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Phytochemical composition and pharmacological impact of natural non-calorie sweetener- monk fruit (*Siraitia grosvenorii*): a review

Shweta Suri
Department of Food and Nutrition, Govind Ballabh Pant University of Agriculture and Technology, Pantnagar, India

Deepika Kathuria
Department of Food Science and Technology, Dr Yashwant Singh Parmar University of Horticulture and Forestry, Nauni, India

Anusha Mishra
Department of Food Engineering and Technology, Institute of Chemical Technology, Mumbai, India, and

Rajan Sharma
Department of Food Science and Technology, Punjab Agricultural University, Ludhiana, India

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Abstract

Purpose – The purpose of this paper is to highlight the biological activities of low-calorie natural sweetener, i.e. monk fruit (*Siraitia grosvenorii*), which are associated with its bioactive constituents.

Design/methodology/approach – Recent investigations focused on biochemical characterization and nutraceutical potential of monk fruit (traditional Chinese perennial vine) have been critically reviewed. Also, the safety and influence of monk fruit on organoleptic characteristics of prepared food products have been documented.

Findings – Biochemistry of monk fruit revealed that mogrosides are the principal compounds responsible for the high-intensity sweetness in the monk fruit. The fruit induces several biological activities including anti-oxidative effect, hypoglycemic response, anti-allergic properties, anti-carcinogenic and anti-tissue damage activities. Attributing to great potential as a bio-functional sweetener in food products, monk fruit extract has been approved as Generally Regarded as Safe.

Originality/value – This paper highlights the biological potential of monk fruit opening the doors to future investigations for its utilization in products of commercial importance including food and pharmaceutical preparations.

Keywords Luohanguo, Antioxidant, Hypoglycemic, Sweetener, Mogrosides, Anti-carcinogenic

Paper type Literature review

Introduction

Monk fruit (*Siraitia grosvenorii*) is an indigenous Chinese endemic plant which is commonly referred as "Luo Han Guo". It is a member of Cucurbitaceae family and predominantly farmed in a Chinese province Guangxi for more than 200 years (Liu *et al.*, 2016b). It is a perennial vine characterized by dark black-brown glandular scales, yellow to brown

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pubescence, robust branches and ovate to cordate leaf blades with fruits mainly oblong or globose having velvety brown to yellow color and enormous ovate yellow seeds (Chen *et al.*, 2019) with fruiting season from July to late September (Wang *et al.*, 2019). Chinese Health Ministry documented monk fruit as edible and medicinal species for its productive potential as an ethnomedical remedy for the common cold, sore throat, lung congestion and cough (Chun *et al.*, 2014; Chen *et al.*, 2019). It attained attention during 20th century when dried fruits were considered as functional ingredient of folk preparations including beverages such as tea and cooling drinks and pork-based recipes against common health disorders (Soejarto *et al.*, 2019). Attributing to excellent phytochemical profile comprising of polyphenols, flavonoids, essential oils, triterpenoids and bioactive polysaccharides, monk fruit has been reported to play a pivotal role against several chronic complications (Chun *et al.*, 2014).

The principal compounds in monk fruit contributing to sweetness are a group of compounds containing siamenoside I, 11-oxo-mogroside V and mogrosides IV, V and VI (Pandey and Chauhan, 2019). Interestingly, ripe fruits have remarkable sweetness attributing to mogroside V while unripe fruits which are visually indistinguishable from ripe fruits contain mogroside III and IIE that have bitter taste (Li *et al.*, 2007a). Owing to high intensity sweetness, it has been suggested as a potent sugar alternate for diabetic and obese subjects as it was found to be 300 times sweeter than sucrose and thus contributed to reduced calorific value (Fang *et al.*, 2017). It has now been given the status of GRAS (Generally Regarded As Safe) in the USA and thus observed a significant upsurge in the consumption pattern as a sugar-free food additive for industrial applications and table-top sweetener after *Stevia rebaudiana* (Çiçek *et al.*, 2020).

