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PHARMACOGNOSTIC AND PHYTOCHEMICAL STUDIES OF *SYZYGIUM CUMINI*: REVIEW

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Antidiabetic, Antineoplastic, Ulcer

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ABSTRACT: *Eugenia jambolana* Lam., commonly known as black plum or "jamun" is an important medicinal plant in various traditional systems of medicine. It is effective in the treatment of diabetes mellitus, inflammation, ulcers and diarrhea and preclinical studies have also shown it to possess chemopreventive, radioprotective and antineoplastic properties. The plant is rich in compounds containing anthocyanins, glucoside, ellagic acid, isoquercetin, kaemferol and myrecetin. The seeds are claimed to contain alkaloid, jambosine, and glycoside jambolin or antimellin, which halts the diastatic conversion of starch into sugar. The present review has been primed to describe the existing data on the information on traditional and medicinal use.

INTRODUCTION: It is a large evergreen tree up to 30 m high. It has been valued in Ayurveda and Unani system of medication for possessing variety of therapeutic properties. The genus Syzygium is one of the genera of the myrtale family Myrtaceae which is native to the tropics, particularly to tropical America and Australia. It has a worldwide, although highly uneven, distribution in tropical and subtropical regions.

The genus comprises about 1100 species, and has a native range that extends from Africa and Madagascar through southern Asia east through the Pacific. Its highest levels of diversity occur from Malaysia to north-eastern Australia, where many species are very poorly known and many more have not been described taxonomically. It is widely distributed throughout India and known as Jamun, Jam, Jambul.

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Plants of this family are known to be rich in volatile oils which are reported for their uses in medicine and many fruits of the family have a rich history of uses both as edibles and as traditional medicines in divergent ethnobotanical practices throughout the tropical and subtropical world. Some of the edible species of Syzygium are planted throughout the tropics worldwide [1].

Synonym:

- Marathi: Jambhool
- Hindi: Jamun, Jomuna, Raja Jambu
- English: Jambul tree, Black plum, Jaman
- Sanskrit: Brahaspati, Jambavam, Mahajambu, Ksudrajambu
- Assamese: Jam
- Bengali: Jaam
- Gujrati: Jambu, Jambuda
- Kannada: Merale, Jamneralae, Jambu, Neralamara
- Malayalam: Njaval, Naval
- Oriya: Jamukoli, Jamu, Jam
- Punjabi: Jammu
- Tamil: Naaval, Navval Sambu, Mahamaram, Nagal

- Telugu: Nesedu
- Urdu: Jamun

Scientific Classification (*Syzygium cumini*) [1, 2]

- Kingdom: Plants, plantae
- Subkingdom: Green plants
- Infra-kingdom: land plants
- Division: vascular plants
- Subdivision: Seed plants
- Infra-division: flower plants
- Class: Magnliopsida
- Super-order: Rosanae
- Order: Myrtales
- Family: Myrtaceae
- Genus: Syzygium
- Species: *Syzygium cumini* (L.) skeels

Parts Used: Fruit, Pulp, Seed, Leaves, bark.

Cultivation and Collection:

Climate and Soil: Since jamun is hardy fruit crop, it can be grown under adverse soil and climatic conditions, it thrives well under both tropical and subtropical climates. It requires dry weather at the time of flowering and fruit setting. Early rains are beneficial for better growth development and ripening of fruit. Young plants are susceptible for frost.

The jamun trees can be grown on wide range of soils-calcareous, saline sodic soils and marshy areas. Deep loam and well drained soils are ideal. It does not prefer very light and sandy soils.

Varieties for Commercial Cultivation: Most common type of grown in North India is known as Rajamun (large/oblong/deep purple colour fruits). Another type in Varanasi without seed (Narendra jamun [6]).

Propogation: Propogated both by seed and vegetative techniques, the most common being by seeds. The seeds have no dormancy. Hence fresh seeds can be sown (within 10 - 15 days) 4 - 5 cm deep at distance of 25 cm × 15 cm. The seed germinate 10 - 15 days after sowing. The seedlings become ready for transplanting in spring or next monsoon.

