Journal of Applied Botany and Food Quality 92, 160 - 171 (2019), DOI:10.5073/JABFQ.2019.092.022

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Plants as a source of natural high-intensity sweeteners: a review

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(Submitted: November 29, 2018; Accepted: March 22, 2019)

Summary

The plants described in this review are a source of natural high-intensity sweeteners, which can be used in food and by the pharmaceutical industry in the future. Most of the plants are still not approved for use, even though they are traditionally used in countries where they appear naturally. Ten of the herein described intense sweeteners are characterized by a much higher sweetness in relation to sucrose. The highest values were received for miraculin, obtained from *Synsepalum dulcificum* (400,000 times sweeter than sucrose, induced by citric acid); thaumatin (1,600 to 3,000 times sweeter), monatin (1,200 - 3,000) and pentadin (500 to 2,000 times sweeter). Some of these substances can also modify the taste, like changing sour into sweet taste (miraculin and neoculin). The most widely used sweeteners are steviol glycosides and thaumatin, which have been admitted for use as a sweetener in the European Union, while in the US, they have the GRAS status (thaumatin as a food enhancer). Mogroside obtained from *Siraitia grosvenorii* (called Luo Han Guo) is not approved for use in the EU, but was granted GRAS status in the US by the FDA. This gives a chance that it will soon be approved as a novel food or food additive in the European Union.

Key words: high-intensity sweeteners, natural sweeteners, sweet plants, sweet proteins

Introduction

The number of diseases related to the excessive consumption of sugar, such as diabetes, obesity, hypertension, and heart disease, is increasing every year (Chattopadhyay et al., 2014; Beltrami et al., 2018). Therefore, the production of sugar-free foods, in which a sweet taste is obtained by using non-caloric intensive sweetening substances, is becoming increasingly popular (Świąder et al., 2011). Artificial high intensity sweeteners like aspartame, acesulfame K, cyclamate and saccharin are widely used in the food industry. However, foreign off-flavours such as bitterness or metallic and astringent taste, which increase with the concentration of sweetening substances (Świąder et al., 2009; Świąder et al., 2011b) and concerns about the safety of their use (Tandel, 2011; Kant, 2005; Sun et al., 2006; Beltrami et al., 2018), lead to a growing need for natural, calorie-free sweeteners with acceptable taste and health-promoting properties (Yadav et al., 2011).

This article describes natural high-intensity sweetening substances that can have a high impact in the new food and pharmaceutical product development in the future. Natural high intensity sweeteners are presented according to the source of origin. The plant parts from which they were obtained and their sweetness potency were also taken into account (Tab. 1). The sweetening properties, advantages and disadvantages resulting from the possibility of natural high intensity sweeteners use in the production of food are described, including sweeteners already in use or whose commercialization is in progress.

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Sweet proteins

Capparis masaikai Lev.

Characteristics of the plant

Capparis masaikai Lev. of the *Capparidaceae* family, grows widely in the subtropical region of Yunnan, China (Masuda and Kitabatake, 2006) on rocky areas, mountains and numerous soil types (good tolerance to volcanic or alkaline soils (Tlili et al., 2011). Its fruits are the size of a tennis ball (Kitada et al., 2008). Seeds from ripe fruits of *C. masaikai* are used in traditional Chinese medicine against pharyngitis. In addition, the Chinese chew the seeds because they are sweet and give a feeling of moisture. During chewing, the seeds cause a bitter-sweet taste with a weak intensity and the taste persists for a long time on the tongue. However, due to an aftertaste, the fruit containing seeds is not accepted by some. Sucking a tablet containing *C. masaikai* extract gives a feeling of moisture in the mouth in adults and the elderly – which is extremely important in salivation disorders (Kitada et al., 2008).

Characteristics of sweeteners and their properties

The sweet component of *C. masaikai* seeds are several isoforms of proteins called mabinlin I-1, mabinlin II, mabinlin III and mabinlin IV (Uher and Wójtowicz, 2003). Mabinlin is approximately 400 times sweeter than sucrose (Gibbs et al., 1996; Kant, 2005). While mabinlin I-1 is unstable and loses sweetness after incubation for 30 minutes at 80 °C and pH 6, other forms are more stable. Mabinlin II is stable at higher temperatures, and its sweetness persists after 48 hours of incubation at 80 °C. The amino acid sequence of mabinlin II was determined and found to be a heterodimer composed of an A chain with 33 amino acid residues and a B chain of 72 amino acids. These chains are connected by two disulphide bonds. It has a molecular weight of approximately 12.4 kDa (Masuda and Kitabatake, 2006). According to Fry (2012), the sweetness of mabinlin II is only 10 times higher than that of sucrose per weight, which is so low that this protein is unlikely to be used as commercial sweetener.

Safety of use

Since mabinlin has no legal status with the European Food Safety Authority in Europe or the FDA in the United States, it is not used as a sweetener in food production (Barclay et al., 2014).

Curculigo latifolia Dryand.

Characteristics of the plant

Curculigo latifolia Dryand (Fig. 1), commonly called lemba, is an herb from the family *Hypoxidaceae*. This plant grows in well-drained, fertile and rich in organic matter soils in highland areas (1,500 - 2,000 meters) on slopes and shaded forests in Malaysia (Farzinebrahimi et al., 2013) and is currently brought into cultivation (Babaei et al., 2014). The edible fruit weighs approximately 1 gram and contains a sweet-flavoured proteins curculin and its heterodimeric form neoculin (Shirasuka et al., 2004), that has flavour-modifying properties (Gibbs et al., 1996), which change a sour taste into a sweet taste (Babaei et al., 2014).

Tab. 1: Characterization of plants and high-intensity sweeteners obtained from them.

Plant species	Family	Plant parts	Country of origin	Sweeteners	Sweetness potency*	Compound	FDA/ EFSA sweetener status	References
***Capparis masaikai* Lev.**	*Capparidaceae*	fruit seeds	China	mabinlin I-1 mabinlin II mabinlin III mabinlin IV	10-400	protein	not approved	Fry, 2012; Kant, 2005; Masuda and Kitabatake, 2006; Uher and Wójtowicz, 2003
***Curculigo latifolia* Dryand (Lemba)**	*Hypoxidaceae*	fruit	Malaysia	neoculin curculin	500** 430-2,070	protein	not approved	Babaei et al., 2014; Barclay et al., 2014 2014; Masuda and Kitabatake, 2006
***Dioscoreophyllum cumminsii* (Stapf) Diels (Serendipity Berry)**	*Menispermaceae*	fruit	West and Central Africa	monellin	3,000	protein	not approved	Flores, 2018; Hobbs et al., 2007; Kant, 2005; Oselebe and Ene-Obong, 2007; Wolski and Najda, 2005
***Pentadiplandra brazzeana* Baill.**	*Pentadiplandaceae*	fruit	Africa	pentadin brazzein	500-2,000	protein	not approved	Barclay et al., 2014; Cimanga et al., 2018; Gibbs et al., 1996; Kant, 2005; Ming and Hellekant, 1994; van der Wel et al., 1989
***Synsepalum dulcificum* Daniell (Miracle fruit)**	*Sapotaceae*	fruit	Africa	miraculin	400,000**	protein	not approved	Barclay et al., 2014; Gibbs et al., 1996; Njoku et al., 2015; Seong et al., 2018
***Thaumatococcus daniellii* (Benn.) Benth (Katemfe)**	*Maranthaceae*	fruit	West Africa	thaumatin I thaumatin II thaumatin a thaumatin b thaumatin c	1,600-3,000	protein	GRAS flavour enhancer / E957 sweetener, flavour enhancer	Drzewiecka, 2016; EFSA, 2015; EC, 2008; Grembecka, 2015; Mitchell, 2006; Świąder et al., 2011a
***Glycyrrhiza glabra* Linn (Licorice)**	*Fabaceae*	root	Europe, Asia	glycyrrhizin	50	terpenoid (triterpenoid glycoside)	GRAS flavour enhancer / not approved EU	Barnes et al., 2002; EFSA, 2003; FDA, 2018d; Fiore et al., 2008; Shabkhiz et al., 2016
***Siraitia grosvenorii* Swingle (Luo Han Guo, Monk Fruit)**	*Cucurbitaceae*	fruit	China	siamenoside I 11-oxomogroside V mogroside V mogroside IVa mogroside IVe	500	terpenoid (triterpenoid glycoside)	GRAS / not approved EU	EC, 2018; FDA, 2018a; FDA, 2018b; Jia and Yang, 2009; Jin and Lee, 2012; Li et al., 2014; Uher and Wójtowicz, 2003
***Stevia rebaudiana* Bertoni (Stevia)**	*Asteraceae*	leaf	Brazil, Paraguay	dulcoside A rebaudioside A rebaudioside B rebaudioside C rebaudioside D rebaudioside E rebaudioside F rebaudioside M rubusoside stevioside steviolbioside	30 200 150 30 221 174 200 250 114 210 90	terpenoid (diterpenoid glycoside)	GRAS steviol glycosides / E 960 steviol glycosides sweetener	EFSA, 2018; FDA, 2018c; Hossain et al., 2017; Kinghorn, 1987; Prakash et al., 2014; USDA, 2018
***Sclerochiton ilicifolius* A. Meeuse (Arruva)**	*Acanthaceae*	root	South Africa	monatin 2R,4R monatin 2S,4S	3,000 1,200	indole	not approved	Barclay et al., 2014; Bassoli et al., 2005; Maharaj et al., 2018; Storkey et al., 2015

*relative to sucrose, **modifying sour taste into sweet taste

Fig. 1: *Curculigo latifolia*

Characteristics of sweeteners and their properties

Curculin is a homodimeric form of protein composed of the basic subunit (NBS), whereas neoculin (Fig. 2) is the heterodimeric form composed of the acidic subunit (NAS), ca. 13kDa, and a basic subunit (NBS) of ca. 11kDa (OHKUBO at al., 2008; NOOKARAJU et al., 2010). Curculin is 430 - 2,070 times sweeter than sucrose on a weight basis, while neoculin is only 500 times sweeter (NOOKARAJU et al., 2010), but has additionally taste-modifying properties to convert sourness to sweetness (NOOKARAJU et al., 2010; BABAEI et al., 2014). After sour lemon tasting, neoculin produces a sweet, orange like taste. This taste-modifying sensation lasts about 30 - 60 minutes (NACAJIMA et at., 2011). Neoculin sweetness depends on pH. It is very sweet at lower pH and slightly sweet at pH 7 (OHKUBO at al., 2015). Neoculin is not thermally stable. Incubation for an hour at temperatures above 50 °C in pH 6 buffer causes a decrease in the ability to cause sweetness, and the total loss of this property occurs at 75 °C. Due to a lack of thermal stability, this protein is not suitable for use in the food industry, where high temperatures are used, because it cannot withstand the pasteurisation (FRY, 2012).

