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Eram S Rao
Department of Food Technology, Bhaskaracharya College of Applied Sciences, University of Delhi, Delhi, India

Rizwana
Department of Food Technology, Bhaskaracharya College of Applied Sciences, University of Delhi, Delhi, India

C Lalmuanpuia
Dept of Food Technology Bhaskaracharya College of Applied Sciences, University of Delhi, Delhi, India

Upadhyay Kumar Krishna
Department of Food Technology, Bhaskaracharya College of Applied Sciences, University of Delhi, Delhi, India

Gayakwad Saloni
Department of Food Technology, Bhaskaracharya College of Applied Sciences, University of Delhi, Delhi, India

Corresponding Author:
Eram S Rao
Department of Food Technology, Bhaskaracharya College of Applied Sciences, University of Delhi, Delhi, India

Naturally occurring non-nutritive sweeteners: A review

Eram S Rao, Rizwana, C Lalmuanpuia, Upadhyay Kumar Krishna and Gayakwad Saloni

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Abstract
Today's well-informed consumer is demanding health promoting foods which not only have natural ingredients and are additive free, but also offer functional properties without compromising on the taste. Excessive consumption of sugar is a leading cause of non- communicable diseases, globally. Not more than 10% of the calories should be derived from sugar for optimal health. This has led to the increase in demand of food products containing sugar free alternatives. Therefore, naturally occurring non-nutritive sweeteners that have positive effects on the body weight as well as metabolism may facilitate in limiting the sugar intake and accomplishing the present recommendations. They are also an excellent alternative both for the consumers as well as the food industry in place of artificial sweeteners. These natural sweeteners are extracted from indigenous plants, provide insignificant calories, taste like sucrose, do not exhibit metallic after taste, and moreover, offer significant health benefits. The steviol glycosides and Luo Han Guo fruit (Monk fruit) are the natural extracts of plants, which are commercialized. In addition, numerous plant proteins such as thaumatin, brazzein, miraculin and several carbohydrates as rare sugars such as D- tagatose, D-allulose, D-sorbose and D-allose are being explored as potential substitutes to intense sweeteners which are reviewed in this paper. These are being extensively studied by the researchers for their physicochemical and functional properties and their possible use in low- calorie food formulations. They have a history of safe consumption by the natives of the country of their origin and have a generally recognized as safe (GRAS) or a novel food status.

Keywords: natural non- nutritive sweeteners, stevia, thaumatin, glycyrrhizin, Brazzein, Rare sugars, D-allulose, D-tagatose, D-sorbose, D-allose, Luo Han Guo fruit (Monk fruit)

Introduction

Today, the health-conscious consumer is yearning to improve the quality of life by reducing the intake of sugar, salt and fat (Siervo M, *et al.*,2014) [76]. According to the recommendation of the World Health Organization, not more than 10% of the calories should be derived from sugar for optimal health (Azaïs-Braesco, *et al.*, 2017) [5]. This has led to the increase in demand of food products containing sugar free alternatives such as non-nutritive sweeteners (NNS). These are intensely sweet compounds as compared to sucrose, are calorie free (except for Aspartame) and are synthetically produced. These artificial sweeteners (AS) are approved for food use as food additives. However, as reported by many investigators substituting sugar with NNS may have unfavourable clinical effects in individuals such as glucose intolerance and disappointment in weight loss. But due to paucity of clinical and epidemiological data, minimal consumption of both sugar and NNS is recommended. (Shankar P *et al.*, 2013) [73].

This has led to renewed interest in identifying alternate natural non- nutritive sweeteners (NNNS) which are not only safe but also provide the characteristic mouth feel of natural sweeteners. (Mooradian *et al.*, 2017) [54]. The steviol glycosides and Luo Han Guo fruit (Monk fruit) are the natural extracts of plants, which are readily available in the market for food use and enjoy a GRAS (generally recognized as safe) status. Besides, some proteins such as thaumatin, brazzein and miraculin which are derived from plants, too have demonstrated remarkable properties of a sweetener.

Moreover, naturally occurring rare sugars have recently emerged as an excellent sweetening alternative. They are monosaccharides which are found in nature and have insignificant calories Several researchers are exploring the possibilities of these rare sugars such as D-allulose (D-psicose), D-tagatose, D-sorbose and D-allose as an alternative to NNS (Mooradian *et al.*, 2017) [54]. They provide the characteristic bulk and mouth feel of table sugar with reduced calories (0.2 kcal/g for D-allulose). These are being further investigated for possible use in the food industry. Several novel approaches including development of bitterness- blockers, coating with mineral carriers or hollowing out the sugar crystals are being pursued to overcome any aftertastes or flavour defects in these sweeteners of natural origin.