Seedlings plants bear fruits of variable size and quality. Therefore, vegetative method is desirable for propagation of improved or selected types. Budding is most successful for commercial raising of plants. It is done on one year root stock having about 10 mm thickness. In low rainfall area, July-August is ideal time.

Planting: Pits of 1m × 1m × 1m size are dug 10m apart for seedling trees and 8m apart for budded plants in a properly cleaned field. Pit digging should be completed before the onset of the monsoon or spring season. They should be filled with a mixture of top soil and well rotten farm-yard manure or compost in a 3:1 ratio.

Monsoon season (July - September) is ideal time of planting. But it can also be planted with a good survival rate in spring (February - March) if irrigation facilities are available. About 100 - 150 plants are required for planting a hectare land.

Training and Pruning: Young plants need training for development of framework. Keep the main stem or trunk clean up to a height of 60 - 90 cm from the ground level by removing the basal branches and sprouts. Jamun plants do not require any pruning except removing diseased and dry and crisscross twigs.

Manuring and Fertilization: In pre-bearing period, 20 - 25 kgs well rotten farmyard manure / plant / year should be applied. For bearing trees, this dose is increased upto 50 - 60 kg / plant / year. The ideal time for giving the organic manure is a month before flowering. Grown up trees should be applied 500 g N, 600g P and 300g K / plant / year. This should be spread near the canopy of the plant and mixed in soil by hoeing.

Aftercare: Green manuring can be done during rainy season. Sprouts arising from base of its plants should be removed timely and the plantation should be kept weed free. Jamun is a cross pollinated crop hence raising of honey bees near the plantation is desirable for maximum fruit set and productivity.

Irrigation: Young plants require 6 - 8 irrigations for better growth. In bearing trees, irrigation should be given from September to October for better fruit bud formation and from May to June for better development of fruits. Normally 5 - 6 irrigations are required.

Harvesting and Post Harvest Management: Seedlings trees start bearing at the age of 9 - 10 years, whereas budded one take 5 - 6 years. Fruits ripen during June-July or with onset of rains. It takes 3 - 5 months to ripen after full bloom. Fruit change colour from green to deep red or bluish black. Fruit does not ripen after harvesting. Fully ripe fruits are harvested daily by hand picking or by shaking and collecting the fruits on a polythene sheet. Jamun trees needs number of pickings, since all fruits do not ripen at a time. The average yield of fully grown budded and seedling tree is 50 – 70 kg and 80 - 100 kg / plant / year.

Jamun fruits are highly perishable. They can be stored only up to 2 days at ambient temperature. Pre-cooled fruits packed in perforated polythene bags can be stored for 3 weeks at 8 - 10 ºC and 85 - 90% humidity. Jamun fruits can be processed into excellent quality fermented beverages such as cider and vinegar, and non-fermented ready to serve beverages and squashes. A good quality jelly can also be prepared from its fruits. The seeds can be processed into powder which is very useful to cure diabetes. The problem of flower and fruit drop can be minimized by spraying of GA3 (60 ppm) twice, one at full bloom and other 15 days after fruit set.

Yield: Fruits 80 - 100 kg / tree / year.

Economics: Ripen fruits Rs.80 per kg. Rs.6400 - 8000 / Tree / Year.

Description of Bark:

A) Macroscopic Characters of Bark: Drugs occurs in slightly curved or flat pieces, 0.5 - 2.5 cm thick, younger bark mostly channelled, external surface more or less rough and rugged due to exafoliation and vertical cracks, light gray to ash coloured, internal surface fibrous, and reddish brown, fracture- short and splintery; taste- astringent.

