A Phyto-Pharmacological Review of *Syzygium cumini* (L.) Skeels.

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Summary

Syzygium cumini (L.) Skeels (Jaman, Indian Blackberry; Myrtaceae) is a widely used medicinal plant throughout India and popular in various Indigenous System of Medicine like Ayurveda and Siddha. In the Traditional System of Medicine, the various plant parts such as bark, fruit, seed and leaf are used as astringent, sweet, sour, acrid, refrigerant, carminative, diuretic, digestive, in diabetes, leucorrhoea, gastric disorder, fever, skin diseases and wounds. The present review is therefore an effort to give a detailed survey of the literature on pharmacognosy, phytochemistry and pharmacological activities of *Syzygium cumini*.

Key words: *Syzygium cumini* (L.) Skeels; pharmacognosy; phytochemistry; pharmacological activities; review; Indian blackberry.

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Introduction

To cure human disease, medicinal plants have been a major source of therapeutic agents since time immemorial. Indian flora and fauna consists of more than 2200 species of medicinal and aromatic plants. The revival of interest in natural drugs started in last decade mainly because of the wide spread belief that green medicine is healthier than synthetic products. Nowadays, there is manifold increase in medicinal plant based industries due to the increase in the interest of use of medicinal plants throughout the world which are growing at a rate of 7 –15 % annually. Despite the major advances in the modern medicine, the development of new drugs from natural products is still considered important. This seems to be even more relevant for the developing countries, where the cost to develop a drug is prohibitive. Since 1980, the World Health Organization has been encouraging countries to identify and exploit traditional medicine and phytotherapy. The evaluation of new drugs especially phytochemically obtained materials has again opened a vast area for research and development. With the emerging worldwide interest in adopting and studying traditional systems and exploiting their potential based on different health systems, the evaluation of rich heritage of traditional medicine is essential. In this regard, one such plant is *Syzygium cumini* (L.) Skeels which is a large tree distributed all over India[1, 2]. In the Traditional System of Medicine, the plant is used as astringent, sweet, sour, acrid, refrigerant, carminative, diuretic, digestive, in diabetes, leucorrhoea, gastric disorder, fever, skin diseases and wounds[3,4,5]. The aim of present review is to highlight the traditional uses, pharmacognostical, phytochemical and pharmacological investigation carried out on the plant so that more pharmacological studies could be conducted to investigate the unexploited potential.

Plant Profile

Syzygium cumini (L.) Skeels (Myrtaceae) commonly known as Indian blackberry; Jaman, is a large tree distributed throughout Upper Gangetic Plains, Bihar, Orissa, planted in West Bengal, Deccan, Konkan region; all forest district of South India[6,7] ; also grown in Thailand, Philippines, Madagascar and cultivated widely throughout Africa, Caribbean and Tropical America. It grows commonly along streams and damp places and in evergreen forests. The tree is planted as an ornamental in gardens and at roadsides[8].

Synonyms

S. jambolanum DC., *Eugenia cumini* Druce, *E. jambolana* Lam., *E. djouat* Perr., *Myrtus cumini* L., *Calyptranthes jambolana* Wild[9].

Taxonomical/ Scientific classification[10]

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Myrtales
Family: Myrtaceae
Genus: *Syzygium*
Species: *cumini*

Classical Names

Jambu, Mahaphala, Phalendra, Surabhipatra, Raj Jambu, Mahajambu.

Among its many colloquial names are Java plum, Portuguese plum, Malabar plum, black plum, purple plum, in Jamaica, damson plum; also Indian blackberry.

In India and Malaya - jaman, jambu, jambul, jambool, jambhool, jamelong, jamelongue, jamblang, jiwat, salam, or koriang.

In Thailand - wa, or ma-ha.

In Vietnam - voi rung.

In Philippines - duhat, lomboy, lunaboy.

In Brazil - jambulao, jalao, jamelao or jambol[9, 11].

Botanical Description

The jambolan is fast growing, reaching full size in 40 years. It ranges up to 100 ft (30 m) in India and it may attain a spread of 36 ft (11 m) and a trunk diameter of 2 or 3 ft (0.6-0.9 m). It usually forks into multiple trunks a short distance from the ground.

Bark- On lower part of the tree it is rough, cracked, flaking and discolored; further up it is smooth and light grey.