Despite of confirmed pharmacological properties of monk fruit including anti-oxidant, anti-tissue damage, anti-allergic, anti-diabetic and anti-carcinogenic activities, studies for optimization of processing technologies and operations which may influence its bio-functional profile are being conducted for effective implementation as value added ingredient and additive in food products. Gong *et al.* (2019a) and Chun *et al.* (2014) have reviewed the structural characteristics of pharmacological compounds and bioactive performance of monk fruit; however, significant number of reports have been documented in the recent past to be reviewed. Therefore, present article aimed an objective to critically examine and document up-to-dated literature reporting phytochemical characterization of monk fruit and related biological activities.

Nutritional and phytochemical characterization

Monk fruit contains carbohydrates, protein, fat, vitamin and minerals. In addition, the fruit comprises of polysaccharides and sugars like glucose and fructose (Li and Xiao, 2008). Further, the crude protein includes all eight essential amino acids involving lysine, valine, methionine, leucine, isoleucine, phenylalanine, threonine and histidine (Chen *et al.*, 2004). On the other hand, seed kernels of monk fruit have been reported to contain 48.5% of fat (Chen *et al.*, 2004). Among vitamins, monk fruit potentially contains ascorbic acid, thiamin and riboflavin (Li and Xiao, 2008). The ripe monk fruit is also embraced with 14 essential trace elements with the highest amount of potassium, calcium and magnesium and other such as Fe, Zn, P, Mn, Cu, Al, Pb, I, Cd, Ni and Se (Xia, 2008).

Besides nutritional composition, monk fruit consists of various bioactive constituents. The major class of bioactive compounds present in monk fruit are glycosides that belong to cucurbitane-type triterpenes (Zhang and Li, 2011). Around 26 forms of cucurbitane-type triterpene glycosides have been identified, among them, three types of triterpene were aglycone, two types of pentacyclic triterpene alcohol and three types of triterpene were

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benzoates (Chaturvedula and Prakash, 2011a, 2011b; Li *et al.*, 2007b; Li *et al.*, 2006). Further, two types of cucurbitane triterpene including siraitic acid C and siraitic acid F were identified from the roots of monk fruit (Si *et al.*, 2005; Yang *et al.*, 2005). In case of cucurbitane-type triterpene aglycone, Li *et al.* (2006) and Zhang *et al.* (2012) identified mogrosides IV, V and VI that share mogrol aglycone structure [(10α,24R)-9β-Methyl-19-norlanosta-5-ene-3β,11α,24,25-tetrol] with two to six glucose units attached. So far, different authors have detected wide number of bioactive components in the monk fruit which are presented in Table 1.

Other phytochemical components in monk fruit included phenolic acid, anthraquinones, sterols, alkaloids, aliphatic acids and flavonoids such as kaempferol, quercetin and vanillic acid (Chun *et al.*, 2014; Zheng *et al.*, 2011; Liao *et al.*, 2008). The total flavones content in fresh fruit ranged from 5 to 10 mg (Chen *et al.*, 2003). The flowers of monk fruit consisted of kaempferol, kaempferol 3-*O*-L-rhamnopyranoside- 7-*O*-[β-D-glucose-based-(1–2)-α-L-rhamnoside], kaempferol 7-*O*-L-rhamnopyranoside, 3-*O*-D-glucopyranoside and 3-*O*-L-rhamnopyranoside while their leaves possess quercetin-3-*O*-D-glucopyranoside-7-*O*-L-rhamnopyranoside and kaempferol 3,7-di-*O*-L-rhamnopyranoside (kaempferitrin) (Li *et al.*, 2007b; Li *et al.*, 2003). According to Wuttisin and Boonsook (2019), 95% ethanolic extracts of monk fruit exhibited total phenolic content of 2.387 mg GAE/mg crude solid and water extract 25.229 μg QE/mg solid crude of total flavonoid content.