A Stem Bark

B Fruit

C Seeds

D Flower

E Leaves

F Whole Plant

FIG. 1: *SYZYGIUM CUMINI* PLANT AND THEIR DIFFERENT PARTS

B) Microscopic Characters of Bark: Mature bark shows a wide zone of cork differentiated into upper and lower cork zones, forming a rhytidoma, cork consisting of tangentially elongated reactangular cells upper few layers thick, stratified and reddish brown having groups of 2 - 4 stone cells crushed elements of phloem, lower cork thin and colourless cork.

Cambium not distinct, secondary phloem composed of sieve elements and phloem rays. Phloem parenchyma thin walled and polyhedral in shape. Stone cells oval to angular elongated fibrous aseptate, both stone cells and fibres single or in groups present throughout this region.

Phloem rays 1 - 4 cells wide; reddish brown content, rosette crystals of calcium oxalate and simple, round to oval starch grains, measuring 5-11u diameter.

C) Powder Characteristics of Bark: Light brown, shows fragments of thin walled cork cells, aseptate fibres, single or in groups, oval to angular, elongated stone cells rosette and prismatic crystals of calcium oxalate and simple round to oval starch grains measuring 5 - 11 u diameter.

D) Identity, Purity and Strength of Bark:

- Foreign matter - not more than 2
- Total ash - not more than 11
- Acid insoluble ash - not more than 1
- Alcohol soluble extractive - not less than 9
- Water soluble extractive - not less than 11

Description of Seed:

A) Macroscopy of Seed: 2 - 5 seeds, compressed together into mass resembling a single seed, the whole seed enclosed in cream colourer, curvaceous covering smooth, oval or roundish, 1cm long, 1 cm wide brownish black and taste astringent.

B) Microscopy of Seed: Shows cotyledons consisting of single layered epidermis, messophyll composed of isodiametric thin walled, parenchymatous cells fully packed with simple starch grains, oval rounded measuring 7 – 28 u in diameter, few schizogenous cavities are also found.

Microscopic Character of Seed:

