumarin[10]

***Hydrangea macrophylla* Seringe var. *thunberghii* (Siebold) Makino**

Family: Saxifragaceae

Vernacular names: Amacha

Origin: Japan and China

Description: Shrub about 4 m tall; leaves – elliptic to broadly ovate or obovate, 7-15 cm long, coarsely toothed and almost glabrous. Flowers – pink or blue; propagation by cuttings

Uses: leaves are used in Japan to make a sweet tea which is imbibed in certain religious ceremonies.

Sweet principle: Phyllodulcin

Obtained from fermented or crushed young leaves It is rated as 400 times sweeter than 3% dilution of sucrose But has several problems as an intense sweetener – delayed onset of sweetness, lingering aftertaste and a low solubility in water

III. Flavonoids[11]

• From the peel of ***Citrus aurantium* L.** and ***Citrus paradisi* Macfad.** (Rutaceae) naturally occurring flavanone glycosides:

Neohesperidin and **Naringin** are bitter. Extraction with dilute alkali and hydrogen leads to intensely sweet dihydrochalcones.

Neohesperidin dihydrochalcone is 250 up to 1,800 times sweeter than sucrose depending upon concentration and used as a saccharin replacement for utilization in chewing gums and various beverages.

IV. Sweet-Tasting Proteins[12]

The existence, in nature, of sweet-tasting proteins has been known for many years. All of these proteins have been found in the fruits of tropical plants, and the indigenous peoples have frequently used them to sweeten their foodstuffs. With the commercialization of Thaumatin, both as a sweetener and as a flavour enhancer, there has been an increase in the interest in these compounds. In recent years, an extraordinary number of sweet-tasting proteins have been discovered, studied, purified and characterized. Their genes have been cloned and sequenced, and in many cases have expressed in foreign hosts.

***Thaumatococcus daniellii* Benth**

Family: Marantaceae

Vernacular names: sweet prayer plant, Katamfe

Origin: Tropical rainforests of West Africa

Description: Perennial herb with fleshy rhizome; the footstalk up to 1-2.5 m tall with alternate oblong leaves. Inflorescence– terminal spikes with violet flowers; fruit– 3-lobed capsule containing black seeds covered with yellow sweet aril.

Uses: Sweetening agent and substitution for agar

Sweet principle: Thaumatin I and II

- Protein 3 000 times sweeter than sucrose
- It has lingering aftertaste that might not be considered acceptable by some palates
- According to current price of thaumatin obtained by extraction from it's natural source, microbial production of this protein would only be economically feasible if the recombinant microbes could produce 1g of product per litre.

***Dioscoreophyllum cumminsii* Diels.**

Family: Menispermaceae

Vernacular names: Serendipity Berry

Origin: Tropical West Africa

Description: Dioecious, herbaceous perennial plant, it has long, thin, twining stems and grows in the humid and heavily shaded understory vegetation of closed forests. The aerial vegetation dies back in the dry season and tubers report to produce climbing vines at the onset of the rains. Red berries are born in clusters of up to 100. The mucilage within each berry is intensely sweet.

Uses: sweetening agent

Sweet principle: Monellin

Protein – 3,000 times sweeter than sucrose. It has been shown to lose it's sweetness when heated above 50°C at acidic pH.

