Journal of Agricultural Engineering and Food Technology
p-ISSN: 2350-0085; e-ISSN: 2350-0263; Volume 6, Issue 2; April-June, 2019, pp. 149-154

http://www.krishisanskriti.org/Publication.html

Taste Modification Using Miracle Berry (*Synsepalum dulcificum*): A Dynamic Approach for Novel Foods

Shikha Goel[1], Ragya Kapoor[2], Kirat Khushwinder Bains[3] and Namrata S.[4]

[1]*Assistant Professor (former), Shaheed Rajguru College of Applied Sciences for Women, University of Delhi*
[2]*Masters, Food Science and Technology, Cornell University, NY*
[3]*M.Sc. Food Technology, Guru Nanak Dev University, Amritsar*
[4]*M.Sc. Food technology and management, M.O.P Vaishnav College for Women, Chennai*
E-mail: [1]shikhagoel1601@gmail.com, [2]kapoor.ragya@gmail.com,
[3]kirat2696@gmail.com, [4]namrata.srinivasan@gmail.com

Abstract—*Red berries of a tropical plant Synsepalumdulcificum, called miracle fruit or miracle berry or miraculous berry lacks taste completely, is known for its taste modifying properties. The fruit itself doesn't have much nutritional value (except for vitamin C) but encloses a unique glycoprotein called 'miraculin', has the power of modifying a disagreeable taste into a pleasant one.Miraculin binds to the taste receptors on the tongue, altering the natural flavors of foods. It not only shields the sour taste, but also makes you believe that what you are eating or drinking is actually sweet. Such an alteration of taste perception by miraculin can persist for few hours. A large segment of population is demanding for low sugar and low-calorie foods without having to compromise on the taste quality. Sugar is not regarded as an avoidable component of diet. Miraculin has dynamic potential to be used for sweetener replacement or as a taste modifier to alter the sour and/or bitter taste of food to be perceived sweet. Hence, miraculin could be introduced as a sweet fix to our palate due to its taste modifying and non-caloric attributes. Use of miracle berry or miraculin in developing novel foods for dietetics and diabetics can revolutionize health food industry. The fruit being high in vitamin C content can also prove to be a good anti-cancer supplement. It is also found to have the ability to improve insulin sensitivity, and so, canbe used as an adjuvant for treating diabetic patients with insulin resistance. This review aims to present an overview of the miracle berry and miraculin with reference to its properties, limitations, and current and potential applications in food as well as clinical industry.*

Keywords*: Miraculin, Taste modifier, Miracle berry, Sweet fix, Diabetics.*

1. INTRODUCTION

Most of the people do not consider sugar as an ingredient to be avoided. However, a fairly large section of the population is compelled to restrict or eliminate sugar specially sweets consumption to control diabetes and obesity. Thus, many alternative sweeteners have been extensively researched. In response to consumers concerns about the calorie content of sugar-sweetened foods, food companies are able to prepare products with zero calorie high potency sweeteners and hence providing the sweetness of sugar with a non calorie alternative ingredient [1].

Nonnutritive sweeteners (NNS) or artificial sweeteners, by offering the taste of sweetness without any calories, have become an important part of everyday life and are increasingly used nowadays in a variety of dietary and medicinal products [2].

There are some studies that show that NNSs are not metabolized in the body, so they are excreted out as it is and hence are considered safe for human consumption. However, the concern over the toxic aspects of 'nonmetabolized' compounds (E.g.: in case of cyclamates) still prevail [3]. Further, some studies contribute that use of NNSs over 1680mg/day may lead to an increased risk of bladder cancer in human beings [4]. Also, high consumption of these types of sweeteners lead to the development of glucose intolerance through initiation of many compositional and functional alterations in the intestinal microbiota [5].

In view of all these studies, many controversies have been raised among the general consumers over the use of artificial sweeteners. This has further led to an increase in demand of natural sweeteners.

