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Various Phytochemical Constituents and Their Potential Pharmacological Activities of Plants of the Genus Syzygium

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ABSTRACT

Syzygium genus contain several plant species which spread across the world, most of them are having diverse biological activity among which some are reported, and some are not. So, Syzygium genus is a subject of interest to researchers. All Syzygium species are actively studied to find new activity or better dose at which they can be used. This review focuses on various species of genus Syzygium, their phytochemical constituents and their pharmacological activities. Syzygium aromaticum (Clove), Syzygium samarangense (Java apple), Syzygium anisatum (Aniseed tree), Syzygium caryophyllatum (Lilly pilly), Syzygium aqeum (Water apple), Syzygium jambos (Mountain Apple), Syzygium cumini (Java plum), Syzygium australe (Brush cherry), Syzygium luehmannii (Riberry) etc., were mentioned in this review article. Biological activities like anti-diabetic, antioxidant, anti-bacterial, anti-inflammatory, platelet inhibition, hepato-protective were found among plants of Syzygium species. Our present review mentions all the activities, anti-diabetic in detail. We tried to gather cumulative data as per our knowledge, hope it is useful to anyone who is studying or researching about Syzygium. Syzygium cumini is given importance in this review article as it has diverse uses and most of the parts of the plant have their own applications in medical field.

Keywords: Syzygium, Anti-diabetic, Syzygium cumini, Myrtaceae.

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INTRODUCTION

Syzygium is the genus of woody flowering plants [(1)], which belongs to the family myrtle, Myrtaceae. The genus comprises about 1200 species. [(1)] Many species formerly grouped as Eugenia are now included in the genus *Syzygium.* [(2)]

Plants of the genus *Syzygium* are used to treat a wide range of illnesses mainly diabetes. In some species the medicinally useful part is leaves while in some it may be root or fruit or seed or bark.

In the genus *Syzygium* plant products of some species are consumed as food, like fruits of *Syzygium* cumini and *Syzygium* jambolanum, *Syzygium* australe and *Syzygium* leuhmani, in *Syzygium* aromaticum bud is used as spice for its flavoring properties, anti-tooth decay and anti-halitosis. As Indians and other Asians know these uses it is widely used in Indian and Asian cuisine, so has economic importance. Except fruits and buds other parts weren't much used except for medicinal purposes.

Syzygium cumini, *Syzygium* aromaticum and *Syzygium* aqeum were discussed in detail in this review article regarding their anti-diabetic activities.

Taxonomical details :[(3)]

Kingdom	**Plantae**
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Clade	Rosids
Order	Myrtales
Family	Myrtaceae
genus	*Syzygium*

Various plant species of genus *Syzygium*, their phytochemical constituents and respective pharmacological activities

S no	Plant species	Plant part	Phytochemical constituents	Pharmacological activity	References
1	*Syzygium* aromaticum	Bud and stem [4]	Acetyl eugenol [4]	platelet inhibitor [5]	T.J. Zachariah et al., 2006[4] K.C. Srivastava KC et al., 1991[5]
			Eugenol [4]	anti-inflammatory and local anesthetic [6]	T.J. Zachariah et al., 2006[4] Kenneth Markowitz et al., 1992[6]
2	*Syzygium* samarangense	Leaves [7]	5'-dimethyl-6'-methoxychalcone 1, 2',4'-Dihydroxy-3', flavanone 5-O-methyl-4'-desmethoxymatteucinol 2 and 2'4'-dihydroxy-6'-methoxy-3'-methylchalcone 3[7]	Hypoglycemic [7]	Resurreccion-Magno et al., 2005[7]
		Pulp and seeds of the fruits [8]	Hyperin [8]	Anti-hyperglycemic [9]	Mario J. Simirgiotis et al., 2008[8] Neeraj Verma et al., 2013[9]
			Myricitrin [8] (Myricetin-3-O-α-rhamnoside) [10]	Antioxidant [10], anti-inflammatory [10]	Mario J. Simirgiotis et al., 2008[8] Domitrović R et al., 2015[10]
			Quercitrin (3-rhamnosylquercetin) [11]	Anti-inflammatory [11]	Mònica Comalada et al., 2005[11]
3	*Syzygium* anisatum	Leaves [12]	Anethole [12]	(Anti-inflammatory, anti-carcinogenic and chemopreventive, anti-diabetic, immunomodulatory, neuroprotein, or anti-thrombotic) [13]. Anti-microbial [12], [14]	Yasmina Sultanbawa 2016[12] Aprotosoaie A.C et al., 2016[13] Krystal Bryant et al., 2016[14]
4	*Syzygium* caryophyllatum	Root [15]	(flavanoids, tanins and alkaloids) [15] Flavanoids [16]	Ani-inflammatory [15]	SN Heendeniya et al., 2018[15] Sasikumar V et al., 2015[16]

