REVIEW ARTICLE

Physicochemical Properties and Metabolic Implications of Selected Artificial and Natural Sweeteners: Sucralose, Aspartame, Stevia, and Monk fruit

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Ann Coll Med Mosul 2026; 48 (1):115-124.
Received: 14th Jan. 2026, Revised 4th March 2026, Accepted: 10th May 2026.
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DOI: 10.33899/acmm.v48.i1.60614

ABSTRACT

Background: The global increase in obesity, diabetes, and other diet-related metabolic disorders has intensified the demand for suitable alternatives to refined sugar. Sweeteners, both natural and artificial, are widely used to reduce caloric intake while maintaining sweetness. However, concerns remain regarding their metabolic effects and long-term safety.

Aim: This review aims to evaluate and compare the physicochemical characteristics, metabolic effects, and safety profiles of selected natural and artificial sweeteners, and to clarify their suitability for industrial food applications and clinical nutrition.

Methods: A narrative review of current scientific literature was conducted on various electronic databases such as PubMed, Scopus, Web of Science and Science Direct, focusing on commonly used natural sweeteners, such as stevia and monk fruit extract, and artificial sweeteners, including aspartame and sucralose. Published studies addressing physicochemical properties, metabolic outcomes, effects on gut microbiota, and safety considerations were analyzed.

Conclusion: Both natural and artificial sweeteners exhibit distinct physicochemical and metabolic properties that influence their safety and effectiveness in food applications. While natural sweeteners are generally perceived as safer due to their biological origin, artificial sweeteners offer advantages in stability and sweetness intensity. Understanding the relationship between the chemical nature of sweeteners and their metabolic effects is essential for their rational selection and safe utilization in the food industry and clinical nutrition.

Keywords: Artificial sweeteners, Natural sweeteners, Metabolic effects, Physicochemical properties.

INTRODUCTION

Sweeteners are compounds that add sweetness to beverages and foods and can be generally classified into noncarbohydrate (noncaloric) sweeteners and carbohydrate (caloric) sweeteners. Caloric sweeteners provide energy and include traditional sugars (e.g., sucrose, glucose, fructose), sugar alcohols (polyols) such as erythritol, sorbitol, mannitol, xylitol, maltitol, lactitol, as well as reducing starch syrups, which yield fewer calories and exhibit lower glycemic indices [1]. Sugar alcohols are partly digested within the gastrointestinal tract and provide fewer calories than sucrose and have a lower glycemic index [1]. Non-nutritive sweeteners (NNSs), another name for noncaloric artificial sweeteners, are a broad class of substances with unique molecular structures. Because they offer a high level of sweetness with little to no calorie contribution, they are frequently used as substitutes for added sugars in foods and beverages [2]. NNSs can be broadly divided into two groups: natural sweeteners (NSs), which come directly from plants, and artificial sweeteners (ASs), which are made synthetically using chemical processes. Sucralose and aspartame are examples of common ASs. On the other hand, NSs are mostly represented by stevia, which is made from the leaves of Stevia rebaudiana, but they also include other sweeteners derived from plants, including hoodia, agave extracts, and Siraitia grosvenorii (monk fruit, or Luo Han Guo) [3]. Compared to sucrose, sucralose has a sweetness potency that is about 600 times greater. Only small amounts are needed to reach desired sweetness levels because of sucralose's high sweetening efficiency. Nevertheless, even at low concentrations, sucralose may have detectable effects on the composition of the gut microbiota [4, 5]. Compared to sucrose, aspartame is about 200 times sweeter. Its varied metabolism and widespread use in diet drinks and food products may influence how it affects gut microbiota and general health [6].

Non-nutritive sweeteners (NNSs) have become widely adopted since their introduction as sugar substitutes for controlling weight and preventing obesity [7]. Over the past

three decades, when childhood and adult obesity rates have dramatically increased worldwide, NNSs use has been especially noteworthy. According to a recent report, the number of obese children and adolescents aged 5 to 19 years increased approximately tenfold globally between 1975 and 2016 [8].