Safety of use

Neoculin and curculin have no legal status in the EU or the USA (FRY, 2012; BARCLAY et al., 2014). There have been no successful attempts to obtain neoculin or curculin in transgenic plants to date (NOOKARAJU et al., 2010).

***Dioscoreophyllum cumminsii* (Stapf) Diels**

Characteristics of the plant

Dioscoreophyllum cumminsii (Stapf) Diels, 'the serendipity berry', belongs to the family *Menispermaceae* (OSELEBE and ENE-OBONG, 2007; WOLSKI and NAJDA, 2005). It is a tropical rainforest vine, that grows in humid and heavily shaded tropical forest regions of West and Central Africa (Nigeria, Ghana) (OSELEBE and ENE-OBONG, 2007). It has long, hairy stems that resemble vines. The leaves consist of three 10-20 cm-long heart-shaped lobes. Small fruit with pips are formed from inflorescences. A jelly mass with an intensely sweet taste spreads around these kernel pips. One kg of fruit can produce 3-6 g of pure protein (monellin) (WOLSKI and NAJDA, 2005). *Dioscoreophyllum cumminsii* is widely used in Nigeria in obesity and diabetes management and treatment (AJIBOYE et al., 2016).

Recently, OLOYEDE et al. (2015) confirmed that the extract from *D. cumminsii* leaves is an antidiabetic agent in the rat-induced diabetic alloxan model. However, the study used a type 1 diabetes model and

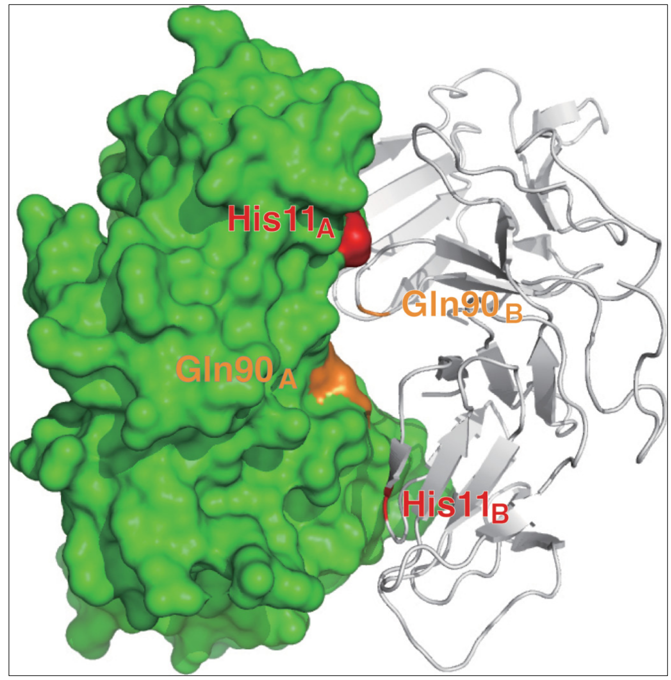

Fig. 2: The dimeric structure of neoculin. One neoculin molecule is depicted as a green surface with $His11_A$ in red (responsible for pH dependent sweetness) and $Gln90_A$ in orange; the other neoculin monomer is represented with grey loop and ribbon structure (image taken from OHKUBO at al., 2015; CC BY 4.0)

the model of type 2 diabetes was omitted. In the AJIBOYE et al. study (2016), the effect of an aqueous leaf extract on hyperglycaemia, dyslipidaemia, insulin resistance, oxidative stress and inflammation in the metabolic syndrome induced by the high supply of fructose in the rat group was evaluated. It was shown that the administration of an aqueous extract from *D. cumminsii* (at a dose of 400 mg / kg body weight) significantly reduced the body weight of rats compared to rats who received metformin (at a dose of 400 mg / kg body weight). Since the treatment of rats significantly ($p < 0.05$) reversed changes in rat serum biochemical parameters, which were induced by a large supply of fructose, the *D. cumminsii* extract may be an effective agent in the treatment of metabolic syndrome.

Characteristics of sweeteners and their properties

D. cumminisii berries contain water-soluble substances of intense sweetness, called monellin (OSELEBE and ENE-OBONG, 2007). In its natural form, monellin is a 10.7 kDa protein composed of two chains (A and B, with 44 and 50 amino acids, respectively) and is unstable at high temperatures or at extreme pH values. Monellin has a secondary structure consisting of five β-strands that form an anti-parallel β-sheet (β1 - β5) and a 17-residue α-helix (α1) located on the concave surface of β2- β strands (HOBBS et al., 2007).

Monellin sweetness is 3,000 times more intense than sucrose by weight and 100,000 times by molar (OSELEBE and ENE-OBONG, 2007). It is 1,500 - 2,000 times sweeter than a 7% sucrose solution. After eating this protein, the sweet taste appears only after a few seconds, but it lasts for almost an hour. In combination with other sweeteners, it shows synergy (TEMUSSI, 2006). Monellin dissolves well in water (OSELEBE and ENE-OBONG, 2007). The isoelectric point is reached at pH = 9.03. Heating to 55 - 65 °C and a pH below 2 and above 9 results in a loss of sweetening properties. The sweetening activity returns after acidification of the environment (GIBBS et al., 1996). A correctly composed three-dimensional structure is a prerequisite for sweetness (REGA et al., 2015). The division of its subunits, A and

B, also causes the disappearance of sweetness (SUAMI et al., 1996). REGA et al. (2015) found that the introduction of modifications in the monellin structure (recombinant Y65R MNEI) makes the protein interact more effectively with the sweet T1R2 receptor: T1R3, which results in even greater intensification of the feeling of sweetness, compared to natural monellin. In the design of monellin-based sweeteners, researchers point to the important role of the three-dimensional parent protein scaffold, increased positive charge density on the surface of protein interaction with the receptor, higher thermal stability and good solubility and low aggregation propensity, even at neutral pH. In another study, due to the use of genetic modifications in the monellin structure, it was found that the stability of the mutant protein (mutant E23A) was superior to natural protein, showing a higher denaturation temperature of up to 85 °C. In contrast, the C41A mutant showed a lower sweetness threshold and increased sweetness compared to the wild-type protein (LIU et al., 2016).

Monellin has a potential application as an alternative to sugar and can therefore be beneficial for diabetics who need to control sugar intake. This substance, like other sweet proteins, activates sweetness in a way that does not require insulin. Therefore, its potential to be an alternative to sugar is of great interest (OSELEBE and ENE-OBONG, 2007).

Safety of use

The *D. cumminisii* berries are rare and difficult to obtain in large quantities from a wild plant, which is why cultivation is unavoidable in order to increase large-scale production of berries to extract sweeteners and then commercialize them in the food industry (OSELEBE and ENE-OBONG, 2007). Currently, since monellin has no legal status with the Food and Drug Administration (FDA) in the US or the European Food Safety Authority (EFSA), it is not used in the food industry (FLORES, 2018).

Pentadiplandra brazzeana Baill.

Characteristics of the plant

Pentadiplandra brazzeana Baill. belongs to the family of *Pentadiplandaceae*. It grows in Africa, from Nigeria to Central and Southern Africa to Angola and the Democratic Republic of Congo (DR Congo), on riverbanks and in secondary forest (CIMANGA et al., 2018). It can be a multi-branched shrub that grows up to 5 m in height or grows as a climbing plant with stems up to 20 m long. The fruit is orange, with a globular berry 2-4 cm in diameter (CIMANGA et al., 2018). The berries contain one to five seeds, which are surrounded by a thick layer of flesh. In this flesh, there are sweet substances called pentadin and brazzein (GIBBS et al., 1996). The native inhabitants have known brazzein for centuries. It is consumed raw or boiled form and is used as a sweetener in beverages and food (HELLEKANT and DANILOVA, 2005).

Root, root bark, leaf and tubers of *P. brazzeana* contain many bioactive substances and are often used in traditional medicine in some African countries to stimulate lactation for women, for treatment of chest pains, lumbago, tooth pains, as aphrodisiac (root bark), in diarrhoea, haemorrhoids, constipation, cough (root), to treat scabies (leaf) or gonorrhoea (tubers) (CIMANGA et al., 2018).

P. brazzeana is used as an antiseptic in the treatment of dental caries and rheumatic diseases and as an anti-ulcer drug, especially in Cameroon as an aphrodisiac and sexual stimulant in men (KAMTCHOUING et al., 2002). In addition, the essential oil obtained from the roots has anti-inflammatory effects (KITAMURA et al., 2015; CIMANGA et al., 2018). Breast-feeding mothers consume *P. brazzeana's* fruits to wean their babies from breastfeeding. After eating the fruit, the mother's milk becomes less sweet and bland, which provokes the child's refusal of the breast. The fruit has also aphrodisiac properties and is used as fish poison (CIMANGA et al., 2018).

