

# An Overview On Diabetic Profile Of Various Syzygium Species

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## Abstract

Diabetes mellitus which is characterised by hyperglycemia, is one of the most serious metabolic conditions, extending alarming common proportions. It maybe on account of the defects in insulin operation, or secretion, or two together. The worldwide predominance of diabetes is supposed at 425 million public in 2017, and anticipated to encourage in activity 629 heap by 2045 due to an growing current of sick behaviors, physical inaction, and corpulence. Syzygium is a florescent plant belonging to the myrtle (Myrtaceae) family and is called after the Greek word “conjugated,” alluding to the paired leaves and branches. There are 1200 to 1800 species of Syzygium and most of them are plants and evergreen shrubs. The largest diversification of these plants is found in Malaysia and north-eastern Australia. The Syzygium species noted to have antidiabetic potential, and examined herein, are *S. cordata*, *S. densiflorum*, *S. paniculatum* and *S. zeylanicum*.

**Keywords :** Diabetes mellitus, Myrtaceae, *S. cordata*, *S. densiflorum*, *S. paniculatum* and *S. zeylanicum*.

## INTRODUCTION

Ayurvedic remedy is still commonly practiced within India with an estimated 85% of Indians still using raw plant preparations for the treatment of broad variety of infections and ailments.[1] Diabetes mellitus (DM) is commonest endocrine disorder that influences more than 100 million people global (6% population). It is caused by inadequacy or ineffective management of insulin by pancreas which results in increase or decrease in concentrations of glucose in the blood. It is found to damage many of body systems especially blood vessels, eyes, kidney, heart and nerves. [2] Diabetes mellitus has been classified into two types i.e. insulin dependent diabetes mellitus (IDDM, Type I) and non-insulin dependent diabetes mellitus (NIDDM, Type II). Type I diabetes is an autoimmune disease characterized by a local inflammatory response in and around islets that is observed by selective devastation of insulin secreting cells whereas Type II diabetes is from peripheral insulin resistance and impaired insulin secretion.[3] The genus *Syzygium* (Family Myrtaceae) is the largest type of flowering plants all over, comprising approximately 1200–1800 species The genus has a extensive range, occurring naturally in subtropical and tropical regions of Africa and Madagascar, Asia, and during the whole of Oceania and the Pacific region. The greatest diversification occurs in Australia and Southeast Asia. It is believed that many species in this area have not yet been correctly categorized taxonomically, and it is likely that new species will be categorized in the future.[4] Most *Syzygium* species range from medium to enormous evergreen trees and bushes, many of which have a history of usage in traditional medicinal systems. This review epitomizes recent research on the diabetic potential of few *Syzygium* species such as *Syzygium cordatum*, *Syzygium densiflorum*, *Syzygium paniculatum* and *Syzygium zeylanicum* and too highlights future areas of research on the medicinal activities of *Syzygium* species

## Syzygiumcordatum

The antibacterial activity of *Syzygiumcordatum* fruits and seeds against bacteria causing GIT infection was studied. The harvested fruits were separated into fruit pulp and seed s, dried and extracted with methanol using soxhlet extraction. The extracts were phytochemically screened and micro dilution assay was used to evaluate antibacterial activity of fruit- pulp and seed extracts against the selected GIT infecting bacteria. The crude extracts of fruit pulp and seed exhibited the percentage yield of 10 and 6, respectively. The extract showed the presence of phytochemicals with the total phenolic content of  $21.4 \pm 1.4 \mu\text{g/ml}$  for seed extract and  $16.4 \pm 1.8 \mu\text{g/ml}$  for fruit pulp extract. The extracts showed the presence of phytochemicals extract. Antimicrobial activity of pulp extract exhibited the lowest minimum inhibitory concentration of  $3.13 \mu\text{g/ml}$  against some bacterial strain which is responsible for GIT infection.<sup>[5]</sup> Essential oil was extracted from dried leaves of *S. cordatum* by hydrodistillation. The components were identified by gas chromatography (GC/FID) and gas chromatography coupled with mass spectrometry (GC/MS). Sixty compounds representing 79% of the *S. cordatum* oil were identified. The main constituents were 6,10,14-trimethylpentadecane-2-one (14.4%), 2,3-butanediol diacetate (13.3%), n-hexadeconic acid (7.2%), ethane, 2-chloro-1,-bis(2-chloroethoxy) (6.2%), Isopentyloxyethyl acetate (5.03%), methane and bis (2-chloroethoxy) (3.8%).<sup>[6]</sup> Oral glucose tolerance tests (OGGT) were conducted in non-diabetic and STZ-diabetic rats using orally administered glucose (1.4 g /100 g body weight) followed by either the leaf extract (6 mg /100 g body weight) or subcutaneous (s.c) injection of metformin (50 mg /100 g). Weekly plasma glucose and terminal hepatic glycogen concentrations were recorded in control STZ-diabetic rats and diabetic rats orally treated with the leaf extract once every third day for 4 weeks. Administration of the leaf extract decreased plasma glucose from  $7.7 \pm 0.9 \text{ mmol/l}$  to  $3.7 \pm 0.6 \text{ mmol/l}$  (n = 6), and  $21.1 \pm 2.2 \text{ mmol/l}$  to  $12.5 \pm 1.8 \text{ mmol/l}$  (n = 7) by 2.5 h in non-diabetic and STZ-diabetic rats, respectively. *Syzygiumcordatum* leaf extract contains compounds that could be effective in mild diabetes mellitus or in cases of glucose tolerance impairment.<sup>[7]</sup>

