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Review article

A review on pharmacological activity of *syzygium cumini* extracts using different solvent and their effective doses

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ABSTRACT

Plants and their extracts have immense potential for the management and treatment of disease. The phyto-medicines used for treatment are not only cheap and affordable but are also purportedly safe as hyper sensitive reactions are rarely encountered with the use of these agents. The *Syzygium cumini* (Myrtaceae) is a popular traditional medicinal plant in India. This plant exhibiting tremendous pharmacological effect in different experimental works. To summarize all the pharmacological effect and their effective doses in diseased conditions this work is done. Different journals especially electronic journals are searched for collecting the data. In this review we concluded that this plant is highly beneficial for the treatment of disease and for the prevention of disease like diabetes, inflammation, hyperglycaemia and CNS related diseases. However, there is a need for scientific validation, standardization and safety evaluation of plants of the traditional medicine before these could be recommended for treatment of the disease in human.

Keywords: *Syzygium cumini,* Diabetes, Antioxidant, Effective dose.

INTRODUCTION

Nature always stands as a golden mark to exemplify the outstanding phenomena of symbiosis. In the western world, as the people are becoming aware of the potency and side effect of synthetic drugs, there is an increasing interest in the natural product remedies with a basic approach towards the nature. *Syzygium cumini* Linn (family Myrtaceae), commonly known as Jamun, jaman, duhat in Hindi and black plum, black plum tree, Indian blackberry, jambolan, jambolan-plum, Java plum, Malabar plum, Portuguese plum in English. S. cumini is one of the most widely distributed trees of India, occurring in the major forest groups except in the very arid regions. It is present in both moist and dry situations, occurring in the tropical wet evergreen forests, tropical semi-evergreen forests, tropical moist deciduous forests, littoral and swamp, tropical dry deciduous, tropical dry evergreen, subtropical broadleaved hills, and subtropical pine forests. The tree favors moist, damp or marshy situations, where it tends to form gregarious crops. It tolerates prolonged flooding and once established, it can tolerate drought. In dry sites, it generally confines itself to the vicinity of watercourses. It can grow on shallow, rocky soils provided the rainfall is sufficient. In the Himalayan valleys, it ascends to about 1200 m and in the Nigrils to 1800 m. *Syzygium cumini* is the Native of India, Malaysia, Myanmar, Philippines, Sri Lanka, Thailand, Algeria, Antigua, Barbuda, Australia, Bahamas, Barbados, Colombia, Cuba, Dominica, Dominican Republic, Ghana, Grenada, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Indonesia, Jamaica, Kenya, Martinique, Mexico, Montserrat, Nepal, Netherlands Antilles, Nicaragua, Panama, South Africa, St Kitts and Nevis, St Lucia, St Vincent and the Grenadines, Sudan, Tanzania, Trinidad and Tobago, Uganda, United States of America, Virgin Islands (US), Zambia and Zimbabwe [1].

Scientific Classification (*Syzygium cumini*)

Kingdom	Plantae – Plantes, Planta, Vegetal, Plants
Subkingdom	Viridaeplantae – Green Plants
Infrakingdom	Streptophyta – Land Plants

Division	Tracheophyta – Vascular Plants
Subdivison	Spermetophytina – Seed Plants
Infradivision	Angiospermae – Flowering Plants
Class	Magnliopsida
Superorder	Rosanae
Order	Myrtales
Family	Myrtaceae - Myrtles
Genus	Syzygium
Speciecs	Syzygium Cumini (L.)Skeels – Java Plum

Botanical Description

Evergreen tree to 25 m (80 ft) tall, with young stems grayish white and lower bark coarse and discolored. Leaves opposite, simple, entire, elliptic to broadly oblong, smooth, glossy, somewhat leathery, 5-10 cm (2-5 in) long, short pointed at tips; petioles to 3 cm (1.2 in) long; leaf midrib prominent, yellowish; blades with many lateral veins closely parallel. Flowers white to pinkish, about 1 cm (0.5 in) across, in branched clusters at stem tips; calyx cuplike; 4 petals, fused into a cap; many stamens. Fruit an ovoid, 1-seeded berry to 2 cm (0.8 in) long, dark purplish red, shiny, with white to lavender flesh.