Characteristics of sweeteners and their properties

The intense sweeteners obtained from *P. brazzeana* fruits are pentadin (VAN DER WEL et al., 1989) and brazzein (MING and HELLEKANT, 1994). Brazzein is 500 times sweeter in comparison to 10% of sugar and 2,000 times sweeter than sucrose (in comparison to a 2% sucrose aqueous solution) (MING and HELLEKANT, 1994). The sweetness intensity of pentadin was ~ 500 times that of sucrose on a per weight basis (VAN DER WEL et al., 1989). Due to the similar amino acid structure of pentadin and brazzein, it was assumed that pentadin can be a heat-induced derivative of brazzein (UHER and WÓJTOWICZ, 2003) and according to ZHAO et al. (2005) a dimeric form of brazzein. The brazzein molecular weight is 6.47 kDa (MING and HELLEKANT, 1994), and 12 kDa pentadin (VAN DER WEL et al., 1989; NOOKARAJU et al., 2010).

Brazzein is thermally stable and its sweetness is maintained at 80 °C for 4 hours in the pH range 2.5-8. It consists of 54 amino acid residues, whose stability is strengthened by four intramolecular bonds, e.g. disulphide bonds. The amino acid chain forms one α-helix and three strands of anti-parallel β-sheets (MASUDA and KITABATAKE, 2006). The solubility of brazzein in water is at least 50 mg/ml, i.e.> 7.7 mM. Therefore, it is considered to be the most water-soluble protein sweetener discovered to date (HELLEKANT and DANILOVA, 2005). It is also stable over a wide pH range (CIMANGA et al., 2018). Brazzein has a taste of pure sweetness, without a sour, salty or bitter aftertaste. Brazzein sweets can be easily removed from the tongue and do not show a cooling sensation. It often improves the taste of beverages in combination with other sweeteners and works well in both citric acid and phosphate systems. Brazzein goes well with most high-intensity sweeteners such as acesulfame-K and aspartame, providing both quantitative and qualitative synergy. It also improves the stability, taste and aftertaste after mixing with acesulfame-K and aspartame, alone or in a mixture. It usually reduces the undesirable off-flavours of other sweeteners – for example, a blend of stevioside and brazzein has a better sensory quality than the stevioside itself (HELLEKANT and DANILOVA, 2005).

Safety of use

The indigenous population of Africa has safely used brazzein to sweeten food for many years, suggesting that this sweet protein poses no particular health risk (LAMPHEAR et al., 2005). In 2007, a low-calorie sweetener called Cweet (CWEET, 2018) was developed. However, the herb has not yet received GRAS status (Generally Recognized As Safe) in the United States, nor has it been authorized as a food additive within the European Union (BARCLAY et al., 2014).

Synsepalum dulcificum Daniell

Characteristics of the plant

Synsepalum dulcificum Daniell (Fig. 3) (common name: miracle fruit) belongs to the family *Sapotaceae*, and is native to tropical west and west Central Africa (NJOKU et al., 2015; SEONG et al., 2018). Its predominant form is shrubby, but it can grow up to 20 feet high and bears fruits after 2-3 years of growing. Sometimes it produces two crops per year (March-April and later, after the rainy season). There are two varieties, distinguished by the production of red and yellow berries. The yellow variety is more prevalent in Nigeria, especially the eastern part of Nigeria (NJOKU et al., 2015). The red berries have an oval shape. Miraculin, a taste-modifying protein, is found in the thin parenchyma layer surrounding the pit (WOLSKI and NAJDA, 2005).

For the first time, the existence of these sweet fruits was documented by the European explorer Chevalier des Marchais during a trip in 1725 to African countries. He noted that local people chewed berries from this bush before meals and added them to improve the taste of acidic dishes from corn and acid drinks (HIRAI et al., 2010).

Fig. 3: Fruits of *Synsepalum dulcificum* Daniell

The yellow berry's pulp has more vitamin C than vitamins A or E. The oxidative vitamin content (vitamin C, A, and E) of the pulp is generally lower than that of other berries like blackberry, raspberry and blueberry (NJOKU et al., 2015). *S. dulcificum* also possesses antioxidant, antibacterial and anticancer activities (SEONG et al., 2018).

Characteristics of sweeteners and their properties

Miraculin was isolated from the red berries of *Richadella dulcifica* (Schumach. & Thonn.) (TCHOKPONHOUÉ et al., 2017), a shrub originating from West Africa. Although miraculin is not sweet, it has taste-modifying properties and transforms the sour taste into a sweet taste, similar to neoculin (KURIHARA and BEIDLER, 1968), which lasts for one to two hours (BROUWER et al., 1968). Its sweetness exceeds 400,000 times the sweetness of table sugar (0.1 µM of miraculin induced by 0.1 M of citric acid) (GIBBS et al., 1996). It consists of 191 amino acids with an N-linked oligosaccharide (THEERASILP et al., 1989). Native miraculin (pure form) is a tetramer of the 25 kDa-peptide (IGETA et al., 1991). The sweetness depends on pH. Miraculin is sweet at lower pH but not sweet at pH 7 (OHKUBO et al., 2015).

Safety of use

Synsepalum dulcificum is characterised by a prolonged juvenile phase of the plant and a very slow growth rate (TCHOKPONHOUÉ et al., 2017). The berries of the plant are considered as novel food and authorisation is required before they can be introduced to the EU market. In this context, no application under Regulation (EU) 2015/2283 has yet been submitted (EU, 2015). Miraculin is not authorised as a sweetener by EFSA or FDA (BARCLAY et al., 2014).

***Thaumatococcus daniellii* (Benn.) Benth.**

Characteristics of the plant

Thaumatococcus daniellii (Benn.) Benth. (Fig. 4), commonly called katemfe, is a plant from the *Maranthaceae* family. It grows throughout the hot, humid tropical rain forest and coastal zone of West Africa (YEBOAH et al., 2003), the Central African Republic and in Angola (DRZEWIECKA, 2016). It has also been introduced to areas in Australia and Singapore (HEAR, 2006). Its natural habitat is the undergrowth of forest trees. The plant flowers most of the year but is most prolific from July until late October, and from January until mid-April fruit formation, maturing and ripening. It seems to be suitable for integration into agroforestry systems (YEBOAH et al., 2003). A single fruit (weighing about 16 g) consists of two or three triangular, fleshy pericarps, each of which contains a large black seed surrounded by a thick, transparent, viscous mucus. Under each seed, there is also a soft, jelly-like coating (VAN DER WEL and LOEVE, 1972).

Fig. 4: *Thaumatococcus daniellii* (image by Ji-Elle, https://commons.wikimedia.org/wiki/File:Thaumatococcus_daniellii-Jardin_botanique_Jean-Marie_Pelt_(3).jpg, CC BY SA 4.0)

In traditional folk medicine, leaf juice is used as an antidote against venoms, stings and bites, as well as a sedative. Katemfe fruits are used as a laxative, while seeds are used as an emetic and for lung problems (UKWUBILE et al., 2017). In West Africa, the fruit pulp of katemfe is traditionally used to sweeten bread, fermented palm wine, acidic fruit desserts and, in general, sour food, to improve the taste of the dishes. Katemfe is also added to dishes such as garri (cake made from fermented manioc flour, usually fried in palm oil), pap (porridge from corn) and tea (LIM, 2012).

Characteristics of sweeteners and their properties

Thaumatin is isolated from *T. daniellii* fruits. There are at least five intensely sweet forms of thaumatin: the most-occurring thaumatin I and thaumatin II and the others: thaumatin a, thaumatin b and thaumatin c. All forms have a molecular mass of 22 kDa, and their isoelectric point is 12. Thaumatin is almost 100,000 times sweeter than sucrose on a molar basis and about 1,600 - 3,000 times sweeter in relation to mass (ŚWIĄDER et al., 2011a; GREMBECKA, 2015).

The taste profile of thaumatin is characterized by the so-called "delayed" appearance of sweet taste and a bitter taste similar to liquorice. Intensification of an adverse aftertaste increases with increasing thaumatin concentration in the product, when using only this sweetener (MITCHELL, 2006). Its sweetness stays on the tongue for a long time. It can improve the mint flavour and the cooling effect of different products. Thaumatin is also used to mask an undesirable aftertaste and the bitterness of other intense sweeteners (saccharin) or the natural bitterness of citrus fruits (DRZEWIECKA, 2016). The possibility of using thaumatin in products with a reduced sodium content was also noted due to the ability to mask the characteristic off-flavour of potassium chloride (sometimes added to table salt) in order to avoid large amounts of sodium ions (ŚWIDERSKI, 2003).

The energy value of thaumatin is 4 kcal / g. But since only small doses of this sweetener are used in practice, it is assumed to not contribute to calories in food intake (GREMBECKA, 2015; DRZEWIECKA, 2016). It is stable at pH 2.5-6 and has quite good resistance to higher temperatures (DRZEWIECKA, 2016). In addition to taste-modifying properties, thaumatin is contraceptive, antibacterial, reduces blood glucose and protects the cardiovascular system (UKWUBILE et al., 2017).

Safety of use

Thaumatin E 957 is a food additive and can be used in confectionery without sugar, chewing gums without added sugar, dietary supplements or energy-reduced ice cream or without added sugar (EC, 2008). Thaumatin is considered one of the sweetest and safest sweeteners. There is no specific dose of ADI for it due to a lack of toxicity and ease of digestion (ŚWIĄDER et al., 2011a; EFSA, 2015). It has GRAS status in the US as a flavour enhancer (no GRAS status as a sweetener) and it has been found that it does not cause harmful health effects (GREMBECKA, 2015). However, the first documented cases of thaumatin allergies emerged. The employees of a chewing gum factory showed that thaumatin has a strong allergenic potential in the upper respiratory tract and appears to induce more intense allergic symptoms than gum arabic (TSCHANNEN et al., 2017).

Sweet terpenoids

***Glycyrrhiza glabra* L.**

Characteristics of the plant

There are different species such as *Glycyrrhiza glabra* (European licorice) and *Glycyrrhiza uralensis* (Chinese licorice). *G. glabra* and *G. uralensis* are considered as beneficial herbs in Japan while *G. glabra, G. uralensis* and *G. inflate* are recognized as medicinal plants in China (PARK et al., 2014). *Glycyrrhiza glabra* L. is a perennial plant from the *Fabaceae* family, originating from central and southwestern Asia, as well as from the Mediterranean basin. It grows in temperate and subtropical climates, including Europe and Asia (FIORE et al., 2005). It is a native to Spain, Iraq, Turkey, Russia, Japan and northern China (THAM et al., 1998). *G. glabra* is very important commercial crop that grows slowly from seed or by micropropagation (BADKHANE et al., 2014) and then can be difficult to eradicate when well established. The active substance (glycyrrhizin) of licorice is contained in the roots of the plant (OMAR et al., 2012).