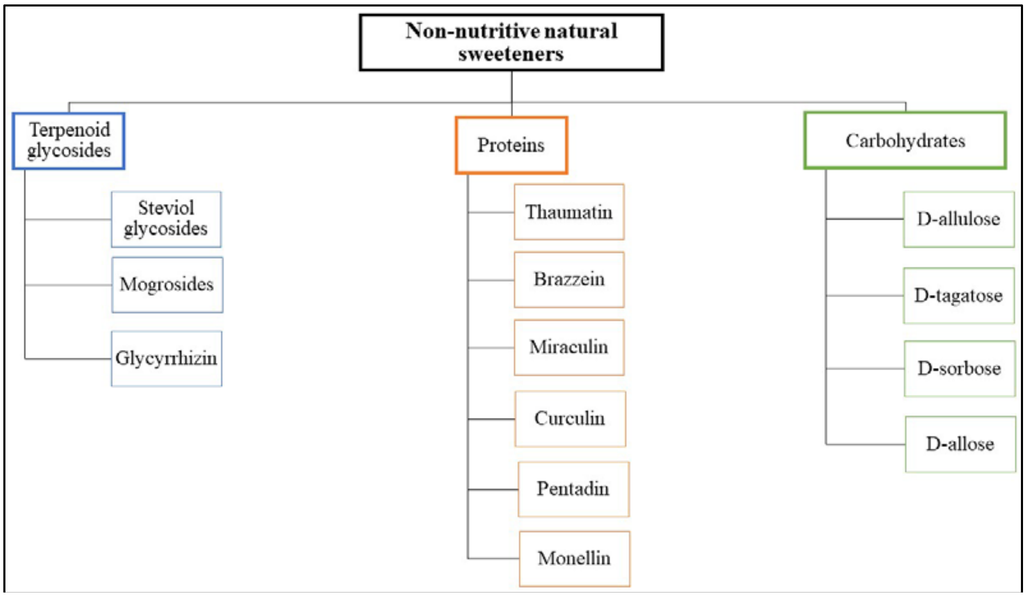

Fig 1: Classification of Natural non-nutritive sweeteners

Naturally Occurring Non-Nutritive Sweeteners

Terpenoid Glycosides

Steviol glycosides

Stevia is a perennial shrub, native to South America called *Stevia rebaudiana bertoni* (Asteraceae). Its cultivation has now spread in other counties of Europe and Asia as well (Hossain *et al.*, 2010) [2]. It is a natural herbal sweetener used for lowering blood sugar for centuries (Carakostas, *et al.*, 2008) [10]. Its white crystalline compound (stevioside) which is extracted and purified from the leaves of the plant. It is an intense sweetener without any calories and is 100−300 times sweeter than table sugar (Lemus-Mondaca, *et al.*, 2012) [42]. Typically, the glycosides represent up to 15% in dried leaves of the plant (Shannon, *et al.*, 2016) [74]. Stevioside and Rebaudioside A are the two main compounds which exhibit sweetness. Stevioside is reported to have slight bitter aftertaste, while Rebaudioside A is the most appealing steviol glycoside due to its high relative sweetness of about 200–300. Physiochemical properties indicate moderate heat and pH stability at broad range of pH range (2- 10). It also resists fermentation and is acid stable. Stevioside and rebaudioside A do not caramelize when food products are subjected to high temperatures. (Muhammad, F. *et al.*, 2020) [55].

Metabolism and Health Aspects

Pawar, *et al.*, (2013) [64] have studied the metabolism of steviol glycosides, it is hydrolysed by the colonic microbiota to steviol and mainly assimilates in the small intestine before being transported to the liver. Here, steviol glucoronides are produced from glucuronic acid by the process of conjugation, which is eventually excreted in urine. It is reported to be a valuable sweetener particularly for those suffering from diabetes, heart disease, obesity and dental caries (Ghanta *et al.*, 2007) [27]. They have also been known to exhibit anti-inflammatory and immunomodulatory diuretic and anti-hypertensive properties (Brahmachari, *et al.*, 2011) [6]. They are safe and suitable for diabetic patients provided their Acceptable Daily Intake (ADI) value is adhered to as calorie contribution of these compounds is nearly non-significant.