## Syzygiumdensiflorum

*Syzygiumdensiflorum* is a tree species categorized as a vulnerable species in the IUCN red list of threatened species. The leaf extracts of *Syzygiumstocksii* and *Syzygiumdensiflorum* were screened for their antimicrobial activity by disc diffusion method. Ethyl acetate extract of these plants were studied using six bacterial strains (*Pseudomonas aeruginosa*, *Proteus vulgaris*, *Klebsiella pneumonia*, *Escherichia coli*, *Staphylococcus aureus* and *Bacillus subtilis*) and three fungal species (*Aspergillusniger*, *Alternariaalternata* and *Penciliumchrysogenum*). The extracts showed higher activity against pathogenic bacteria whereas the fungal species were more resistant. MICs and MLCs were also determined for the bacterial species.<sup>[8]</sup> *S. densiflorum* dried fruits which were subjected to successive extraction with n-hexane, ethyl acetate, and ethanol using a Soxhlet extractor. Further, preliminary phytochemical screening was carried out with a series of tests. Preliminary phytochemical estimation confirmed the presence of alkaloids, flavonoids, sterols, terpenoids, anthocyanin, phenols, carbohydrates, fixed oils, and fats in fruits of *S. densiflorum*. Ethyl acetate and n-hexane extracts showed less free radical scavenging and  $\alpha$ -amylase inhibition activity than ethanol extract. IC<sub>50</sub> values of ethanol extracts for 2,2- diphenyl-1-picrylhydrazyl radical, superoxide radical, hydroxyl radical, lipid peroxidation, and  $\alpha$ -amylase inhibition assays were found to be 0.01, 0.16, 0.66, 0.46, and 0.46 mg/mL respectively. Ethanol extract of *S. densiflorum* fruits showed higher activity with statistical significance vs. ethyl acetate and n-hexane extracts.<sup>[9]</sup> The fresh leaf samples of *S. densiflorum* which were collected from a wild tree and essential oil fraction was extracted by hydrodistillation process and the compounds were identified using GC-MS analysis. A total of 84 compounds were identified among which  $\beta$ -maaliene (17.43 %), isodene (12.46 %),  $\alpha$ -gurjunene (10.44 %),  $\beta$ -elemene (9.9 %) and  $\beta$ -vatirenene (8.50 %) were major constituents.<sup>[10]</sup> Phytochemical analysis of the leaves of *Syzygiumcaryophyllatum* and *Syzygiumdensiflorum* revealed the existence of flavonoids, tannins, glycosides, terpenoids and protein. Methanol extract of *S. caryophyllatum* exhibited highest DPPH radical scavenging activity and ferric reducing power followed by ethyl acetate and hexane extracts (81.97, 78.69, 34.34 % and 0.978, 0.916 & 0.691 %). Ethyl acetate extract of *S. densiflorum* exhibited highest DPPH radical scavenging activity and ferric reducing power (98.76, 87.36 & 43.39) and (1.560, 1.037 & 0.604).<sup>[11]</sup> Mohan et al planned to explore the antidiabetic and antioxidant (in vivo and in vitro) potential of leaves. The ethanolic extract significantly and dose-dependently reduced the hyperglycaemic condition and also decreased the elevated levels of cholesterol (CHL) and triglyceride (TGL). The extract significantly decreased TBARS and SOD levels but was insignificant on CAT levels. The extract showed an IC<sub>50</sub> value of  $53.56 \pm 0.20$  and  $79.00 \pm 0.12$  in DDPH and nitric oxide method

respectively.<sup>[12]</sup>Two different compounds were isolated from ethanolic extract of *S. densiflorum* fruits and purified using HPLC. The structures of the compounds were elucidated on the basis of their <sup>1</sup>H NMR, <sup>13</sup>C NMR, <sup>1</sup>H-<sup>1</sup>H COSY, HMBC, HRESIMS, and FT-IR data. Further, the chemical reactivity of the compounds was analyzed by density functional theory calculations and its therapeutic role in diabetic management was examined by comparing the structure of isolated compounds with previously reported bioactive compounds. Of the two compounds ((6,6 & 1-kestopentaose (1) and 6-(hydroxymethyl)-3-[3,4,5-trihydroxy-6-[(3,4,5-trihydroxyoxan-2-yl)oxymethyl]oxan-2-yl]oxyoxane-2,4,5-triol)(2)).  $\beta$ -glucosidase,  $\beta$ -galactosidase,  $\alpha$ -glucosidase and  $\beta$ -amylase inhibition activity of the compounds were predicted by structure activity relationship.<sup>[13]</sup>