		Leaves [17]	phenol, flavonoids and tannins [18]	Anti-microbial [17] Antioxidant [18]	Annadurai G et al., 2012[17] Stalin N 2018[18]
				Anti-diabetic [19]	H P T Wathsara et al., 2020[19]
5	*Syzygium* aqeum	Leaves [20]	(epigallocatechin, epigallocatechin gallate, vescalagin, castalagin, and samarangenins A and B) [21]	(Antioxidant, Hepatoprotective, Painkilling and Anti-inflammatory) [20]	Mansour Sobeh et al., 2018[20] Nonaka, G et al., 1992[21]
6	*Syzygium* jambos	bark and leaves [22]	(polyphenols, anthraquinones, tannins, and steroids) [22]	Anti-bacterial [22]	E. N. Wamba et al., 2018[22]
7	*Syzygium* alternifolium	Seeds [23]	Cinnamic acid [23]	Antihyperglycemic [23]	Ramesh Babu Kasetti et al., 2012[23]
8	*Syzygium* cumini	Seeds [24]	(alkaloid, jambosine, and glycoside jambolin or antimellin) [24]	diabetes mellitus [25]	Muniappan Ayyanar et al., 2012[24] Shrikant Baslingappa Swami et al., 2012[25]
		Bark [26]	Gallic acid, umbelliferone [26]	Anti-diabetic [26]	Perera PR et al., 2017[26]
9	*Syzygium* australe	Fruit [27]	Ascorbic acid, benzoic acid, flavanols, flavanones [28]	Anti-microbial [27] Antioxidant [28]	C. Sautrona et al., 2014[27] Goyal MR et al., 2018[28]
10	*Syzygium* leuhmannii	Leaves [29]	Phenols, flavonoids and tannins [18]	Anti-microbial [29]	I.E. Cock 2012[29] Stalin N 2018[18]
		Fruit [27]	vitamins (β-carotene, vitamins C and E), flavonoids and other polyphenolic compounds [18]	Anti-microbial [27]	C. Sautrona et al., 2014[27] Stalin N 2018[18]

***SYZYGIUM* CUMINI**:

Synonyms:

Syzygium cumini is also referred as *Syzygium* jambolanum and Eugenia cumini. Common names are Jambul, Black Plum, Java Plum, Indian Blackberry, Jamblang, Jamun etc. [25]

Habitat:

These trees are found growing throughout Asia, Eastern Africa, South America, Madagascar and have also in Florida and Hawaii in the United States of America. [30] In India S. Cumini is widely grown and its fruits are widely consumed for its anti-diabetic activity and also as natural food and for making jam etc.,

Taxonomical details: [3]

Kingdom	**Plantae**
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Clade	Rosids
Order	Myrtales
Family	Myrtaceae
Genus	*Syzygium*
Species	S. cumini

Pharmacological uses:

Cumini is known to have various pharmacological activities against diabetes mellitus [31], [25], [32], [33], inflammation [25], [31], ulcers [25] and diarrhea [25], [34] and preclinical studies have also shown it to possess chemopreventive, [35] radioprotective and antineoplastic [35] properties. The plant contains anthocyanins, glucoside, isoquercetin, kaempferol, ellagic acid, and myricetin in large amounts.