The aim of this review is to discuss in details the physicochemical characteristics and metabolic implications of selected artificial and natural sweeteners.

METHODOLOGY

A narrative review of current scientific literature was conducted on various electronic databases such as PubMed, Scopus, Web of Science, and Science Direct, focusing on commonly used natural and artificial sweeteners. Published studies addressing physicochemical properties, metabolic outcomes, effects on gut microbiota, and safety considerations were analyzed.

Sucralose

C12H19Cl3O8 is a chlorinated disaccharide derived from sucrose through selectively substituting chlorine atoms at positions C-4, C-1′, and C-6′ for three hydroxyl groups in sucrose, to produce 4,1′,6′-trichloro-4,1′,6′-trideoxygalactosucrose (Fig. 1). In comparison to sucrose, this modification improves sweetness by almost 600 times and raises molecular weight to about 397.63 g/mol. Its non-caloric nature is explained by the addition of chlorine atoms, which significantly increases resistance to enzymatic hydrolysis and decreases digestibility [9].

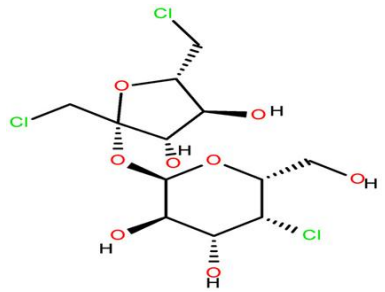

Fig. 1. Chemical structure of sucralose [9].

Polarity and Solubility

Sucralose has a high aqueous solubility (28–30 g/L at 25 °C) because of its numerous hydroxyl groups, which allow for extensive hydrogen bonding with water molecules and make it highly hydrophilic. Nevertheless, it is poorly soluble in nonpolar solvents like organic media and lipids. The molecule's high dipole moment due to its strong polarity affects how it partitions and restricts its use in lipid-based systems [10].

Thermal and pH Stability

One of the most valuable physicochemical properties of sucralose is its exceptional thermal stability. It maintains its chemical stability through baking and pasteurization process up to 120-130℃ [11]. However, degradation occurs at higher temperature, where browning and dichlorination may be the outcome of thermal breakdown [12].

Due to the stability of sucralose over a wide pH range (pH 3-8), it can be used in both acidic beverages and neutral pharmaceutical suspension. Nevertheless, extreme pH value and high temperature may result in partial hydrolysis or rearrangement of the glycosidic bond [13].

Compatibility and Reactivity

The overall activity of sucralose is remarkably decrease by chlorine atoms, which decrease its ability to oxidation and Maillard-type reactions. Sucralose is non-reducing as it lacks a free aldehyde or ketone group, which clarifies why it stays stable in formulations containing reducing sugars or amino acids. The compound in aqueous solutions persists inert under normal storage conditions, degrading very little over extended periods of time [14].

Physical Form and Perceptual Features

Sucralose is a white, crystalline powder that has a melting point of about 119-121 ℃ and a density of 1.59 g/cm 3. Although it has clean sucrose-like taste with little bitterness or metallic after taste, a slight lingering sweetness may occur at higher concentrations. Its intense sweetness profile is related to receptor binding kinetics and molecular configuration, which influence sensory perception [15].

Metabolic Effects of Sucralose

Upon consumption of sucralose-containing products, the compound traverses the gastrointestinal tract with restricted absorption and undergoes minimal metabolic processing in human body and mainly excreted unchanged in the urine, which explains its negligible calorie contribution and supports its widespread as low-calorie sugar alternative for individuals with diabetes or those looking for lower calorie intake while maintaining sweetness [16].