Leaves- Turpentine-scented, opposite, 2 to 10 in (5-25 cm) long, 1 to 4 in (2.5-10 cm) wide, oblong-oval or elliptic, blunt or tapering to a point at the apex, pinkish when young, when mature leathery, glossy, dark green above, lighter beneath, with yellowish midrib.

Flowers- 1 to 4 in (2.5-10 cm) clusters, 1/2 in wide, have funnel shaped calyx and 4 to 5 united petals, white at first, then rose pink.

Fruits- They are in cluster of few or 10-40, is round or oblong, often curved, 1/2 to 2 in (1.25-5 cm) long, turns from green to light-magenta, then dark purple or nearly black as it ripens. The skin is thin, smooth, glossy, and adherent. The pulp is purple or white, very juicy, and normally encloses a single seed.

Seed- Oblong, green, or brown, 4 cm in length[7, 11, 12, 13].

Climate, Soil and propagation

The loamy, deep and well drained soils are considered suitable for optimum growth and development of the plant. Dry weather during flowering and fruit setting and early rains thereafter are considered beneficial for proper developing and ripening of fruits. Artificial reproduction can be carried out by direct sowing or by stump planting. It can also be propagated by inarching, grafting by approach and by the modified Forket method of budding. Trees from seedling begin to bear fruits in 8-10 years and budded or grafted ones in 6-7 years. Flowering starts in March and extends up to May. Fruits ripen during June- August and should be immediately harvested to avoid spoilage[14, 15, 16].

Pharmacognostical studies

Macroscopical characteristics[17, 18, 19, 20]

Stem bark: Drug occurs in slightly curved or flat pieces,0.5-2.5 cm thick, younger bark mostly channeled; external surface more or less rough and rugged due to exfoliation and vertical cracks, light grey to ash colored; internal surface fibrous, rough and reddish brown; fracture short and splintery; taste astringent. Seeds: 2-5 seeds, compressed together into a mass resembling a single seed, the whole seed enclosed in a cream colored, coriaceous covering, smooth, oval or roundish, 1 cm long,1 cm wide, brownish – black.

Microscopical and Powder Characteristics

Transverse section of mature bark shows a wide zone of cork which consists of tangentially elongated rectangular cells and gets differentiated as upper and lower cork, the former with few layers thick, stratified and reddish brown, having groups of 2-4 stone cells and latter being thin and colorless. Cork cambium is not distinct. Secondary phloem consists of sieve elements, phloem rays 1-4 cm wide, phloem parenchyma thin-walled and polyhedral in shape, oval to angular elongated stone cells, aseptate fiber, reddish brown content, rosette crystals of calcium oxalate and simple starch grains are also present.

Transverse section of seed shows cotyledons consisting of single layered epidermis, mesophyll composed of isodiametric, thin walled, parenchymatous cells fully packed with simple starch grains and few schizogenous cavities also are found.

The powder microscopy of seed powder shows parenchymatous cells and numerous oval, rounded starch grains.

The physical constants of the stem bark and seed are shown in Table No.1.

Table No.1: Physical constants of stem bark and seeds

Part of plant	Foreign organic matter % w/w	Total ash % w/w	Acid insoluble ash % w/w	Alcohol soluble extractive % w/w	Water soluble extractive % w/w
Stem bark	2	11	1	9	11
Seed	1	5	1	6	15

Important Marketed Formulations[3, 21, 22]

Panchapallava yoga, Pathadya churna, Brihallavangangadya churna, Jambvadya taila, Amradi kvatha, Karanjadya ghrita.

Doses

Juice: 10-20 ml

Powder: 3-6 g

Traditional uses[23, 24]

Plant parts used: bark, fruit, seed, leaf.

Fruit and seed: sweet, acrid, sour, liver tonic, haematinic, cooling, used in diabetes, diarrhoea, pharyngitis, splenopathy, urinary disorder, ringworm, to strength teeth and gums, digestive ailments.

Bark: astringent, sweet, sour, acrid, refrigerant, carminative, diuretic, digestive, anthelmintic, febrifuge, constipating, stomachic, antibacterial, used in diabetes, leucorrhoea, intrinsic hemorrhage, gastric disorder, strangury, fever, skin diseases and wounds.