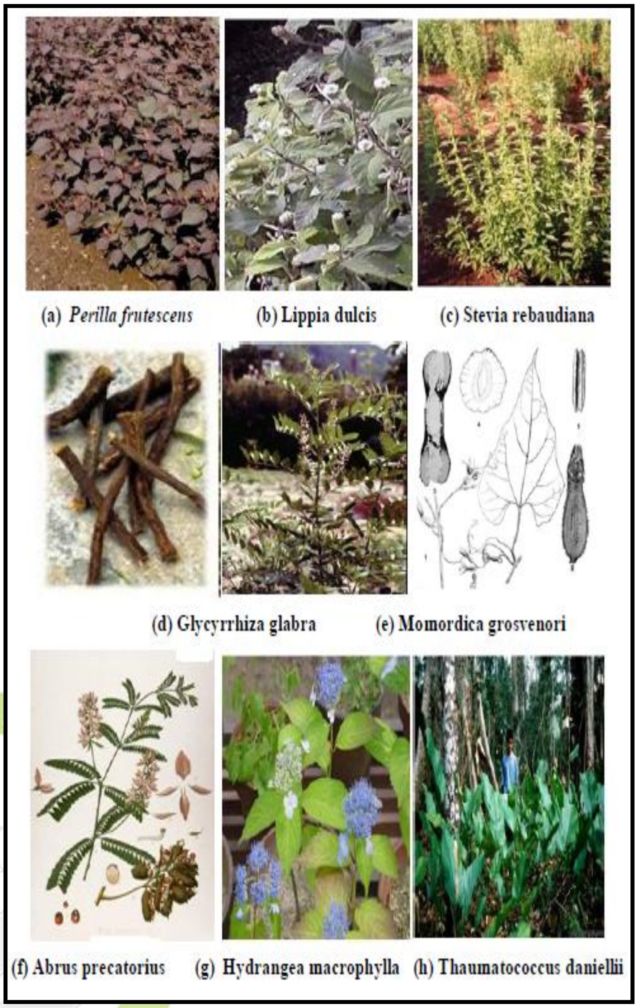

Figure 1: Morphology of some Plant Sweeteners

V. Other Sweet-Tasting Proteins[12,13]

- ***Capparis masaikai* Levl** bears fruits that contains sweet-tasting protein **Mabinlin** (100 times sweeter than sucrose)
- ***Pentadiplandra brazzeana* Baillon** provide two sweet proteins from its fruit –**Pentadin** and **Brazzein** (500 times sweeter than sucrose)
- ***Curculigo latifolia* (Ridl.) D.J.L.Geerinck** provides sweet and also sweet-modifying protein **Curculin**– it is able to turn sour taste into sweet one similarly like **Miraculin** ***Synsepalum dulcificum* Baill.** It's fruits contain a taste- modifier named **Miraculin**. Miraculin by itself does not elicit a sweet response. Like curculin however it can modify a sour taste into a sweet taste.

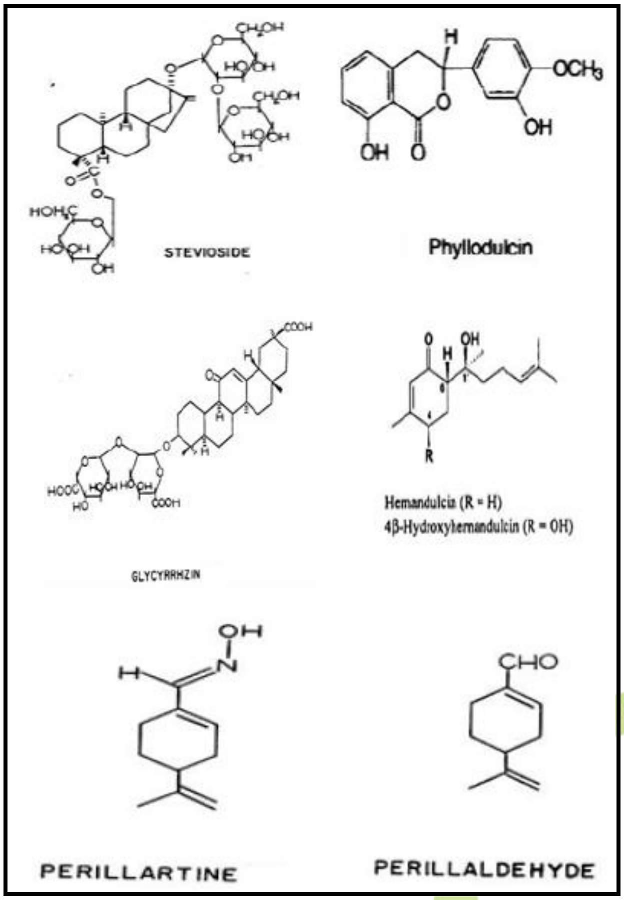

Figure 2: Chemical Structure of some Plant Sweeteners

Future Research Needs

New methods for detection of nonsacchariferous sweet compounds (method based on evaluation of content of saccharides and polyols) – Safety of natural sweeteners (cheaper and faster methods) – Evaluation of sweetness (High Throughput Screening – immunoassays) Industrial production of sweet-tasting proteins through genetically modified microorganisms.