Sweeteners are commonly used to enhance the flavor of diet drinks and confectionaries as they provide sweetness without calorie load of sucrose. But recent studies have connected using artificial sweeteners to a higher risk of type 2 diabetes and heart disease, which raises enquiries about their long-term metabolic effects and emphasizes the need for more research [17].

Excessive consumption of artificial sweeteners has been linked to increased appetite and weight gain [18]. Undesirable sensory effects like bitterness and metallic aftertaste in addition to sweetness can be produced by these substances. Complex temporal dynamics like changes in the onset, persistence, and a decline of flavor intensity during consumption, affect how taste is perceived. As the primary sweet sensation may be followed by lingering unpleasant taste, such sensory attributes are critical in determining consumer

acceptance [19]. Furthermore, it seems that sucralose affects the physiological mechanisms that controls hunger and fullness, potentially leading to overeating. Recent studies indicate that the composition of gut microbiota may be altered by sucralose, potentially lowering the quantity of beneficial bacteria and disturbing gastrointestinal homeostasis. This proposes that the conformation of gut microbes may be negatively affected, which could lead to metabolic disturbances and difficulties in weight management [20].

Sucralose consumption has been also linked to the upregulation of key metabolic enzymes, including cytochrome P450 2D1 (CYP2D1), cytochrome P450 3A4 (CYP3A4), and P-glycoprotein (P-gp). As the expression of these enzymes increases, the systemic bioavailability of some orally adminstrated medications decreases due to their significance in drug metabolism and oral bioavailability. This could diminish therapeutic efficacy and necessitate clinical consideration of varying dosage or using alternative medication strategies [21].

Impact of Sucralose on Insulin Sensitivity and Glucose Metabolism

Consuming sucralose has been linked to alterations in glucose metabolism and reduced insulin sensitivity. In a 10-week open-label human trial involving 40 healthy young adults, sucralose consumption was linked to altered glucose and insulin responses; however, the small sample size, lack of blinding, reduce the strength and generalizability of these findings [22]. In addition, an earlier randomized crossover study in 17 obese adults found that sucralose altered acute glycemic and insulin responses during a 5-hour oral glucose tolerance test (OGTT), but because the study is short-term, its findings can't be used to infer long-term metabolic effects [23]. Therefore, while these studies suggest that sucralose may negatively affect glucose metabolism and insulin sensitivity, the evidence should be interpreted cautiously until confirmed by larger, longer, blinded human studies [22, 23].

Impact of Sucralose on Lipid Metabolism

In a 12-week, parallel-arm randomized controlled trial in 210 Indian adults with type 2 diabetes, replacing added sucrose in coffee/tea with sucralose show no significant change in serum lipid profile (total cholesterol, HDL-C, LDL-C, and triglycerides) compared with continuning sucrose. This trial had arelatively large sample size but was short duration for lipid outcomes and conducted in free-living setting, which can introduce dietary variability, and biochemical outcomes were collected only at baseline and week 12 [24].

In contrast to the neutral human lipid findings, a mouse study reported that six months of sucralose intake (within the acceptable daily intake) altered gut microbiome functions related to bile acid metabolism, reduced hepatic farnesoid receptor (FXR) activation, upregulated key lipogenic gene, and was associated with mildly increase hepatic lipid accumulation and higher hepatic cholesterol. These results suggest that long-term sucralose exposure may perturb hepatic lipid and cholesterol homeostasis through a gut microbiome-bile acid-FXR pathway in mice [25].

Aspartame

Aspartame ($C_{14}H_{18}N_2O_5$) is a methyl ester dipeptide (L-aspartyl-L-phenylalanine 1-methyl ester), widely used as a powerful artificial sweetener (Fig. 2). It has a molecular weight of ~ 294.30 g/mol. It is usually an odorless white to off-white crystalline powder, with a very sweet taste, some 160-200 times sweeter than sucrose in solution in water [26, 27].

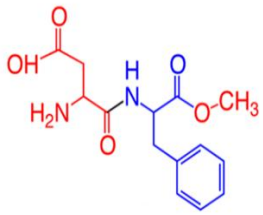

Fig. 2. Chemical Structure of Aspartame[26].

