

SYNSEPALUM DULCIFICUM [MIRACLE FRUIT] A COMPREHENSIVE REVIEW OF BIOACTIVE COMPOUNDS, TASTE-MODIFYING MECHANISMS, AND THERAPEUTIC APPLICATIONS IN CLINICAL NUTRITION

Arpith Kumar L M

Lecturer and Residential Medical Officer, Yenepoya Naturopathy and Yogic Sciences College and Hospital, Mangalore
Yenepoya [Deemed to be University]

ABSTRACT

Background: *Synsepalum dulcificum*, commonly known as miracle fruit, is a West African plant renowned for its unique taste-modifying properties attributed to the glycoprotein miraculin. By temporarily altering taste perception, specifically converting sour tastes into sweet. *S. dulcificum* has gained attention not only as a novelty but as a promising candidate in clinical nutrition and therapeutic applications. This review provides a comprehensive synthesis of current scientific and clinical evidence surrounding the potential health benefits and applications of *S. dulcificum*. The fruit's phytochemical profile includes antioxidants, flavonoids, and polyphenols, which contribute to its proposed anti-inflammatory, antihyperglycemic, and lipid-lowering effects. Recent studies have explored its role in managing chemotherapy-induced taste disturbances [dysgeusia], aiding glycemic control in diabetic patients, and supporting weight management in obesity. Its potential to improve appetite and nutritional intake in patients undergoing cancer treatment or suffering from metabolic disorders highlights its relevance in clinical nutrition. While preclinical studies show promising pharmacological activity, human trials remain limited, with variability in study design and outcomes. This review critically examines the available literature, discussing mechanisms of action, therapeutic efficacy, safety profile, and potential for integration into functional foods or medical nutrition therapy. Overall, *S. dulcificum* represents a novel, natural agent with emerging clinical relevance. However, further well-designed, large-scale clinical trials are necessary to validate its efficacy and ensure safe application in medical practice. This review aims to guide future research and support healthcare professionals considering *S. dulcificum* in nutritional and therapeutic interventions.

Keywords: *S. dulcificum*, Miracle plant, Miraculin, Anticancer, Antidiabetic, Antioxidant

INTRODUCTION

Synsepalum dulcificum is an evergreen shrub that is a member of the Sapotaceae family and is sometimes referred to as the Miracle plant, Miracle berry plant, or red berry. The miracle plant was initially found in West and Central Africa, more precisely in Nigeria, Ghana, and Congo [1].

The Yoruba and Igbo people of southern Nigeria refer to the plant as Agbayun and Uni, respectively. In cultivation, miracle plants reach a height of roughly 3 meters, whereas in their natural habitat, they reach 6.1 meters. The leaves measure 5–10 cm in length and 2–3.7 cm in width. When they mature, the cream-colored flowers turn dark crimson or brown. The flowers have two sexes. There are four to five sepals in the calyx, four to five petals in the corolla, and five stamens in the androecium. The gynoecium has an unimpressive stigma and is upright [2].

The fruit is red when it is mature. Compared to other berry fruits like blueberries, blackberries, cran-

berries, and grapes, the miracle berry is less prevalent. The fruit measures around 2 cm in length and 1 cm in width, making it about the size of a coffee bean. Its comparatively large seed is enclosed by a thin layer of skin covering a translucent pulp. The pulp contains the sweetening action. Typically, the fruits are grouped at the branches' tips [1].

Miracle fruit can be used as an ingredient in cosmetic products or as a raw or processed ingredient in food and medicine. The fruit of the plant has historically been called a "miracle plant" due to its special ability to change the flavour of sour foods to sweet ones [3].



PHYTOCHEMICAL COMPOSITION

Nutritionally, the fruit is rich in essential vitamins [A, C, E, K], minerals [like calcium, iron, and zinc], and both essential and non-essential amino acids.



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Correspondence: Dr. Arpith Kumar L M, Lecturer and Residential Medical Officer, Yenepoya Naturopathy and Yogic Sciences College and Hospital, Mangalore, Yenepoya [Deemed to be University] Email: drarpithkumarlm@gmail.com

The presence of potent antioxidants such as anthocyanins and flavonoids including quercetin, myricetin, and kaempferol enhances its profile as a functional food with chemopreventive potential. Miraculin is the active ingredient that gives the fruit its ability to change its flavor [4].