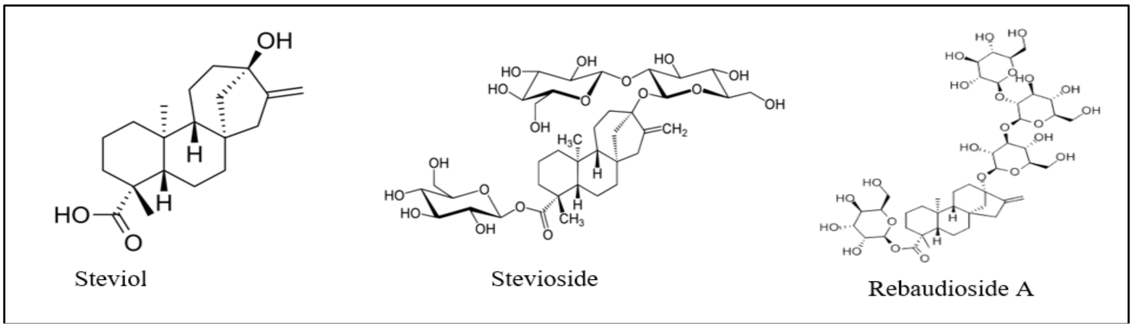

Fig 2: Chemical structure of Steviol, Stevioside and Rebaudioside A

Food applications and Regulatory status
It is ideally suited for a wide variety of foods as it enhances sweet and savoury flavours. Typically, in bakery and confectionary, dairy products, chocolates, preserves such as jams, jellies, sauces and beverages. However, it has a liquorice aftertaste and lacks bulking property. The ADI of steviol glycosides is 4 mg/kg of body weight/day limit (Younes, *et al*., 2020) [18].

Glycyrrhizin
Glycyrrhizin is a plant glycoside which is sweet in taste and obtained from the roots of liquorice plant *Glycyrrhiza glabra L.* (Fabaceae). It grows extensively in Europe and Central Asia. The dried roots are extracted using ammonia and then crystallized with 95% alcohol giving crude ammonium glycyrrhizin (AG). After further treatment mono- ammonium glycyrrhizin (MAG), a white crystalline form is obtained. The sweetness index of both the derivatives is alike but have different solubility rates and sensitivity to pH. Ammonium glycyrrhizin (AG) is highly soluble both in hot and cold water as well as in alcohol, stable at high temperatures for short time but precipitates at pH below 4.5. Whereas, mono- ammonium glycyrrhizin (MAG) is stable at low pH and can be employed in food applications where colour rule out AG. (M. Gloria, 2003) [47]

Metabolism and health Aspects
Glycyrrhizin is hydrolysed by the human gut and is completely metabolized with no effect on glycemic index. According to J.C. Fry, (2012) [24, 25] glycyrrhizin could have beneficial effects on intestinal microbiota. The glycyrrhizin extract has been traditionally used as herbal medicine, to treat cough, stomach ulcers and for constipation (M. Zeece, 2020) [49]. Excessive intake of glycyrrhizin increases sodium levels in blood and decreases the potassium levels leading to hypertension and arrhythmia.

Food applications and regulatory status
It is about 30–50 times sweeter than sucrose and exhibits a sweet woody flavour, which limits its use as a pure sweetener. However, glycyrrhizin is known to enhance food flavours, masks bitter flavours, and increases the perceived sweetness of sucrose. It also has the potential to provide functional properties to foods such as foaming, viscosity control, gel formation, and possibly antioxidant characteristics too. Glycyrrhizin can be used in bakery, confectionery, ice creams, gums and beverages. In Japan it is permitted to be used as a sweetener. However, in USA and EU it is not permitted as a sweetener but as a flavouring agent and a flavour enhancer. It has a GRAS status as a food additive (Noori *et al.,* 2018) [58]. At present there is no ADI for glycyrrhizin, but the intake should be restricted to 100mg/day as prescribed by the EU. (Michael Zeece,2020) [49].

Luo Han Guo (Monk fruit)
Siraitia grosvenorii is a perennial herb which belongs to family Cucurbitaceae native to southern China and is best known for its fruit, the luo han guo. The word “Luo Han” means monk and “Guo” means fruit, thus, is known as Monk Fruit in the west. It has been used in Chinese traditional medicine as a remedy for cold and sore throat for almost 1,000 years. Mogrosides, are triterpene glycosides which are the sweet principles of the plant. Several mogrosides are produced by the plant, of which the most common have been designated mogroside IV and mogroside V (Fry, J.C., 2012) [24, 25]. Majorly, mogroside V occurs in about 1% of the dried fruit and is sweetness potential is approximately 200–250 times that of sucrose. Mogrosides are classified by the US Food Drug Administration (FDA) as a GRAS product. There are no restrictions on consuming the fruit or its extracts.