The cumini is used to relieve stomach pain, carminative and diuretic. Jamun

vinegar is used to reduce enlargement of spleen, diarrhea, and people with urine retention problems. [3]

Phytochemicals and their respective pharmacological activities

S.no	Plant parts	Phytochemical constituents	Pharmacological use	Reference
1	Bark[25], [34]	tannins and carbohydrates [25], [34]	Dysentery [25], [34]	S. Swami et al., 2012[25] Rekha. N et al., 2008[34]
2	Fruit (pulp) [35]	Anthocyanins- cyaniding, malvidin, peonidin, petunidin, and delphinidin and other phenolics [35]	Anti-carcinogenic [35]	Shavez Khan et al., 2019[35]
			cough, diabetes, dysentery, inflammation & ringworm[25], [31]	K. Reynertson et al., 2005[31] S. Swami et al., 2012[25]
		anthocyanins, tannins and flavanol [36]	Antimicrobial and antioxidant [36]	A. Gordon et al., 2011[36]
		flavonoids, phenolics, carotenoids and vitamins [37]	antioxidant [37]	J. Kubola et al., 2011[37]
3	Seed [25], [32]	Jamboline [25], [32]	Antidiabetic [25], [32]	S. Swami et al., 2012[25] A. Ratsimamanga et al., 1973[32]
		Ellagitannins [25],[33] (corilagin, 3,6-hexa hydroxyl diphenoyl glucose its isomer 4,6-hexahydroxy diphenoyl glucose, 1- galloylglucose, 3-galloylglucose, gallic acid, and ellagic acid)	Anti-diabetic [25], [33]	S. Swami et al., 2012[25] Helmstadter 2008[33]
		alkaloid, jambosine, glycoside jambolin or antimellin [38]	Anti-diabetic [38]	P. Prince et al., 1998[38]
		Glucoside, Jamboline and Ellagic acid [25], [39]	Biomarker (check the conversion of starch into sugar in case of excess production of glucose) [25], [39]	S. Swami et al., 2012[25] J. Giri et al., 1985[39]
		triterpenoids, saponins and tannins [40]	anti-inflammatory [25]	S. Swami et al., 2012[25] Kumar et al., 2010[40]
		ellagitannins, flavonols, and phenolic acids [35], [38]	chemopreventive effects [35], antioxidant [38]	Mohammad Shavez Khan et al., 2019[35] P. Prince et al., 1998[38]
4	fruit seeds and pulp	Anthocyanins- (pulp cyaniding, malvidin, peonidin, petunidin, and delphinidin and other phenolics [33], [41]	delaying diabetic complications including neuropathy and cataracts [33], [41]	Helmstadter 2008[33] H. Sagrawat 2006[41]
5	leaves	Tannin, limeonene and dipentene, sesquiterpene, azulenic sesquiterpene	Hypoglycemic [42]	D. C. Damasceno et al., 2002[42]
			radioprotective effects [43]	G. Jagetia et al., 2004[43]

Phytochemicals of jamun with reported chemopreventive effects:

Oleanolic acid, Ellagic acid, Gallic acid, Quercetin, Myricetin, Kaempferol, Betulinic acid, β-sitosterol, Delphinidin. [25]

Phytochemicals of Jamun with reported radioprotective activities: Oleanolic acid, Quercetin, Gallic acid, Ellagic acid. [25]

Anti-diabetic activity of *Syzygium* cumini:

Fruit:

Syzygium cumini fruit is known to exhibit anti-diabetic activities upon alloxan-induced diabetes rats [38], in a dose dependent manner.

Administration of 100 and 200 mg of aqueous extract of *Syzygium* cumini fruit mash per kilogram of diabetic rat body weight, eventually decreased the blood glucose level. which shows that the fruit extract is anti-diabetic. Treatment with *Syzygium* cumini increased body mass, indicating prevention of muscle wasting. [25]

Leaf: [42]

Syzygium cumini leaf extract exhibited anti-diabetic action in diabetic rats. [42]

Bark: [44]

As we know that *Syzygium* cumini bark contain alkaloids, glycosides, tannin and carbohydrate [25], [34] etc., the bark possesses biological activities like dysentery [25], [34] and anti-diabetic [44]. Tripathi AK, Kohli S. 2014, conducted the following experiment to explore anti-diabetic activity of *Syzygium* cumini bark.

