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Synsepalum Dulcificum: A Review

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Abstract

Synsepalum dulcificum also regarded as a miracle berry, belonging to the Sapotaceae family. It is cultivated for its mild fruits, which makes sour foods to give a sweet taste, the effect lasts for about 30 minutes. The plant is a shrub, containing red coloured fruits and localised to West Africa. They used this plant as their palm wine and also used this for certain other beverages to make it sweetened regionally. Because of its remarkable sweet potential used to make the sour foods taste sweet. Miraculin is the glycoprotein present in the plant responsible for the sweet taste. Some of the reported health benefits are anti-diabetic, effective food enhancer, taste disorder in cancer, alter the taste. The plant is known for its production of transgenic tomatoes. Ethnobotany uses of the plants includes in the treatment of male infertility, Asthma, Haemorrhoids, Anti-cancer etc. The aim of the present review was to brief the literature survey of the plant through the internet like PubMed and Google scholar for forming the platform to illustrate the ethnopharmacology of the plant, information about the traditional usage, important chemical constituents and selected pharmacological activities of the plant were gathered from available research papers to frame the review. The current review also highlights the phytochemical and pharmacological aspects of *Synsepalum dulcificum* which will have been helped in the researchers for the further qualitative research.

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INTRODUCTION

Synsepalum dulcificum also recognized as Miracle fruit, Miracle berry, and miraculous berry. Berry when eaten it makes sour food like lemons to sweet taste (Obafemi *et al.*, 2019). The effect usually lasts around half an hour, with the potency decreasing over time (Lipatova and &campolattaro, 2016). Hence there was a significant preference obtained by the cancer patients to the fruit vendors because the fruit had the property of masking the metallic taste in mouth caused by chemotherapy (Obafemi *et al.*, 2017; Kant, 2005). Miracle fruit(MF) has been considered as a possible food colorant while incorporated into carbonated sugar and water solutions due to the development of an orange-red color (Bartoshuck *et al.*, 1974). MF is very famous in Japan amongst diabetic patients and dietitians (Buckmire and Francis, 1976, 1978).

Miracle fruit (MF) plant belongs to the family Sapotaceae, indigenous to tropical West Africa (Chen *et al.*, 2006) commonly used to provide sweetness to sour palm wine by Africans (Du *et al.*, 2014a). The entire plant has medicinal uses (Inglett and Chen, 2011), as it is used in the treatment of hemorrhoids (Sanematsu *et al.*, 2016) used in the treatment of male infertility (Jeremiah

et al., 2015), and other health benefits reported are helps in the treatment of obesity, treating Dysgeusia and improves well-being (Kurihara and Beidler, 1968), Hyperuricaemia (Bepoliverbever, 2009), Hyperlipidemia (Mccurry, 2015), and as Anti-tyrosinase (Wang *et al.*, 2011).

The history behind the discovery of the plant

The Miracle Fruit crop was discovered in the 1700s by European explorers named Chevalier des Marchais traveling to West Africa (Bepoliverbever, 2009). The first mention of the fruit in the literature occurred in 1852 and was called the "miraculous berry" (Kurihara and Beidler, 1968). Once the food was eaten by West African natives and chewed the "miraculous berry" to make acidic foods taste sweet.

Pharmacognostical characters and Phytochemistry

This study showed the presence of various minerals like iron, calcium, chromium, zinc, cobalt, copper and the absence of minerals like potassium, manganese, magnesium, sodium, lead in the pulp. Various vitamins like Vitamin A, Vitamin D, Vitamin K and a high concentration of Vitamin C were analysed. Proximate analysis showed 3.26% of fat,7.75 % of protein, 18.84% of carbohydrates, 59.55% of moisture content, 4.46% of ash, 6.24 % of crude fiber were reported (Nkwocha *et al.*, 2014).