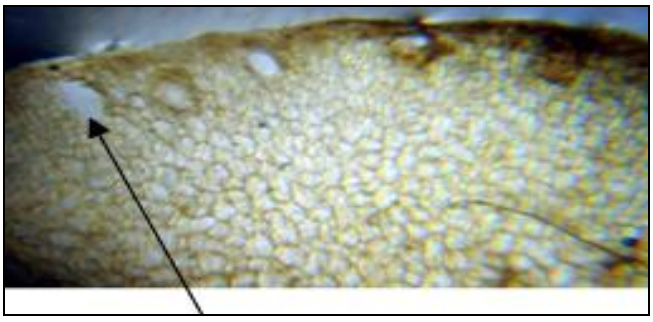

FIG. 2: SCHIZOGENOUS CAVITIES

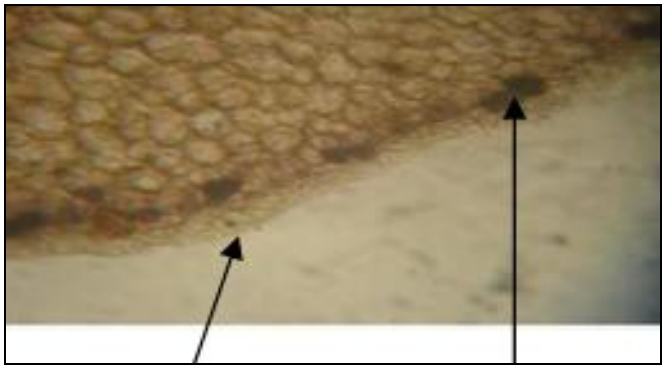

FIG. 3: EPIDERMIS AND STARCH GRAIN

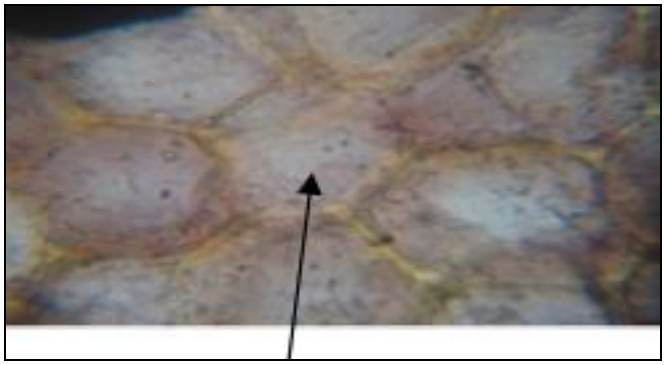

FIG. 4: MESOPHYLL

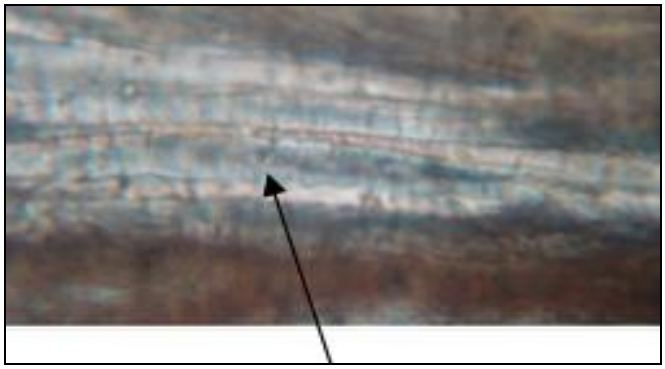

FIG. 5: TESTA

C) Powder Characteristics of Seed: Brown coloured, shows few parenchyamatous cells and numerous oval rounded starch grains, measuring 7-28u in diameter.

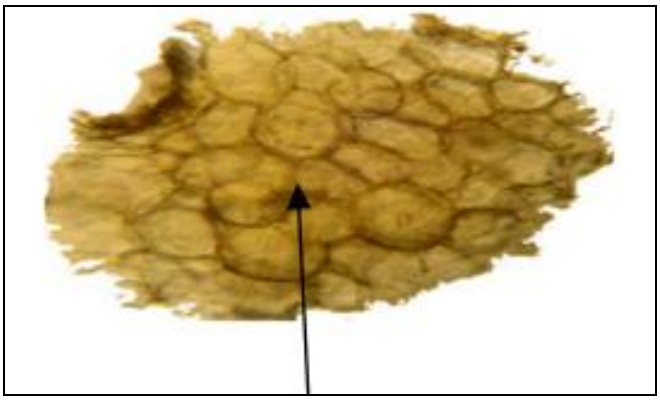

FIG. 6: ENDOSPERM

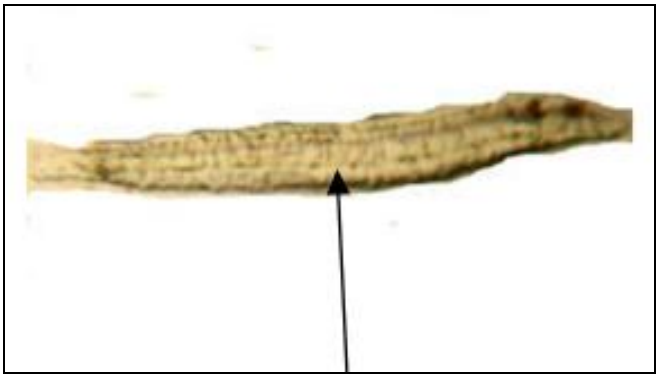

FIG. 7: TESTA

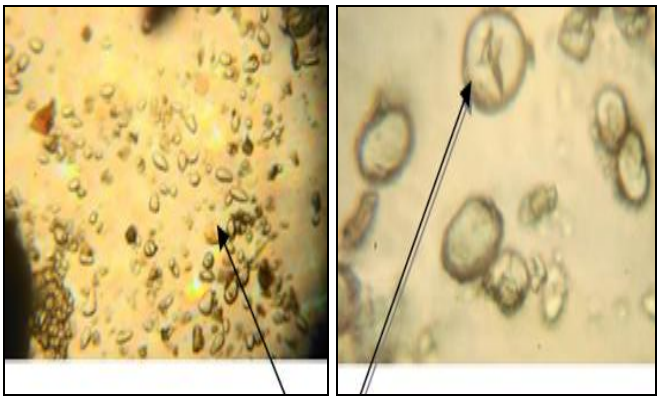

FIG. 8: STRACH GRAINS

D) Identity, Purity and Strength:

- Foreign matter- not more than 1.
- Total ash- not more than 5.
- Acid insoluble ash-not more than1.
- Alcohol soluble extractive- not less than 6.
- Water soluble extractive-not less than 15.