Leaves: antibacterial, for prevention of vomiting, to strengthen teeth and gums.

Ayurvedic properties[3, 22, 23]

Rasa: Kashaya, Madhura, Amla

Guna: Laghu, Ruksha

Veerya: Sheeta

Vipaka: Katu

Doshaghnata: Pittashamaka

Rogaghnata: Raktasrava, Vrana, Shoola, Pravahika, Madhumela, Udakameha, Prameha, Upadansha.

Karma: Stambhana, Dahaprashamana, Raktastambhana.

Phytochemical Studies

Considerable amount of phytochemical isolations have been carried out and number of phytoconstituents have been isolated[25, 26,27,28,29]. The details are given below.

Stem bark: Betulinic acid, friedelin, friedelinol, daucosterol, kaempferol,kaempferol-3-O-glucoside, quercetin, myricetin, astragalin, β- sitosterol, β-sitosterol glucoside, sucrose, gallic acid, ellagic acid[30],cuminiresinol, 5'-hydroxy- methyl piperitol, syzygiresinol A, syzygiresinol B, demethyl-5-hydroxypinoresinol, dimethylpinoresinol, didemethoxypinoresinol,pinoresinol, 4'-methyl-5'-hydroxypinoresinol[31],bergenin[32].

Leaves: Heptacosane, nonacosane, triacontene, hentriacontane, octacosanol, triacosanol, dotriacosanol, betulinic acid, crotegolic acid[33], myricetin-4'-methyl ether, myricetin-3-O-(4"-O-acetyl-2"-O-galloyl)-α-L-rhamnopyranoside[34],quercetin, myricetin-3-O-(4"-acetyl)-α-L-rhamnopyranoside[35], ferulic acid, catechin[36], dihydromyricetin,iso-rhamnetin-3-O-rutinoside[29].

Flowers: Myricetin-3-L-arabinoside, dihydromyricetin, quercetin-3-D-galactoside, oleanolic acid, acetyl oleanolic acid, eugeniatriterpenoid A and B, ellagic acid, isoquercetin, kaempferol, myricetin, quercetin[37, 38].

Fruit:Delphinidin-3-gentiobioside,malvidin-3-laminaribioside,petunidin-3-gentiobioside, pconidin, pelargonidin, petunidin, mallic acid, oxalic acid, tannins, cyanidin diglycoside, waxy component, triterpenhydroxy acid, oleanolic acid[39].

Seeds: Gallic acid, ellagic acid, corilagin, ellagitannins, 3,6- hexahydroxydiphenoyl glucose,4,6-hexahydroxydiphenoyl glucose, 1-galloyl glucose,3-galloyl glucose, quercetin, 3,3',4' tri-O-methyl ellagic acid, 3,4'-di-O-methyl ellagic acid, caffeic acid, ferulic acid, guaiacol, resorcinol dimethyl ether, veratrole[40], lignanglucoside, medioresinol 4"-O-β-glucoside,(+)-pinoresinol-O-β-glucoside,(+)-syringaresinol-O-β-glucoside, dihydrodehydrodiconiferyl alcohol-4'-O-β-glucoside, 5- hydroxy methyl furfural[22], betulinic acid, 3,5,7,4'-tetrahydroxy flavanone[36].

Root: Myricetin-3-O-robinoside, myricetin-3-O-glucoside[29].

Essential oil from leaves, stem and fruits: α-Pinene, β-pinene, bornyl acetate, myrcene, β-pinene, α-terpinene, terpinolene, β-phellandrene, bornylene, cuminaldehyde, α-terpineol, eugenol, borneol[29]

Seed oil: Oleic, myristic, linoleic, stearic, palmitic, vernolic, lauric, sterculic, malvalic acids[28].

Pharmacological Studies

Antidiabetic Activity

Administration of powdered seeds of *E. jambolana* do not produce appreciable difference in blood sugar levels in rabbits but, its ethanol extract showed hypoglycemic activities in rabbits which was comparable with that of standard tolbutamide [41].

The effect of ethyl acetate, methanol and isolated compound mycaminose were evaluated for its antidiabetic activity in streptozotocin (STZ) induced diabetes.