Metabolism and health Aspects
Mogroside V has been reported to be non-mutagenic. Pandey. A & Chauhan. O, (2020) [63] have reported that the monk fruit extract and mogrosides have shown effective anti- diabetic properties by increasing the blood glucose uptake in the diabetic population. Pharmacological studies on monk fruit in recent years have exhibited many health protective properties. They have demonstrated high anti-oxidative and anti- inflammatory properties which helps in suppressing stress mediated diabetes mellitus. Mogrosides have been found to be anti-carcinogenic as well as anti -asthmatic and offers liver protection (Li *et al*., 2014) [43]. Similarly, San *et al*. (2012) studied anti-obesity property of total mogrosides extracted from monk fruit as well as, mogrosides IV and V by analysing their effect on pancreatic lipase in-vitro. They found significant inhibitory effect of total mogrosides, mogrosides IV and V on pancreatic lipase activity. The increase in body weight as well as triglyceride and total cholesterol level in mice was suppressed during in-vivo study by the oral administration of mogrosides. Therefore, ripe monk fruit mogrosides extract might be an effective replacement of sugar for diabetic and obese patients. (Fang *et al*., 2017) [20].

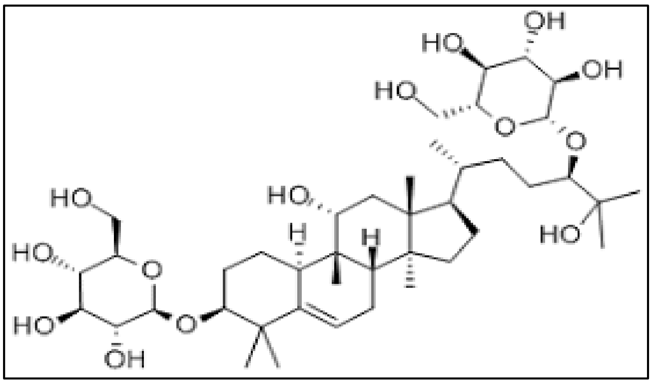

Fig 3: Mogroside structure

Food Applications and regulatory status
The increasing demand of non-nutritive sweeteners from natural sources have increased the popularity of monk fruit in international market including nutraceutical, food and beverage industries (Pawar *et al*., 2013) [64]. They are used to sweeten soft drinks, juices, desserts, candies and condiments. It is often blended with other non-nutritive sweeteners too. The health benefits of monk fruit have encouraged its use in low calorie foods and beverages such as jams, chocolate and sweet juices. It is used as a non-nutritive tabletop sweetener and as a dietary supplement. It has been approved by many countries like Australia, Japan, United States and New Zealand. Mogrosides V has been approved by Japan as a natural sweetening agent. USA has approved the extract of monk fruit as GRAS (generally recognized as safe) for non-nutritive sweetening and as a flavour enhancer (Tu *et al*, 2017).

Table 1: Health implications of Natural non-nutritive sweeteners

	Natural sweetener	Health implications	References
Terpenoid Glycosides	Steviol glycosides	Non-genotoxic, non-carcinogenic, non-allergic, non-teratogenic and non-mutagenic	Saraiva *et al.*, 2020 [70]
	Glycyrrhizin	Anticancer, antiviral, antioxidant, anti-inflammatory, and hepatoprotective	Saraiva *et al.*, 2020 [70]
	Monk fruit	liver protection, anti-hyperglycaemic, anti-oxidative, anti-asthmatic, anti-cancer and anti-inflammatory action	Buchilina *et al.*, 2021 [8]
Proteins	Thaumatin	Does not induce tooth decay; not toxic and non-allergic	Ariana Saraiva *et al.*, 2020 [70]
	Brazzein	Anti-inflammatory, antioxidative,anti-allergic,	Chung *et al.*, 2018 [14, 15]
	Miraculin	Antidiabetic, anti-hyperuricaemia, antioxidative, anticancer and anticonvulsant in nature	Akinmoladun *et al.*, 2020 [1]
	Curculin	Unknown	-
	Pentadin	Unknown	-
	Monellin	Unknown	-
Carbohydrates	D-allulose	antihyperglycemic, antihyperlipidemic, and antiobesity	Kishida *et al.*, 2019 [38]
	D-allose	Antioxidant, anti-inflammatory, anti-cancer, anti-tumor, anti-osteoporotic, anti-hypertensive, neuroprotective and cryoprotective properties	Li *et al.*, 2019 [44]
	D-tagatose	prebiotic, anticariogenicity, and antiglycemic activity, effective against type II diabetes	Li *et al.*, 2019 [44]
	D-sorbose	antihyperlipidemic, and antiobesity	Furuse *et al.* 1994

Naturally occurring plant proteins sweeteners

Naturally occurring proteins as sweeteners have captured the attention of researchers in recent times. They are isolated from indigenous plants and far superior to carbohydrate sweeteners in their sweetening potential. The taste profile is much like table sugar and the relative sweetness is many thousand times greater than sucrose. They provide 4 kcal/g but being intensely sweet the amount used in food application makes them virtually calorie free. Interestingly these amino acids / proteins do not initiate the insulin response on food consumption (Gloria, 2003) [47]. Some of the plant proteins which have the potential of being used in the future as substitute for carbohydrate sweeteners are being discussed. These include thaumatin, brazzein, mabinlin, monellin, miraculin, pentadin, curculin (neoculin). Although these proteins have a long history of safe use, but more studies are needed to make sure that these sweeteners do not cause any hypersensitivities in susceptible individual when consumed in foods. (Rao, E.S, 2021) [68]