E) T. L. C: T. L. C. of alcoholic extract of the drug on Silica gel 'G' plate using n-Butanol: Acetic acid: Water (4: 1: 5) shows under U.V. (366 nm) three spots at R_f. 0.34, 0.54 and 0.84 (all violet). On exposure to Iodine vapour six spots appear at Rf. 0.10, 0.29, 0.39, 0.49, 0.63 and 0.90 (all yellow). On spraying with 5% Methanolic-Sulphuric acid reagent and heating the plate at 105 °C for ten minutes three spots appear at R_f. 0.34 (grey), 0.54 (yellow), 0.84 (brown).

Description of Leaves, Flower and Fruits:

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.

8. Important Marketed Formulations and Doses: Panchapallava yoga, Pathadya churna, Brihallavangangadya churna, Jambvadya taila, Amradi kvatha, Karanjadya ghritam, Pusyanuga Curna, Usirasava.

Doses:

- Juice - 56-112 ml.
- Bark powder - 0.5-1 gm.
- Seed powder - 1-3 gm.

Phytochemical Studies: [5, 6] Considerable amounts of phytochemical isolations have been carried out and numbers of phyto constituents have been isolated. 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, cuminiresinol, 5'-hydroxy-methyl piperitol, syzygiresinol A, syzygiresinol B, demethyl- 5- hydroxy- pinoresinol, dimethyl pinoresinol didemethoxypinoresinol, pinoresinol, 4'-methyl-5'-hydroxypinoresinol, bergenin.

Seeds: Gallic acid, ellagic acid, corilagin, ellagitannins, 3, 6- hexahydroxydiphenoyl glucose, 4, 6- hexahydroxy diphenoyl 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, lignanglucoside, medioresinol 4"-O-β-glucoside, (+)-pinoresinol-O-β- glucoside, (+)- syringaresinol-O –β -glucoside, dihydrodehydrodiconiferyl alcohol- 4'- O- β-glucoside, 5- hydroxy methylfurfural, betulinic acid, 3, 5, 7, 4'-tetrahydroxy flavanone.

Heptacosane, nonacosane, triacontene, hentriacontane, octacosanol, triacosanol, dotriacosanol, betulinic acid, crotegolic acid, myricetin-4'-methyl ether, myricetin-3-O- (4"-O-acetyl-2"-O-galloyl-α-L-rhamnopyranoside, quercetin, myricetin-3-O-(4"-acetyl)- α- L- rhamnopyranoside, ferulic acid, catechin, dihydro- myricetin, isorhamnetin-3-O-rutinoside.

Flowers: Myricetin- 3- L- arabinoside, dihydro-myricetin, quercetin-3-D-galactoside, oleanolic acid, acetyl oleanolic acid, eugeniatriterpenoid A and B, ellagic acid, isoquercetin, kaempferol, myricetin, quercetin.

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.

Root: Myricetin- 3- O-robinoside, myricetin- 3- O-glucoside.

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.

Seed Oil: Oleic, myristic, linoleic, stearic, palmitic, vernolic, lauric, sterculic, malvalic acid.

Pharmacological Studies:

Diabetes Mellitus:

a) Introduction of Diabetes: Diabetes mellitus is one of the most common and serious chronic diseases. Diabetes is the leading cause of adult blindness, end-stage renal disease, and nontraumatic lower-extremity amputations (as a result of nerve disease). People with diabetes are 2–4 times more likely to have coronary heart disease and stroke than people without diabetes. In addition, poorly controlled diabetes can complicate pregnancy-birth defects are more common in babies born to women with diabetes.