Phytochemicals, including volatile oils, alkaloids, glycosides, flavonoids, tannins, and resins, have been used in a variety of commercial and industrial uses, including natural pigments, flavours, preservatives, medicine, and cosmetics [5].

Spectroscopic methods were used to identify thirteen bio constituents in the *S. dulcificum* stem's methanol extract. Dihydro-feruloyl -5-methoxytyramine, [β]-syringaresinol, [β]-epi-syringaresinol, 4-acetonyl-3, 5-dimethoxy-p-quinol, cis-p-coumaric acid, trans-p-coumaric acid, p-hydroxybenzoic acid, syringic acid, vanillic acid, veratric acid, N-cis-feruloyl tyramine, N-trans-feruloyl tyramine, and N-cis-caffeoyl tyramine are among the molecules [6].

Similar to this, six pure chemicals were identified from the methanol extract of the plant stem: nicotinic acid, 3, 4, 5-trimethoxybenzoic acid, 2, 5-dimethoxyphenol, propane-1, 2, 3-triol, β-sitosterol, and stigmaterol. [β] - epi-syringaresinol and [β]-syringaresinol, the isolated compounds, were reported to have anti-oxidative and anti-ageing properties as well as the ability to inhibit human skin cancer cells in vitro [7].

Accordingly, [β]-epi-syringaresinol, 4-acetonyl-3,5-dimethoxy-p-quinol, trans-p-coumaric acid, p-hydroxybenzoic acid, cis-p-coumaric acid, vanillic acid, and N-cis-feruloyl tyramine decrease the activity of mushroom tyrosinase, which gives them the unbounded ability to prevent melanin synthesis and, on the other hand, to treat hyperpigmentat [8]

Glycoprotein Oil substance	Miraculin 4-hydroxy-2-oxetanone Anthocyanins	Fruit [9]
Phenolic acid	cis-p-coumaricacid trans-p-coumaricacid p-hydroxybenzoicacid syringicacid vanillicacid isovanillic veratricacid methylparaben	Stem and root [10]
Lignan	β-sitosterolandstigma-sterol pheophytin-a pheophytin-b lupeol lupenone lupeolacetate α-tocopherylquinone 26.α-amyrin 27.β-amyrinacetate	Leaf [11]

gives the fruit its taste-altering ability is called miraculin. Miraculin is a single polypeptide glycoprotein consisting of two sugars linked to two amino acid residues and with a molecular weight ranging from 24,000 to 45,000 Da. The two amino acid residues are held together by intramolecular disulfide bonds and are composed of 191 amino acid residues [12]. When miraculin attaches itself to taste cell membranes close to the sweet receptor location, the sweetening effect occurs. A conformational shift in the receptor membrane as a result enables the carbohydrate component of miraculin to attach to the sweet receptor site, resulting in the perception of sweetness. Protons [H+] must be present for the conformational shift to occur. In other words, miraculin's ability to create sweetness by causing conformational changes in the receptor membrane depends on pH. Miracle fruit has a taste-modifying property that works on all acids and lasts for around 30 minutes [3].

Mechanism of action: Miraculin's mode of action was assessed in monkeys by Five distinct acids were used in the study to assess the acceptance rate. The outcome demonstrates that pretreatment with 0.3–0.5 mg miraculin boosted the acceptability rate. Following pretreatment with miraculin, the nerve response to acid was twice as compared to the sucrose response. The miraculin effect was found to last for an hour before gradually disappearing after 20 minutes. The outcome demonstrated that miraculin increased the acid sensitivity of sweet-sensing cells [13]. Another study investigated the brain mechanism of the sweet taste elicited from the consumption of miracle fruit that is, how the fruit converts the sour taste of acids to sweet

Chemical Class	Compound Name	Part
Alkaloid	dihydro-feruloyl-5-methoxytyramine	Stem and root [7]
	N-cis-Caffeoyl tyramine	
	N-cis-Feruloyl-tyramine	
	N-trans-Feruloyl-tyramine	
	4-acetonyl-3,5-dimethoxy-p-quinol	