Melting Point and Thermal Behavior

Aspartame has a melting point of approximately 246-248 °C, although melting is frequently followed by decomposition. It shows good thermal stability under dry conditions, with only minor degradation (e.g., less than 5% conversion to diketopiperazine under 105 °C after prolonged time). According to thermal analysis, mass loss in tabletop powder sweetener formulations starts at moderate temperatures (about 65°C) when moisture is present; under similar circumstances, natural sweeteners typically exhibit higher thermal stability than aspartame [27].

Solubility, pH, and Stability in Solution

Aspartame dissolves somewhat in ethanol and sparingly in water. High temperature and acidity both increase solubility. Temperature, moisture content, and pH all have a significant impact on the stability of the molecule in solution. At room temperature, maximum stability occurs at pH ~4.2–4.3. Aqueous solutions can have a long half-life (hundreds of days) at that pH [9]. Sweetner is degraded by hydrolysis of the ester bond (producing aspartyl-phenylalanine + methanol) and/or cyclization to diketopiperazine at higher pH (basic) or extremes of acidity [27, 28].

Degradation and Photostability

Research on soft drinks indicates that aspartame breaks down over time; weeks of storage at room temperature result in a considerable conversion to degradation products (such as diketopiperazine, α-Asp-Phe, and β-Asp-Phe) [27]. Aspartame in soft drinks breaks down more quickly in neutral pH and with photosensitizing ingredients, according to a more recent study of

photolytic transformation under simulated sunlight. New photoproducts, some of which have not been previously described, were discovered, raising concerns about their safety in specific storage and light-exposure scenarios [29].

Solid State Stability and Form

As long as moisture is kept to a minimum, aspartame is fairly stable in dry solid form; moisture and high temperatures hasten degradation. In order to change the kinetics of solubility and dissolution, some research also investigates aspartame as a co-former in co-amorphous systems [30].

Consequences and Use-Restrictions

Aspartame is less appropriate for uses requiring extended heating (such as baking) or in high pH environments due to its sensitivity to moisture, high temperatures, light, and pH extremes. Drinks are a better medium, especially those that are acidic. Aspartame's sweetness can be maintained and the development of off flavors or breakdown products can be decreased with the use of formulation techniques (such as protective encapsulation, blending, and storage in dry, cool, and light-protected conditions) [29].

Metabolic Effects of Aspartame

The food and beverage industries frequently use aspartame (L-aspartyl-L-phenylalanine methyl ester), a low-calorie artificial sweetener that is about 200 times sweeter than sucrose, to reduce calories without sacrificing sweetness intensity. When aspartame is consumed, it is quickly hydrolyzed in the digestive system into its component parts, methanol, phenylalanine, and aspartic acid. These metabolites enter various metabolic pathways and have been associated with a number of biochemical and physiological alterations related to energy balance, glucose homeostasis, and oxidative stress [31].

Aspartame has been suggested to promote oxidative stress through the action of its metabolites, via generating reactive oxygen species (ROS)and impairing antioxidant defenses [31]. Animal studies provide some support for this effect, as long-term exposure in Wistar rats has been associated with altered antioxidant defense markers (e.g., superoxide dismutase, catalase, glutathione peroxidase) and increased level of malondialdehyde (MDA), although the relevance of these findings to human intake remains uncertain because of species differences and relatively high experimental doses [32]. Similarly, recent review literature indicates that aspartame may alter the gut microbiota and influence metabolic regulations, but the available human evidence is inconsistent, and a definitive relationship has not yet been established [33].