Investigation was done on *S. cumini* seeds to isolate and identify the putative antidiabetic compound. The mycaminose (50 mg/kg) and ethyl acetate and methanol extracts produced significant reduction in blood glucose level suggesting that all the three possess anti-diabetic effects [42].

The methanol extract of jamun (*Syzygium cumini*) and root of Kadali (*Musa paradisiaca*) in separate or in composite manner in STZ-induced diabetic rat resulted a significant recovery in the activities of hexokinase, glucose-6-phosphate and glucose-6-phosphate dehydrogenase in liver along with correction in fasting blood glucose as well as liver and skeletal muscle glycogen level and plasma insulin level in comparison to diabetic group. It can be concluded that composite extracts of the two plants have some potential antidiabetogenic activities than that of separate extract [43].

Oral administration of seeds at 170, 240 and 510 mg/rat for 15 days caused maximum reduction in blood glucose. The result obtained from the 240 mg/rat doses was comparable with that of rats treated with chlorpropamide. In addition there was a 2.4-6.8 fold and 9.2 fold increases in cathepsin B activity pertaining to proteolytic conversion of proinsulin to insulin by seed extracts of *E. jambolana* and chlorpropamide respectively in rats [44].

The effect of oral administration of *E. jambolana* seeds on the hypoglycemic activity in normal and streptozotocin-induced diabetic rats was evaluated with sulfonylurea, glibenclamide as standard. There was significant decrease in blood glucose level in the treated group [45].

Oral administration of pulp extract of fruits of *S. cumin*i has shown to possess hypoglycemic activity in 30 min which was possibly mediated by insulin secretion *in* normoglycaemic and streptozotocin induced diabetic rats. In addition, the extract inhibited insulinase activity in the liver and kidney. Further studies with oral administration of alcoholic extracts of dried seeds of *E. jambolana* showed hypoglycemia and reduced glucosuria in rats suggesting the use as antidiabetic agent [46].

Daily oral administration of lyophilized powder of *E. jambolana* seeds (200 mg/kg) showed maximum reduction of blood glucose level to 73.51, 55.62 and 48.81% as compared to their basal value in mild (21 days), moderate (120 days) and severe (60 days) in diabetic condition in rats. In addition the treatment also partially restored altered

hepatic and skeletal muscle glycogen content and hepatic glucokinase, hexokinase, glucose-6-phosphate and phospho-fructokinase levels [47].

Investigation have been done on the hypoglycemic and hypolipidemic effect of ethanol extracts (100mg/kg, p.o.) of seeds in alloxan induced sub diabetic, mild diabetic and severe diabetic rabbits which showed significant fall in the fasting blood glucose level on 15 days administration. They also observed 32.85 and 26.95% increase in insulin level in mild and severe respectively and fall in total serum cholesterol/HDL ratio [48].

There is significant decrease in serum glucose and cholesterol levels on oral administration of aqueous extracts of seeds and bark of *E. jambolana* to alloxan diabetic rats for 60 days and the total RBC, T- lymphocytes were also significantly increased in treated animals [49].

An ethereal fraction of the ethanol extract of the seeds of *S.cumini* which contain ferulic acid was evaluated for its antidiabetic activity in STZ induced diabetes in rats. There was significant increase in level of glycogen, hepatic glucose-6-phosphate dehydrogenase, catalase, peroxides and decrease in the hepatic levels of thiobarbituric acid reactive substances (TBARS) and conjugated dienes with the drug treatment. The possible therapeutic activity of ferulic acid could be due to its pancreatic β cell regeneration[50].

The ethanol extract of seed of *S.cumini* when fed orally in various doses significantly increased body weight and decreased blood sugar level in alloxan induced diabetes. Once the level dropped to normal level, even after discontinuing the extract for 15 days, the blood sugar level was not elevated[51].

The effect of methanol extract of *S.cumini* at a dose of 100 ng/ml on a battery of target glucose transporters (Glut-4), peroxisome proliferator activator receptor gamma (PPAR gamma) and phosphatidyl inositol 3'-kinase (PI3 kinase) involved in glucose transport was evaluated. Elevation of Glut-4, PPAR gamma and PI3 kinase by *S.cumini* in association with glucose transport supported the up regulation of glucose uptake which suggests that the plant activate glucose transport in a PI3 kinase dependent fashion[52].