Fruit part	Bio-active compounds	Bioactivities	References
Dried fruit	Siamenoside I and group of mogrosides comprising of IIe, III, IIIe, IV, V and isomogroside V	•*Anti-carcinogenic activity* •*Hypoglycemic activity* •*Antioxidant properties* •*Anti-microbial properties* •*Anti-inflammatory properties*(Chun *et al.*, 2014; Gong *et al.*, 2019a; Jia *et al.*, 2019)	Wang *et al.* (2019)
Fresh fruit	Grosvenorine I, Grosvenorine Il, Kaempferol-7-O-α-Lrhamnopyranosideb, 11-O-mogroside VI, 7-O-mogroside III, Mogroside VI/Neomogrosided, Kaempherol, Rutin, Quercitrin, Kaemferol-3O-β-rutinoside in addition to predominant group of mogrosides, i.e. IIa, IIe, III, IIIe, IVa, IVe, V and 11-O-mogroside V		Fang *et al.* (2017)
Dried fruits	Mogroside III, mogroside IV, siamenoside I, mogroside V and 11-oxomogroside V		Shen *et al.* (2014)
Dried fruits	Grosvenorine I, grosvenorine II, mogroside IIE/isomer, 11-O-mogroside III, mogroside III/isomer, 11-Dehydroxy-mogroside III, mogrosideIV/siamenoide I/isomer, mogroside V isomer and other similar compounds		Zhang *et al.* (2012)
Commercial monk fruit extract	Mogroside IVa and IVe, mogroside V, isomogroside V, mogroside VI, 11-oxomogroside V and siamenoside I		Chaturvedula and Prakash (2011a)
Commercial monk fruit extract	Mogroside III A2 and 11-deoxymogroside III		Chaturvedula and Prakash (2011b)
Fresh unripe fruit	Cucurbitane triterpene glycosides and group of mogrosides in addition to flavonoids		Li *et al.* (2006)

Table 1. Different bioactive compounds present in monk fruit (*Siraitia grosvenorii*)

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Role of monk fruit as a sweetener

Among the human population, the sweetness is an essential component for pleasure, and to satisfy this desire, consumption of sugar has been followed 250 years ago. The principal component that gives ripe monk fruit its sweet taste is mogrosides. The backbone structure of mogrosides is mogrol along with glucose unit linked with glycoside bond at C3 and C24 of the mogrol. This compound is not absorbed by upper gastrointestinal tract and therefore contributes zero calories in the diet and when it reaches to colon, the glucose unit are cleaved by gut microbes and used as source of energy (Zhou *et al.*, 2018; Xu *et al.*, 2015). Depending on the structure of mogrosides, the taste of fruit varies accordingly. Mogrosides III, IV, V, VI, 11-oxo-mogroside V and cucurbitane glycosides, i.e. Siamenoside I were identified for sweet taste with intensity of sweetness as 195, 300, 256–378, 125, 68 and 456 times, respectively in comparison to sucrose (Suzuki *et al.*, 2007). While, glycosides of the 11α-hydroxy series (R4: α-OH) taste sweet, while mogrosides I, mogrosides II, glycosides of the 11β-hydroxy (R4: β-OH) are tasteless; dehydro derivatives and 11-oxo compounds (more in unripe fruit) taste bitter (Kasai *et al.*, 1988). In addition, a novel iso-mogroside V has been identified with high potency sweetener (500 times sweeter than sucrose) and flavor enhancer (Jia and Yang, 2014).