Impact of Aspartame on Insulin Sensitivity and Glucose Metabolism

Aspartame, as a non-carbohydrate sweetener, appears to exert little direct effect on fasting blood glucose or insulin levels in human studies, including both healthy and diabetic [34]. Nevertheless, the available human evidence is based largely on small, short-duration trials summarized in systematic reviews, which limits confidence regarding chronic exposure and long-term metabolic outcomes [34]. Although animal studies suggest that prolong aspartame intake may induce physiological disturbances, including altered glucose metabolism and changes in insulin secretion, these data are derived from in vivo rat models and should not be considered directly applicable to human glucose regulation [35].

Impact of Aspartame on Lipid Metabolism

Although aspartame provides negligible caloric intake, its long-term effect on lipid metabolism and weight control remains controversial. Compared to sucrose, some human trials reveal no significant effect on lipid profile or body mass index (BMI) [36]. Nevertheless, according to experimental models, long-term exposure to aspartame may elevate lipid peroxidation, low density lipoprotein (LDL)cholesterol, and serum triglyceride possibly due to oxidative stress mechanism. Also, it may produce changes in hormones that control appetite, such as leptin and ghrelin, suggesting a possible interference with satiety signals [37].

Stevia

Steviol glycosides (SGs) that are extracted from stevia rebaudiana leaves and referred to as stevia sweeteners are stevioside, rebaudioside A (Reb A), and rebaudioside M (Reb M), (Fig. 3). Solubility, stability, sweetness intensity is all impacted by the pattern and degree of glycosylation of the common diterpenoid (steviol) aglycone found in these substances [38].

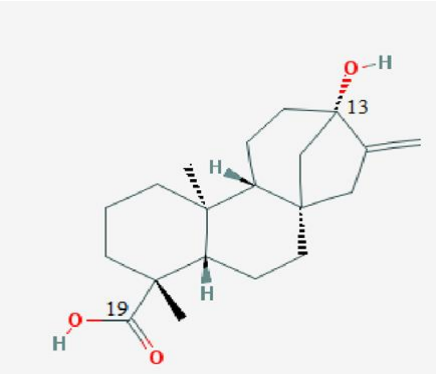

Fig. 3. chemical structure of stevia [38].

Steviol glycosides are odorless, white to off-white crystalline powders with a high sweetness potency that is typically 200-300 times greater than sucrose. Glycosylation affects handling and solubility properties via molecular weights changing (stevioside ≈805 g/mol; Reb A ≈ 967g/mol) [39].

Dissolution and Solubility

Steviol glycosides are generally soluble in water while their crystalline forms, especially those that are highly

glycosylated such as Reb M, show modest solubility at room temperature and low intrinsic dissolution rates. Amorphous or glucosylated forms exhibit higher apparent solubility [38]. A number of formulation techniques have been investigated to increase their solubility and improve their sensory qualities, such as solid dispersion, enzymatic glucosylation, and microencapsulation [38, 40].

Thermal and pH stability

Steviol glycosides have significant hydrolytic and thermal stability, maintaining their structural integrity and sweetness at regular food processing temperatures and within the pH range (3-8) but hydrolysis or isomerization may be enhanced by high acidity or prolonged heating. Protein or polymer encapsulation offers additional protection during processing and storage [41].

Functional derivatives and technological advancements

Derivatives with enhanced solubility, reduced bitterness, and a faster onset of sweetness have resulted from recent advancements which have focused on enzymatic or microbial glucosylation. Dispersibility and flavor masking in food and beverage formulation can be improved by encapsulation techniques. Consequently, steviol glycosides' stability, solubility, and hygroscopicity are among physicochemical properties that show how well they work in culinary application. Although stevia is stable in most situation, its taste and solubility limitation encourage continued research into molecular formulation, encapsulation, and process optimization to create next generation stevia sweetener with better performance [42].