Table 01: Phytochemical composition

MECHANISM OF TASTE MODIFICATION

Structure of Miraculin: The active ingredient that

and appetizing taste. Recording of human cerebral cortex using magnetic fields to monitor the sweet taste elicited by miracle fruit was performed. In the report, the preliminary taste responses were limited to the fronto-parietal cortex described as the brain site that received neuronal signal for taste [14]. The response latency of sucrose and citric acid, after mastication of miracle fruit, was shown to be equivalent whereas there was a large difference [250–300 ms] between sucrose and citric acid in the absence of the fruit. The sour taste vanishes at the subcortical level while the sweet taste neuronal signal gets to the cortical level. Miraculin binds to the epithelial plasma membrane of the receptor taste receptor type 1 member 3 [T1R2-T1R3] and acts as antagonist in any sour solution [15].

THERAPEUTIC APPLICATIONS

Antioxidant activity:

Antioxidants shield the body from harmful substances that lead to oxidative stress. Flavonoids and other antioxidant phytochemicals are prevalent in Miracle berry pulp. A few studies assessed and validated the methanol extracts of *S.dulcificum*'s flesh and seeds in vitro antioxidant and radical scavenging properties. Antioxidants shield the body from harmful substances that lead to oxidative stress. Flavonoids and other antioxidant phytochemicals are prevalent in Miracle berry pulp. A few studies assessed and validated the methanol extracts of *S.dulcificum*'s flesh and seeds in vitro antioxidant and radical scavenging properties [16]

Among the techniques used were FRAP tests, ferric-reducing antioxidant power, DPPH [1,1-diphenyl-2-picrylhydrazyl] and ABTS [2,20-azino-bis[3-ethyl 49 benzothiazoline-6-sulfonic acid] 6 radical scavenging activities. Additionally, the fish oil emulsion model was used to analyse how the extract stabilised lipid oxidation. It was found that the sample decreased fish oil's polyunsaturated fatty acid oxidation. As a result, the *S.dulcificum* plant may be a fruit that is high in antioxidants and might support good health. Flavonoids and phenols that have been extracted from fruits, leaves, and roots may be the cause of the known antioxidant properties of *S.dulcificum* plant component extracts [17,18]

Anticancer activity:

Bioconstituents derived from the stem of *S. dulcificum* were tested on melanoma cells [A375.S2] and mushroom tyrosinase. Tyrosinase is a crucial enzyme that directly regulates the body's melanin synthesis. According to earlier research, two of the chemicals in *S. dulcificum*, {[β]-syringaresinol and [β]-epi-syringaresinol}, exhibit significant antioxidant activity in vitro and inhibit human skin cancer cells. The activity of mushroom tyrosinase was sup-

pressed by substances such as [β]-epi-syringaresinol, 4-acetyl-3,5-dimethoxy-p-quinol, cis-p-Coumaric acid, trans-p-coumaric acid, p-hydroxybenzoic acid, vanillic acid, and N-cis-feruloyl-tyramine. Tyrosinase inhibitors are used in the cosmetics industry and in medicine to treat hyperpigmentation [17].

Another study examined how aqueous leaf extracts of miracle fruit affected 4-nitroquinoline-N-oxide [4-NQO] and 2-aminoanthracene [2-AA]. Oxidative damage and induced mutation were assessed. The mutagenicity of 2-AA, an indirect mutagen, and 4-NQO, a direct mutagen, toward *Salmonella typhimurium* TA 98 and TA 100 was inhibited by the leaf extracts in a concentration-dependent manner. P-hydroxybenzoic acid, vanillic acid, syringic acid, trans-p-coumaric acid, and veratric acid are among the active phenolics found in the sample [18].