2. MIRACLE BERRY

Miracle berry (*Synsepalumdulcificum*) has been studied as a sweetness enhancer. This berry, is a fruit of a tropical plant, *Synsepalumdulcificum*, which is an evergreen shrub that is native to tropical West Africa. The plant is commonly found growing in the wild, in fringes of virgin forests. Although, in its native environment, the plant reaches up to 20 feet in height at maturity, its main form is shrubby [6]. The plant first bears fruits after growing for approximately 2–3 years. It has a large seed that is surrounded by a thin layer of berry flesh with a faint cherry-like flavor. The plant has two varieties, the red and the yellow ripe berry varieties. The red berry is not really sweet to taste by itself but has a unique effect on the taste

buds, such that flavors of foods consumed after eating the fruit are generally modified [7].

3. MIRACULIN – THE TASTE MODIFYING PROTEIN FROM MIRACLE BERRY

A component has been identified in the fruit which could be held responsible for masking the sour taste and bringing out the sweet sensation of any generally consumed food.This effect is seen within a short period after the tongue comes in contact with the pulp of miracle fruit, consequently causing the normal food to taste pleasingly sweet [8]. Therefore, when the taste receptors on the human tongue are exposed to the miracle fruit, any sour tasting food could be made to taste sweet without the addition of any sugar or artificial sweetener.

This taste modifying principle in the miracle berry known as miraculin and it is a 191 amino acid protein composed of a single polypeptide chain having a molecular weight of 24,600kDa [9].This glycoprotein binds itself to the taste-receptors thus exhibiting the unique property of altering the sensory perception of the sour taste in foods eaten after the miracle berry. It has been found that, two histidine residues, located in exposed regions, are mainly responsible of miraculin activity. Its monomer is flavorless at all pH as well as at high concentration; the dimer form elicits its taste-modifying activity at acidic pH; a tetrameric form is also reported as active [10].

Due to this unique taste modifying property, miracle berry has great potential to be used in food as a sugar substitute in some foods or as a taste modifier to mask undesirable sour tastes in food products. However, more studies are needed to characterize and compare the sensory profile of miracle berry to other sweeteners in order to better elucidate its dynamic potential for development of novel food products.

4. NUTRITIONAL PROFILE OF MIRACLE BERRY

Since plant is not used as a food crop and only exploited for its taste-modifying effect, it makes it highly underutilized. Therefore, its nutritional profile was studied, and it was found that each miracle fruit berry contains only 1 calorie. In addition to that, it contains a sufficient amount of vitamins and in comparison with other berries and fruits, more quantity of the berry pulp may be consumed.

Also, miracle fruit berries are a great source of Vitamins C (1.33 mg/100 g), vitamin A (2.54 µg), and vitamin E (0.78 mg/100 g) and essential amino acids, particularly leucine (2.35 g/100 g protein) and followed by lysine (1.60 g/100 g protein). Leucine is unique among amino acids because it is the only amino acid that promotes protein synthesis in muscles.

The nonessential amino acids were also discovered, with glutamic acid (3.43 g/100 g protein) being the highest and glycine (0.38 g/100 g protein), the lowest. Norleucine was not detected. The values of the amino acids – isoleucine, leucine, lysine, threonine, and valine – in the miracle berry, were all above the reference values of 2.8 mg/100 g protein, 6.6 mg/100 g protein, 5.8 mg/100 g protein, 3.4 mg/ 100 g protein, and 3.5 mg/100 g protein, respectively(As prescribed by FAO/ WHO/UNU 1991). The methionine + cysteine and phenylalanine + tyrosine reference values of 2.5 mg/100 g protein and 6.3 mg/100 g protein, respectively, were all exceeded in the miracle berry [11].

This information is helpful in understanding the full potential of the fruit and also to increase the acceptability among consumers, so that the utilization of the fruit is improved. The amino acids profile in the pulp of miracle berry have high biological values, therefore it could contribute to the commercial potential of the berry as it could be processed to get useful by products.

5. DYNAMIC APPLICATIONS OF MIRACLE BERRY

Other than the ability to trick the receptors present in the tongue, the berry is also known to have many health benefits and applications. Some of the benefits and useful applications of this berry are as follows:

5.1. Development as a health food

Hyperuricemia, which is associated with inflammation, is caused as result of increased uric acid production or impaired renal uric acid excretion. In most patients with primary gout, ineffective renal excretion is the cause behind hyperuricemia. Hyperuricemia, through inflammasome activation, is mediated by ROS and cytokine generation. Furthermore, MSU (Monosodium- urate) is known to activate the inflammasome, thereby triggering oxidative stress and inflammation in monocytes or macrophages [12]. Presently, there are a number of anti-gout medications are available which includes non-steroidal anti-inflammatory drugs. These agents are most often used a first-line treatment for acute gout. However, their use is questioned when adverse reactions including gastrointestinal toxicity, renal toxicity, and gastrointestinal bleeding are seen.Therefore, it becomes necessary to identify better anti-gout arthritis drugs.