G. glabra root is used as a flavouring and sweetening agent for tobacco, chewing gums, candies, toothpastes and beverages (DONG et al., 2007). Licorice is also the most popular ingredient in over 70% of Chinese medicines and has been used by people for at least 4,000 years. It was used as an analgesic, antispasmodic or expectorant (WANG and NIXON, 2001), as well as for the treatment of tuberculosis, infectious hepatitis and bronchitis (NIU et al., 2005).

G. glabra contains flavonoids and isoflavonoids, which show antiproliferate and oestrogen-like activity (THAM et al., 1998; KLASIK-CISZEWSKA et al., 2016). *G. glabra* extract shows a distinctive gene expression profile, which indicates the presence of potentially useful components other than glycine, which may be effective in hormonal therapy or in anti-cancer therapy (DONG et al., 2007). The smooth phytoestrogens contained in the root can be used to treat or alleviate the effects of postmenopausal osteoporosis. Glabridin is the main isoflavan present in the root of *G. glabra*. In addition to oestrogenic activity, it has a protective effect on the cardiovascular, anti-inflammatory, anti-oxidant and anti-neoplastic systems (KLASIK-CISZEWSKA et al., 2016).

Characteristics of sweeteners and their properties

Glycyrrhizin (Fig. 5) is the main triterpenoid saponin in the licorice root (1-9% licorice extract) and it is considered the primary component of *G. glabra* responsible for the characteristic taste and sweetness (BARNES et al., 2002). Glycyrrhizin is a triterpenoide glycoside (saponin) with glycyrrhetinic acid, which is condensed with O-β-d-glucuronosyl-(1'→2)-β-d-glucuronic acid (GLORIA, 2003). It is completely absorbed in the digestive system. During hydrolysis, it releases two molecules: D-glucuronic acid and 18-β-glycyrrhizinium aglycone (SHAMS et al., 2015). It is about 50 times sweeter than sucrose and it leaves a characteristic aftertaste in the mouth for a long time (SHABKHIZ et al., 2016), that limits its use as a pure sweetener. It

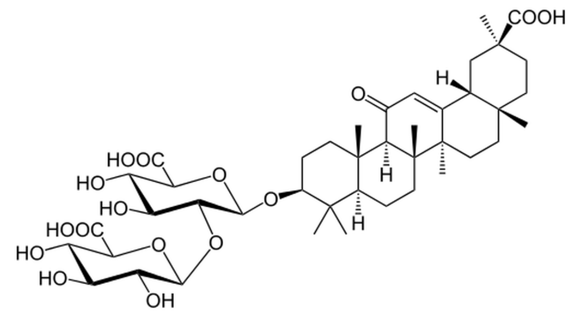

Fig. 5: Chemical structure of glycyrrhizin

can still be used as a food enhancer. Glycyrrhizin masks bitter flavors and increases the perceived sweetness level of sucrose. It has also other functional properties and can regulate gel formation, foaming and viscosity control (GLORIA, 2003).

Safety of use

Licorice extracts were generally recognized as safe (WANG and NIXON, 2001), although, chronic excessive intake can cause high blood pressure and low potassium levels, which can lead to heart and muscle problems (KHAN et al., 2013; NCCIH, 2016). Biochemical studies have shown that glycyrrhizin inhibits the 11βHSD enzyme, which catalyzes the conversion of cortisol into its inactive cortisone metabolite. This results in slowing the excretion of cortisol and prolonging its action in the body. Elevated levels of cortisol stimulate mineralocorticoid receptors in the channels of distal kidneys, which in turn causes pseudohyperaldosteronism: retention of salts and fluids in the body, edema, hypertension and lowering the level of potassium in the blood (ISBRUCKER and BURDOCK, 2006). Pregnant women and people taking diuretics should avoid using liquorice root as a supplement or eat it in large quantities (NCCIH, 2016). Glycyrrhizin is a food additive (as a flavour enhancer) and has the status of GRAS (FDA, 2018d) in the US, but is not approved as a sweetener in the EU (EFSA, 2003).

***Siraitia grosvenorii* Swingle**

Characteristics of the plant

Siraitia grosvenorii Swingle (common name: Luo Han Guo, Monk Fruit) is a perennial vine from the *Cucurbitaceae* family. It is an endemic species for Guangxi province in China, where it has been cultivated for over 200 years. Its fruit is widely known in China as Luo Han Guo (LI et al., 2014) or "luo han kuo", in Vietnamese "la han qua"; or in English arhat, Buddha, or monk fruit (JIN and LEE, 2012). The vine reaches a length of 3 to 5 m, climbing over other plants with the help of creepers, which wrap around the obstacles encountered. Narrow, heart-shaped leaves are 10-20 cm long. The fruits (Fig. 6) are round, 5-7 cm in diameter, smooth, yellow-brown or green-brown with hard, thin skin covered with thin hairs. Inside the fruit there is an edible pulp which, after drying, forms a thin, light-brown, brittle shell with a thickness of about 1 mm. The seeds are elongated and almost spherical (DHARMANANDA, 2004).

The first information about Luo Han Guo appeared in the thirteenth century, when monks started using it for the first time. Due to the limited natural area of cultivation (mainly the mountain sides in Guangxi and Guangdong) and the difficulty in its effective cultivation, this fruit did not enter the general Chinese herbal tradition. This plant became more popular in the twentieth century. Its fruit was often used as the main ingredient in cold drinks. The interior of the fruit is eaten fresh and the bitter skin is used to make tea (DHARMANANDA, 2004).

Fig. 6: *Siraitia grosvenorii* fruit cut open (image by David Badagnani, https://commons.wikimedia.org/wiki/File:Luohanguo-open.jpg, CC BY 3.0)

Luo Han Guo has been used for hundreds of years as a natural sweetener and as a traditional medicine to treat pharyngitis, as well as an anti-tussive agent in China. In 1987, the fruit of *S. grosvenorii* was classified as a product with medicinal properties by the Chinese Ministry of Health (Li et al., 2014).

Characterization of sweeteners and their properties

The sweet taste of Luo Han Guo comes mainly from mogrosides, a group of terpene glycosides, present in around 1% of the fleshy part of the fruit. Both fresh and dried fruits are extracted to obtain a powder with 80% or more of mogroside. Five types of mogroside were identified: siamenoside I, 11-oxomogroside V, mogroside V, mogrosides IVa and IVe (Jia and Yang, 2009) of which mogroside V (Fig. 7) is in the highest concentration (Dharmananda, 2004) and is about 500 times sweeter than 0.5% sucrose (Jia and Yang, 2009). Mogrosides also have anti-diabetic, anti-cancer and anti-allergic effects. Mogroside V inhibits the initiation and promotion of cancer and can also be valuable as a chemotherapeutic agent against chemical carcinogenesis. In addition, 11-oxomogrozide V significantly inhibits the oxidation of low-density lipoprotein (LDL), with a dose-dependent delay in LDL oxidation. The monk's fruit extract is used in China as a natural low-calorie sweetener for people suffering from diabetes and / or obesity (Jin and Lee, 2012).

Safety of use

Luo Han Guo fruit extract has GRAS status. In application No 629, the extract is used as a table-top sweetener and a non-nutritive sweetener for general use in food, excluding mixtures for infants and meat and poultry products, whereas application No 706 refers to its use as a sweetener in food, excluding food regulated by the USDA and infant formula (FDA, 2018a; FDA, 2018b). The powder concentrate from Luo Han Guo is known under the name PureLo. The overall sweetness of PureLo concentrate is estimated at 200 times greater than sucrose (Marone et al., 2008). To date, the EFSA has not confirmed the safety of monk's fruit extract, however, in 2017 the EFSA conducted a risk assessment and scientific opinion on the safety of the use of Luo Han Guo fruit extract (LHG) as a food additive (EFSA, 2017). At the same time, an application was made for the Novel Food status of the monk fruit extract. Due to the lack of a safety evaluation of Luo Han Guo extract in food, this product cannot be marketed in the EU as a food or food ingredient (EC, 2018).

Stevia rebaudiana Bertoni

Characteristics of the plant

Stevia rebaudiana Bertoni (Fig. 8), commonly called Stevia, is a perennial belonging to the *Asteraceae* family, originally occurring in Brazil (Mato Grosso do Sul, Minas Gerais) and Paraguay (Amambay, Concepcion) (USDA, 2018). It is also cultivated commercially in Brazil, Paraguay, Central America, Thailand, Korea, China and India (Hossain et al., 2017). Stevia grows on sandy soils, characterized by high moisture and good permeability with an acid reaction or on soils mud (Madan et al., 2010). This plant usually reaches about 50-120 cm in height. The shoots are erect and usually branched. Leaves are mostly arranged in an opposite or winding position and are of the petiole or sitting type. The leaf blade has one- or three-strands, a rounded end and a serrated edge stretching from half-length to the tip. The flowers are concentrated in disc-shaped, loose or dense baskets. The corolla is light purple, and bell shaped (Bugaj et al., 2013). Stevia leaves have traditionally been used for hundreds of years in Paraguay and Brazil for sweetening tea, medicines and as sweet snacks (Hossain et al., 2017). Stevia became more widely-known outside central South America after being discovered and described in 1887 by the botanist Antonio Bertoni. Because of its sweetness, stevia has received many names, including honey leaf, sweet leaf from Paraguay, sweet tea, sweet herb and honey yerba (Carakostas et al., 2008). The commercial use of stevia increased after Japanese researchers developed an extraction and refinement process of sweeteners from its leaves (Yadav et al., 2011). The extract from *S. rebaudiana* leaves has traditionally been used to treat diabetes. It has anti-