The biosynthetic pathways for the formation of mogrosides involve numerous enzyme (cytochrome P450, α-ketoglutaric acid, Fe, NAD or FAD linked) and steps from squalene to mogroside V. The first step involves cyclization of 2, 3-oxidosqualene using oxidosqualene cyclase enzyme (cucurbitadienol cyclase) that convert 2, 3; 22, 23-diepoxysqualene into 24, 25-epoxycucurbitadienol. Then hydroxylation reaction proceeds further using epoxide hydrolase to produce 24, 25-dihydroxycucurbitadienol from 24, 25-epoxycucurbitadienol, is expressed strongly during early stage of fruit development. In addition, CYP87D18 is used for the hydroxylation of C-11 of 24, 25-dihydroxycucurbitadienol to create 11, 24, 25-trihydroxycucurbitadienol that corresponds to aglycone form of mogrosides i.e. mogrol. Once the mogrol is formed a chain of glycosylations reaction takes place for the addition of 5 glucose molecules, 2 at the C-3 position and 3 at C-24 position, for the production of most essential sweetness component, i.e. mogroside V (Itkin *et al.*, 2016).

Pharmacological impact of monk fruit

Presence of some components like flavonoids, polysaccharides and essential oils in monk fruit induce anti-asthmatic, antitussive, glucose-lowering and immune regulating actions. Further, monk fruit is a commonly used folk remedy in China from ancient times. It is used for treating the common cold, pulmonary congestion, pharyngitis, cleaning of lung-heat, elimination of phlegm and bowels relaxation, even the roots of this fruit are involved in curing carbuncle, furuncle and swollen boils while the fruit hair are used for healing cuts (Li and Zhang, 2000). Monk fruit as an emollient and a pulmonary demulcent are used during dry coughs, dire thirst, sore throats and constipation (Lu *et al.*, 2012). Different biological activities associated with monk fruit is presented here under.

Hypo-glycemic activity

Diabetes mellitus is a chronic endocrine disorder described by reduced secretion of insulin thus resulting in hyperglycemia. Significance of zero-calorie sweeteners arises from the fact that hypoglycemic drugs are only effective in controlling the blood glucose levels but associated chronic complications such as cardiac concerns and nephropathy may not be prevented (Gong *et al.*, 2019b). Mogrosides, a non-sugar compounds of monk fruit imparts strong sweetness and depict positive impact on regulation of blood glucose levels by

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augmenting the postprandial insulin levels and inhibiting the dietary sugar conversion (Liu *et al.*, 2019b). Anti-diabetic activity of monk fruit has been attributed majorly to mogrosides and their derivatives including mogroside IA_1, mogroside IE_1, mogroside II E, mogroside IV E, mogrol and siamenoside I as seen in experiment-subject rats (Murata *et al.*, 2010; Zhang *et al.*, 2020). Elevation of insulin release, reduction in α-glucosidase activity, healing of pancreatic injury and prevention of oxidative stress by scavenging free radicals are thought to be mechanisms inducing hypoglycemic response (Wan *et al.*, 2016; Gong *et al.*, 2019a); however, detailed and absolute mechanism remains to be explored. Liu *et al.* (2019a) observed considerable drop in fasting blood glucose level, serum insulin, glycated serum proteins with considerable increment in insulin tolerance and anti-atherogenic lipid profile at high-dose supplementation of mogroside rich extract to diabetic mice. Furthermore, mogroside V has presented promising results in prevention of tissue damage and muscle atrophy by improving carbohydrate utilization and body weight because weight loss and polyphagia are often followed by the onset of diabetes (Liu *et al.*, 2019b, 2019c). Interestingly, Zhang *et al.* (2020) confirmed that low-polar glycosides in monk fruit comprising of mogroside II A_1, mogroside I A_1 and mogroside III had prominent hypoglycemic impact when compared to other fractions of the fruit opening newer routes for future investigations revealing their other similar biological activities.