Antioxidants are known to show shielding effects by blocking MSU-induced inflammasome activation. Some studies have shown that miracle fruit has antioxidant properties and it was found that miracle fruit powder (MFP) has more total phenolic compounds, flavonoids, and anthocyanins than miracle fruit water extract (MFWE). Therefore, miracle fruit powder has a greater free radical scavenging activity as compared to MFWE. Furthermore, both MFP and MFWE inhibited xanthine oxidase activity [12].

Currently, MFP, MFWE, and various fractions from miracle fruit have antioxidant effects and can reduce hyperuricemia. Also, it has been found that butanol extract from miracle fruit may prove to be an effective therapy for acute gouty arthritis

and therefore, this could be developed in the form of a new health food [12]. Other than this, it is noteworthy that all parts of this plant have medicinal importance [13]. Some studies aimed atinvestigating the antioxidant properties of phenolics and flavonoids in the skin, pulp, and seeds of miracle fruit and suggested it as a good source of antioxidants for functional food applications [14]. Some scientists studied the total phenolic content and DPPH radical scavenging activities of extracts from the skin, pulp, and seed of miracle fruit, while some researched the phenolic and flavonoid content and antioxidant activity of miracle fruit flesh and seed methanol extracts, which could be used as an antioxidant-rich fruit to promote human health [15-16].

It has also been verified that polyphenols in seed extracts of miracle fruit were powerful antioxidants [17]. Wang et al [18] studied the antioxidant and anti-tyrosinase effects of constituents of the stems of miracle fruit, suggesting the potential applications in food supplementation and medical cosmetology. Chen et al [19] reported the inhibitory effects of aqueous extracts of miracle fruit leaves on oxidative and mutation damage and attributed them partially to its active phenolic components.

5.2. As anti-cancer supplement

Taste dysfunction in patients living with cancer is a complex problem and is associated with alterations in taste. Taste and Smell Alterations (TSAs) are very common and usually take place as a result of the some disease or its treatment. During a disease or some treatment, there are changes observed in body such as altered cell structure, receptor surface changes, interruption in neural coding or a decrease in the number of normal cells[20]. All these changes often lead to TSAs.

Anti-neurotic drugs and radiation treatment given to cancer patients can affect the tongue receptors due to which individual can easily lose the ability to taste. Cancer patients whilst going through radiation treatment feel metallic taste and this is the reason behind their health degeneration because of their incapacity to taste food. [21] Taste changes in patients with cancer undergoing chemotherapy are common but understudied. Abnormal or bad tastes as a result of treatment can result in negative outcomes that affect nutrition, response to treatment, and quality of life. Good nutrition has a direct relationship to immune health. Chemotherapy suppresses the immune system, making individuals more prone to infection, the number one killer of patients of cancer [22].

Miracle fruit supplementation can lead to improved nutritional intake which would further lead to more positive outcomes among the patients. Miraculin, binds to taste receptors in an acidic environment to produce a sweet perception of the foods consumed, thus improving the palatability of foods by masking some unpleasant tastes. Patients undergoing chemotherapy or radiotherapy, who consumed miracle fruit supplements before regular meals were found to have an increased food intake because of positive taste changes produced by miraculin [23].

Given the responses from the study participants, healthcare providers should consider offering a Miracle Fruit supplement to patients experiencing taste changes as a result of chemotherapy.

5.3. As protein supplement

The fruit pulp can be safely exploited as food or an ingredient in food processing as a considerable amount of carbohydrate, lipid and protein was estimated during the proximate evaluation of the *Synsepalumdulcificum* berry pulp. The results of some studies conducted showed a moisture content of 45.12%, protein content of 2.48% and a carbohydrate content of 48.84%.The anti-nutrients content include Tannin 2.90 ± 0.64mg/100g, phytate 5.21 ± 0.92 mg/100g, glycosidic cyanide 0.03 ± 0.00mg/100g, steroid 1.56±0.03 mg/100g and oxalate 11.04 ± 0.29%. The anti-nutritional levels were all found to be within the recommended safety limits. Some phytochemicals like flavonoids, resins and steroids were also identified, which were all below their respective lethal doses [24].