Recombinant Miraculin Synthesis

Closed Cultivation system of height 86cm, 88cm width, 86 cm length was built that is on small scale, where tomatoes were cultivated by maintaining the conditions required for the growth of transgenic tomatoes. The amount of miraculin produced in these transgenic tomatoes was 90 μg/g fruit yield and the miraculin content was stable. Whereas there was a difference in miraculin contents produced by transgenic tomatoes grown in netted greenhouse (Hirai *et al.*, 2010; Achigan-Dako *et al.*, 2015).

MF plant has lipophilic, hydrophilic phytochemicals (Du *et al.*, 2014a) and anthocyanin, flavonol pigments in leaves and berry (Buckmire and Francis, 1976; Njoku *et al.*, 2015). Miracle berry has both essential and non-essential amino acids (Njoku *et al.*, 2015). Miraculin is a glycoprotein containing 191 amino acid residues along with two glycosylated polypeptides, Asn-42 and Asn-186, cross-linked by a disulfide bond. Miraculin is 4,00,000 times sweeter than sucrose on a molar basis (Theerasilp *et al.*, 1989), which subjected for the sweet taste, the protein binds to sweetness receptors, resulting in sour-tasting foods to be perceived sweet (Tafazoli *et al.*, 2019). Miracle berries leave, and roots are rich in carbohydrate, fibers, tannins, cardiac glycosides, polyphenols, flavonoids and minerals (Osabor *et al.*, 2016).

Miraculin can be synthesized by tomatoes, strawberry, lettuce (Sun *et al.*, 2006, 2007; Sugaya *et al.*, 2008). Tomatoes host was more recommended for its high miraculin content (Yano *et al.*, 2010). Around 50 to 200mg of miraculin can be procured from 1kg of MF. Miraculin can be purified by using different solvents from polar to non-polar and vice versa (Inglett *et al.*, 1965). Miraculin degrades at high temperature (Kurihara and Beidler, 1968). Miraculin by itself is not sweet (Sun *et al.*, 2007). The berry itself has low sugar content (Vos *et al.*, 2013). Table 1 and Figure 1 shows,

Morphological Characteristics

1. Miracle fruit plant is a shrub that grows up to 5-20 feet.

2. Leaves are 5-10cm long and 2-3.7 cm wide

3. Gives 2 crops per year

4. Flowers are white in color turns to red drupe fruits of about 2-3 cm length.

5. The plant requires 3-4 years to bear fruit after growing.

6. Seeds are ovoid in shape. The seeds need around 10 days to germinate.

7. Propagation can be by stem cuttings.

Common names

1. Magic fruit

2. Miracle fruit

3. Miracle berry

4. Miraculous berry

5. Sweet berry

6. Synsepalum wood

Vernacular names

1. African - Abayunkun, Agbayun

2. Danish – Irakelbaer, Mirakelfrugt

3. German - Wunderbeere

4. Japanese- Mirakurufuruutsu

5. Russian – Magicheskijfrukt

6. Spanish - Bayamágica, Frutamaravillosa, Frutamilagros

Taxonomic classification

Botanical name: *Synsepalum dulcificum*

Kingdom: Plantae

Table 1: Ethnobotany

Part of the plant	Used by	Used in the form	Treatment	References
Leaves	South Western Nigeria	Decoction	Hemorrhoids	(Soladoye *et al.*, 2011)
Leaves	Badagry group Nigeria	Decoction	Asthma, Male infertility	(Sco et al. n.d.)
Leaves	Egun indigenous tribal group, Nigeria	Decoction	Weight loss,Anticancer, Diabetes.	(Adedeji *et al.*, 2018)