Dose selection based on acute oral toxicity study (300-5,000 mg/kg body weight) as per OECD guidelines. Diabetes is induced to rats by a single dose of STZ at 50 mg/kg body weight intraperitoneally. The impact of *Syzygium* cumini bark extracts (500 mg/kg) on post-meal blood glucose level was determined in fasted diabetic and normal rats. Blood glucose levels were measured at 0 min, 30 min, and 90 min after the glucose administration in the OGTT study. The cumini bark extracts were administered orally at a dose of 500 mg/kg for 21 days in case of chronic study. Glibenclamide (2.5 mg/kg) was used as a standard treatment drug.

Administration of *Syzygium* cumini extracts 30 min before oral glucose administration significantly decreased ($p<0.001$) the rise in levels of postprandial blood glucose in treated rats in comparison with control rats but less significant than glibenclamide treated diabetic rats. Continuous oral treatment of STZ-induced diabetic with various extracts of *Syzygium* cumini for at least 3 weeks resulted in significant reductions in fasting blood glucose levels compared with diabetic controls. The ethanol and aqueous extracts of cumini bark were most active.

Seeds:

The seed powder of *Syzygium* cumini is reported to have hypoglycemic action in streptozotocin induced diabetic rats. [45, 46]

Anti-inflammatory activity of *Syzygium* cumini seeds: [40]

Following experiment was conducted by Kumar, Ayanagounder et al 2010.

Preparation of extracts

The S. cumini fruits were washed well and seeds were separated from pulp. Seeds were washed with distilled water to remove the traces of pulp on them and were dried at room temperature and coarsely powdered. To remove lipids the powder was extracted with hexane. The extract is then filtered. Extraction of the residue is done with methanol and ethyl acetate by cold percolation method. The percentage yields in ethyl acetate was 1.81% and in methanol 10.36%. The phytochemical screening shown the presence of triterpenoids, saponins and tannins. [40]

Animals

Wistar rats of either sex weighing 160-180 g were selected for experimental study. They were fed with commercial pelleted rats chow and had free access to water. Drug for the experimental study Extracts and the standard drugs were administered as suspension in water with 1% sodium carboxy methyl cellulose (SCMC) as suspending agent. [40]

Anti-inflammatory activity

The animals either sex was divided into six groups each composed of six animals.

Group I – Control animals were given 1% SCMC 10 ml/kg p.o.

Group II – Animals received ethyl acetate extract of cumini seed at the dose of 200mg/kg p.o.

Group III – Animals received ethyl acetate extract of cumini seed at the dose of 400 mg/kg p.o.

Group IV – Animals received methanolic extract of cumini seed at the dose of 200mg/kg p.o.

Group V – Animals received methanolic extract of cumini seed at the dose of 400mg/kg p.o.

Group VI- Animals received standard Diclofenac sodium 5 mg/kg, p.o.

Paw oedema was induced injecting 0.1 ml of 1% carrageenan in physiological saline into the left paw of each rat. The extracts (Ethyl acetate and Methanol) of S. cumini were administered orally 30 min prior to carrageenan administration. The paw volume was measured at intervals of 60 min, 120 min, 180 min and 240 min by using a plethysmograph. The percentage inhibition of paw volume in drug treated group was compared with the carrageenan treated control group (Group- I). Diclofenac sodium (5 mg / kg / p.o.) was used as standard drug. In this study, the anti-inflammatory activity of the ethyl acetate extract and methanolic extracts of S. cumini seed has been established. The extracts did inhibit the carrageenan-induced rat paw oedema, a test for anti-

inflammatory agents acting by inhibiting the mediators of acute inflammation. Carrageenan induced inflammation is useful in detecting oral anti-inflammatory agents. Oedema formation due to carrageenan in the rat paw is a diphasic event. At initial phase the release of histamine and serotonin occurs. The extracts of S. cumini seed possessed anti-inflammatory activity when tested at doses of 200 and 400 mg/kg. The methanolic extract at a dose of 400 mg/kg showed high anti-inflammatory activity at 4 h, where it caused 62.6% inhibition, as compared to that of 5 mg/kg of diclofenac sodium.