In oral glucose tolerance test, the bark of *S.cumini* exhibited antihyperglycemic activities when fed simultaneously with glucose. It showed significant decrease in blood glucose at 30 min and from 45 minutes onwards[53].

Crude ethanol, aqueous and butanol fraction (200-2000 mg/Kg twice daily p.o.) of *S.cumini* reduced glycemia of non diabetic mice which was associated with a reduction of food intake and body weight indicating that this may not be a genuine hypoglycemic effect[54].

The effect of feeding orally for 21 days along with diet containing 15% powdered unextracted seeds with water soluble gummy fiber, 15% powdered defatted seeds from which lipid and saponins were removed only and 6 % water soluble gummy fiber obtained from the seeds of *S.cumini* were tried on fasting blood glucose and glucose tolerance in normal and alloxan diabetic rats. All these lowered blood glucose level and improved oral glucose tolerance[55].

Oral administration of an aqueous and alcohol extract of Jamun seed for 6 weeks caused a significant decrease in lipid TBARS; an increase in catalase and superoxide dismutase in the brain of alloxan induced diabetic rats. The result were better than the glibenclamide which shows that the extract reduce tissue damage in diabetic rat brain[56].

The potential antihyperglycemic effect of tea and extracts prepared from leaves of jambolan (*Syzygium cumini* and *Syzygium jambos*) were studied. The experiments with normal rats, rats with streptozotocin-induced diabetes, normal volunteers and patients with diabetes were all negative in regard to an antihyperglycemic effect of this plant. In view of the pharmacological inertia of jambolan in the clinical model, patients and physicians should not rely on its putative antihyperglycemic effect[57].

Patients with type 2 diabetes mellitus were enrolled in a double-blind, double-dummy, randomized clinical trial to evaluate antihyperglycaemic effect in patients with type 2 diabetes mellitus. The three experimental groups received a tea prepared from leaves of *S.cumini* plus placebo tablets, placebo tea plus glyburide tablets or placebo tea plus placebo tablets. Fasting blood glucose levels decreased significantly with glyburide and did not change with *S. cumini* tea or placebo. Body mass index, creatinine, gamma-glutamyl transferase, alkaline phosphatase, aspartate aminotransferase (SGOT), alanine aminotransferase (SGPT), 24-h glucosuria, 24-h proteinuria, triglycerides, total, low-density lipoprotein and high-density lipoprotein cholesterol did not vary significantly between the different groups. Tea prepared from leaves of *S. cumini* has no hypoglycaemic effect[58].

There is lot of ambiguity regarding the use of *S.cumini* as antidiabetic agents as few researchers have shown potent hypoglycemic effect while few others have shown no hypoglycemic activity.

Alpha amylase inhibitor activity

One of the complications of diabetes is post prandial hyperglycemia (PPHG). Glucosidase inhibitors, particularly alpha amylase inhibitor are a class of compounds that helps managing PPHG. The chloroform, methanol and aqueous extracts of *S.cumini* seeds have shown to possess significant alpha amylase inhibitory activity[59].

Bioactivity guided fractionation of aqueous extract of *S.cumini* seeds led to the isolation of betulinic acid and 3,5,7,4'-tetrahydroxyflavone which showed higher inhibition against the procine pancreatic alpha amylase[36].

S.cumini seed kernel extracts were evaluated for the inhibition of alpha glucosidase from mammalian, bacterial and yeast in *in vitro* studies. The extracts are more effective in inhibiting maltase when compared to the acarbose control. In an *in vivo* study using Goto-Kakizaki rats, the acetone extract was found to be a potent inhibitor of alpha glucosidase hydrolysis of maltose when compared to untreated animals[60].

Antioxidant activity

It has been observed that oral administration of ethanol extract of *Eugenia jambolana* seed kernel to streptozotocin induced diabetic rats significantly decreased the levels of glycosylated hemoglobin, increased the body weight, hemoglobin and restored the activities of superoxide dismutase, catalase, glutathione peroxidase back to the normal level. They also found an increase in glutathione content and lipid peroxidation and hydroperoxides levels in liver and kidney. Similar results were observed in plasma and pancreas along with the capacity to bring level to near normal [61, 62].