Also, a study shows that *S.dulcificum* pulp contains 8.055% tryptophan, 1.35% phenylalanine, 0.7% isoleucine, 0.5% tyrosine, 1.05% methionine, 0.4% proline, 0.69% valine, 1.1% threonine, 0.4% histidine, 0.5% alanine, 1.02% glutamine, 1.6% glutamic acid, 0.7% glycine, 0.3% serine, 1% arginine, 0.1% aspartic acid, 1.23% asparagine, 0.6% lysine, 0.6% and leucine. A study of the amino acid profile infers that the fruit pulp contains both essential as well as non-essential amino acids that too in considerable concentration. This make the fruit unique and exceptional as a raw material or an ingredient for the production of therapeutically agents and diet supplements. In one of the study, it was found that the fruit contains sufficient amount of essential amino acids conveying valuable nutritious potential of this fruit [25].

5.4. As an anti- diabetic ingredient

It has been shown that the berry and its leaves have hypoglycemic effects on the blood glucose level of albino rats. This effect is primarily attributed to the presence of some natural compounds that can be found in miracle berry fruits and leaves. These compounds are basically reported to be antioxidant-rich phytochemicals, such as phenolic, flavonoids and the glycoprotein, miraculin [26]. Also, it has been found that the leavesof the plant are rich in protein, fiber, polysaccharides, and moisture along with different phytochemicals such as tannin, cardiac glycosides, polyphenols, saponin and also flavonoids [27-28].

Many natural compounds, mainly plants-derived drugs, have the ability to treat diabetes mellitus through the anti-oxidative mechanism as found in experimental animal and human trial studies [29]. Numerous studies infer that that herbal constituents such as those found in miracle berry fruit and leaf

extracts have shown to exhibit considerable free radical scavenging activity in the biological systems. However, among all the phytochemicals present, saponins and flavonoids are primarily attributed for antidiabetic action [30-32].

Flavonoids, being the potentantioxidants and free radical scavengers, have been shown to protect cell membranes from damage. Studies show that flavonoids have anti-diabetic, anti-inflammatory, anti-microbial and anticancer activities as well [33]. Also, Flavonoid compounds are found to be responsible for improvement and stabilization of the secretion of insulin from pancreatic beta cells [34]. Saponins, on the other hand, are known to reduce cholesterol at the gut. They may also aid in lessening the metabolic burden that are should be in the liver and are also known to inhibit the structure dependent biological activities [35]. On the other hand, the glycoprotein, miraculin, which is responsible for modifying sour taste as sweet in the mouth, has the ability to improve insulin sensitivity.

Therefore, it can be used in the development of health food for treating diabetic patients with insulin resistance [36].

5.5. Anti-microbial agent

Studies conducted on the essential oil obtained from the leaves of *S. dulcificum* showed that it possess antibacterial activity against tested bacteria. It also showed antitumor activity against human cancer cell line. Total flavonoids present in the leaf extract can enhance mice liver glycogen and antitumoral activity. The *Synsepalumdulcificum* leaf extracts can improve heartburn, indigestion, poorappetite and other symptoms, such as atherosclerosis, high blood pressure anddiabetes. It also can enhance liver function and immunity [37-38].

5.6. As potential food colorants

On extraction and purification of the red anthocyanin pigments of Miracle fruit, it was found that it could be used as an effective food colorants by concentrating it.

This pigment provided an orange red solution when added to carbonated water and other carbonated sugar solutions. Its stability was found to be comparable to that of anthocyanins from other sources. At pH 1.0, in water, the ratio of the extinction coefficient of the pigment preparation compared to that of FD&C Red No. 2 was 2.03. At pH 2.8 and 3.0 the ratios were 1.2 and 0.85, respectively.

Therefore, anthocyanin and flavanol pigments found in the miracle fruit could have potential to be used as natural food colorants [39].