Anti-carcinogenic activity

Presently, millions of individuals succumb to cancers and tumors across the world and survivors experience poor quality of life associated with health and normal body functioning. Although chemotherapeutic drugs have been thought of as a promising approach to prolong survival, their adverse effects are also not ignorable (Liu *et al.*, 2016b). Carcinogenesis is a multistage course comprising of initiation, promotion and progression occurring as a consequence of epigenetic alteration, mutation and cell death (Trosko, 2005) which are majorly triggered by modern lifestyle and dietetic patterns. Recent biochemical understanding of carcinogenesis has suggested that drugs treatment may have adverse influence on normal cells posing the risk of toxigenic outcomes (de Alencar *et al.*, 2019). Thus, dietary sources inducing anti-proliferative activity against cancers are being explored and significant rise in resources and investment for these projects have been noted in the recent past. Several clinical studies have documented the potential of monk fruit to impart anti-carcinogenic effect in different *in vivo* models. Mogroside V is the principal component of monk fruit responsible for apoptosis and inhibition of tumor growth and progression with minimal damage to normal cells (Liu *et al.*, 2016b). Moreso, mogroside IVe protects from laryngeal and colorectal cancers evident from inhibition of HT29 and Hep 2 cells growth and proliferation under *in vitro* models (Liu *et al.*, 2016a). This has been attributed to apoptosis of the cancer cells as a consequence of modulated expression of MMP-9 and p53 which are important markers in tumor cell invasion and migration (Liu *et al.*, 2016a). Jin and Lee (2012) reported that 11-oxo-mogroside and mogroside V shown anti-tumor activity as early antigen of Epstein–Barr virus was stimulated by 12-O-tetradecanoylphorbol-13-acetate (TPA) which is a preliminary screening analysis of anti-cancer agents. In addition, Weerawatanakorn *et al.* (2014) found suppressive action of monk fruit extract on skin carcinogenesis by inhibition of and TPA induced tumor proliferation and suggested strong correlation between onset of cancers and inflammation. Antioxidative mechanism and anti-inflammatory properties may also contribute indirectly to anti-carcinogenic activity of monk fruit.

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Antioxidant activity

Free radicals are hyper-reactive because of the presence of unpaired electrons which attempt to bind with the electrons from the neighboring atoms initiating chain reaction (Shrivastava *et al.*, 2019), and they can disturb the intracellular unsaturated fatty acids and exaggerate the lipid peroxidation reactions thereby lead to alterations in the morphology and functionality of cell membrane (Liu *et al.*, 2018a). Antioxidant potential, a predominant property of phytochemicals, reduces the risk of inception of modern lifestyle diseases by quenching the pro-oxidants and scavenging free radicals generated in the body. Monk fruit has been reported to inhibit the origination of superoxide anions and exhibit antioxidant activity comparable to ascorbic acid. Furthermore, elimination of free radicals, reduction in hemolysis of Fe^{2+} and lowering the threat of oxidation induced hepatic tissue damage were major biological activities of monk fruit extracts (Gong *et al.*, 2019a; Zhu *et al.*, 2015). Glycosides present in the monk fruit are effective against the oxidative damage to the cell. Mogroside extract acted as a potent scavenger of the peroxide radicals (Liu *et al.*, 2018b). Significant inhibitory effects were demonstrated by themogroside V and 11-oxo-mogroside V against the reactive oxygen species such as oxygen (O_2-), peroxides (H_2O_2) and hydroxyl radical (•OH) as well as oxidative damage to DNA. 11-oxo-mogroside V was reported to have high scavenging activity on oxygen (EC_{50} 0.479 μg/ml) plusperoxides (EC_{50} 016.52 μg/ml) as compared to mogroside V, while the mogroside V also revealed a high scavenging effects on hydroxyl radical (EC_{50} 0 48.44 μg/ml). Additionally, the significant inhibition of hydroxyl radical induced damage to DNA (EC_{50} 0 3.09 μg/ml) was displayed by 11-oxo-mogroside V (Chen *et al.*, 2007). Besides, the crude extracts of monk fruit were found to have high scavenging capacity on the reactive oxygen species (ROS); moreover, the antioxidant effect shown by the monk fruit extract was similar to that of the potent natural antioxidant compound, i.e. ascorbic acid (Zhu *et al.*, 2015).