Thaumatin

Thaumatin is a naturally occurring sweetener composed of a mixture of proteins, isolated from a West African fruit *Katemfe* (*Thaumatococcus danielli*) (Das, *et al*., 2016) [16]. It consists of two proteins namely, Thaumatin I and Thaumatin II which have similar properties, amino acid composition, sweetness, molecular weight and 207 amino acids. Its sweetness potency is roughly 2000 times more than table sugar, sucrose. Traditionally, Katemfe has been used to flavour foods and beverages and possess flavour modifying/ masking properties. Its sweetness lingers longer than sucrose, but its perception is more gradually. However, at high concentrations it leaves a liquorice like after taste. When combined with other sweeteners or sucrose its acceptability as a sweetener is enhanced (Michael. Z, 2020) [49]. Thaumatin is highly soluble and stable at a wide range of pH 2.0-10 at room temperature. However, the protein losses its sweetness at temperatures more than 70 ^{0}C.

Metabolism and health Aspects

Thaumatin is metabolized in the human body like any other proteins. It provides 4 kcal/g but since it is an intense sweetener the amounts used to impart sweet taste are very small thus, it is classified as a non-nutritive sweetener. It is nontoxic and its protein value is insignificant in the diet. However, there seems to be a possible risk of allergic reactions due to the structural similarities of the proteins present in thaumatin with those found in apple and kiwi fruit allergens. The proteins are resistant to thermal and gastric digestion. (Bublin *et al*., 2008) [7].

Food applications and regulatory status

The major uses of thaumatin in foods include chewing gum, dairy products, processed vegetables, soups, sauces. However, it is not suitable for use in beverages as it leads to loss of sweetening potency when it comes in contact with the colour additives (Miele *et al.*,2017) [50]. Thaumatin works well as flavour enhancer at very low concentrations and thus works very well synergistically with other intense sweeteners and sugar alcohols (Spillane, 2006) [76]. The only exception reported by Gloria (2003) [47] are aspartame and cyclamate. Thaumatin is considered safe for food applications and is therefore have been permitted by United States and European Union. It has been given generally recognized as safe (GRAS) status. In ice cream and sweets, it is permitted to be used as a sweetener at a dosage of 50 mg/kg. As a flavour enhancer it is suitable for dairy products and soft drinks in the range of 0.5 mg/L and 5 mg/kg (Saraiva, 2020) [70].

Brazzein

Brazzein is a small sweet tasting protein obtained from an indigenous wild African plant, *Pentadiplandra brazzeana Baillon* having 54 amino acid residues with four intramolecular disulphide bonds. Its sweetness index is 2000- 500 times sweeter than sucrose. Brazzein tastes more like sugar, than thaumatin and has a clean non- metallic after taste. It is water soluble and has very good thermal and pH stability and does lose its sweetness when heated at 80 C for 4 h. (Ming D, *et al.*, 1994) [52].

Metabolism and health aspects

Brazzein has been consumed by the natives of West Africa as a sweetener from ancient times with no adverse health effects. This testifies its safety (Rajan V, 2018) [67]. Kim. H, *et al.*, (2020) [34] investigated the use of brazzein as a possible natural sugar substitute and its link with obesity, metabolic disorder and inflammation. They reported lack of adiposity hypertrophy and no disruption of glucose homeostasis or insulin resistance and inflammation. Kim and co-workers suggested that it could perhaps be used as a potential sugar substitute reducing obesity.

Food applications and regulatory status

Being heat and pH stable and easily soluble in water makes brazzein a suitable sweetener for food formulations. With a clean sweet taste like sugar, it can be used as a masking agent with other sweeteners of high intensity by reducing their aftertastes. It blends very well with stevia. It is still to be approved as a sweetener and therefore not available commercially. However, this natural non-nutritive sweetener with the taste profile akin to sucrose has unlimited potential to be used for food applications in future. (Chung, *et al*. Food Chemistry (2017).

Miraculin

Miraculin as the name suggests is a unique sweetener which makes sour foods taste sweet. It's a glycoprotein which is present in the berries of so called 'Miracle Fruit' which is native of West Africa named *Richadella dulcifica* synonym *Synsepalum dulcificum* (Kurihara, *et al*., 1994) [41]. It is not sweet by itself but can alter a sour taste into sweet (Ezura, H *et al*., 2018) [19]. Thus, when the berries are chewed, they coat the tongue and bind to the receptors that react to sweet substances (Kurihara K, Beidler LM, 1968). The resultant change in taste lasts from fifteen minutes to over an hour.