***SYZYGIUM* AROMATICUM**:

Cloves are the pink flowering bud of a form evergreen tree (Eugenia aromatica), which are dried until brown and used for medicinal and spicing purposes. [47]

Taxonomical classification: [3]

Kingdom	**Plantae**
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Clade	Rosids
Order	Myrtales
Family	Myrtaceae
Genus	*Syzygium*
Species	S. aromaticum [3]

Phytochemicals present: [48]

Phenolic molecules	hidroxibenzoic acids, flavonoids, hidroxiphenyl propens, hidroxicinamic acids, and eugenol
Gallic acid derivatives	hidrolizable tannins
Flavonoids	quercetin and kaempferol
Phenolic acids	ferulic, caffeic, ellagic, and salicylic acids.

Flower buds contain up to 18% of essential oil which consists of eugenol, eugenol acetate and β-cariofileno. [48]

Pharmacological uses:

Analgesic, antioxidant, anticancer, antiseptic, anti-depressant, antispasmodic, anti-inflammatory, antiviral, antifungal, and antibacterial activity of eugenol against several pathogenic bacteria including methicillin-resistant Staphylococcus epidermidis and S. aureus. [43] In tropical Asia cloves have been used to treat diverse infections like Malaria, Cholera and Tuberculosis, as well as Scabies. In America it is traditionally used to treat worms, viruses, candida, various bacterial and protozoan infections. [47]

Phytochemicals present in *Syzygium* aromaticum and their respective pharmacological activities

S. No	Phytochemical	Pharmacological activity	References
1	Eugeniin	antiviral efficacy [49,50]	Cortés-Rojas et al., 2014[49] Hussein, G et al., 2000 [50]
2	Carvacrol and eugenol	fungicidal	Velluti et al., [51] Manohar, V et al., 2004[52] Tampieri, M.P et al., 2005[53]
3	Eugenol	anti-depressant	Tao, G et al., 2005[54]
4	carvacrol and thymol, cinnamaldehyde and eugenol	Ani-bacterial	Pei, R.S et al., 2009[55]
5	cinnamaldehyde	Ani-bacterial	Amanda A et al., 2019[56]

Anti-diabetic activity of *Syzygium* aromaticum: [57]

According to a study conducted by Shukri R et al 2010 the following conclusions and results were drawn. Clove oil was known to reduce diabetes in streptozotocin-induced diabetic rats. This study is to evaluate the protective effects of cloves (*Syzygium* aromaticum) in chronic hyperglycemia. The cloves (of 100 mg total eugenol per kg body weight/day) was orally given to streptozotocin-induced diabetic male Sprague-Dawley rats. Fasting blood glucose levels, organ tissue physical and biochemical markers, were monitored. Dietary intake of cloves decreased tissue damage, protect lens and decrease cardiac muscle damage, and to a lesser extent in the liver but not the kidneys. The cloves treatment significantly reduced blood sugar and lipid peroxidation in streptozotocin-induced diabetic rats by improving the antioxidant enzyme levels. Cloves decrease hyperglycemia-induced oxidative tissue damage and cataract formation in the eye lens. This study shows the in vivo antioxidative organ protective effects of clove in diabetics.

***SYZYGIUM* AQUEUM**

Syzygium aqueum is widely grown in India, its fruits are edible and widely consumed.

Taxonomic classification: [3], [54]

Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Clade	Rosids
Order	Myrtales
Family	Myrtaceae
Genus	*Syzygium*
Species	S. aqueum [54]

Phytochemicals present:

Biologically active compounds have been isolated from the plant, among them, epigallocatechin, epigallocatechin gallate, vescalagin, castalagin, and samarangenins A and B. [21]

Biological activity:

Antioxidant, hepatoprotective, anti-inflammatory, anti-nociceptive, analgesic activity.