The antioxidant activity of the fruit skin has been analyzed using different assays, such as hydroxyl radical, superoxide radical, DPPH radical scavenging assay, lipid peroxidation assay, total antioxidant capacity. In all the systems, a significant correlation existed between concentration of the extract and percentage inhibition of free radicals and percentage inhibition of lipid peroxidation. The antioxidant property of the fruit skin may come in part from the antioxidant vitamins, phenolics or tannins and anthocyanins present in the fruit [63].

The antioxidant activity of *S.cumini* leaf extracts was investigated using DPPH and ferric reducing antioxidant power (FRAP) assay. The methanol extract and its four water, ethyl acetate, chloroform and n-hexane fraction were prepared and subjected to above antioxidant assay. The results showed that the ethyl acetate fraction had stronger antioxidant activity than the other ones[64].

In-vitro antioxidant activity of seeds of *S.cumini* was studied for total phenolic content and antioxidant activity by DPPH method. It showed a high total phenol content (72-167.2 mg/g) and high antioxidant activity (69.6-90.6 %) [65].

Antibacterial activity

Antibacterial activity of ethanol extracts of *E. jambolana* against gram positive and gram-negative organisms have been reported [66].

The antibacterial activity of methanol and ethyl acetate extracts of the seeds of *E. jambolana* have been determined at a concentration of 200 µg/disc against five gram positive bacteria (*Bacillus aureus, B.subtilis, B.megaterium, Streptococcus β-haemolyticus, Staphylococcus aureus*) and nine gram-negative bacteria (*Shigella dysenteriae, Sh. shiga, Sh. boydii, Sh. flexneriae, Sh. sonnei, E.coli, S.typhi B, S. typhi B-56* and *Klebsicella species*) by disc diffusion method where the MIC for methanol extract was 64, 128 and 64µg/ml against *Bacillus creus, E. coli* and *Sh. flexneria* respectively whereas for ethyl acetate extract, the MIC were found to be 256, 256 and 64 µg/ml against *Bacillus aureus, E. coli* and *Sh. flexneria* respectively [67].

The leaf essential oils of *S. cumini* and *S. travancoricum* were tested for their antibacterial property. The activity of *S. cumini* essential oil was found to be good, while that of *S. travancoricum* was moderate [68].

Anti-inflammatory activity

The ethanol extract of *S.cumini* bark extract was investigated for its anti-inflammatory activity in carragennin, kaolin-carragennin, and formaldehyde induced paw edema and cotton pellet granuloma tests in rats. The result suggests that the extract has a potent anti-inflammatory action against different phases of inflammation without any side effect on gastric mucosa [69, 70].

The ethanol extract of *S.cumini* bark was tested at the dose of 100, 300 and 1000 mg/Kg p.o. against inflammation induced by histamine, 5-HT, bradykinin and PGE2 in

rat paw edema. It was concluded that S. cumini exhibits inhibitory role on inflammation response to histamine, 5-HT and PGE2[71].

Anti-inflammatory activity of ethyl acetate and methanol extracts of *S. cumini* seed in carrageenan induced paw oedema in Wistar rats at the dose level of 200 and 400 mg/kg p.o. was carried out. Both the extracts exhibited significant anti-inflammatory activity, which supports the traditional medicinal utilization of the plant. This study established anti inflammatory activity of the seed of *S. cumini* [72].

Antifertility activity

The antifertility effect of oleanolic acid isolated from the flowers of *E. jambolana* significantly decreased the fertilizing capacity of the male albino rats without any significant change in body or reproductive organ weights. It causes significant reduction in conversion of spermatocytes to spermatides and arrest of spermatogenesis at the early stages of meiosis leading to decrease in sperm count without any abnormality to spermatogenic cells, leyding interstitial cells and sertoli cells [73].

Antidiarrohoeal activity

The ethanol extract of the bark of *E. jambolana* at dose of 400 mg/kg p.o. reduced diarrohea by inhibiting gastrointestinal motility and PGE2 – induced enteropolling in castor oil induced diarrohea in rats [74].

Gastro protective activity

The gastro protective effect of quantified tannins (13.4%) from *S. cumini* was determined. Gastric mucosal damage was induced by oral gavage administration of HCl/ethanol solution. Examination using Best's Ulcer Staging Index showed that tannins had a very significant decrease in gastric mucosal damage. A dose which consisted of 20.0 g tannins/kg rat weight showed significantly lower stomach free radical concentrations. These findings suggest that tannins extracted from *S. cumini* have gastroprotective and anti-ulcerogenic effects [75].