## Syzygiumpaniculatum

Lilly pilly (LP) fruit (*Syzygiumpaniculatum*Gaertn.) is widely grown in eastern Australia and has been used as food by indigenous Australians. However, there is limited information on its bioactivity. The LP extract was water-soluble and possessed a total phenolic content of 96 mg of gallic acid equivalents (GAE)/g, flavonoid levels of 52 mg catechin equivalents (CAE)/g, proanthocyanidin levels of 29 mg CAE/g. Several phenolic compounds such as gallic acid, chlorogenic acid, catechin and epicatechin were identified in the LP extract with levels of 0.39, 2.35, 0.47 and 2.9 mg/g, respectively. The LP extract (200  $\mu$ g/mL) significantly reduced the viability of MiaPaCa-2 and ASPC-1 pancreatic cancer cells to levels comparable to that of the chemotherapeutic agent gemcitabine.<sup>[14]</sup>The ethnopharmacological significance of the fruits of *Syzygiumpaniculatum*Gaertn (Magenta Cherry) is widely recognized in the Indian traditional medicine system to treat various disorders, such as diabetes, hyperlipidaemia, hypertension, and cardiovascular problems. The supplementation of the aqueous extract of *S. paniculatum* fruit (AESPF) on liver function; the molecular effects on the expression of the protein of insulin receptor (IR) and insulin receptor substrate 1 (IRS-1) in high-fat diet-induced hepatic insulin resistance in the rat model. The supplementation of AESPF with a dose of 100 mg/kg bw significantly reduced bodyweight, blood sugar, insulin, lipid profiles, and liver enzymes. Hepatic insulin resistance was improved with a reduced level of IR and IRS-1 to protein levels. HFD alters the sensitivity of hepatocytes to insulin due to the down-regulation of insulin receptor proteins.<sup>[15]</sup>The *Syzygiumpaniculatum*extract with significant antihyperglycemic activity evaluated for antihyperlipidemic, antioxidative stress, antioxidant activity and also for insulin resistance by OGTT. Histopathological examination of pancreas sections carried by hematoxylin and eosin stain. The findings confirm that *S. paniculatum* possesses potential antihyperglycemic, antihyperlipidemic, antioxidative stress and antioxidant activity. The histological changes also coincide with its potential on insulin secretion, glycemic control, lipid metabolisms, oxidative stress and antioxidant enzyme activities.<sup>[16]</sup>The hydrodistilled volatile oil (VO) from the aerial parts of *Syzygiumpaniculatum* was characterised by GC-MS and Kovat's index, while the antioxidant property was investigated using spectrophotometric techniques. Antioxidant capacities of the aerial parts VOs range from 0.12 to 0.93 mg/mL in scavenging 2, 2-diphenyl-1-picrylhydrazyl radicals (DPPH). Overall, 75 and 67 compounds were identified from the summer and winter VOs, respectively. The main compounds were  $\alpha$ -pinene (33.13%), n-hexadecanoic acid (19.14%), limonene (14.26%), farnesol (14.21%),  $\beta$ -ocimene (13.04%), citronellol (12.67%), linoleic acid (11.50%), octahydro1,4-dimethyl azulene (11.57%), citral (9.91%), phytol (5.07%), linolenic acid (4.85%) and thymol (2.23%).<sup>[17]</sup>

## Syzygiumzeylanicum

The leaves of *Syzygiumzeylanicum* were extracted using hexane, ethanol and water; and evaluated for its phytochemicals, total phenolic content and antioxidant activities. The highest yield of extract was from the ethanol (64.52  $\pm$  0.05%), followed by water (17.65  $\pm$  0.84%) and hexane (4.61  $\pm$  0.56%). Phytochemical screening on the leaves extracts showed the presence of flavonoids, saponins, tannins, alkaloids, terpenoids and steroids. Total phenolic content was highest in the extract of water (0.24  $\pm$  0.02  $\mu$ g/mL GAE), followed by ethanol (0.19  $\pm$  0.01  $\mu$ g/mL GAE) and hexane (0.02  $\pm$  0.001  $\mu$ g/mL GAE). Both free radical scavenging assays of ethanol and water extracts demonstrated stronger antioxidant activities in which the IC<sub>50</sub> values were 79.48  $\mu$ g/mL and 75.98  $\mu$ g/mL respectively, than the commercial butylated hydroxyl toluene which was 197.60  $\mu$ g/mL. A strong antioxidant capacity in both water (751.75  $\pm$  12.36 mg/mL) and ethanol 741.64  $\pm$  6.96 mg/mL extracts were also shown in the FRAP method.<sup>[18]</sup>Successive solvent extraction of shade dried leaves were carried out using solvents of increasing polarity and all the extracts were subjected to estimation of total phenolics and the extract containing