Food applications and regulatory status

Miraculin is known as an excellent taste modifier. It has the potential to sweeten sour beverages. This protein changes sour taste to sweet, at an acidic pH by an unknown mechanism. Although at neutral pH it tastes flat. Being a natural product, it contains practically no calories and has zero glycemic index which makes it a suitable sweetener for diabetics. However, miraculin is yet to be approved as a sweetener. It is not permitted for use in USA but has been given a novel food status in the EU. A novel food is defined as a type of food that does not have a significant history of consumption or is produced by a method that has not been previously used for food. (M. Zeece, 2020) [49]

Curculin (Neoculin)

Curculin is another unique sweet tasting protein, extracted from the fruit of *Curculigo latifolia*, grown in Malaysia (Kurihara, *et al*., 1994) [41]. The active protein responsible for the sweet taste in curculin has been renamed neoculin. The fruit contains approximately 1-3mg (Okubo *et al.* 2008). Like miraculin it can also alter the sour taste to sweet which lasts for a few minutes only as compared to miraculin which is up to an hour. However, renewed sweetness is observed after the intake of water or acidic solutions. But unlike miraculin, curculin has a sweet taste of its own. It's about 550 times as sweet as sugar (Fry, J.C, 2012) [24, 25]. It consists of two identical 114 amino acid residue subunits (Shirasuka *et al*., 2004). It is believed to affect the taste buds in two different ways: one is to register as a molecule on the receptors that identify sweetness. the opposite is to connect to the sour receptor buds and alter the signal to sweet (H. Yamashita, *et al*., 1990) [82].

Food applications and regulatory status

This high intensity sweetener is heat labile and loses it sweetening potency at temperatures higher than 50^0C and at pH 6.0, therefore has limited use in food industry. However, as a masking agent, neoculin could improve the acceptability of unpalatable substances. So far it has also only been approved in Japan as a food additive but not in other countries.

Monellin

Monellin is the first naturally occurring protein sweetener to be discovered in 1969. It is obtained from a West African plant *Dioscoreophyllum cumminsii* and consists of 94 amino acids. It is an intense nutritive sweetener approximately 3000 times sweeter than sugar. Being a protein monellin contains 4 calories per gram but being extremely sweet, it is practically non- nutritive (Zhao, *et al*., 2018) [83]. The perception of sweetness is best between the pH range of 2.0-5.0. Although unlike other protein sweeteners, the onset of sweetness is slow and has a lingering aftertaste.

Food applications and regulatory status

Monellin is not heat and pH stable. It denatures at low pH and high temperatures (above 50 C) leading to loss in sweetness (Qiulei Liu, Ietal *et al*., 2016) [66]. This limits its use in the processed food industry. Being pH labile, it adversely affects the flavour of soda drinks due to the fruit acid (lemon etc) and hence are not suitable for beverages. Other than local consumption by natives in Africa it has not yet found use as a sweetener (M.F. Rega, *et al*, 2015) [69]. No safety concerns have been known so far. Japan is the only country so far to have approved of monellin as a sweetener.

Pentadin

Pentadin is a lesser known sweet tasting protein which is isolated from a shrub native of Africa *Pentadiplandra brazzeana.* It is 500 times sweeter than sucrose on a weight basis. Not much is known about this sweetener despite its discovery several years ago. It is metabolized like proteins in the body, has zero calorific value and glycemic index. It has been safely consumed by the Africans for decades. It is not commercially available in the market nor does it have the regulatory approval as a sweetener by any country. (Kant, 2005) [32, 33]

Mabinlin

These sweet tasting proteins are obtained from the seeds of a Chinese plant named Mabinlang (*Capparis masaikai*) (Kurihara, *et al*., 1994) [41]. They are approximately 400 times sweeter than sucrose on weight basis with a lingering but weak sweetness of 0.1% threshold. They are known to exhibited extremely good heat stability, due to the presence of four disulphide bridges. (Guan *et al*., 2000) [29]. It consists of 33 and 72 amino acids residues respectively in chain A and B which are linked with two intramolecular disulphide bonds each. (Nirasawa S, 1993) [56]

There are at least four homologues of Mabinlin with different thermal stability profiles. Mabinlin I is heat sensitive which after heating for 30 minutes at 80 °C and pH 6 loses its sweetness. Mabinlin II is the most heat tolerant and remains unaffected even after heating for 48 hours at 85 C. Whereas, Mabinlin III and IV remain unaffected after 1 hour at 80 C. However, the sweetness potency of Mabinlin II is very low as compared to sucrose. Thus, its commercial viability as a sweetener in food applications is not encouraging (Nirasawa S, 1994) [57].