Central Nervous System activity

The ethyl acetate and methanol extracts of seed were investigated for 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[76].

Antistress activity

The seed extracts of *E. jambolana* produce alteration in the general behavior of test animal such as reduction in locomotion, decrease in aggressiveness and increase in phenobarbitone induced sleeping time in dose dependent fashion in a stress reducing study. It also has significant analgesic effect against acetic acid induced writhing movement and reduction in body temperature and also reduces plasma cortisone level, which was elevated due to stress [77].

Hepatoprotective activity

The hepatoprotective effect of aqueous extract of *S.cumini* leaves (either in single dose or by 7 days pretreatment) was evaluated against hepatotoxicity induced by carbon tetra chloride in rats. The levels of SGOT and SGPT were lowered by preadministration with the aqueous extract but not by a single dose[78].

S. cumini peel extract rich in anthocyanins (SCA) offers considerable protection against carbon tetrachloride (CCl_4)-induced damage in rat hepatocytes. SCA itself being non-toxic to primary rat hepatocytes at concentrations ranging from 50 to 500 ppm was found to suppress CCl_4-induced LDH leakage by 54% at 50ppm, thereby improving the cell viability by 39%. The SCA significantly reversed the CCl_4 induced changes in cellular glutathione (GSH) level, lipid peroxidation and activity of the antioxidant enzyme glutathione peroxidase. Exposure of hepatocytes to SCA after CCl_4 treatment was found to elevate GSH and GPx activities by 2-folds, whereas the activities of catalase and superoxide dismutase were not significantly affected. These observations suggest that the fruit peel extract of *S. cumini*, is largely responsible for the reversal of CCl_4-induced oxidative damage in rat hepatocytes[79].

Antileishmanial activity

The antileishmanial activity of methanol extract of *S.cumini* was evaluated against two species of *Leishmani* (*L. amazonenesis* and *L. chagasi*) and was found to be active against both the species of Leishmania[80].

Antifungal activity

The antifungal activity of methanol extract of *S.cumini* was evaluated against two yeasts (*Candida albicans* and *Crytococcus neoformans*). It exhibited the best activity against *C.neoformans* with MIC value of 0.078 mg/ml[80].

Antiallergic activity

Oral administration of SC (25-100 mg/kg) in Swiss mice inhibited paw edema induced by compound 48/80 (50% inhibition, 100 mg/kg) and, to a lesser extent, the allergic paw edema (23% inhibition, 100 mg/kg). SC treatment also inhibited the edema induced by histamine (58% inhibition) and 5-HT (52% inhibition) but had no effect on platelet-aggregating factor-induced paw edema. SC prevented mast cell degranulation and the consequent histamine release in Wistar rat peritoneal mast cells (50% inhibition, 1 microg/mL) induced by compound 48/80[81].

Pre-treatment of BALB/c mice with 100 mg/kg of the extract significantly inhibited eosinophil accumulation in allergic pleurisy (from 7.662 +/- 1.524 to 1.89 +/- 0.336 x 10(6)/cavity). This effect was related to the inhibition of IL-5 (from 70.9 +/- 25.2 to 12.05 +/- 7.165 pg/mL) and CCL11/eotaxin levels (from 60.4 +/- 8.54 to 32.8 +/- 8.4 ng/ml) in pleural lavage fluid, using ELISA. These findings demonstrate an anti-allergic effect of SC indicating that its anti-edematogenic effect is due to the inhibition of mast cell degranulation and of histamine and serotonin effects, whereas the inhibition of eosinophil accumulation in the allergic pleurisy model is probably due to an impairment of CCL11/eotaxin and IL-5 production[81].