Metabolic effects of stevia

The leaves of the Asteraceae family are used to make stevia (Stevia rebaudiana Bertoni), a naturally occurring non-nutritive sweetener. Steviol glycosides, its primary sweetening agents, including stevioside and rebaudioside A, are 200–300 times sweeter than sucrose and have been recognized by regulatory bodies such as the European Food Safety Authority (EFSA) and the U.S. Food and Drug Administration (FDA) as safe sugar substitutes worldwide. Beyond its sweetness, there is growing evidence that stevia has a variety of metabolic effects, such as modifying oxidative balance, lipid metabolism, and glucose homeostasis [43].

Stevia has very little nutritional value despite being extremely sweet. Contrary to some artificial sweeteners that may change hunger signaling, stevia consumption does not appear to increase appetite or energy intake, according to a number of studies. In high-fat diet models, long-term steviol glycoside administration has been linked to decreases in body weight and visceral adiposity; this may be because it improves leptin sensitivity and modifies gut microbiota [44].

Stevia may help with metabolism because of its anti-inflammatory and antioxidant properties. Stevioside lowers malondialdehyde (MDA) levels while increasing the activity of endogenous antioxidant enzymes such as catalase (CAT) and superoxide dismutase (SOD). Oxidative stress, a major contributor to insulin resistance and metabolic syndrome, may be lessened by these effects. Additionally, pro-inflammatory mediators like TNF-α and IL-6 are downregulated by steviol glycosides [45].

Impact of stevia on insulin sensitivity and Glucose Metabolism

Stevia has been investigated for possible beneficial effects on glucose metabolism, but the strength of evidence differs by study design. Human clinical data suggest that stevia may improve postprandial glycemic responses in some settings. In a crossover trial comparing stevia, aspartame, and sucrose preloads, stevia was associated with lower postprandial glucose levels than sucrose, but this study assessed mainly acute responses rather than long-term insulin sensitivity, and its findings cannot be taken as proof of sustained metabolic benefit [46].

Mechanistic and preclinical evidence is more supportive. In vitro and in vivo work has shown that steviol glycosides can enhance glucose-induced insulin secretion by potentiating Transient Receptor Potential Melastatin 5 (TRPM5) channel activity in pancreatic beta cells, a calcium-dependent pathway relevant to insulin release. In the same line of research, daily stevioside exposure improved glycemic outcomes in high-fat-diet mouse models, suggesting a possible role in glucose regulation; however, these findings come from experimental systems and animal models, so they should not be directly extrapolated to humans [47].

Impact of stevia on the Lipid Metabolism

Human clinical evidence does not currently demonstrate a consistent lipid-lowering effect of stevia. A systematic review and meta-analysis of randomized controlled trials found no significant overall effect of steviol glycosides on total cholesterol, LDL-C, HDL-C, or triglycerides, although the included studies were heterogeneous and varied in quality [48].

In contrast, animal studies suggest a possible beneficial effect on lipid metabolism; for example, stevia extract reduced serum triglyceride and lowered total cholesterol in high-fat-fed mice, together with changes in lipid-metabolism-related genes such as Peroxisome Proliferator-Activated Receptor Alpha (PPAR-α) and Carnitine Palmitoyltrasferase I (CPT-I) [49].

Monk fruit extract

Mogroside V is the main sweet ingredient in commercial extracts of the mogrosides, a family of extremely sweet, non-caloric cucurbitane-type triterpene glycosides that are produced from monk fruit (Luo Han

Guo; Siraitia grosvenorii) (Fig. 4). Depending on the assay and matrix, mogroside V is typically reported to be between 250 and 425 × sweeter than sucrose. The temporal profile and sweetness intensity are determined by the relative composition of mogrosides (V, IV, III, neo-mogrosides, siamenside I, etc.) [50].