Chief Chemical Constituents of *Syzygium Cumini* (Skeels)

The stem bark is rich in eugenin and fatty acid ester. It also contains quercetin kaempferol, bergenins, flavianoids tannins pentacyclic triterpenoid betulinic acid, ester of epi-friedelanol, Friedelin and a plant sterol B-sitosterol is found in almost all part of plant gallic acid, ellagic acid, resin, myricetin . phytostrols, Betulinic acid is a naturally occurring triterpenoid, which has demonstrated selective cytotoxicity against a number of specific tumor and active against a verity of infectious agent like HIV, malaria , immunomoduatory and the inflammatory action. It has much beneficial pharmacological activity like anti-inflammatory and lowering blood cholesterol. The presence of gallo- and ellagi –tannins may be responsible for the astringent property of stem bark Acetone extract of the bark contain partially methylated derivatives of ellagic acid i.e. 3,3'-di-O-methyl ellagic acid and 3,3', 4-tri-O-methyl ellagic acid. Alcoholic extraction of tannins results into their extensive degradation into simple phenolic compounds. The Roots are rich in flavanoids glycosides and isorhaminetin-3-rutinoside, The essential oils isolated from the freshly collected leaf stem, seed, fruits contain α - Pinene, camphene, β -Pinene, myrcene, Ocimene, γ -T erpinene, terpinoline, bornyl acetate , α copaene, β-caryophyllene, α –Humuline, γ-cedinene and δ-cadinene· trance-ocimene,cis- ocimene, β-myrcene, α- tripineol, β-caryophyllene, , α –humuline, β-selinene, calacorene, α -muurolole, , α –santalol, cis-farnesol: lauric ,myrisitic,palmitic,stearic,oleic,linoleic, malvalic,sterculic,and vernolic acid unsaponifiable matter of the seed fat was also chemically investigated. The plant leaves contain an essential oil with pleasant odour. The oil contains terpenes, 1- limonene and dipentene, sesquiterpenes of cadalane type, and sesquiterpenes of azulene type. This essential oil is reported to be responsible for the antibacterial activity of the leaves, the leaves are rich in acylated flavonol glycosides quercetin, myricetin, myricetin 3-O-4- acityl-L-rhamnopyranoside esterase, galloyl carboxylase, and tannin. The ethanolic extracts of leaves were tested for the presence of various phytoconstituents like tannins, alkaloids, carbohydrates, flavonoids, sterols, & glycosides. The methanolic extract of leaves content Flavonoid. The HPLC data indicated that leaf extracts contained erulic acid and catechin.. A significant linear relationship between antioxidant potency, free radical-scavenging ability and the content of phenolic compounds of leaf extracts supported this observation.The flower are rich in kaempferol, quercetin, myricetin- (quercetin-3-glucoside), myricet-3-L-Arabinoside, quercetin-3-D-galactoside, dihydromyricetin Flower of plant contains Oleanolic acid and other three triterpenoids also reported in the flowers are acetyl oleanolin acid melting point (260-262oC), Eugenia- triterpenoid A and Eugenia triterpenoid B . Flowers also contain ellagic acid. Ellagic acid arises from lactonization of hexa-hydroxdiphenic acid during chemical hydrolysis of tannins. The whole fruit consisted of pulp, kernel and seed coat. Total fatty matter was not significant in all three parts of fruit. Detailed mineral analysis showed calcium was abundant in all fruit parts and extracts·

The fruits contains citric acid a nthocynanis delphinididin-3-gentiobioside, maividin-3-laminaribioside, pentunidin -3-gentiobioside cyaniding diglycoside petunidin and malvidin. The sourness of fruits may be due to the presence of gallic acid .The color of fruits might be due to the presence of anthocyanin The purple colour of the fruit is due presence of one or two cyanidin diglycosides. The fruit contains moisture, protein, fat, crude fiber, ash, calcium, magnesium, phosphorus, iron, potassium, copper, sulfur, chlorine, vitamin A, thiamine,riboflavin, niacin, choline , folic acid of edible portion. One of the varieties of jambolan found in Brazil possesses malvidin-3-glucoside and pentinudin -3-glycoside. The peel powder of jambolan also can be employed as a colorant for foods and pharmaceuticals and anthocyanins pigments from fruit peels were studied for their antioxidant efficiency stability as extract and in formulations [2].The edible pulp of plant forms 75% of the whole fruit. Various mineral amino acid and vitamins were reported like vitamin C, nicotinic acid. Fructose are the principle source of sweeteners in ripe fruit with no trace of sucrose. The sugar part is mainly glucose, galactose is probably present, but there is no pentose or rafinose. Cyanidin diglycoside are sap pigments and the actual colour depends on the pH. Maleic acid is the major acid (0.59% of the weight of fruit. Small quantity of Oxalic acid has been also reported. Tannins mainly Gallic acid isresponsible for the astringency effect of the fruits. The