Radioprotective activity

The effects of various concentrations (5, 10, 20, 30, 40, 50, 60, and 80 mg/kg body weight of the leaf extracts of *S. cumini* (SCE) on the radiation-induced sickness and mortality in mice exposed to 10 Gy gamma-irradiation was studied. The treatment of mice with different doses of SCE, consecutively for five days before irradiation, delayed the onset of mortality and reduced the symptoms of radiation sickness when compared with the non drug-treated irradiated controls. All doses of SCE provide protection against the gastrointestinal death increasing the survival by 66.66% after treatment with 20, 30, and 40 mg/kg SCE versus a 12% survival in the irradiated control group (oil and irradiation). Similarly, SCE provided protection against the radiation-induced bone marrow death in mice treated with 10-60 mg/kg b.wt. of SCE[82].

The radio protective activity of the hydro alcoholic extract of jamun seeds (SCE) was studied in mice exposed to different doses of gamma radiation. The mice were injected with 0, 5, 10, 20, 40, 60, 80, 100, 120, 140 or 160 mg/kg body weight of SCE,

before exposure to 10 Gy of gamma radiation, to select the optimum dose of radiation protection. The mice treated with 80 mg/kg body weight SCE intraperitoneally before exposure to 6, 7, 8, 9, 10 and 11 Gy of gamma radiation showed reduction in the symptoms of radiation sickness and mortality at all exposure doses and caused a significant increase in the animal survival when compared with the concurrent double distilled water and irradiation group. The SCE treatment protected mice against the gastrointestinal as well as bone marrow deaths[83].

The effects of various concentrations (0.0, 1.56, 3.125, 6.25, 12.5, 25, 50 and 100 µg/ml) of the leaf extract of *S. cumini* (SC) were studied on the alteration in the radiation-induced micronuclei formation in the cultured human peripheral blood lymphocytes. Treatment of lymphocytes to various concentrations of SC resulted in a dose dependent increase in the micronuclei-induction, especially after 25-100 µg/ml extract. The exposure of human lymphocytes to various concentrations of SC extract before 3 Gy gamma-irradiation resulted in a significant decline in the micronuclei-induction at all the drug doses when compared with the non-drug treated irradiated cultures. Our study demonstrates that the leaf extract of *S. cumini*, a plant traditionally used to treat diabetic disorders protects against the radiation-induced DNA damage[84].

Clinical Evaluation

A clinical trial was conducted on 80 patients on non insulin dependent diabetes mellitus. All the patients were treated with *E.jambolana* seed powder, 12 gm per day, in three divided doses for 3 months. The drug produced good symptomatic relief along with regulation of blood sugar. It did not show any side effects[85].

In another study, 80 non insulin dependent diabetes mellitus cases, an Ayurvedic formulation was orally administered for a period of 24 weeks. Fasting and post prandial blood sugar were estimated for 6 week intervals. There was significant reduction in both fasting and post prandial blood sugar in all the patients[86].

A clinical study was conducted on 25 patients of type II diabetes with a herbomineral proprietary preparation of which jambu seed was one of the constituents. The patients were administered 2 tablets, 3 times a day in addition to regular sulphonyl urea over a period of 6 weeks. It showed improvement in glycaemic parameter viz.,

fasting and post prandial blood sugar and fructosamine level which suggest that it can be a useful adjuvant in poorly controlled type II diabetes[87].

Efficacy of a proprietary herbal preparation consisting *of E. jambolana, Tinospora cordifolia, Pterocarpus marsupium, Ficus glomerata, Momordica charantia* and *Ocimum sanctum* was evaluated on 28 cases of persistent post prandial hyperglycemia. After 12 weeks of treatment, a persistent fall in fasting and post prandial blood glucose levels was recorded[88].

Conclusion

In recent years, ethnomedicinal studies received much attention as this brings to light the numerous little known and unknown medicinal virtues especially of plant origin which needs evaluation on modern scientific lines such as phytochemical analysis, pharmacological screening and clinical trials[89]. In the present review, the literature pertaining to botanical, pharmacognostical, phytochemical and pharmacological activities has been given comprehensively. The plant is having antidiabetic, antioxidant, antidiarrhoeal, antiviral, neuropsychological, antifertility, anti-inflammatory, antidiarrohoeal activity, hepatoprotective, antiallergic activity and gastro protective activity. A literature survey also pinpoints the fact that although the number of diseases for which *S. cumini* finds use as a medicine is fairly large but its therapeutic efficacy has been assessed only in few cases with few models. Therefore, it is imperative that more clinical and pharmacological studies should be conducted to investigate the unexploited potential of this plant.

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