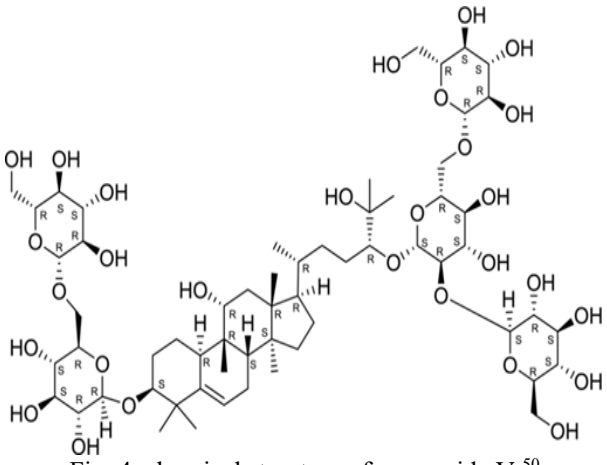

Fig. 4. chemical structure of mogroside V [50].

Physical and molecular properties

Large glycosylated triterpenes, known as mogrosides, have varying molar masses depending on the degree of glycosylation. Their crystallinity, particle size, and residual sugars have a significant impact on the rate of dissolution and the perceived sweetness in applications, even though they are water-dispersible due to their multiple sugar moieties and are isolated as white to off-white powders in commercial concentrates [51]. The relative mogroside profile and impurity levels are changed by processing (drying, extraction conditions), which in turn affects functional behavior, according to analytical work (HPTLC, HPLC-MS) [52].

Dissolution and solubility

Although mogrosides are soluble in water, their apparent solubility and dissolution kinetics vary depending on the type of mogroside (more glycosylation typically makes a mogroside more soluble in water) and product form (purified vs. crude extract; crystalline vs. amorphous). At low concentrations, poor dissolution of crystalline fractions can reduce the intensity of sweetness, which is why amorphous preparations or co-formulation with bulking agents are used to increase dispersibility [52].

Thermal and pH stability

Overall, mogrosides demonstrate good stability under typical food processing conditions (pasteurization, moderate heating) and across a broad pH range used in beverages and many foods. However, severe heating or prolonged exposure to extreme pH can cause glycosidic cleavage or minor degradation; encapsulation and protective carriers are used when additional thermal/pH protection is required (e.g., in bakery matrices or highly acidic formulations) [53].

Formulation and sensory factors

Manufacturers frequently mix monk fruit extract with other sweeteners or masking ingredients to match sucrose-like temporal profiles and lessen off-tastes, even though mogroside V has a high sweetness potency. Its sensory profile (onset, linger, and bitterness) however, depends on purity and co-ingredients. In order to maximize solubility, mouthfeel, and stability while maintaining clean sweetness, recent developments include enzymatic modification, fermentation production of particular mogrosides, and microencapsulation [54].

Metabolic Effects of Monk Fruit extract

As monk fruit sweetener is a natural non-nutritive sweetener extracted from the fruit of the Cucurbitaceae family, it has gained attention as a safer alternative to artificial sweeteners for individuals seeking to manage glucose levels and metabolic health [55].

Monk fruit extract exhibits strong anti-inflammatory and antioxidant properties in addition to a positive impact on the extent of glycemic control. Mogrosides have been shown to increase endogenous antioxidant enzymes like catalase and superoxide dismutase (SOD) and scavenge reactive oxygen species (ROS) .By reducing oxidative stress-induced insulin resistance and vascular inflammation, which are prevalent characteristics of metabolic syndrome, these effects may indirectly promote metabolic health .Furthermore, in models of macrophages and adipocytes, monk fruit extract has demonstrated suppression of inflammatory mediators such as TNF-α and IL-6 [56].

Preliminary data indicates that monk fruit sweetener has a neutral or slightly positive impact on the composition of the gut microbiota, in contrast to certain artificial sweeteners that upset the balance of gut microbes. Mogrosides are not substantially metabolized by gut bacteria, according to in vitro fermentation studies, reducing the risk of dysbiosis linked to some artificial sweeteners [57]. To validate these results and their long-term metabolic implications, additional human trials are required.