astringency activity is due to efficiency to combine with tissues and proteins and precipitate them. Tannins are also efficient for gastroprotective and antiulcerogenic activity [3]. The waxy component of the fleshy pericarp contains a sterol essential oil. The major component appears to be triterpene hydroxyl acid, oleanolin acid. Fresh pulp was rich in carbohydrates. Total phenolics, anthocyanins and flavonoid Jambolan is rich in compounds containing ellagic acid, kaemferol and myrecitin. The seeds are claimed to contain alkaloid jambosine and glcolide jamboline or antimellin, which halts the distatic conservation of starch into sugar .The seeds have been reported to be rich in flavonoids, a well known anti oxidant, which accounts for the scavenging of free radicals and protective effect on antioxidant enzymesand also found to have high total phenolics with significant antioxidant activity and are fairly rich in protein and calcium.java palms are reach in sugar ,mineral salt,vitamin c, pp which fortifies the beneficial effects of vitamin c, anthocyanins and flavanoids starch, Myricyl alcohol in the unsaponified fraction of seeds and a small quantity of pale yellow essential oil, [α] D are also present.Presence of ellagic acid, corilagin and related ellagitannins, 3, 6-hexahydroxydiphenoyl-glucose and its isomer, 4,6-hexahydroxydiphenoyl glucose, 1-galloyl glucose, 3-galloyl glucose and quercetin is reported in the alcoholic extraxt of Jambul seeds. Fixed oils & Fats are absent, Proteins, Steroids, Triterpenoids are present , Phenols,are present in more quantity.

Pharmacological Activity and There Effective Dose

Anti-diabetic activity

Syzygium cumini extract (aqueous suspension) was tested for its antibiadetic activity at the different dose levels of 1gm., 2gm., 4gm. and 6 gm. /kg body weight. 4 gm./ kg dose level was found to exhibit maximum hypoglycemic effect (42.64%) in rabbits. it also produced a significant decrease in the blood sugar level (17.04%) in alloxan diabetic rats. The administration of different doses of aqueous suspension of dried seed kernels in rabbit's changes blood sugar level viz., 1gm., 2gm., 4gm. and 6 gm/kg body weight indicate that the optimum dose level is 4 g/kg. The reduction was maximum for the 4 g/ kg body weight dose level being 42.64% as compared to the other dosages. Oral administration of ethyl acetate and methanol extracts of *Syzygium cumini* (200 and 400 mg/kg) showed significant decrease in blood sugar level. The isolated compound from *Syzygium cumini* mycaminose at a dose level of 50 mg/kg also showed significant decrease in blood sugar level. Oral administration of Syzygium cumini bark extract at dose of 300mg/kg body weight exhibited antidiabetic activity by significantly lowering blood glucose in rats but in case of clinical trial, experiments showing that the tea and extracts prepared from leaves of are pharmacologically inert. Patients and physicians should not rely on the putative antihyperglycemic effect of this tea, and perhaps of other folk medicines, that pretend to have such an effect. The investigation of plants with potential clinical utility could start with a clinical trial testing the effect of folk preparations in order to isolate the active principles of those products that show pharmacological activity in this model [4].

Antibacterial Activity

Syzygium cumini seed extracts prepared in methanol and ethanol was evaluated for antibacterial by disc diffusion and broth dilution assays. Both extracts exerted a broad spectrum of bacteriostatic action against different gram-positive and gram-negative bacteria. Their minimum inhibitory concentration (MIC) against susceptible organisms ranged from 154-656 μg/mL. Highest total activity was registered by the ethanol extract against *Staphylococcus epidermidis*. Zone Of Inhibition obtained in case of methanol extract of *S. cumini* seeds at 110 mg/mL and its ethanol extract at 250 mg/mL against *E. coli* and *V. cholerae* was of identical diameter. This means that methanol extract is 2.27 times more potent than the ethanol extract against these organisms. *S. paratyphi* A proved to be most susceptible among all test organisms, against both the extracts. Both extracts exerted a bacteriostatic action against susceptible organisms. However none of them was effective against *S. typhi* and drug-resistant strain of *S. paratyphi.*

Antioxidant Activity

The antioxidant activity of *Syzygium cumini* leaf extracts was investigated using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical-scavenging and ferric-reducing antioxidant power (FRAP) assays. The different solvent used for extraction of extract that are methanol, water, ethyl acetate, chloroform, and *n*-hexane fractions amongst this. Tannins extracted from *S. cumini* fruit showed a very good DPPH radical scavenging activity and ferric reducing/antioxidant power.the effective dose for antioxidant activityis abou 500 μg [5].