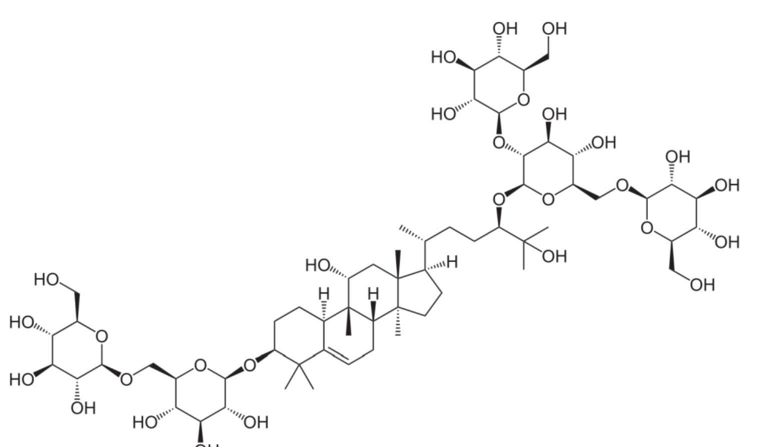

Fig. 7: Chemical structure of mogroside V

Fig. 8: *Stevia rebaudiana* (image by Manuel Martin Vicente, https://www.flickr.com/photos/martius/37147164031, CC BY 2.0)

bacterial, anti-fungal, anti-inflammatory, anti-viral, anti-microbial, diuretic, hypoglycaemic and vasodilatory effects (SHARMA et al., 2009). Stevia was reportedly used as an oral contraceptive by women from the Paraguayan Matto Grosso Indian tribes (KINGHORN, 2002).

Characteristics of sweeteners and their properties

Steviol glycosides are non-nutritive sweeteners which have been found to be 200 to 400 times sweeter than table sugar (FDA, 2017e). Although steviol glycosides are produced by the stevia plant and are not chemically altered by any of the extraction steps and purification, glycosides cannot be referred to as "natural sweetener (sweeteners)". However, the word "natural" may be possible with reference to the source plant material (stevia leaf) (IFST, 2018). The sweetness of steviol glycosides is more noticeable and lasts much longer than the sweetness of sucrose or aspartame (KOLANOWSKI, 2013). Stevia has a mild, licorice flavour that is slightly bitter. Eleven diterpene glycosides with sweetening properties have been identified in the stevia leaf tissues. The four main ones are stevioside, rebaudioside-A (Fig. 9), rebaudioside-C and dulcoside-A. According to KINGHORN (1987) and PRAKASH et al. (2014), the sweetness of these compounds in relation to sucrose is - 210, 200-242, 30 and 30 times, respectively. The two major glycosides are stevioside (5-10% of the dry weight of the leaves) and rebaudioside-A (Reb-A, 2-4% of the dry weight of the leaves), which are the sweetest compounds. The other compounds isolated from Stevia leaves are rebaudioside B, D, E, F and rebaudioside M which are 150, 221, 174, 200 and 250 times sweeter than sucrose and steviolbioside (90 times sweeter) and rubusoside (114 times sweeter) (PRAKASH et al., 2014).

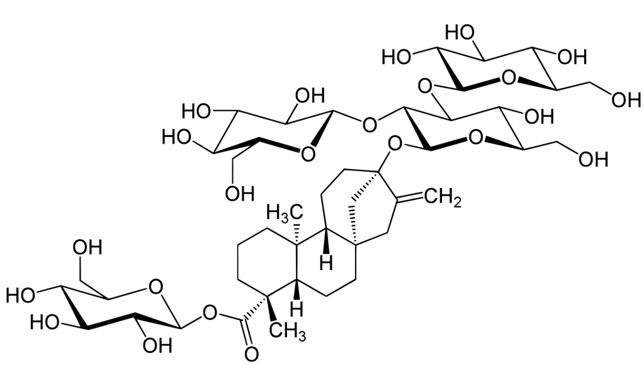

Fig. 9: Rebaudioside A, a steviol glycoside from *Stevia rebaudiana*

Steviosides exhibit remarkable stability in an aqueous solution over a wide range of pH and temperatures. In heat treatment in the 1-10 pH range for 2 hours at 60 °C, slight degradation of the stevioside was observed, with only slight decreases to 5% (at pH 2 and 10) noted when heated to a temperature of 80 °C. At pH 1, a forced decomposition of the stevioside was observed, resulting in its complete decomposition after incubation at 80 °C for 2 h. Steviol glycosides have low solubility, although rebaudioside A (1 g/100 ml) is more soluble than stevioside in water and they also have high melting temperatures (LEMUS-MONDACA et al., 2012). Rebaudioside-A is the most interesting steviol glycoside due to its desirable taste profile, while stevioside is responsible for the bitter aftertaste. The rebaudioside-A-to-stevioside ratio measures the acceptability of the quality of sweetness (the more rebaudioside-A, the better). If rebaudioside-A is the same as the stevioside, it seems that the characteristic aftertaste has been eliminated (YADAV et al., 2011).

The use of different mixtures of sweeteners improves the taste and time profiles, in which the sweet taste persists, which often also improves the stability of rebaudioside A. Steviol glycosides can be combined, among others, with mogroside, monatin, aspartame, acesulfame salts, cyclamate, sucralose, erythritol, sorbitol, xylitol and glycerol, as well as with sucrose, glucose or fructose. In addition, sweet amino acids (glycine, alanine and serine) also improve the taste of rebaudioside A (PRAKASH et al., 2008).

Stevioside and rebaudioside A are not digested by human digestive enzymes, although they are hydrolysed to steviol in the intestine with the participation of bacteria of the genus Bacteroides. This metabolite attaches a glucuronic acid molecule to itself, which causes the steviol to be inactivated and removed very quickly from the body, without showing negative effects on the body (BUGAJ et al., 2013; KULCZYŃSKI et al., 2015). Due to the very small amounts of stevia consumption, it can be concluded that it does not bring a higher nutritional value to a standard diet, hence its caloric value is assumed to be 0 kcal (YADAV et al., 2011).

Unlike many low-calorie sweeteners, stevioside is stable at high temperatures (198 ºC) and in a wide range of pH values. In addition, it dissolves very well in water (YADAV et al., 2011; BUGAJ et al., 2013; KULCZYŃSKI et al., 2015). Rebiana (commercial sweetener based on rebaudioside A) is stable in dry conditions and has much better stability than aspartame or neotame in water (PRAKASH et al., 2008). *S. rebaudiana* does not ferment and does not change colour after cooking (YADAV et al., 2011). Parts of the stevia plant contain different amounts of glycosides, which decrease in the following order: leaves, flowers, stems, seeds and roots. Roots are the only parts of a plant that do not contain stevioside, while sweetness in leaves is twice as high as in inflorescence (YADAV et al., 2011; BUGAJ et al., 2013).

Safety of use

Stevia leaves are not an approved food additive and have not been confirmed as GRAS in the US due to insufficient toxicological information. GRAS status has been obtained for steviol glycosides, which are purified extracts obtained from leaves (FDA, 2018c; FDA, 2018e). Toxicological studies conducted as part of the safety assessment by EFSA have shown that these substances do not cause genotoxic or carcinogenic effects and are not associated with adverse effects on the human sexual system or developing foetus (URBAN et al., 2013). Experts have set an acceptable daily dose (ADI) for steviol glycosides of 4 mg / kg body weight / day (expressed as stevia). The daily intake level of a given sweetener E 960 is the same as that set by the Joint FAO / WHO Expert Committee on Food Additives - JECFA (EFSA, 2018).

Sweet indoles

***Sclerochiton ilicifolius* A.Meeuse**

Characteristics of the plant

Sclerochiton ilicifolius A.Meeuse (common name: arruva) belongs to family Acanthaceae and is native to South Africa (Bassoli et al., 2005; Storkey et al., 2015). This spiny-leaved hardwood shrub is growing wild in the rocky hills of the Limpopo, Zoutpansberg and Mpumalanga provinces in South Africa (Maharaj et al., 2018).

Characteristics of sweeteners and their properties

Monatin (Fig. 10), commonly known as arruva, is a high-intensity sweetener isolated from the bark of the roots of *S. ilicifolius*. Two isomers with high sweetness occur naturally (2S,4S and 2R,4R) (Vleggar et al., 1992; Maharaj et al., 2018). Monatin 2R,4R is more than 3,000 times sweeter than 5% sucrose (Storkey et al., 2015), while 2S,4S is 1,200-1,400 times sweeter than 5% and 10% sucrose solutions, respectively (Bassoli et al., 2005). Monatin has a sweet, pleasant taste, similar to sucrose and does not notably increase the calorific value of products in which it is used. Long-term UV/visible photolysis has an influence on the loss of sweetness and occurrence of unpleasant flavours (Storkey et al., 2015).

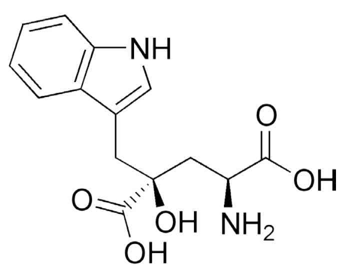

Fig. 10: Monatin, an indole-derived sweetener from *Sclerochiton ilicifolius*

Safety of use

There have been many *in vivo* toxicology studies conducted for the 2R,4R monatin isomer to make it easier for commercialization (Maharaj et al., 2018), but it is not yet approved by the FDA and EFSA for use as a sweetener (Barclay et al., 2014).

Conclusions

The plants described in this review are a source of natural high-intensity sweeteners that can have a big impact on the creation of new food and pharmaceutical products in the future. Most of them are still not approved for use, even though they are traditionally used in countries where they appear naturally. Those substances have a high application potential in both qualitative and quantitative terms. They shape the sweet taste of the products which contain them, and either modify the sweetness of products themselves or act in combination with other sweetening substances. They can replace sucrose, thus, helping to reduce the development of obesity and diseases arising from sucrose consumption. However, many have not been allowed yet for use in food products due to the lack of safety evidence. Some have already been tested for safety and are allowed to use in food products in United States, so it gives a chance that they will be soon approved in the European Union as a novel food or as food additives.