Diabetes is a metabolic disease in which the body does not produce or properly use insulin, a hormone that is needed to convert sugar, starches, and other food into energy needed for daily life. There are three main types of diabetes, all of which are characterized by high levels of blood glucose (sugar).

b) Classification of Diabetes:

A) Type1 Diabetes (IDDM): Also called insulin-dependent diabetes mellitus (IDDM) or juvenile-on set diabetes

B) Type 2 Diabetes (NIDDM): Also called noninsulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes. Diabetes is called a self-managed disease, meaning that your loved one can probably take responsibility for his or her own day-to-day care. Much daily care involves keeping blood glucose near normal levels at all times. Studies show that controlling blood sugar levels lowers the risk of some complications of diabetes, such as eye and heart disease and nerve damage, so it's important for your loved one to stick to his or her diabetes management plan as closely as possible. This article has an objective to collect scattered scientific information on the herbs of hypoglycemic activity and to provide present status of plants on which antidiabetic activity has been done.

c) Mechanism of Action: The antidiabetic action of *Syzygium cuminui* is not fully understood. It exerts a dual effect namely a combination of mechanism of action of sulfonylurea and biguanide, they may bring about its hypo- glycemic action through stimulation of surviving β - cells of islets of Langerhans to release more insulin.

However according to some other studies it increases Glucose-6-Phospate content in liver indicating an overall increase in glucose influx thus it is having an overall effect in increasing glucose utilization. It may be acting as hypoglycemic agent by increased the insulin content through increasing activity of cathepsin B. Anti oxidants has observed that oral administration of ethanolic extracts of *Syzygium cumini* seed kernel to streptozotocin induced diabetic rats significantly decreased the levels of glycosylated hemoglobin, increased the body weight and hemoglobin, restored the activities of superoxide dismutase, catalase, glutathione peroxidase to the normal level. They also found an increase in glutathione content and increased levels of lipid peroxidation and hydroperoxides in liver and kidney.

The same group in the plasma and pancreas observed later similar results along with the capacity to bring level to near normal of Vitamin C concomitant to Vitamin E and ceruloplasmin in plasma.

d) Animal Models Used in Antidiabetic Activity: [7]

1) *In-vivo* Animal Models for Diabetes Mellitus:

1. Pharmacological induction of Diabetes.
2. Surgical models of Diabetes
3. Genetic models of diabetes

a) Animal strains that spontaneously develop Diabetes.
b) Genetically engineered Diabetic mice.

4. Other models of type-2 diabetes to evaluate the reduction of pancreatic β-cell Mass.

2) *In-vitro* Studies:

1. *In-vitro* studies on insulin secretion:

a) Studies using isolated pancreatic islet cell lines.
b) Studies using insulin-secreting cell lines.

2. *In-vitro* studies on glucose uptake.

e) Antidiabetic Activity: [7, 8] Administration of powdered seeds of *Syzygium cumini* 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. 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.

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. 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 *Syzygium cumini* and chlorpropamide respectively in rats. The effect of oral administration of *Syzygium cumini* 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. Oral administration of pulp extract of fruits of *Syzygium 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 *Syzygium cumini* showed hypoglycemia and reduced glucosuria in rats suggesting the use as antidiabetic agent. Daily oral administration of lyophilized powder of *Syzygium cumini* 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 (60days) 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. Investigation have been done on the hypoglycemic and hypolipidemic effect of ethanol extracts (100 mg/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. There is significant decrease in serum glucose and cholesterol levels on oral administration of aqueous extracts of seeds and bark of *Syzygium cumini* to Allegan diabetic rats for 60 days and the total RBC, T- lymphocytes were also significantly increased in treated animals. An ethereal fraction of the ethanol extract of the seeds of *Syzygium cumini* which contain ferule 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 dehydrogenate, 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.