Vibriocidal Activity

To assure whether *ogawa* and *inaba* were antibiotic resistant or not, antibiogram of these strains was determined using some common antibiotics such as erythromycin, gentamicin, tetracycline, ampicilin, penicillin G, trimethoprim and ceftazidim. Both of the organisms showed resistance against all the above antibiotics tested (data not shown). The extract of *S. cumini* effectively inhibits the growth and activity of multi-drugs resistant *ogawa* and *inaba*, the *Vibrio* serogroup. The antibacterial activity of the extract and its potency was assessed by the presence or absence of inhibition zone. In observation it was clear that *S. cumini* extract was active in inhibiting the growth of *ogawa* and *inaba*. The extract was active with the concentrations ranging from 200-1000 μg/ml, however, the MIC was found to be 600μg/ml for both *V. ogawa* and *inaba*. High value of MIC may indicate a lower efficacy or the potential of the organisms for developing resistance against the bioactive compounds [6].

Antiallergic Activity

The anti-allergic properties of an aqueous leaf extract of *Syzygium cumini* (L.) Skeels (SC). To assess the effect of SC extract (crude extract obtained from fresh leaves by decoction in water) on allergic reactions, anaphylaxis edema caused by the mast-cell degranulator C48/80 or by OVA in sensitized animals. Oral pre-treatment with SC extract inhibited edema formation at doses of 25, 50, and 100 mg/kg (maximal inhibition of 50% at 25 mg/kg) to almost the same extent as promethazine, an anti-histaminic compound (65% inhibition at the dose of 10 mg/kg. It is noteworthy that oral treatment with 200 or 400 mg/kg SC extract inhibited edema formation at the same intensity (64 and 58%). The mouse paw edema induced by PAF (1 μg/paw; 30 min) was not affected by oral pre-treatment with SC extract at the doses of 25, 50, or 100 mg/kg. Experiments suggest that the anti-edematogenic effect of oral SC extract on allergen-induced paw swelling was due to an anti-histamine and anti-serotonin effect [7].

Inotropic and Chronoscopic Effects

cumulative administration (936.55 μg/ml) of the ethanolic extract of *Syzygium cumini* seed relaxed (55 %) the rat uterus smooth muscle against 22.36 mmol/l of Potassium chloride (KCl) induced smooth muscle contraction. Also, the inotropic and chronotropic effects of the extract using Langendorff's isolated heart perfusion method are reported. Upon addition of 4 mg/ml of *Sc* to the isolated heart, there was a significant increase in the number of beats in the isolated heart (42.85 %). This effect continued even upon the addition of 8 mg/ml of *Sc*, where the heart rate increased two fold (60 %). The possible mechanism behind this would be the extracellular K+ promoting the influx of Ca2+ into the cell. Extracellular potassium ion influences the ATP sensitive potassium channel which leads to an increase in the intracellular potassium ion concentration. This prevents the hyper polarization of the cellular membrane thereby increasing the cytosolic calcium and by further cell signaling cascades, muscle contraction takes place. The relaxation produced by *Sc* might possibly act via these signaling pathways.

Central nervous system activity

Ethyl acetate and methanolic extract of Syzygium *cumini* seed were undergone for investigating its Central Nervous System activity (CNS) of Albino mice in rota rod and actophotometer at the dose level of 200 mg/kg and 400 mg/kg. Both the extract exhibited significantly CNS activity. The ethyl acetate and methanol extracts of *Syzygium cumini* seed at the dose level of 200 and 400 mg/kg administrated orally exhibited significant reduction of activity compared with control group of animalsThis study established CNS activity in *Syzygium cumini* seed.

α Amylase inhibitors

The aqueous extract of *S. cumini* or *Eugenia jambolana* seeds showed higher inhibition against the porcine pancreatic α-amylase among the medicinal plants studied. The α-amylase inhibitors from *S.cumini* seeds were separated from the extract by preparative thin layer chromatography into fractions with different Rf values. The fraction with R*f* value between 0.285 and 0.43, which showed maximum inhibitory activity, was eluted and analyzed through LC-MS. The compounds identified from the seed extract of *S. cumini* were betulinic acid and 3, 5, 7, 4`-tetrahydroxy flavanone, which were reported earlier from *S. formosanum* and other plants [8].