Anti-microbial activity

Monk fruit and its mogrosides exhibit anti-microbial properties by inhibiting the growth of several microorganisms. The extract obtained from leaf, stem and fruit of *S. grosvenorii* plant had a robust inhibitory effect against *Streptococcus mutans*, *Pseudomonas aeruginosa* and *Escherichia coli* (Gong *et al.*, 2019a). Monk fruit extract was found to have immense potential as pharmaceutical or dietary supplements for the treatment of infections (Zhou and Huang, 2008). *In vitro* activity of nine antibacterial compounds isolated from monk fruit against the oral bacterial species such as *Streptococcus mutans*, *Fusobacterium nucleatum* and *Actinobacillus actinomycetemcomitans* and also the yeast species *Candida albicans* were determined and reported the significant antibacterial activity of the monk fruit leaves. Glucosyltransferase enzyme (GTF) of the *S. mutans* supported the metabolism and was also known to be the virulence component during the pathogenesis of dental caries. Antioxidant properties of five flavonols isolated from the monk fruit flowers were analyzed using different assays. Also, the association between structure and activity of the flavonol compounds was examined. The study revealed that out of the five flavonol compounds, the two major flavonols showed major antioxidant activity. However, on the basis of the association amongst the activity and structure of these compounds, 7-hydroxyl as well as 3-hydroxyl groups on the aglycone showed a positive correlation with the activity but either the methylation of the 7-hydroxyl part or the glycosylation of the 3-hydroxy part showed a decrease in the activity (Mo and Li, 2009). Another compound *Siraitiflavandiol* isolated from monk fruit showed inhibitory action on certain bacterial species such as *Streptococcus mutans, Porphyromonas gingivalis* and yeast such as *Candida albicans* with minimum

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inhibition concentrations of *S. mutans* (6 mg/ml), *P. gingivalis* (24 mg/ml) and *C. albicans* (6 mg/ml), respectively (Zheng *et al.*, 2009).

Anti-inflammatory activity

Several studies have examined that the administration of mogrosides derived from the monk fruit exhibited inhibitory response against the inflammation. Mogroside V is the key compound involved in declining the inflammatory effects in asthma ensuring efficient drug ability properties for the preparation of new drug-combating β2AR-mediated respiratory ailments (Jia *et al.*, 2019). Likewise, studies have shown the shielding action of mogroside V on the ovalbumin-induced experimental asthma caused by allergy in the mice. Addition of mogroside V lowered the levels of different interleukin viz. IL-4, IL-5 and IL-13 in broncho alveolar lavage fluid (BALF) plus serum levels of ovalbumin (OVA)-induced inflammation in the asthmatic mice (Song *et al.*, 2019). Mogrosides exhibited anti-inflammation properties in murine macrophage RAW 264.7 cells by down regulation of certain inflammatory genes such as iNOS, cyclooxygenase-2 COX-2 and interleukins (ILs) and upregulation of protective genes TRP53, PARP1, MAPK9 and BCL2l1. Besides mogrosides also demonstrated anti-inflammatory effects in the murine ear edema model, it protected against inflammation by down regulation of COX-2 and interleukins-6(IL-6) and up-regulation of TRP53, PARP1, MAPK9, BCL2l1 and PPARδ gene expression (Di *et al.*, 2011). Furthermore, *M. grosvenorii* Swingle extract (MSE) inhibited lipopolysaccharide induced nitric oxide synthase and cyclooxygenase-2 gene expression. Administration of mogroside lead to the fall of the lipopolysaccharide-induced translocation of nuclear factor (NF-kB) and dependent transcription action of NF-kB through hindering the phosphorylation of the inhibitor jB (IjB) a. Moreover, mogrosides also hindered the transcriptional effects of NF-kB in lipopolysaccharide-stimulated macrophages in mouse. Correspondingly, mogrosides were effective in the inhibition of lipopolysaccharide (LPS)-induced PI3K/Akt activation. Altogether, mogrosides were effective in downregulating the expression of the inflammatory genes in macrophages via preventing NF-kB activation, through interference with the PI3K/Akt/IKK and MAPK activation (Pan *et al.*, 2009). Therefore, the aforementioned studies implicated the usage of mogrosides as an effective anti-inflammatory compound.