maximum of phenolics were subjected to anti-inflammatory studies. Preliminary phytochemical analysis was done on all extracts. Ethyl acetate extract and aqueous extract found to contain maximum of phenolics by Folin-ciocalteu method. Anti-oxidant activity study by using nitric oxide scavenging activity showed the ethyl acetate extract has maximum activity (IC<sub>50</sub> = 125 mcg/ ml). The evaluation of anti-inflammatory activity by inhibition of Cyclooxygenase (70.71 and 78.79% at 100 and 500 mcg/ ml), 5-lipoxygenase (65.95 and 70.26% at 100 and 500 mcg/ ml) and by determination of protein denaturation (64.43 and 76.92% at 100 and 250 mcg/ml) showed the ethyl acetate extract possess good anti-inflammatory activity.<sup>[19]</sup> The major fatty acids were cis-oleic acid (43.47±0.62 %) and linoleic acid (31.14±0.35%). Total monounsaturated fatty acids in the sample was 44.21%. Omega-6, omega-7 and omega-9 fatty acids were detected. The polyunsaturated fatty acids in the fruits were linoleic acid (31.14±0.35 %) and arachidonic acid (0.15±0.22 %), whereas 24.51 % of the total fatty acids were saturated. The ratio of unsaturated to saturated fatty acids was approximately 3:1. The order of abundance of fatty acids, in some of the healthiest oils, viz. olive, canola, peanut oils is, Oleic acid>Linoleic acid>Palmitic acid>Stearic acid and the same order was observed in the present study.<sup>[20]</sup> In the microscopic studies, the *Syzygium zeylanicum* leaf was found to be dorsiventral and the chief characters of transverse section includes single plano convex and collateral vascular bundle, which consists of several short 3 celled xylem rows and a thin layer of phloem on the lower end and mesophyll consists of 2 layer of thin, vertically oblong, compact palisade cells and lower part of 5 or 6 much lobed spongy parenchyma. Chief characters of powder include thick, wavy epidermal cells, the cells being much lobed; stomata appear in deep pits and calcium oxalate druses seen scattered in surface view of the lamina. Leaf constants were analysed. Physicochemical parameters such as moisture content, chlorophyll estimation, ash values and extractive values were evaluated.<sup>[21]</sup> This water extract was further fractionated by column chromatography with various concentrations of methanol solutions. Among the 6 resultant fractions, the fraction developed with 20% methanol exhibited the most potent antioxidant activity. The one peak among the three major HPLC peaks in this fraction was isolated and purified using a preparative HPLC. The structure of a pure compound was elucidated as a novel macrocyclic ellagitannin using a <sup>1</sup>H/<sup>13</sup>C NMR and a high-resolution electrospray ionization mass spectrometer. This newly isolated compound, which was named zeylaniin A, exhibited potent antioxidant activities in the assays of DPPH, oxygen radical absorbance capacity, and malonadehyde/gas chromatography.<sup>[22]</sup> The fatty acid analysis of the seeds and pulp was carried out separately by gas chromatography. The wild fruits were nutritionally rich in comparison to the cultivated fruits. The percentage of unsaturated fatty acid was found to be higher than saturated fatty acid. The major fatty acids present were oleic acid, linoleic acid and palmitic acid. The fruit methanol extract of the *S. caryophyllatum* was independent of gram reaction inhibiting the growth of both gram-positive and gram-negative bacteria. The minimum inhibitory values ranged from 8 to 10 mg/ml. The calorific value of both the fruits increased upon fermentation, and the alcohol content was 4 and 5% in *S. zeylanicum* and *S. caryophyllatum*, respectively.<sup>[23]</sup>

## CONCLUSION

In conclusion, very few species have been investigated for the phytochemical compounds from the *Syzygium* genus. The common curative effect that was often stated from the *Syzygium* genus is its antidiabetic activity. Evidence from current literature highlights the potential of seed, leaf, and fruit extracts from various *Syzygium* species in improving level of glucose in blood and insulin regulation. This promising antidiabetic effect is combined by its common non-toxic nature at moderate doses, bringing focus to a desirable role in clinical remedy for type 1 or 2 diabetes. Future work emphasizes a need to isolate and characterize various bioactive compounds derived from *Syzygium* species into antidiabetic agents, and their effects should be validated in vivo and in clinical studies.

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