6. SAFETY ASPECT OF THE MIRACLE FRUIT

Presently, there is not enough scientific information to determine the appropriate dosage for the consumption of miracle fruits. However, it is found that the appropriate dose of miracle fruit depends on several factors such as the user's age, health, and several other conditions.

In general, there is no harm concerned to the consumption of glycoproteins and they are known to be nontoxic. Also, glycoproteins are readily metabolized and excreted by the body. However, one study shows that excessive quantities of miracle fruit concentrate i.e. about 3,000 times ordinary human consumption, were proven to cause absolutely no ill effects [40-41].

7. LIMITATIONS

Sour taste is perceived sweet for a period of time after ingestion of miraculin, irrespective of whether a person likes it or not. For example: the sour taste of the green apple is desirable to many people. However, after ingestion of miraculin, the apple may no longer be desirable. Thus, miraculin affects the overall flavor of a particular food which may not always be desirable. Another problem with the miracle fruit is related to its availability. As the fruit is only able to grow under specific conditions, it is not profound in mature and therefore not readily available to the consumers. Also, the fruit is very delicate. Miraculin, being a glycoprotein is thermolabile. Furthermore, it is stable only in the pH range of 3-12 [42]. pH lower than 3 or higher than 14 leads to the proteolytic modification in the protein backbone of miraculin which leads to the loss in activity [43]. Another limitation is that the miracle berry is perishable, i.e. it has a short shelf life, and is spoiled in about two days [44]. But, to overcome this deficit, potential preservation techniques are being studied, one of which includes application of a coating of the polysaccharide chitosan on the surface of the fruit in order to extend its shelf life. [45]. Studies suggest that the miracle berry can be stored at -20° F for about three to four months before use without any concern [46].

8. REGULATORY ISSUES

The use of miracle berry has been well recognized by Japan’s Ministry of Health and Welfare. However miraculin has not been yet legally recognized as a food additive by the U.S. Food and Drug Administration (FDA) and the European Union. Therefore, it still faces regulatory impedances. But unlike the FDA, the U.S. Department of Agriculture (USDA) does not have any restrictions on growing, selling and eating miracle berry [47].

In the late 1980s, a company in U.S established large scale plantations of *Synsepalumdulcificum* in the West Indies and Brazil in order to manufacture a tablet from the miracle fruit extract. It also contained hydrolyzed cereal solids. The company also used to design special diets and menus incorporating miracle fruit extract as an aid to reduce caloric intake. Despite extensive toxicological evaluation and substantial investment, the extract did not meet with approval of the FDA and because of this the company was liquidated

and all products of *Synsepalumdulcificum* were finally denied food additive status.

9. CONCLUSION

The miracle berry and miraculin, hold a huge potential to be used in the development of foods in order to improve health and control various diseases.Miracle berry could be used to design products to meet the demand for patients with diseases related to sugar or patients undergoing radio or chemo therapy as this berry effects your taste, or it could be used to meet the market demands for products with low calorific value and low level of artificial sweeteners. Also, research could be conducted on development of products not just using the fruit itself but their stems, leaves, roots or because their own components in fruit. Analyzing the current scenario of usage and safety of berries of *Synsepalumdulcificum,* authors intended to fill the gaps by identifying its future prospects to be used as a perfect element for the consumers having a sweet tooth including the alarming diabetic population worldwide. Since, miracle berry has not been studied extensively in terms of its structure, safety and potential uses, a carefully planned approach would be needed which would direct toward its introduction as a product of great potential which meets the needs of food and pharmaceutical industries, in the most natural ways.

REFERENCES

[1] S. Goel, "Formulating low calorie dairy foods: challenges and opportunities. ," *Advances in Food Science and Technology, National Conference Proceedings. SRCASW, New Delhi*, pp. 64–70, 2016.

[2] A. Sharma, Amarnath, S, Thulasimani, M, and Ramaswamy, S, "Artificial sweeteners as a sugar substitute: Are they really safe? ," *Indian Journal of Pharmacology*, vol. 48(3), p. 237, 2016.

[3] C. R. Whitehouse, J. Boullata, and L. A. Mccauley, "The Potential Toxicity of Artificial Sweeteners," *AAOHN Journal*, vol. 56, no. 6, pp. 251–259, 2008.