Naturally occurring rare sugars as sweeteners

Rare sugars are monosaccharides which are found in very minute quantities in nature. They have recently gathered momentum as a suitable alternative to artificial sweeteners due to their natural occurrence, absence of aftertaste, low glycemic index and lesser calories as compared to sucrose (Mooradian *et al.,* 2017) [54]. International Society of Rare Sugars (ISRS) have defined them as carbohydrates which represent a group of different monosaccharides and their derivatives that are found in low abundance in nature are called rare sugars (Izumori K, 2006) [30]. There are more than fifty rare sugars that exists in nature but so far only four i.e. D-allulose, D-tagatose, D-sorbose, and D-allose have been studied as potential low energy substitutes for sucrose (Mooradian *et al.*, 2017) [54]. D-allulose and D-tagatose have been approved for food use by the USFDA and have been given a generally recognized as safe (GRAS) status (Oshima H, 2006) [61].

D-Allulose

D-allulose is a rare monosaccharide sugar which can be naturally found in some fruits, wheat, processed cane and beet molasses, heat processed fruit juices and steam-treated coffee in traces. It can also be synthesized through the isomerization of D-fructose by D-tagatose 3-epimerases (DTEases) or d-allulose 3-epimerases (DAEases) (Jiang, S.,*et al*., 2020) [31]. It is an excellent low calorie substitute for sucrose as it provides only 0.2 kcal/g as compared to 4 kcal/g with 70% sweetening potency (Mooradian *et al.*, 2017) [54]. Unlike sucrose, D-allulose has a lower peak sweetness but similar sweetness decay. In order to achieve an acceptable sweetness profile like table sugar, D- allulose combination with sucrose in a 1:1 ratio was found to be effective. This could be used to partially replace sucrose in food products (Tan *et al*., 2019)

Food applications and regulatory status

D-allulose has been approved for food products and dietary supplements and has been given a GRAS status. No adverse effects have been reported in humans after sustained consumption. In addition, it also exhibits diverse physiological functions such as high solubility and improved antioxidative activity during storage as compared to D-fructose and D-glucose. It is suitable for type II diabetes, obese and those suffering from hyperlipidemias. D-allulose has shown hypoglycemic, improved insulin resistance, hypolipidemic and obesity properties. It has anti-inflammatory, anti- artherosclerotic properties and serves as a neuroprotectant (Mijailovic, N, 2021) [51]. The exceptional physiochemical properties make it a viable substitute for D-sucrose in foods.

D-Tagatose

D-Tagatose is a rare naturally occurring keto-sugar present in very minute quantities in *Sterculia setigera* gum exudate of the cacao tree, fruits such as apples, oranges, pineapple and dairy products (C. Vera, 2016) [9]. In dairy products it is present in sterilized milk, milk powder, hot cocoa, cheese and yogurt, when they are heat processed and stored for long periods (Sohini Roy, *et al.*,2018) [75]. Tagatose makes a good low-calorie substitute, as it has a clean after taste and sweetness is quite like table sugar. Its sweetness potency is 92% as compared to sucrose and provides only half of the calories i.e. 2kcal/g (Mooradian *et al.*, 2017) [54]. Moreover, it has a comparable relative sweetness without any unpleasant off notes at varied concentrations of sucrose ranging from 4.5% to 18%, usually seen in foods and beverages (Fujimaru *et al.*, 2012).

D- Tagatose is a structural epimer to fructose, which exhibits a slightly faster rate of rise in sweetness than sucrose, much like fructose (Levin, 2002). It has a low glycemic index as it is gradually metabolized and only partially absorbed in the body. It is a suitable sweetener for diabetics too, as it did not increase the blood glucose levels after consuming up to 75 g of tagatose. (C. Vera, 2016) [9] D-Tagatose has excellent physio- chemical properties. It is highly soluble reducing sugar, stable at pH range of 2.0 – 7.0. At high temperatures, it undergoes browning (Maillard) reactions and easily caramelizes. It is also known to have prebiotic and flavour enhancing properties. (Carocho M., 2015) [11].

Food Application and regulatory status

Due to its flavour modifying properties, it is a potential low-calorie substitute used in confectionary, bakery and low-calorie soft drinks particularly in combination with other intense sweeteners (Bertelsen *et al*. 2001a). Some of the popular food applications of tagatose are in yoghurts, frostings, cereals, beverages, chewing gum, fudge, caramel, fondant, chocolate and ice cream. D- Tagatose was initially evaluated as a food additive but now it is considered a novel food. Australia, New Zealand, Korea and European Union has permitted its use as a food or novel food. Whereas, US has given it a generally recognized as safe (GRAS) status to be used as a sweetener in foods. (G.W. R. Lipinski, 2006) [26]. D-Tagatose has demonstrated exceptional physio chemical and therapeutic benefits as a natural low-calorie sweetener, making it a promising sweetener for special dietetic food formulations. WHO (2004) [81] has established “No Observed Adverse Effect Level” (NOAEL) for tagatose at 45 g/day or 0.75 g/kg body weight/day.