References

Ajiboye, T.O., Aliyu, H., Tanimu, M.A., Muhammad, R.M., Ibitoye, O.B., 2016: *Dioscoreophyllum cumminsii* (Stapf) Diels leaves halt high-fructose induced metabolic syndrome: Hyperglycemia, insulin resistance, inflammation and oxidative stress. J. Ethnopharmacol. 192, 472-478. DOI: 10.1016/j.jep.2016.08.024

Babaei, N., Abdullah, N.A.P., Saleh, G., Abdullah, T.L., 2014: An efficient in vitro plantlet regeneration from shoot tip cultures of *Curculigo latifolia*, a medicinal plant. Scien. World J. ID 275028, 9. DOI: 10.1155/2014/275028

Badkhane, Y., Yadav, A.S., Bajaj, A., Sharma, A.K., Raghuwanshi, D.K., 2014: *Glycyrrhiza glabra* L. a miracle medicinal herb. Indo Americ. J. Pharm. Res. 4, 5808-5816.

Barclay, A., Sandall, P., Shwide-Slavin, C., Brand-Mille, J., 2014: The ultimate guide to sugars and sweeteners: discover the taste, use, nutrition, science, and lore of everything from agave nectar to xylitol. New York: The Experiment LCC.

Barnes, J., Anderson, L.A.A., Phillipson, J.D., 2002: Herbal Medicines 2nd edn. Pharmaceutical Press: London.

Bassoli, A., Borgonovo, G., Busnelli, G., Morini, G., Drew, M.G.B., 2005: Monatin and its stereoisomers: chemoenzymatic synthesis and taste properties. Eur. J. Org. Chem. 8, 1652-1658. DOI: 10.1002/ejoc.200400589

Beltrami, M.C., Döring, T., De D. Lindner J., 2018: Sweeteners and sweet taste enhancers in the food industry. Food Sci. Technol. Campinas. 38, 181-187. DOI: 10.1590/fst.31117

Brouwer, J.N., Van Der Wel, H., Francke, A., Henning, G.J., 1968: Miraculin, the sweetness-inducing protein from miracle fruit. Nature. 220, 373-374.

Bugaj, B., Leszczyńska, T., Pysz, M., Kopeć, A., Pacholarz, J., Pysz-Izdebska, K., 2013: Charakterystyka i prozdrowotne właściwości Stevia rebaudiana Bertoni. ŻYW. Nau. Tech. Jakość. 3, 27-38.

Carakostas, M.C., Curry, L.L., Boileau, A.C., Brusick, D.J., 2008: Overview: The history, technical function and safety of rebaudioside A, a naturally occurring steviol glycoside, for use in food and beverages. Food Chem. Toxicol. 46, 1-10. DOI: 10.1016/j.fct.2008.05.003

Chattopadhyay, S., Raychaudhuri, U., Chakraborty, R., 2014: Artificial sweeteners – a review. J. Food. Sci. Technol. 51, 611-621. DOI: 10.1007/s13197-011-0571-1

Cimanga, K.R., Lubiba, N.Z., Makila Bool-Miting, F., Tona, L.G., Kambu, K.O., Vlietinck, A.J., Pieters, L., 2018: Biological activities of arredoul jaune, a phytomedicine based ethanol extract from fresh roots of *Pentadiplandra brazzeana Baill*. (*Pentadiplandaceae*) used as an antidiarrhoeal drug in Kisangani – Democratic Republic of Congo. Europ. J. Biomed. Pharma. Sciences. 5, 130-139.

CWEET, 2018: Retrieved 2nd November 2018, from http://www.cweet.com/.

Dharmananda, S., 2004: Luo han guo: Sweet fruit used as sugar substitute and medicinal herb. Institute for Traditional Medicine. Retrieved 6th November 2018, from http://www.itmonline.org/arts/luohanguo.htm.

Dong, S., Inoue, A., Zhu, Y., Tanji, M., Kiyama, R., 2007: Activation of rapid signaling pathways and the subsequent transcriptional regulation for the proliferation of breast cancer MCF-7 cells by the treatment with an extract of *Glycyrrhiza glabra* root. Food Chem. Toxicol. 45, 2470-2478. DOI: 10.1016/j.fct.2007.05.031

Drzewiecka, A., 2016: Charakterystyka użytkowa i właściwości fizykochemiczne naturalnej substancji słodzącej taumatyny. Nauki Inżynierskie i Technologie, 1, 33-39.

EFSA, 2003: Opinion of the Scientific Committee on Food on glycyrrhizinic acid and its ammonium salt. Retrieved 3rd November 2018, from https://ec.europa.eu/food/sites/food/files/safety/docs/fs_food-improvement-agents_flavourings-out186.pdf [dostęp: 10.05.2018].

EFSA, 2015: Scientific Opinion on the safety of the extension of use of thaumatin (E 957). EFSA J. 13, 4290. DOI: 10.2903/j.efsa.2015.4290

EFSA, 2017: Scientific Panel on Food Additives and Nutrient Sources added to Food (ANS). Retrieved 3rd November 2018, from https://www.efsa.europa.eu/sites/default/files/event/170926-m_0.pdf [dostęp: 20.03.2018].

EFSA, 2018: EFSA evaluates the safety of steviol glycosides. Retrieved 3rd November 2018, from https://www.efsa.europa.eu/en/press/news/ans100414.

EC, 2008: Regulation (EC) No 1331/2008 of the European Parliament and of the Council of 16 December 2008 establishing a common authorisation procedure for food additives, food enzymes and food flavourings (OJ L 354, 31.12.2008, 1-6 with amendments) Retrieved 5th November 2018, from http://data.europa.eu/eli/reg/2008/1333/oj.

EC, 2018: Novel Food catalogue – Search „Siraitia grosvenorii". Retrieved 3rd November 2018, from http://ec.europa.eu/food/safety/novel_food/catalogue/search/public/index.cfm#.

EU, 2015: Regulation (EU) 2015/2283 of the European Parliament and of the Council of 25 November 2015 on novel foods, amending Regulation (EU) No 1169/2011 of the European Parliament and of the Council and repealing Regulation (EC) No 258/97 of the European Parliament and of the Council and Commission Regulation (EC) No 1852/2001 (OJ L 327, 11.12.2015, 1-22 with amendments) Retrieved 5th November 2018, from http://data.europa.eu/eli/reg/2015/2283/oj.

Farzinebrahimi, A., Taha, R.M., Rashid, K.A., 2013: Effect of light intensity and soil media on establishment and growth of *Curculigo latifolia* Dryand. J. Appl. Hort. 15, 224-226.

FDA, 2018a: GRAS Notice No. 629 GRAS exemption claim for Luo Han Guo fruit extracts (SWEETMONK™) manufactured by HUNAN NUTRAMAX, INC.® (NUTRAMAX®). Retrieved 6th November 2018, from https://www.fda.gov/downloads/Food/IngredientsPackagingLabeling/GRAS/NoticeInventory/ucm505159.pdf.

FDA, 2018b: GRAS Notice No. 706: Determination of the generally recognized as safe (GRAS) status of *Siraitia Grosvenori* Swingle (Luo Han Guo) fruit extract as a food ingredient. Retrieved 6th November 2018, from https://www.fda.gov/downloads/Food/IngredientsPackagingLabeling/GRAS/NoticeInventory/ucm590281.pdf.

FDA, 2018c: Additional Information about high-intensity sweeteners permitted for use in food in the United States – Steviol glycosides. Retrieved 4th November 2018, from https://www.fda.gov/Food/IngredientsPackagingLabeling/FoodAdditivesIngredients/ucm397725.htm.

FDA, 2018d: Food additive status list. Retrieved 5th November 2018, from https://www.fda.gov/food/ingredientspackaginglabeling/foodadditivesingredients/ucm091048.htm#ftnG.

FDA, 2018e: Import Alert 45-06, Retrieved 4th November 2018, from https://www.accessdata.fda.gov/cms_ia/importalert_119.html.

Fiore, C., Eisenhut, M., Krausse, R., Ragazzi, E., Pellati, D., Armanini, D., Bielenberg, J., 2008: Antiviral effects of Glycyrrhiza species. Phytother. Res. 22, 141-148. DOI: 10.1002/ptr.2295

Flores, R. 2018: Monellin (Serendipity Berry) sources, health risks. Retrieved 4th November 2018, from https://www.naturalpedia.com/monellin-serendipity-berry-sources-health-risks.html.

Fry, J.C., 2012: Natural low-calorie sweeteners. In: Baines, D., Seal, R. (Eds.), Natural Food Additives, Ingredients and Flavourings. Sawston: Woodhead Publishing.

Gibbs, B.F., Alli, I., Mulligan, C., 1996: Sweet and taste-modifynig proteins: A review, Nutr. Res. 16, 1619-1930.

Glória, M.B.A. 2003: Glycyrrhizin. Encyclopedia of Food Sciences and Nutrition (2nd Ed.). USA: Academic Press.

Grembecka, M., 2015: Natural sweeteners in a human diet. Rocz. Państ. Zakł. Hig. 66, 195, 197, 199.

HEAR, 2006: Hawaiian Ecosystems at Risk project. Pacific Island Ecosystems at Risk (PIER)- Thaumatococcus daniellii. Retrieved 5th November 2018, from http://www.hear.org/pier/species/thaumatococcus_daniellii.htm.