Impact of Monk Fruit Extract on Insulin Sensitivity and Glucose Metabolism

Human evidence suggests that monk fruit-sweetened beverages do not increase postprandial glucose or insulin compared with sucrose-free sweetened alternatives, and generally produce much smaller glycemic and insulinemic responses than sucrose. In a randomized crossovertrial in 30 healthy male participants, monk fruit-sweetened beverages were tested across seprate study visits and showed minimal effects on postprandial glucose and insulin compared with sucrose-containing beverages. However, this study assessed acute response only and include only healthy men, limiting

generalizability to women, people with diabetes, and long-term metabolic outcomes [58].

In rodent models of diabetes, mogroside-rich preparations have shown potential metabolic benefits. In a high-fat diet/streptozocin-induced diabetic mouse model, mogroside-rich extract administrated for 5 weeks reduced fasting blood glucose and indices related to insulin resistance and improved glucose/insulin tolerance. Alongside evidence of hepatic activated protein kinase (AMPK) activation consistent with reduced gluconeogenesis and increased fat oxidation-related gene expression. Key limitations include the relatively short duration, and the fact that intervention tested a mogroside-rich extract rather than purified mogroside-V, so the findings cannot be assumed to apply directly to typical monk-fruit sweeteners [59].

Impact of monk fruit extract on lipid metabolism

In high-fat diet models, animals were fed a high-fat diet and then treated with different doses of mogroside V during the final 8 weeks of the feeding period; the study used a control group and a high-fat diet group that was divided into four groups, each group has 9 mice. Mogroside V has been reported a dose-dependant improved lipid-related outcomes including reductions in serum triglycerides and total cholesterol, alongside increased expression of lipid oxidation-related markers such as PPAR-α and CPT-1A[60].

Similarly, in a high-fat dietd/streptozocin-induced diabetic mouse model, a mogroside-rich monk fruit extract given for 5 weeks (150 or 300 mg/kg) improved the serum lipid profile. Compared with untreated diabetic mice, monk fruit extract reduced serum triglycerides, total cholesterol, and LDL-C in a dose-dependant manner.

These lipid improvements were accompanied by reduced hepatic lipid accumulation and activation of hepatic AMPK signaling, with downregulation of lipogenic gene expression and upregulation of fatty-acid oxidation related genes including CPT1A and PPAR-α, supporting a plausible mechanism for improved lipid handling [59]. However, these findings should be interpreted cautiously because they derived from short-duration rodent experiments. Therefore, human trials are needed to confirm monk fruit sweetener's effect on lipid profile.

CONCLUSIONS

Both artificial and natural sweeteners hold significance in contemporary nutrition because they provide glycemic control and calorie reduction alternatives to sucrose. Stevia and monk fruit extract are examples of natural sweeteners that come from plants and provide sweetness through glycosides or mogrosides, which have little effect on metabolism and may have anti-inflammatory or antioxidant properties. The dietary management of obesity and diabetes, on the other hand, benefits greatly from the use of artificial sweeteners, such as sucralose, aspartame, and saccharin, which are manufactured artificially and have a strong sweetness but very little nutritional value.

In spite of the technological and metabolic benefits of these sweeteners, studies remain in progress to determine their long-term physiological effects, including probable effects on gut microbiota, appetite regulation, and glucose homeostasis. Although natural sweeteners may offer greater bioactivity and consumer preference for "clean label" products, the comparative analysis of these two groups establishes that artificial sweeteners are still necessary because of their affordability, stability, and reliable sweetness intensity. Further studies gathering metabolic, toxicological, and sensory viewpoints are necessary to clarify health effects, ensure safety, and guide the rational formulation of sweetness in the food and pharmaceutical industries.

Acknowledgements

The authors would like to thank College of Medicine/ University of Mosul for providing the necessary facilities to conduct this review.

Authors' contributions

The author1, 2, and 3 contributed to the preparation, writing, and presentation of this article to the journal in its current form.

Conflict of interests

There are no conflicts of interest among the writers.

Funding

None

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