Phytoconstituents and biological activities of *Syzygium* aqeum

S.no	Phytoconstituents	Biological activity	Reference
1	Six flavonoid compounds, 4-hydroxybenzaldehyde, myricetin-3-O-rhamnoside, europetin-3-O-rhamnoside, phloretin, myrigalone-G and myrigalone-B [58]	antihyperglycemic activity [58]	T Manaharan et al., 2012[58]
	(epigallocatechin, epigallocatechin gallate, vescalagin, castalagin, and samarangenins A and B) [21]	(Antioxidant, Hepatoprotective, Painkilling and Anti-inflammatory) [20]	Mansour Sobeh et al., 2018[20] Nonaka, G et al., 1992[21]
2	Terpenoids: γ-terpinene [59]	antioxidant activity [59]	Tehrani, M et al., 2011[59]
3	Epigallocatechin [61]	Blood anticoagulation and antiplatelet activity [61]	Chen XQ et al., 2013[61]

Anti-inflammatory activity: [20]

The following is an experiment conducted by Mansour sobeh et al 2018.

The capacity of the extract to inhibit lipoxygenase was determined using a lipoxygenase inhibitor screening assay kit. The ability of the extract to inhibit ovine COX-1 and COX-2 was determined by using an enzyme immunoassay (EIA) kit according to the manufacturer's instruction and reported studies. The data are given as IC50 value, which is the concentration causing 50% enzyme inhibition (IC50). Furthermore, the COX-2 selectivity index (SI values) which is defined as IC50 (COX-1)/IC50 (COX-2) was calculated and compared to that of celecoxib, indomethacin, and diclofenac which were used as standards.

Carrageenan-induced hind-paw edema: [20]

Carrageenan solution (1% in 0.9% NaCl, 0.1 mL) was injected in right paw to induce edema in rats. 1 h earlier, the vehicle, S. aqueum extract (300 mg/kg, p.o.) or diclofenac (10 mg/kg) were given orally according to their groups. The paw thickness (mm) was measured before and after the carrageenan injection at hourly intervals for 6 hours and then at 24 hours. The overall anti-inflammatory effect during the whole period (0–24 h) was estimated by calculating the area under changes in paw thickness-time curve.

Inhibition effect of the extract on LOX, COX-1, and COX-2 enzymes. [20]

	IC50 (mg/mL)		IC50 (mg/mL)	
Treatment	LOX	COX-1	COX-2	SI
S. aqueum extract	2.54 ± 0.19		0.12 ± 0.005	59.3
Celecoxib	-	15.1 ± 0.72	0.049 ± 0.002	308.2
Diclofenac	2.11 ± 0.14	3.8 ± 0.17	0.84 ± 0.04	4.5
Indomethacin	-	0.041 ± 0.001	0.51 ± 0.02	0.08
Zileuton	3.51 ± 0.21	-	-	-

SI is COX selectivity index which is defined as IC50 (COX-1)/IC50 (COX-2).

***SYZYGIUM* CARYOPHYLLATUM:** [17]

The following is a study conducted by Annadurai G et al 2012.

Antimicrobial activity of ethyl acetate extract of S. caryophyllatum was tested with different concentrations (100 to 1000 μg/disk) that have produced a maximum zone of inhibition against Staphylococcus aureus and minimum zone of inhibition against Enterobacter faecalis and antifungal activity effective against Alternaria alternata. The zone of inhibition increased on increasing the concentration of the extract for all the strains

***SYZYGIUM* ALTERNIFOLIUM:** [23]

The following study is done by Kasetti RB et al 2012.

Cinnamic acid is a component with antihyperglycemic activity. A detailed study was undertaken to elucidate its mode of antidiabetic action by giving fraction C – cinnamic acid (50 mg/kg b.w) orally, once a day for 30 days in STZ induced diabetic rats. The altered enzyme activities of carbohydrate metabolism in liver and kidney of diabetic rats were significantly ($p < 0.01$) got back to near normal levels by the administration of fraction C. Fraction C lowered blood glucose as expected, immediately following treatment, it led to glibenclamide-like modulatory effects on enzyme activities related to glucose homeostasis after 30 days treatment, indicating that cinnamic acid may prove useful in diabetes management**.**

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