Antinociceptive activity

The analgesic potential of *S. cumini* leaf extracts using hydro-alcoholic solventwas assessed in rats. Hot plate and formalin tests were used to estimate cutaneous nociception whereas measurements of forelimb grip force were done to assess muscular nociception under normal and inflammatory conditions. In the hot plate test, *Syzygium jambos* extract produced a significant increase in the withdrawal response latencies in a dose-dependent manner (10–300 mg/kg i.p.). The extract (100–300 mg/kg i.p.) significantly reduced pain scores in all the phases of the formalin test with an analgesic efficacy.

Anti-inflammatory activity

Significant anti-inflammatory activity was observed in carrageenin (acute), kaolin-carrageenin (subacute), formaldehyde (subacute)-induced paw oedema and cotton pellet granuloma (chronic) tests in rats. The extract did not induce any gastric lesion in both acute and chronic ulcerogenic tests in rats. The extracts of *S. cumini* seed possessed varying degree of anti-inflammatory activity when tested at various doses. The methanol extract at the dose of 400 mg/kg showed high significant anti-inflammatory activity at 4 h, where it caused 62.6% inhibition, as compared to that of 5 mg/kg of diclofenac sodium.

In Vitro Glucose uptake activity

Syzygium cumini act on glucose transporter (Glut-4), peroxisome proliferator activator receptor gamma (PPARγ) and phosphatidylinositol 3′ kinase (PI3 kinase) involved in glucose transport. *Activity sugesst that.* S. *cumini* activate glucose transport in a PI3 kinase-dependent fashion.*S. cumini* are anti-diabetic medicinal plants being used in Indian traditional medicine. Different solvent extracts extracted sequentially were analysed for glucose uptake activity at each step and methanol extracts were found to be significantly active at 100 ng/ml dose comparable with insulin and rosiglitazone [9].

Chemopreventive activity

Syzygium cumini seed extract can possibly play an important role as a chemopreventive agent against oxidative stress and genomic damage. Aqueous and ethanolic extracts of *Syzygium cumini* seed extract showed significant protective effects against hydroxyl radical induced strand breaks in pBR322 DNA. The *in vivo* experiments with aqueous *Syzygium cumini* seed extract showed significant protective effects against chromosomal damage induced by the genotoxic carcinogens URE and DMBA. Biochemical assays registered

significant inhibition of hepatic lipid peroxidation and increase in GSH level and activity of GST, SOD (superoxide dismutase) and CAT (catalase) [10].

Antifungal activity

Aqueous, ethanol and *n*-hexane extracts from leaves, fruit, root-bark and stem-bark of *Syzygiumcumini* (L.) Skeels were tested for their antifungal activity against *Ascochyta rabiei* (Pass.) Lab., the cause of blight disease of the chickpea (*Cicer arietinum* L.). Different concentrations, namely 1, 2, 3, 4, 5% of both aqueous and the two organic solvent extracts were used in this study. Aqueous extracts of all the four test plant parts, namely leaves, fruit, stem-bark and root-bark, showed significant antifungal activity.

CONCLUSION

Chemical nature, stability and bioefficacies of anthocyanins from fruit peel of *syzygium cumini* Skeels. In the present review it is concluded that the plant having the potential of treating various highly dangerous disease which are responsible for mortality in different age group. *Syzygium cumini* (Jamun) reduces the radiation-induced DNA damage in the cultured human peripheral blood lymphocytes in preliminary level study in the dose of 100 µg/ml [21].Plant extracts have been examined for their antidiabetic properties in an effort to identify alternative treatment strategies that pose less of a risk for diabetics. *Syzygium cumini* Ameliorates Insulin Resistance and *β*-Cell Dysfunction via Modulation of PPAR*γ*, Dyslipidemia, Oxidative Stress, and TNF-*α* in Type 2 Diabetic Rats *Syzygium cumini* (L.) skeels effective on post-prandial blood glucose levels in non-diabetic rats and rats with streptozotocin-induced diabetes mellitus. The different doses are used for treatment of various diseased groups. In this point it is concluded that in many treatment a small amount of drug is effective. Drug possesing the fewer side effects up to the dose of 200mg/kg body weight. It contains many phytochemical like which are responsible for the beneficial effect of the drug in many disease situations. This study suggest that many clinical trials are required for the better utilization of this plant so that many people take the benefit of this plant to treat the life threatening diseases.

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