D-Allose

D-Allose is a rarely occurring carbohydrate found in select plant species in traces, such as *Solanum tuberosum*, *Tamarindus indica* (potato, tamarind etc.). It is a C-3 epimer of D-glucose, which is a low- calorie sweetener. Its sweetness index is 80% as compared to sucrose and is easily soluble in water. However, its calorific value is yet to be determined. (Mooradian *et al*., 2017) [54]. Lim, Y.R, (2011) [45] have reported exceptional health and physiological functions associated with allulose, including anti-inflammatory, anti-oxidative, anti-cancer, anti- tumour activities. In addition, this rare sugar has demonstrated hypoglycemic effects in Asian populations. However, there is not enough data for other populations (Franchi F, *et al.*, 2021) [23].

D-Sorbose

has a 70% sweetness profile like sucrose with no clarity on calorific value of this rarely occurring sugar (Mooradian *et al*., 2017) [54]. The taste profile of D-sorbose matches that of fructose, xylose, xylitol, and glucose.

Table 2: Summary of natural non-nutritive sweeteners

Attributes	Source	Geographic distribution	Caloric value (kcal/g)	Potency	Stability	Applications
Steviol glycosides	*Stevia rebaudiana bertoni*	South America	0	200-300	Stable to heat and pH variation.	Confectionery, baked goods, yoghurts, ice cream, gums, sauces, dairy products and beverages.
Glycyrrhizin	*Glycyrrhiza glabra*	Japan	0	30-110	Sensitive to pH variation	Baked goods, ice cream, confectionery, gums and beverages.
Thaumatin	*Thaumatococcus daniellii Benth*	West Africa	4	3000	Stable to heat and acidic pH variation.	Processed vegetables, sauces, soups, fruit juices, wine and bread.
Brazzein	*Pentadiplandra brazzeana baillon*	West Africa	4	1000-2000	Stable to heat and pH variation.	Beverages, fruits, vegetables and flour.
Miraculin	*Richadella dulcifa*	West Africa	-	Not sweet themselves but have taste modifying properties.	Heat labile, stable to pH variation.	Sour beverages, ice lollies
Curculin	*Curculingo latifolia*	Malaysia	-	550	Heat labile	Medicines
Monellin	*Dioscoreophyllum cumminsii diels*	West Africa	4	2500-3000	Unstable to heat and pH variation.	Barely used in processed and preserved foods due to limited stability.
Pentadin	*PentadipZandra brazzenna Baillon*	West Africa	0	~500	-	No commercial use
Monk fruit	*Siraitia grosvenorii*	China	0	~250	Stable at pH range of 3-7	Jams, jellies, beverages
D-allulose	Epimerization product of Dfructose at the C-3 position.	-	0.2	0.70	Unstable to heat	Pharmaceuticals and dietary supplements.
D-allose	converted from D-allulose	-	-	0.80	-	Table sugar substitute
D-tagatose	produced by several biocatalyst sources like L-arabinose isomerase using D-galactose as a substrate.	-	0	0.92	Stable at pH 2–7	Non-chronic drugs, tooth paste, and mouth wash and in a wide variety of foods, beverages, health foods, and dietary supplements
D-sorbose	produced by biological oxidation of sorbitol by *Acetobacter suboxydans*	-	-	0.70	-	-

*Potency is expressed as times sweeter than sucrose. (for potency – Priya *et al*, 2011) [65]

Conclusions

The growing health consciousness amongst the consumers have led to the demand of sugar- free food products in the market. The consumers are keen to buy food products which are manufactured using ingredients of natural origin, without additives and with clean labels. Naturally derived sweeteners from tropical plants such as stevia, monk fruit, thaumatin, brazzein, miraculin and several rare monosaccharide sugars such as D- tagatose, D-allulose, D-sorbose and D-allose are emerging as a viable substitute for artificial sweeteners. As compared to intense sweeteners they provide a clean sweet taste like sucrose, have negligible calories, have a low glycemic index and are non-toxic. There physicochemical and technological properties are of great interest to the food processor and this makes them superior to the conventional non-nutritive sweeteners. However, there is a need to produce these sugars on a commercial scale which is cost effective. Meanwhile, more studies are needed to evaluate the temporal properties along with allergenicity and safety of these novel sweeteners. Presently, they seem to be promising alternatives to sugar with optimal health benefits and non -negotiable taste of sucrose.

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