CONCLUSION

The demand of low calorific intense sweeteners is growing not only because of sugar related health problems but also due to rising number of diabetic patients especially in Indian subcontinent. Thus, the extensive efforts are necessary for the search of new sweeteners from various biodiversity regions of India. Although in past, ethnobotanical approach played significant role in discovering sweeteners, an integrated multidisciplinary approach is much more anticipated which can involve phytochemist, ethnobotanist, pharmacologist, pharmacognosist, plant biochemist, etc. to ensure fruitful results. The commercialization of plant sweeteners is currently attempted by large scale cultivation and or biotechnological means. The latter approach is found promising for protein as well as some small molecule sweeteners. It was also realized that several phytoconstituents besides being sweet in taste exhibit various pharmacological activities. It will be, therefore, highly appropriate to categorize these sweeteners according to the disease groups (e.g. sweeteners for diabetic patients) to get benefit of their dual properties.

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REFERENCES

1. Mehtani, S., Kak, R. D. and Singla, P. (2003). *Plant sweeteners for diabetics. In: Recent progress in medicinal plants* Vol. 8. D.K. Majumdar, J. N. Govil, and V. K. Singh (Eds.). Studium Press, LIC, USA, pp. 219-233.

2. Sardesai, V. M. and Waldshan, T. H. (1991). Natural and synthetic intense sweeteners. *J Nutr Biochem, 2(5)*, 236-244.

3. Inglett, G.E. (1976). A history of sweeteners — natural and synthetic. *J Toxicol Environ Health, 2(1)*, 207-214.

4. Douglas, K. and Djendoel, S. (2002). Discovery of terpenoid and phenolic sweeteners from plants. *Pure Appl Chem, 74(7)*, 1169-1179.

5. Compadre, C. M., Pezzuto, J. M., Kinghorn, A. D. and Kamath, S. K. (1985). Hernandulcin: an intensely sweet compound discovered by review of ancient literature. *Science, 227(4685)*, 417-419.

6. Takasaki, M., Konoshima, T., Murata, Y., Sugiura, M., Nishino, H., Tokuda, H., Matsumoto, K., Kasai, R. and Yamasaki, K. (2003). Anticarcinogenic activity of natural

sweeteners, cucurbitane glycosides from *Momordica grosvenori*. *Cancer Lett*, *198(1)*, 37-42.

7. Kaneda, N., Lee, I. S., Gupta, M. P., Soejarto, D. D. and Kinghorn, A. D. (1992). (+)-4 Beta- hydroxyhernandulcin, a new sweet sesquiterpene from the leaves and flowers of *Lippia dulcis*. *J Nat Prod*, *55(8)*, 1136-1141.
8. Jakinovich, W. C., Moon, Y. H. and Kinghorn, A. D. (1990). Evaluation of plant extracts for sweetness using the *Mangolian gerbil*. *J Nat Prod*, *53*, 190
9. Hashimoto, Y., Ishizone, H., Suganuma, M., Ogura, M., Nakatsu, K. and Yoshioka, H., Periandrin, I. (1983). A sweet triterpene-glycoside from *Periandra dulcis*. *Phytochemistry*, *22(1)*, 259-264.
10. Raouf, A. H., Yuh-Meei, L., Luis, J. P., Eugenia, B., Bo, S. C., John, M. P., Djaja, D. S. and Kinghorn, A. D. (1990). Plant-derived sweetening agents: Saccharide and polyol constituents of some sweet-tasting plants. *J Ethnopharmacol*, *28(1)*, 103-115.
11. Nanayakkara, N. P., Hussain, R. A., Pezzuto, J. H., Seejarto, D. D. and Kinghorn, A. D. (1988). An intensely sweet dihydroflavonol derivative based on a natural product lead compound. *J Med Chem*, *31(6)*, 1250-1253
12. Gibbs, B. F., Alli, I. and Mulligan, C. (1996). Sweet and taste-modifying proteins. *Rev Nutr Res.*, *16(9)*, 1619-1630.
13. Hussain, R. A., Poveda, L. J., Pezzuo, J. H., Seejarto, D. D. and Kinghorn, A. D. (1990). Sweetening agents of plant origin. *Econ Bot.*, *44*, 174.