Weight management

Monk fruit is a zero-calorie sweetener. There is an utmost need to replace the sugar from our diet due to continually increasing metabolic disorders like diabetes, obesity and other related conditions. As per World Health Organization, 2019 statistics, around 38 million children are obese or overweight under the 5 years of age. This is no more a trend in developed countries but developing and low-income countries are at equal risk. In comparison to rural conditions, urban settings are more prone due to easy availability and accessibility. Rapid industrialization has led to negative implications on the health of children and adults. Therefore, it is essential to replace sugar as an ingredient that are excessively being used in various sectors of food processing. The non-nutritive sweeteners follow a different metabolic pathway in the body and thus do not result in calorie increment (O'Donnell and Kearsley, 2012). They help in increased breakdown of fat, reduction in weight, reduced blood glucose level and ultimately weight reduction (Mejia and Pearlman, 2019).

Sun *et al.* (2012) conducted a study to assess the anti-obese property of mogrosides IV and V by evaluating their impact on pancreatic lipase under *in vitro* conditions on pancreatic lipase. It was concluded that the triglyceride and total was reduced in the body

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leading to weight reduction by oral administration of mogrosides to the mice. Triglyceride content of mice plasma decreased within 1 to 3 h after oral consumption of total mogrosides with the premix of lipid emulsion. The problem of overweight cannot be solved by focussing on single nutrient control. The overall consensus lies in the fact that total energy input shall be equal to energy output to prevent fat deposition in the body (Jebb, 2015; Marriott *et al.*, 2010).

Sensory profile

Mogrosides are the cucurbitane triterpene glycoside that is majorly present in monk fruit. They are responsible for sweetness and medical applications. Monk fruit extract has a different sensory profile compared with other intense sweeteners. It has a relative lack of bitter taste, especially when compared with saccharin and acesulphame K (Kuhn *et al.*, 2004). Monk fruit extract has been found to exhibit bitterness roughly equivalent or less than that of sucrose (Kim *et al.*, 2015). Scarce data have been published in detail on the flavour profile of mogrosides. The sensory characteristics may help make monk fruit extract a more palatable and appealing choice of intense sweetener for some consumers compared with other intense sweeteners currently available in the market. Non-calorie sweetener with enhanced taste and with reduction in the undesirable aftertaste using natural glycosides was developed by Quinlan and Zhou (2017). The developed sweetener composed of mogroside extract and sweet steviol glycosides of namely rebaudiosides A and B. They stated that the addition of rebaudioside B to a threshold level helped to reduce the perceived bitterness and taste profile. Alternative sweeteners obtained from plants have varied profile affected by purity and amount of extract present in the sweetener (Cadena *et al.*, 2013). The sweetness profile and off flavour can be reduced by blending of various other compounds. The synergy created by the blends lead to improved taste and the sweetness intensity was better than individual compounds (Wilson, 2013). The flavour technology can be explored extensively to overcome the undesirable aftertaste. Procter and Gamble (P&G) patented the process for making monk fruit sweetener (Downton *et al.*, 1995). They successfully developed a process to reduce the undesirable flavour characteristics in order to make the sweetener widely acceptable.

Safety assessment of monk fruit

Monk fruit has been recognized as safe (GRAS) status by United States Food and Drug Administration (USFDA, 2015). Government of several countries such as Australia, New Zealand, China and Japan have approved its use in only table-top packets and food products. According to the FDA, monk fruit sweetener is safe to be consumed by children, pregnant women and individuals with diabetes (Palmer, 2018). The studies in animals have illustrated no detrimental reproductive or developmental effects on mother or offspring, despite of animals being exposed to high levels of mogrosides daily over long periods [Yang *et al.*, 2015; Food Standards Australia New Zealand (FSANZ), 2008]. There is a lack of toxicological analysis of monk fruit extract examined through animal studies, (Jin *et al.*, 2007; Marone *et al.*, 2008; Matsumoto *et al.*, 2009). Tey *et al.* (2017a) and Tey *et al.* (2017b) observed that a beverage containing monk fruit had no effect on total daily energy consumption, glucose and insulin responses in healthy human males.