Hellekant, G., Danilova, V., 2005: Brazzein a Small, Sweet Protein: Discovery and Physiological Overview. Chem. Senses. 30, 88-89. DOI: 10.1093/chemse/bjh127

Hirai, T., Sato, M., Toyooka, K., Sun, H.J., Yano, M., Ezura, H., 2010: Miraculin, a taste-modifying protein is secreted into intercellular spaces in plant cells. J. Plant. Physiol. 167, 209-215. DOI: 10.1016/j.jplph.2009.08.001

Hobbs, J.R., Munger, S.D., Conn, G.L., 2007: Monellin (MNEI) at 1.15A° resolution. Acta. Crystallogr Sect. F Struct. Biol. Cryst. Commun. 63, 162, 164. DOI: 10.1107/S1744309107005271

Hossain, M.F., Islam, M.T., Islam, M.A., Akhtar, S., 2017: Cultivation and uses of Stevia (*Stevia rebaudiana* Bertoni): a review. Afr. J. Food, Agric., Nutr. Dev. 17, 12746, 12751-12753. DOI: 10.18697/ajfand.80.16595

IFST, 2018: Institute of Food Science & Technology: Stevia – a non-caloric sweetener of natural origin. Retrieved 5th November 2018, from https://www.ifst.org/knowledge-centre/information-statements/stevia-non-caloric-sweetener-natural-origin-1.

Igeta, H., Tamura, Y., Nakaya, K., Nakamura, Y., Kurihara, Y., 1991: Determination of disulfide array and subunit structure of taste-modifying protein, miraculin. Biochim. Biophys. Acta. 1070, 303-307. DOI: 10.1016/0167-4838(91)90073-9

Isbrucker, R.A., Burdock, G.A., 2006: Risk and safety assessment on the consumption of Licorice root (*Glycyrrhiza* sp.), its extract and powder as a food ingredient, with emphasis on the pharmacology and toxicology of glycyrrhizin. Regul. Toxicol. Pharmacol. 46, 167-92. DOI: 10.1016/j.yrtph.2006.06.002

Jia, Z., Yang, X., 2009: A minor, sweet cucurbitane glycoside from *Siraitia grosvenorii*. Nat. Prod. Commun. 4, 769-72.

Jin, J.-S., Lee, J.-H., 2012: Phytochemical and pharmacological aspects of *Siraitia grosvenorii*, luo han kuo. Orient. Pharm. Exp. Med. 12, 233-239. DOI: 10.1007/s13596-012-0079-x

Kant, R., 2005: Sweet proteins – Potential replacement for artificial low calorie sweeteners. Nutr. J. 4, 5. DOI: 10.1186/1475-2891-4-5

Kamtchouing, P., Mbongue Fandio, G.Y., Dimo, T., Jatsa, H.B., 2002: Evaluation of androgenic activity of *Zingiber officinale* and *Pentadiplandra brazzeana* in male rats. Asian J. Androl. 4, 299-301.

Khan, R., Khan, A.Q., Lateef, A., Rehman, M.U., Tahir, M., Ali, F., Hamiza, O.O., Sultana, S., 2013: Glycyrrhizic acid suppresses the development of precancerous lesions via regulating the hyperproliferation, inflammation, angiogenesis and apoptosis in the colon of wistar rats. PLoS One 8, e56020. DOI: 10.1371/journal.pone.0056020

Kinghorn, A.D., 1987: Biologically active compounds from plants with reputed medical and sweetening properties. J. Nat. Products. 50, 1009-1024.

Kinghorn, A.D., 2002: Stevia: the Genus Stevia (Medicinal and Aromatic Plants – Industrial Profiles), New York/London: Taylor & Francis/CRC Press.

Kitada, K., Ishikawa, M., Shibuya, K., Nakasugi, T., Oho, T., 2008: Enhancing oral moisture using an extract of *Capparis masaikai* Levl. J. Ethnopharmacol. 115, 57-60. DOI: 10.1016/j.jep.2007.09.002

Kitamura, S., Morisseau, C., Inceoglu, B., Kamita, S.G., De Nicola, G.R., Nyegue, M., Hammock, B.D., 2015: Potent natural soluble epoxide hydrolase inhibitors from *Pentadiplandra brazzeana* Baillon: synthesis, quantification, and measurement of biological activities in vitro and in vivo. PLoS ONE. 10, e0117438. DOI: 10.1371/journal.pone.0117438

Klasik-Ciszewska, S., Wojnar, W., Kaczmarczyk-Sedlak, I., 2016: Lukrecja gładka (*Glycyrrhiza glabra* L.) i jej zapobiegawczy wpływ na rozwój osteoporozy. Post. Fitoterapii. 17, 108-110.

Kolanowski, W., 2013: Glikozydy stewiolowe – właściwości i zastosowanie w żywności. Brom. Chem. Toksykol. 2, 140-150.

Kulczyński, B., Gramza-Michałowska, A., Człapka-Matyasik, M., 2015: Charakterystyka żywieniowa stewii – aktualny stan wiedzy. Brom. Chem. Toksykol. 1, 11-18.

Kurihara, Y., Beidler, L.M., 1968: Taste-modifying protein from miracle fruit. Science 161, 1241-1243.

Lamphear, B.J., Barker, D.K, Brooks, C.A., Delaney, D.E., Lane, J.R., Beifuss, K., Love, R., Thompson, K., Mayor, J., Clough, R., Harkey, R., Poage, M., Drees, C., Horn, M.E., Streatfield, S.J., Nikolov, Z., Woodard, S.L., Hood, E.E., Jilka, J.M., Howard, J.A., 2005: Expression of the sweet protein brazzein in maize for production of a new commercial sweeteners. Plant Biotechnol. J. 3, 103-114. DOI: 10.1111/j.1467-7652.2004.00105.x

Lemus-Mondaca, R., Vega-Gálvez, A., Zura-Bravo, L., Ah-Hen, K., 2012: *Stevia rebaudiana* Bertoni, source of a high-potency natural sweetener: A comprehensive review on the biochemical, nutritional and functional aspects. Food Chem. 132, 1121-1132. DOI: 10.1016/j.foodchem.2011.11.140

Li, C., Lin, L.-M., Sui, F., Wang, Z.-M., Huo, H.-R., Dai, L., Jiang, T.-L., 2014: Chemistry and pharmacology of *Siraitia grosvenorii*: A review. Chin. J. Nat. Med. 12, 89-100. DOI: 10.1016/S1875-5364(14)60015-7

Lim, T.K., 2012: Edible medicinal and non-medicinal plants. Fruits. Volume 3. New York: Springer Science Business Media.

Liu, Q., Li, L., Yang, L., Liu, T., Cai, C., Liu, B., 2016: Modification of the Sweetness and Stability of Sweet-Tasting Protein Monellin by Gene Mutation and Protein Engineering. BioMed Research International. 1-7. DOI: 10.1155/2016/3647173

Madan, S., Ahmad, S., Singh, G.N., Kohli, K., Kumar, Y., Singh, R., Garg, M., 2010: *Stevia rebaudiana* (Bert.) Bertoni – A Review. IJNPR. 1, 267-286.

Maharaj, V.J., Moodleyb, N., Vahrmeijerc, H., 2018: Characterization of natural monatin isomers, a high intensity sweetener from the plant *Sclerochiton ilicifolius* from South Africa. S. Afr. J. Bot. 115, 37-43. DOI: 10.1016/j.sajb.2017.12.007

Marone, P.A., Borzelleca, J.F., Merkel, D., Heimbach, J.T., Kennepohl, E., 2008: Twenty eight-day dietary toxicity study of Luo Han fruit concentrate in Hsd:SD® rats. Food Chem. Toxic. 46, 910-919. DOI: 10.1016/j.fct.2007.10.013

Masuda, T., Kitabatake, N., 2006: Developments in Biotechnological Production of Sweet Proteins. J. Biosci. Bioeng. 102, 375-389. DOI: 10.1263/jbb.102.375

Ming, D., Hellekant, G., 1994: Brazzein, a new high-potency thermostable sweet protein from *Pentadiplandra brazzeana*. FEBS Lett. 355, 106-108.

Mitchell, H., 2006: Sweeteners and sugar alternatives in food technology, Oxford: Blackwell Publishing.

Nakajima, K.-I., Yokoyama, K., Koizumi, T., Koizumi, A., Asakura, T., Terada, T., Masuda, K., Ito, K., Shimizu-Ibuka, A., Misaka, T., Abe, K., 2011: Identification and modulation of the key amino acid residue responsible for the pH sensitivity of neoculin, a taste-modifying protein. PLoS ONE. 6, e19448. DOI: 10.1371/journal.pone.0019448

NCCIH, 2016: National Center for Complementary and Integrative Health, Licorice Root. Retrieved 6th November 2018, from https://nccih.nih.gov/health/licoriceroot.

Niu, G.G., Xie, Y.C., Lou, J.F., Liu, H.Z., 2005: Isolation and purification of glycyrrhizic acid with solvent extraction. Separat. Purif. Tech. 44, 189-196.

Njoku, N.E., Ubbaonu, C.N., Alagbaoso, S.O., Eluchie, Ch.N.M, Umelo, C., 2015: Amino acid profile and oxidizable vitamin content of *Synsepalum dulcificum* berry (miracle fruit) pulp, Food Sci. Nutri. 3, 252-256. DOI: 10.1002/fsn3.213

Nookaraju, A., Upadhyaya, Ch.P., Pandey, S.K., Young, K.E., Hong, S.J., Park, S.K., Park, S.W., 2010: Molecular approaches for enhancing sweetness in fruits and vegetables, Sci. Horticultur. 127, 1-15. DOI: 10.1016/j.scienta.2010.09.014

Okubo, S., Asakura, T., Okubo, K., Abe, K., Misaka, T., Akita, T., Abe, K., 2008: Neoculin, a taste-modifying sweet protein, accumulates in ripening fruits of cultivated *Curculigo latifolia*. J. Plant. Physiol. 165, 1964-1969. DOI: 10.1016/j.jplph.2008.04.019

Ohkubo, T., Tamiya, M., Abe, K., Ishiguro, M., 2015: Structural basis of pH dependence of neoculin, a sweet taste-modifying protein. PLoS ONE. 10, e0126921. DOI: 10.1371/journal.pone.0126921

Oloyede, H.O.B., Bello, T.O., Ajiboye, T.O., Salawu, M.O., 2015: Antidiabetic and antidyslipidemic activities of aqueous leaf extract of *Dioscoreophyllum cumminsii* (Stapf) Diels in alloxan-induced diabetic rats. J. Ethnopharmacol. 166, 313-322. DOI: 10.1016/j.jep.2015.02.049

Omar, H.R., Komarova, I., El-Ghonemi, M., Fathy, A., Rashad, R., Abdelmalak, H.D., Yerramadha M.R., Ali, Y., Helal, E., Camporesi, E.M., 2012: Licorice abuse: time to send a warning message. Ther. Adv. Endocrinol. Metab. 3, 125-138. DOI: 10.1177/2042018812454322

Oselebe, H.O., Ene-Obong, E.E., 2007: Organogenesis in *Dioscoreophyllum cumminsii* (Stapf) Diels. Tropicultura. 25, 37.