Antidiabetic activity:

Chen et al. assessed the impact of miraculous fruit [*Synsepalum dulcificum*] on insulin resistance in male Wistar rats produced by fructose-rich chow [19]. Insulin-resistant mice treated with 0.02, 0.04, and 0.2 mg/kg extract of miracle fruit showed improvement in the time interval for response to tolbutamide [10.0 mg/kg, i.p.] and the effect of fructose-rich diet on the glucose-insulin index. Additionally, the use of miracle fruit powder resulted in a notable improvement in insulin sensitivity. According to Dioso et al., *S. dulcificum* fruit [50% and 100%] and leaf [50% and 100%] extracts had hypoglycemic effects on the blood glucose levels of diabetic albino rats produced by alloxan. *dulcificum*'s fruits and leaves both exhibited a notable hypoglycemic effect [20].

Anticonvulsant activity:

Studies employing seizure-induced mouse models have demonstrated the significant anticonvulsant effect of *Synsepalum dulcificum* seed extract. In maximal electroshock tests, it greatly shortened recovery time and offered 33.33% protection against seizures caused by strychnine and pentylenetetrazole. The extract most likely enhances inhibitory neurotransmission by interacting with the picrotoxin binding site on the GABA receptor. These results point to the plant's potential for treating seizures, but more investigation is required to verify its safety and therapeutic efficacy [21].

Anti-hyperuricaemic activity:

The anti-hyperuricaemia action of *S. dulcificum* fruit extract in xanthine oxidase and monosodiumurate [MSU]-treated RAW264.7 macrophages. Uric acid is produced through the action of xanthine oxidase. In animals, xanthine oxidase catabolizes uric acid to

allantoin; hence, xanthine oxidase inhibition will directly prevent the synthesis of uric acid. Butanol extract of *S. dulcificum* fruits reduced the raised serum uric acid in mice with potassium salt-induced hyperuricaemia, according to the study. Additionally, butanol extract reduced the activity of xanthine oxidase in RAW264.7 macrophages treated with monosodium urate [MSU] [22].

Cholesterol-lowering effect:

A hamster model fed an experimental diet that included 2% ethanolic and water extract of *S. dulcificum* seed, leaves, and dry pulp was used to assess the plant's ability to decrease cholesterol. While lupeol acetate and β -amyrin acetate, which are triterpenoids extracted from the seed extract, lower plasma total cholesterol by 15% to 20% in hamsters, experimental meals including *S. dulcificum* seed extract decreased plasma total cholesterol. The ethanol extract of the seed was found to lower plasma total cholesterol, which may be related to the extract's active triterpenoids [23].

CONCLUSIONS

Synsepalum dulcificum, commonly known as miracle fruit, is emerging as a significant natural agent in clinical nutrition and therapeutic science due to its unique taste-modifying glycoprotein, miraculin, and its rich phytochemical composition. Indigenous to West Africa, this plant has attracted global interest for its potential to transform sour flavors into sweet, offering novel applications especially for individuals with dietary restrictions or taste disorders. Scientific studies have revealed that *S. dulcificum* contains essential vitamins, amino acids, and powerful antioxidants, such as flavonoids and polyphenols, which contribute to its antioxidant, anti-inflammatory, and anticancer properties.

The pharmacological activities of *S. dulcificum* are broad and promising. Its antidiabetic potential has been demonstrated through improved insulin sensitivity and glucose regulation in animal models. Additionally, its anticonvulsant effects have been linked to enhanced inhibitory neurotransmission via interaction with GABA receptors. The plant's anti-hyperuricaemic activity, driven by inhibition of xanthine oxidase, and cholesterol-lowering effects, attributed to triterpenoids like lupeol acetate, further underscore its value in metabolic health management. Moreover, its bioactive compounds exhibit tyrosinase inhibition and anti-mutagenic properties, highlighting its utility in dermatology and cancer prevention.

In clinical nutrition, miracle fruit shows promise in enhancing appetite and taste perception in patients undergoing chemotherapy, managing diabetes-related complications, and supporting weight man-

agement. However, despite encouraging preclinical data, human trials are currently limited and vary in methodological rigor and outcomes. For *S. dulcificum* to be integrated into evidence-based medical and nutritional practices, further well-structured clinical studies are essential to validate its efficacy and safety. With continued research, standardized formulations, and regulatory evaluations, this plant could significantly contribute to personalised nutrition and integrative healthcare. Its multifaceted benefits make it a valuable resource worthy of further scientific exploration and clinical application.

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Author ORCID: 0009-0004-5061-7428

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