European Food Safety Authority (EFSA) panel on Food Additives and Flavourings (FAF) has provided the guidelines regarding the secure use of extract obtained from monk fruit in food preparations as an additive. As per EFSA, the major mogroside (mogroside V) was absorbed to certain extent and had systemic bioavailability. The study done by panel reported that extract containing 25 and 55% mogroside V showed negative effects on the

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bacterial reverse mutation and also caused no damage to the structure and/or number of chromosomes. Conversely, the panel disclosed that *in vitro* toxicity studies comprising the study with the metabolic activation were scarce to analyze the genotoxic strength of the metabolites produced after metabolism of microbes including aglycone. Also, no impact of reproductive, parental or development toxicity was reported in the toxicity study done on rats for reproductive and developmental screening. The panel reported a lack of monk fruit toxicity database to advocate the safe use of monk fruit as food additive (EFSA Panel on Food Additives and Flavourings FAF, 2011).

Food Standards Australia, New Zealand reported that mogroside V (about 30–40% of the total extract) was a major constituent of the commercial monk fruit extract. The metabolism of mogroside V indicated its degradation in the intestinal lumen along with the formation of several metabolites. These metabolites could be measured through urine, plasma, liver and other organs, which indicated the systemic absorption; however, the excretion was also through faeces, which indicated the partial systemic absorption of the mogroside V. The sub chronic toxicity studies of repeated dose of monk fruit extract exhibited no harmful effects from higher doses of the extract tested at 5 g/kg body weight/day in mice, 7.48 g/kg bw/day in female rats, 7.07 g/kg bw/day in male rats and 3 g/kg bw/d in dogs [Food Standards Australia New Zealand (FSANZ), 2008]. However, a study done by Hussain *et al.* (1990) explained the acute toxicity of methanol: water (80:20) extracts of monk fruit in mice and reported that none of the extracts showed acute toxicity at ≤ 2 g/kg body weight.

Future prospects and conclusion

It can be suggested that this fruit has great potential to be used in food and beverage, nutraceutical and pharmaceutical sector. Also, the effect of applying heat on monk fruit extract have no clear evidence, and only little work have recorded the involvement of monk fruit extract in products processed at higher temperature. Therefore, to obtain more information related to high temperature processing of monk fruit–related researches are needed to be done. In view of the fact that, a lot of processed products available in the marketplace consists of natural high-caloric sweetening agents therefore needed to be changed fully or partially with natural low caloric sweeteners. These substances have possessed great interest among food manufactures for the production of low-calorie products to meet the demand of health professionals and consumers. The United State Food and Drug Administration has published a regulation regarding the safe consumption of sweeteners such as aspartame, saccharin, sucralose, acesulfame potassium, neotame, stevioside and mogroside. The use of monk fruit extract or powder can be used in functional foods to provide targeted benefits. Efforts are required to study the effect of monk fruit extract and mogrosides on human beings during consumption for longer period as area of research in upcoming years. The harmful effect of artificial sweeteners has escalated the demand for natural sweeteners and the unique characteristics of mogrosides have further resulted in its increased utilization at industrial upfront. Considerable progress has been made on processing and extraction of components derived from the fruit. Also, there are no documented limitations or any known toxic or side effects of monk fruit. However, the disadvantage of monk fruit is that it is hard to grow and import of the fruit is expensive. In the food industry, monk fruit extract may act as an alternative of sugar in different product. However, there is a need to conduct research on utilization of fruit sweetener in variety of products to attain wide acceptability.

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Corresponding author

Rajan Sharma can be contacted at: ranchanrajan@gmail.com

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