Park, C.-G., Lee, A.Y., Lee, J.M., Lee, S.-H., Lee, J.H., Choi, A.J., Park, C.B., Cho, E.J., Lee, S., 2014: Comparison of biological activities of *Glycyrrhiza glabra* and *G. uralensis*. Arch. Biol. Sci., Belgrade. 66, 1431-1439. DOI: 10.2298/ABS140431P

Prakash, I., Dubois, G.E., Clos, J.F., Wilkens, K.L., Fosdick, L.E., 2008: Development of rebiana, a natural, non-caloric sweeteners. Food Chem. Toxicol. 46, 75-82. DOI: 10.1016/j.fct.2008.05.004

Prakash, I., Markosyan, A., Bunders, C., 2014: Development of next generation stevia sweetener: rebaudioside m, Foods. 3, 162-175. DOI: 10.3390/foods3010162

Rega, M.F., Di Monaco, R., Leone, S., Donnarumma, F., Spadaccini, R., Cavella, S., Picone, D., 2015: Design of sweet protein based sweeteners: Hints from structure – function relationships. Food Chem. 173, 1180, 1185. DOI: 10.1016/j.foodchem.2014.10.151

Seong, J., Oyong, G.G., Cabrera, E.C., 2018: *Synsepalum dulcificum* extracts exhibit cytotoxic activity on human colorectal cancer cells and upregulate c-fos and c-jun early apoptotic gene expression. Asian. Pac. J. Trop. Biomed. 8, 173-178. DOI: 10.4103/2221-1691.227999

Shabkhiz, M.A., Eikani, M.H., Sadr, Z.B., Golmohammad, F., 2016: Superheated water extraction of glycyrrhizic acid from licorice root. Food Chem. 210, 396-401. DOI: 10.1016/j.foodchem.2016.05.006

Shams, K.A., Abdel-Azim, N.S., Kamal, S.A., Husseiny, H.A., Hammouda, F.M., 2015: Green extraction: enhanced extraction yield of glycyrrhizic acid from *Glycyrrhiza glabra* L. J. Chem. Pharma. Res. 7, 725-728.

Sharma, N., Mogra, R., Upadhyay, B., 2009: Effect of Stevia Extract Intervention on Lipid Profile. Ethno-Medicine. 3, 137-140. DOI: 10.1080/09735070.2009.11886351

Shirasuka, Y., Nakajima, K.-I., Asakura, T., Yamashita, H., Yamamoto, A., Hata, S., Nagata, S., Abo, M., Sorimachi, H., Abe, K., 2004: Neoculin as a new taste-modifying protein occurring in the fruit of *Curculigo latifolia*, Biosci. Biotechnol. Biochem. 68, 1403-1407. DOI: 10.1271/bbb.68.1403

Storkey, C., Pattison, D.I., Koehler, J.A., Gaspard, D.S., Evans, J.C., Hagestuen, E.D., Davies, M.J., 2015: Prevention of degradation of the natural high potency sweetener (2R,4R)-monatin in mock beverage solutions. Food Chem. 173, 645-51. DOI: 10.1016/j.foodchem.2014.10.054

Suami, T., Hough, L., Machinami, T., Watanabe, N., 1996: Molecular mechanisms of sweet taste Part 6: the sweet protein, Monellin. Food Chem. 56, 275-281. DOI: 10.1016/0308-8146(96)00024-6

Sun, H., Cui, M.L., Ma, B., Ezura, H., 2006: Functional expression of the taste-modifying protein miraculin, in transgenic lettuce. FEBS Lett. 580, 620-626. DOI: 10.1016/j.febslet.2005.12.080

Świąder, K., Waszkiewicz-Robak, B., Świderski, F., Kostyra, E., 2009: Sensory properties of some synthetic high-intensity sweeteners in water solutions. J. Sci. Food Agric. 89, 2030-2038. DOI: 10.1002/jsfa.3687

Świąder, K., Waszkiewicz-Robak, B., Świderski, F., 2011a: Substancje intensywnie słodzące – korzyści i zagrożenia. Probl. Hig. Epidemiol. 92, 392-396.

Świąder, K., Waszkiewicz-Robak, B., Świderski, F., 2011b: Substancje intesywnie słodzące w żywywnosci. Przem. Spoż. 65, 32-36.

Świderski, F., 2003: Żywność wygodna i żywność funkcjonalna. Warszawa: Wydawnictwo Naukowo-Techniczne.

Tandel, K.R., 2011: Sugar substitutes: Health controversy over perceived benefits. J. Pharmacol. Pharmacother. 2, 236-243. DOI: 10.4103/0976-500X.85936

Tchokponhoué, D.A., N'danikou, S., Hale, I., Van Deynze, A., Achigan-Dako, E.G., 2017: Early fruiting in *Synsepalum dulcificum* (Schumach. & Thonn.) Daniell juveniles induced by water and inorganic nutrient management. F1000Res. 6, 399. DOI: 10.12688/f1000research.11091.1

Temussi, P.A., 2006: Natural sweet macromolecules: how sweet proteins work, Cell. Mol. Life Sci. 63, 1876-1888. DOI: 10.1007/s00018-006-6077-8

Tham, D.M., Gardner, C.D., Haskell, W.L., 1998: Potential health benefits of dietary phytoestrogens: a review of the clinical, epidemiological and mechanistic evidence. The J. Clin. Endocrinol. Metabol. 83, 2223-2235. DOI: 10.1210/jcem.83.7.4752

Theerasilp, S., Hitotsuya, H., Nakajo, S., Nakaya, K., Nakamura, Y., Kurihara, Y., 1989: Complete amino acid sequence and structure characterization of the taste-modifying protein Miraculin. J. Biol. Chem. 264, 6655-6659.

Tlili, N., Elfalleh, W., Saadaoui, E., Khaldi, A., Triki, S., Nasri, N., 2011: The caper (*Capparis* L.): Ethnopharmacology, phytochemical and pharmacological properties. Fitoterapia. 82, 93-101. DOI: 10.1016/j.fitote.2010.09.006

Tschannen, M.P., Glück, U., Bircher, A.J., Heijnen, I., Pletscher, C., 2017: Thaumatin and gum arabic allergy in chewing gum factory workers. Am. J. Ind. Med. 60, 664-669. DOI: 10.1002/ajim.22729

Uher, M., Wójtowicz, H., 2003: Naturalne i syntetyczne niecukrowe substancje słodkie. Wiad. Chem. 5-6, 510-522.

Ukwubile, C.A., Musa, Y.D., Troy, S.M., 2017: *Thaumatococcus daniellii* Benn. (Marantaceae) leaf methanol extract possessed hepatoprotective effect against Acetaminophen induced liver injury in albino rats. Int. J. Med. Biosci. 1, 4. DOI: 10.28933/ijbm-2017-09-2002

Urban, J.D., Carakostas, M.C., Brusick, D.J., 2013: Steviol glycoside safety: Is the genotoxicity database sufficient? Food Chem. Toxicol. 51, 386-90. DOI: 10.1016/j.fct.2012.10.016

USDA, 2018: Agricultural Research Service, National Plant Germplasm System, 2018. Germplasm Resources Information Network (GRIN-Taxonomy). National Germplasm Resources Laboratory, Beltsville, Maryland. Retrieved 3rd November 2018, from https://npgsweb.ars-grin.gov/gringlobal/taxonomydetail.aspx?id=35581.

van der Wel, H., Loeve, K., 1972: Isolation and characterization of thaumatin I and II, the sweet-tasting proteins from *Thaumatococcus daniellii* Benth. Eur. J. Biochem. 31, 221-225.

Van Der Wel, H., Larson, G., Hladik, A., Hladik, C.M., Hellekant, G., Glaser, D., 1989: Isolation and characterization of pentadin, the sweet principle of *Pentadiplandra brazzeana* Baillon; Chem. Senses. 14, 75-79. DOI: 10.1093/chemse/14.1.75

Vleggaar, R., Ackerman, L.G.J., Steyn, P.S., 1992. Structure elucidation of monatin, a highintensity sweetener isolated from the plant *Schlerochiton ilicifolius*. J. Chem. Soc., Perkin Trans. 1, 0, 3095-3098. DOI: 10.1039/P19920003095

Wang, Z.Y., Nixon, D.W., 2001: Licorice and cancer. Nutr. Cancer. 39, 1-11. DOI: 10.1207/S15327914nc391_1

Wolski, T., Najda, A., 2005: Substancje słodzące pochodzenia naturalnego. Post. Fitoterapii. 1-2, 15-28.

Yadav, A.K., Singh, S., Dhyani, D., Ahuja, P.S., 2011: A review on the improvement of Stevia [*Stevia rebaudiana* (Bertoni)]. Canad. J. Plant Sci. 91, 1-27. DOI: 10.4141/cjps10086

Yeboah, S.O., Hilger, T.H., Kroschel J., 2003*: Thaumatococcus daniellii* (Benn.) Benth. – a natural sweetener from the rain forest zone in West Africa with potential for income generation in small scale farming. J. Applied Sci. 6.

Zhao, Q., Song, J., Jin, Z., Danilova, V., Hellekant, G., Markleya, J.L., 2005: Probing the sweet determinants of brazzein: Wild-type brazzein and a tasteless variant, brazzein-ins(R18a-I18b), exhibit different pH-dependent NMR chemical shifts. Biochem. Biophys. Res. Commun. 335, 256-263. DOI: 10.1016/j.bbrc.2005.07.049

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