Figure 1: *Synsepalum dulcificum* at the natural habitat

Subkingdom: Tracheobionta

Division: Magnoliophyta – Flowering plants

Class: Magnoliopsida - Dicotyledons

Subclass: Dilleniidae

Order: Ebenales

Family: Sapotaceae

Genus: Synsepalum

Antioxidant activity

Phenolic content was assessed by the Folin Ciocalteau colorimetric technique with slight changes and flavonoids by aluminum chloride colorimetric report. Antioxidant activity was determined by the 2, 2-diphenyl-1-picryl-hydrazyl (DPPH) method and showed that phenolic content was 3 times more in the skin and 4 times that of pulp. More flavonoids were found to be present in skin, the free antioxidant activity of pulp, the skin was comparatively more than seeds, bound antioxidant activity was least found in pulp, followed by skin. Hence the study concluded that the presence of antioxidant activity in the skin, pulp of miracle fruit but total antioxidant activity is more in seeds by the presence of more total phenolic content and flavonoid content (Inglett and Chen, 2011; Du *et al.*, 2014b).

Improve Food Palatability for Patients Receiving Chemotherapy

The taste receptor cells in the mouth can be changed by chemotherapy drugs, this pilot study was done to know whether miraculin does better for the patients receiving chemotherapy. The study was conducted on 8 cancer patients of all cancer types and each of them was said to consume MF before meals.The effect of foods was tracked for 4 weeks.The data reported clarified improved the food taste in all the participants, 5 reported metallic taste disappeared with supplement and even the food intake in a few increased. The experimental group showed improved taste but after shifting to control group food tasted bad. This pilot study revealed that with the intake of miracle fruit supplemented all the negative tastes improved (Wilken and Satiroff, 2012).

Sweet proteins

The study aimed to identify whether MF increases sweetness and acceptance of low sugar dessert, sourfood, reduces energy intake.13 subjects were supplied with standard food each day like lemon juice popsicles (sweetened popsicles) (REG), sour/low sugar popsicles (DIET) were ingested by the subjects accordingly. Data generated showed no change in hedonic preference. The subject did not show the change in the sweetness for REG comparison MF produced lower energy intake. Thus, Miracle fruit enhanced the sweetness of low sugar dessert with reducing energy intake (Wilken and Satiroff, 2012).

Taste Sensation and Perception

The aim of this laboratory exercise was to broaden student's recognition of sweet taste receptor, neural mechanisms and to illustrate the psychophysical importance of taste perception.19 students were selected for the study. Jelly beans-sweet

taste receptor, lemon wedges-sour taste receptor, Goldfish® crackers-salty taste receptors, raw broccoli pieces-bitter taste receptor additionally grapefruit, greenapple, sour candy,lime,apple cider were used for the taste effect of miracle fruit.Students witnessed no change in the perception of salty/bitter tastes. Paired t-tests reported Goldfish® crackers bitterness rating of broccoli and saltiness did not affect after consumption of the fruit but paired t-tests showed that the apparent sweetness of every acidic food like lemon, grapefruit, lime, sour candy, cider vinegar was more after eating the fruit whereas sense of sweetness of bitter broccoli and salty Goldfish® crackers, sweet (jelly bean) flavors did not alter (Lipatova and &campolattaro, 2016).

Insulin Resistance

The lyophilized powder of MF was given through oral route for male Wister rats at the dose of 0.02,0.004,0.2 mg/kg. Fasting glucose was measured for 4 weeks. The intraperitoneal glucose tolerance test indicated a decrease in the glucose-insulin index. The tolbutamide action of reducing plasma glucose is exerted by insulin secretion. After the treatment with Miracle fruit time for loss of plasma glucose levels were reduced in the response of tolbutamide in fructose-rich chow-fed rats remarkably prolonged, hence it reports production of insulin resistance in rats delayed by the administration of MF orally (Chen *et al.*, 2006).

Anticonvulsant activity

The aqueous fraction of methanol extract of miracle berry was injected to the albino mice of dose 10ml/kg through the IP route and pentylenetetrazole maximal electro shock-induced seizures tests, strychnine induced convulsion was conducted and analysed for the anticonvulsant activity. The report generated showed aqueous fraction possesses 33.33% protection against mortality in all the 3 tests conducted, hence aqueous fraction of *Synsepalum dulcificum* is found to have anticonvulsant activity (Jeremiah *et al.*, 2015).