[4] M. R. Weihrauch and V. Diehl, "Artificial sweeteners—do they bear a carcinogenic risk?," *Annals of Oncology*, vol. 15, no. 10, pp. 1460–1465, 2004.

[5] M. Boothby, "Faculty of 1000 evaluation for Artificial sweeteners induce glucose intolerance by altering the gut microbiota.," *F1000 - Post-publication peer review of the biomedical literature*, 2014.

[6] I.K. Opeke, "Effects of Certain Growth Substances on the Growth and Morphogenesis of Immature Embryos of Capsella in Culture," *Plant Physiology*, vol. 39, no. 4, pp. 691–699, 1984.

[7] S. Issanchou and S. Nicklaus, "Measuring consumers' perceptions of sweet taste," *Optimising Sweet Taste in Foods*, pp. 97–131, 2006.

[8] S. J. Sijtsema, M. J. Reinders, S. Hiller, and M. D. Guardia, "Fruit and snack consumption related to sweet, sour and salty taste preferences.," *British Food Journal*,vol. 114(7), pp. 1032–1046, 2012.

[9] J. Rodrigues, R. Andrade, S. Bastos, S. Coelho and A. Pinheiro, "Miracle fruit: An alternative sugar substitute in sour beverages", *Appetite*, vol. 107, pp. 645-653, 2016. Available: 10.1016/j.appet.2016.09.014.

[10] A. Paladino, S. Costantini, G. Colonna and A. Facchiano, "Molecular modelling of miraculin: Structural analyses and functional hypotheses", *Biochemical and Biophysical Research Communications*, vol. 367, no. 1, pp. 26-32, 2008. Available: 10.1016/j.bbrc.2007.12.102.

[11] N. Njoku, C. Ubbaonu, S. Alagbaoso, C. Eluchie and M. Umelo, "Amino acid profile and oxidizable vitamin content ofSynsepalumdulcificumberry (miracle fruit) pulp", *Food Science & Nutrition*, vol. 3, no. 3, pp. 252-256, 2015. Available: 10.1002/fsn3.213.

[12] Y. Shi et al., "Miracle Fruit (Synsepalumdulcificum) Exhibits as a Novel Anti-Hyperuricaemia Agent", *Molecules*, vol. 21, no. 2, p. 140, 2016. Available: 10.3390/molecules21020140.

[13] E. Achigan-Dako, D. Tchokponhoué, S. N'Danikou, J. Gebauer and R. Vodouhè, "Current knowledge and breeding perspectives for the miracle plant Synsepalumdulcificum (Schum. et Thonn.) Daniell", *Genetic Resources and Crop Evolution*, vol. 62, no. 3, pp. 465-476, 2015. Available: 10.1007/s10722-015-0225-7.

[14] G. Inglett and D. Chen, "Contents of Phenolics and Flavonoids and Antioxidant Activities in Skin, Pulp, and Seeds of Miracle Fruit", *Journal of Food Science*, vol. 76, no. 3, pp. C479-C482, 2011. Available: 10.1111/j.1750-3841.2011.02106.x.

[15] Z. He, J. Tan, S. Abbasiliasi, O. Lai, Y. Tam and A. Ariff, "Phytochemicals, nutritionals and antioxidant properties of miracle fruit Synsepalumdulcificum", *Industrial Crops and Products*, vol. 86, pp. 87-94, 2016. Available: 10.1016/j.indcrop.2016.03.032.

[16] L. Du, Y. Shen, X. Zhang, W. Prinyawiwatkul and Z. Xu, "Antioxidant-rich phytochemicals in miracle berry (Synsepalumdulcificum) and antioxidant activity of its extracts", *Food Chemistry*, vol. 153, pp. 279-284, 2014. Available: 10.1016/j.foodchem.2013.12.072.

[17] F. Cheng, S. Huang, M. Lin and J. Lai, "Polyphenol Measurement and Antioxidant Activity of Miracle Fruit", *International Journal of Chemical Engineering and Applications*, vol. 6, no. 3, pp. 211-214, 2015. Available: 10.7763/ijcea.2015.v6.483.