The ethanol extract of seed of *Syzygium 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. The effect of methanol extract of *Syzygium cumini* at a dose of 100 mg/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 *Syzygium 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. In oral glucose tolerance test, the bark of *Syzygium cumini* exhibited antihyperglycemic activities when fed simultaneously with glucose. It showed significant decrease in blood glucose at 30 min and from 45 minutes onwards.

Crude ethanol, aqueous and butanol fraction (200-2000 mg/Kg twice daily p.o.) of *Syzygium 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. 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 *Syzygium 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.

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. 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.

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 *Syzygium 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 *Syzygium cumini* tea or placebo. Body mass index, creatinine, gammaglutamyl transferase, alkaline phosphatase, aspartate aminotransferase (SGOT), alanine aminotransferase (SGPT), 24-h glucosuria, 24-h proteinuria, triglycerides, total, lowdensity 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.

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. 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.

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.

f) Clinical Evaluation: A clinical trial was conducted on 80 patients on non insulin dependent diabetes mellitus. All the patients were treated with *Syzygium cumini* 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. 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.

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. Efficacy of a proprietary herbal preparation consisting *of Syzygium cumini* 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.

Other Pharmacological Activities: [9, 10]

a) Antioxidant Activity: It has been observed that oral administration of ethanol extract of *Syzygium cumini* 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. 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.

The antioxidant activity of *Syzygium 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. *In-vitro* antioxidant activity of seeds of *Syzygium 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 %).

b) Antibacterial Activity: Antibacterial activity of ethanol extracts of *Syzygium cumini* against gram positive and gram-negative organisms have been reported. The antibacterial activity of methanol and ethyl acetate extracts of the seeds of *Syzygium*

cumini 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.

The leaf essential oils of *Syzygium 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.

c) Anti-inflammatory Activity: The ethanol extract of *Syzygium 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.

The ethanol extract of *Syzygium 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. 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 *Syzygium cumini*.

d) Antifertility Activity: The antifertility effect of oleanolic acid isolated from the flowers of *Syzygium cumini* 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.

e) Antidiarrohoeal Activity: The ethanol extract of the bark of *Syzygium cumini* 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.

f) Gastro Protective Activity: The gastro protective effect of quantified tannins (13.4%) from *Syzygium 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.

g) 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.

h) Antistress Activity: The seed extracts of *Syzygium cumini* produce alteration in the general behaviour 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.

i) Hepatoprotective Activity: The hepato-protective effect of aqueous extract of *Syzygium cumini* leaves (either in single dose or by 7 days pretreatment) was evaluated against hepatotoxicity

induced by carbontetra chloride in rats. The levels of SGOT and SGPT were lowered by pre-administration with the aqueous extract but not by a single dose.

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 CCl4 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.

j) Antileishmanial Activity: [10, 11] The anti-leishmanial activity of methanol extract of *Syzygium 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.

k) Antifungal Activity: The antifungal activity of methanol extract of *Syzygium 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.

l) 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. 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 × 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.

m) 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 *Syzygium cumini* on the radiation-induced sickness and mortality in mice exposed to 10 Gygamma - irradiation was studied. The treatment of mice with different doses of *Syzygium cumini*, 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 *Syzygium cumini* provide protection against the gastrointestinal death increasing the survival by 66.66% after treatment with 20, 30, and 40 mg/kg *Syzygium cumini* 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 SCE82.

The radio protective activity of the hydro alcoholic extract of jamun seeds (*Syzygium cumini*) 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 SC 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.

n) Gastrointestinal as well as Bone Marrow Deaths: The effects of various concentrations (0.0, 1.56, 3.125, 6.25, 12.5, 25, 50 and 100µg/ml) of the leaf extract of *Syzygium 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 Gygamma-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.

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, pharma-cognostical, phytochemical and pharmacological activities has been given comprehensively. The plant is having antidiabetic, antioxidant, antiviral, neuropsychological, antifertility, anti-inflammatory, antidiarrohoeal activity, hepatoprotective, anti-allergic 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 plasma.

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