Anti-hyperuricemic activity

Numerous miracle fruit extracts like water, butanol, ethyl acetate, hexane fractions were assessed to find its antioxidant effects and thus found that the extracts possess the capacity in reducing uric acid also hindered xanthine oxidase activity in vitro and in monosodiumurate (MSU) treated RAW 264.7 macrophages serum uric acid levels were lowered in ICR mice by the MF butanol extracts. Hence MF butanol extract is found to have novel antihyperuricemic activity (Shi *et al.*, 2016).

Protective action

In this study methanolic and flavonoid rich leaf extracts of MF were selected for the protective effect on lead acetate induced toxicity in Wistar albino rats. Rats were divided into 9 groups,5 in each Group. where group 1 was control, only distilled water was administered, group 2 was lead-induced and 50mg of lead acetate was given, group 3 was given with 50mg/kg lead acetate and 25mg/kg of methanolic leaf extract, group 4 was given with 50mg/kg lead acetate and 50 mg/kg of methanolic leaf extract, group 5 with 80 mg/kg lead acetate and 25mg/kg of methanolic leaf extract, group 6 was given with 50 mg/kg lead acetate and 25mg/kg flavonoid-rich leaf extract, group 7 was given with 50 mg/kg lead acetate and 50 mg/kg flavonoid-rich leaf extract, group 8 was administrated with 50 mg/kg lead acetate and 80 mg/kg flavonoid-rich leaf extract, group 9 was served with 50 mg/kg lead acetate and 40mg/kg vitamin c for 2 weeks. By various histopathological analysis, biochemical analysis, hematological analysis the study concluded the presence of the protective effect of methanolic and flavonoid rich leaf extracts against lead acetate induced toxicity in Wistar albino rats.

Antidiabetic activity

This research is targeted to study the antidiabetic activity of flavonoid-rich and methanolic leaf extracts of MF in type 2 diabetic rats. Wistar albino rats were divided into 9 groups 7 in each group.Group 1 acting as a control, group 2, 3, 4,5,6,7 were administered orally with 10% fructose through water for 2 weeks, followed by administration of 40mg/kg streptozotocin. Group 2 is considered as diabetic control.Group 3 was given with 30m/kg of Methanolic leaf extract (MSD), group 4 was given with 60mg/kg of MSD. Group 5 was administered with 30mg/kg of flavonoid-rich leaf extract (FSD), group 6 with 60 mg/kg of FSD. Group 7 with 5mg/kg glibenclamide, group 8,9 has healthy animals with 60mg/kg MSD and FSD respectively. The results showed greatly reduced serum glucose levels in diabetic animals treated and MSD, FSD has antihyperglycemic activity in type 2 diabetic rats (Obafemi *et al.*, 2017).

CONCLUSIONS

Natural sweeteners are obtained from sources like plants, fruits or honey because of the low glycaemic index, natural sweeteners do not increase in blood glucose level. The body often absorbs natural sweetening agents slowly compared with regular sugar. Natural sweeteners such as honey, fruit pulps, dates, palm sugar, and others are also known to be bene-

ficial to people with diabetes. Artificial sweeteners claimed to increase the risk of cancer, blood sugar and gut health, and obesity. Hence people nowadays are preferring natural sweeteners, one such sweetener can be obtained by miracle fruit.

Present review on *Synsepalum dulcificum* supports the usage of "Miracle Fruit" to improve food palatability for patients receiving chemotherapy, and successful replacement for artificial low-calorie sweeteners. The study on taste sensation and perception and other biological activities such as antioxidant activity, anti-hyperuricemia, improvement of insulin resistance in chow-fed rats, anticonvulsant activity, protective action on lead acetate toxicity, recombinant miraculin produced by transgenic tomatoes, antidiabetic activity are noted. Still few pharmacological activities are yet to be reported therefore there is a need for further studies on *Synsepalum dulcificum*.

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Conflict of Interest

None.

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