[18] H. Wang et al., "Bioconstituents from stems of SynsepalumdulcificumDaniell (Sapotaceae) inhibit human melanoma proliferation, reduce mushroom tyrosinase activity and have antioxidant properties", *Journal of the Taiwan Institute of Chemical Engineers*, vol. 42, no. 2, pp. 204-211, 2011. Available: 10.1016/j.jtice.2010.05.008.

[19] T. Chen, Z. Kang, M. Yen, M. Huang and B. Wang, "Inhibitory effect of aqueous extracts from Miracle Fruit leaves on mutation and oxidative damage", *Food Chemistry*, vol. 169, pp. 411-416, 2015. Available: 10.1016/j.foodchem.2014.08.022.

[20] L. McLaughlin and S. Mahon, "Understanding Taste Dysfunction in Patients With Cancer", *Clinical Journal of Oncology Nursing*, vol. 16, no. 2, pp. 171-178, 2012. Available: 10.1188/12.cjon.171-178.

[21] I. IJpma, R. Renken, G. ter Horst and A. Reyners, "Metallic taste in cancer patients treated with chemotherapy", *Cancer Treatment Reviews*, vol. 41, no. 2, pp. 179-186, 2015. Available: 10.1016/j.ctrv.2014.11.006.

[22] T. Tarver, "Cancer Facts & Figures 2012. American Cancer Society (ACS)", *Journal of Consumer Health On the Internet*, vol. 16, no. 3, pp. 366-367, 2012. Available: 10.1080/15398285.2012.701177 [Accessed 1 April 2019].

[23] T. Thorne, K. Olson and W. Wismer, "A state-of-the-art review of the management and treatment of taste and smell alterations in adult oncology patients", *Supportive Care in Cancer*, vol. 23,

no. 9, pp. 2843-2851, 2015. Available: 10.1007/s00520-015-2827-1.

[24] N. Chinelo C., N. Obi U and E. Florence N, "Phytochemical, Antinutrient and Amino Acid Composition of Synsepalumdulcificum Pulp", *IOSR Journal of Pharmacy and Biological Sciences*, vol. 9, no. 2, pp. 25-29, 2014. Available: 10.9790/3008-09252529.

[25] Suree, N., Surat, K. and Akekachai, N. (2004). Phytate and Fiber Content in Thai Fruits commonly consumed by diabetic patients. *J. Med. Assoc.* Thai 87(12): 1444-1446.

[26] L. Du, Y. Shen, X. Zhang, W. Prinyawiwatkul and Z. Xu, "Antioxidant-rich phytochemicals in miracle berry (Synsepalumdulcificum) and antioxidant activity of its extracts", *Food Chemistry*, vol. 153, pp. 279-284, 2014. Available: 10.1016/j.foodchem.2013.12.072.

[27] C. Ragasa, K. Cornelio, T. Bauca, S. Chua and C. Shen, "Chemical Constituents of the Leaves, Stems, and Fruits of Synsepalumdulcificum", *Chemistry of Natural Compounds*, vol. 51, no. 3, pp. 588-589, 2015. Available: 10.1007/s10600-015-1356-y.

[28] V. Osabor, R. Etiuma and M. Ntinya, "Chemical Profile of Leaves and Roots of Miracle Fruit (Synsepalumdulcificum)", *American Chemical Science Journal*, vol. 12, no. 1, pp. 1-8, 2016. Available: 10.9734/acsj/2016/20456.

[29] L. Qi, E. Liu, C. Chu, Y. Peng, H. Cai and P. Li, "Anti-Diabetic Agents from Natural Products — An Update from 2004 to 2009", *Current Topics in Medicinal Chemistry*, vol. 10, no. 4, pp. 434-457, 2010. Available: 10.2174/156802610790980620.

[30] C Han; Q Hui; Y Wang. Nat Products Res, 2008, 22:11, 12-19.

[31] M.Misra, "Flavonoids and phenolic acids: Role and biochemical activity in plants and human", *Journal of Medicinal Plants Research*, vol. 5, no. 31, 2009. Available: 10.5897/jmpr11.1404.

[32] A. Muthuraman, S. Krishan, P. Perumal and P. Anaswara, "Therapeutic potency of saponin rich aqueous extract of Scopariadulcis L. in alloxan induced diabetes in rats", *AYU (An International Quarterly Journal of Research in Ayurveda)*, vol. 35, no. 2, p. 211, 2014. Available: 10.4103/0974-8520.146261.

[33] C Han; Q Hui; Y Wang. Nat Products Res, 2008, 22:11, 12-19.

[34] S. Mohan and L. Nandhakumar, "Role of various flavonoids: Hypotheses on novel approach to treat diabetes", *Journal of Medical Hypotheses and Ideas*, vol. 8, no. 1, pp. 1-6, 2014. Available: 10.1016/j.jmhi.2013.06.001.

[35] S. Patel, D. Santani, M. Shah and V. Patel, "Anti-hyperglycemic and Anti-hyperlipidemic Effects of BryoniaLaciniosa Seed Extract and its Saponin Fraction in Streptozotocin-induced Diabetes in Rats", *Journal of Young Pharmacists*, vol. 4, no. 3, pp. 171-176, 2012. Available: 10.4103/0975-1483.100024.

[36] M. Kanauchi, S. Yamano, K. Kanauchi and Y. Saito, "Homeostasis Model Assessment of Insulin Resistance, Quantitative Insulin Sensitivity Check Index, and Oral Glucose Insulin Sensitivity Index in Nonobese, Nondiabetic Subjects with High-Normal Blood Pressure", *The Journal of Clinical Endocrinology & Metabolism*, vol. 88, no. 7, pp. 3444-3446, 2003. Available: 10.1210/jc.2002-021641.

[37] C. Chen, I. Liu and J. Cheng, "Improvement of insulin resistance by miracle fruit (Synsepalumdulcificum) in fructose-rich chow-fed rats", *Phytotherapy Research*, vol. 20, no. 11, pp. 987-992, 2006. Available: 10.1002/ptr.1919.

[38] Lu Sheng Lou (2013). Hainan Normal University : Chemical Analysis of Nutritional Components and Essential Oil from *Synsepalumdulcificum* Leaf and Its Extraction and Puriifcation Process of Total Flavonoids and Pharmacological Activities Assessment

[39] T. Lim, "Synsepalumdulcificum", *Edible Medicinal And Non-Medicinal Plants*, pp. 146-150, 2012. Available: 10.1007/978-94-007-5628-1 26 [Accessed 1 April 2019].

[40] "Miracle Fruit", *Hawley's Condensed Chemical Dictionary*, 2007. Available: 10.1002/9780470114735.hawley11022 [Accessed 1 April 2019].

[41] I. Morton, "Cancer testing technology and saccharin", *Food Policy*, vol. 3, no. 3, pp. 233-234, 1978. Available: 10.1016/0306-9192(78)90031-3.

[42] G. Inglett and J. May, "Tropical plants with unusual taste properties", *Economic Botany*, vol. 22, no. 4, pp. 326-331, 1968. Available: 10.1007/bf02908127.

[43] E. Giroux and R. Henkin, "Purification and some properties of miraculin, a glycoprotein from Synsepalumdulcificum which provokes sweetness and blocks sourness", *Journal of Agricultural and Food Chemistry*, vol. 22, no. 4, pp. 595-601, 1974. Available: 10.1021/jf60194a033.

[44] M. Witty, "New technologies for taste modifying proteins", *Trends in Food Science & Technology*, vol. 9, no. 7, pp. 275-280, 1998. Available: 10.1016/s0924-2244(98)00048-x.

[45] C. Liu, C. He, T. Xie, Y. Yang and T. Liang, "Research on Preservation of SynsepalumDulcificum by Coatings", *Advanced Materials Research*, vol. 239-242, pp. 2158-2162, 2011. Available: 10.4028/www.scientific.net/amr.239-242.2158.

[46] V. Danilova and G. Hellekant, "Elucidating coding of taste qualities with the taste modifier miraculin in the common marmoset", *Brain Research Bulletin*, vol. 68, no. 5, pp. 315-321, 2006. Available: 10.1016/j.brainresbull.2005.09.008.

[47] T. Sugaya, M. Yano, H. Sun, T. Hirai and H. Ezura, "Transgenic strawberry expressing the taste-modifying protein miraculin", *Plant Biotechnology*, vol. 25, no. 4, pp. 329-333, 2008. Available: 10.5511/plantbiotechnology.25.329.