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MORPHOLOGY, PHYTOCHEMISTRY AND PHARMACOLOGY OF *SYZYGIUM CUMINI* (LINN.) - AN OVERVIEW

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ABSTRACT: *Syzygium cumini* (L.) is a widely used medicinal plant for the treatment of various ailments. The plant contains anthocyanins, glucoside, ellagic acid, isoquercetin, kaempferol, and myricetin as its chief active constituents. These active cons isoquercetin, kaempferol tituents impart multiple pharmacological activities to the plant which includes antidiabetic, anticancer, antioxidant, antibacterial, antifungal and antidiarrhoeal activity. The present review presents specific information on botany, phytochemical constituents, traditional uses and pharmacological actions of *S. cumini* (L.). Further applications of *Syzygium cumini* (L.) in the field of novel drug delivery has been also elaborated in the review. Apart from its application in the treatment of various diseases there is need to explore chemical and toxicity concern of *S. cumini* (L.).

INTRODUCTION: There has been an increasing demand for health promoting food products by the consumers all over the world. This has led to the new hybrid term between nutrients and pharmaceuticals, 'nutraceuticals' coined by Dr. Stephen L. DeFelice, in the year 1989. [1] Nutraceuticals are diet supplements that deliver a concentrated form of a bioactive component from a food and used with the purpose of enhancing health in dosages that sometimes exceeds that of the normal foods. [2] The medicinal properties of several herbal plants have been documented in ancient Indian literature and the preparations have been found to be effective in the treatment of diseases.

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Therefore to meet the increasing demand of manufacturing modern medicines and export, the need of the medicinal plants have enormously increased. This demand is generally met with by cultivating uprooted medicinal plants. [3] To cure human disease, medicinal plants have been a major source of therapeutic agents since time immemorial. Indian flora and fauna a 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 tradi tional 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.[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.

1.1 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] It is a large evergreen tree up to 30 meters height and girth of 3.6 meters with a bole up to 15meters. [9]

The tree was also introduced to Florida, USA in 1911 by the USDA, and is also now commonly planted in Suriname. In Brazil, where it was introduced from India during Portuguese colonization, it has dispersed spontaneously in the wild in some places, as its fruits are eagerly sought by various native birds such as thrushes, tanagers, and the Great Kiskadee. [10]

Common names from worldwide: [11-12]
Brazil - Azeitona
Pakistan - Jaman
West Indies - Jambol
Nepal - Java plum
Thailand - Lukwa
Japan - Madan
Madagascar - Rotra

Other names: [11-12]
Hindi - Jaman, Jam
Bengali - Jam, Kalajam
Gujarati - Jambu, JamLi
Telugu - Jambuvu
Marathi - Jaman, Jambul

Taxonomic classification: [13]
Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Myrtales
Family: Myrtaceae
Genus: Syzygium
Species: *Cumini*

2. Occurrence and distribution: The original home of jamun is India, distributed throughout India, in forest up to 1800m usually along the bank and moist localities, also cultivated as shade trees along road sides. It is widely cultivated in Haryana as well as the rest of the Indo- Gangetic plains on a large scale. Its habitat starts from Myanmar and extends up to Afghanistan. It is also found in Thailand, Philippines, Madagascar and some other country. The plant has been successfully introduced into many other tropical countries such as the West Indies, West Africa and some subtropical regions including Florida, California, Algeria and Israel.[14] It was cultivated in England by Miller in 1768.[15]

3. Botanical Discription:

3.1 *S. cumini* may reach 30 m tall in India and Oceania or up to 12-15 m in Florida, USA, with a broad crown up to 11 m in diameter and a trunk diameter of 0.6-0.9 m though it usually has a multi-stemmed from branching close to the ground.

FIG. 1: *SYGZIUM CUMINI* TREE

3.2 Bark: is rough, cracked, flaking and discoloured on the lower part of the trunk, becoming smooth and light-grey higher up.

FIG. 2: *SYGZIUM CUMINI* BARK

3.3 Leaves: have a turpentine smell, and are opposite, 5-25 cm long, 2.5-10 cm wide, oblong-oval or elliptic, blunt or tapering to a point at the apex; pinkish when young, becoming leathery, glossy, dark-green above, lighter beneath, with a conspicuous, yellowish midrib when mature.

FIG. 3: *SYGZIUM CUMINI* LEAVES

3.4 Flowers: are fragrant and appear in clusters 2.5-10 cm long, each being 1.25 cm wide and 2.5 cm long, with a funnel-shaped calyx and 4-5 united petals, white at first, becoming rose-pink, shedding rapidly to leave only the numerous stamens.

FIG. 4: *SYGZIUM CUMINI* FLOWERS

3.5 Fruit: appear in clusters of just a few or 10-40, are round or oblong, often curved, 1.25-5 cm long, turning from green to light-magenta, then dark-purple or nearly black, although a white-fruited form has been reported in Indonesia. The skin is thin, smooth, glossy, and adherent. The pulp is purple or white, very juicy, and normally encloses a single, oblong, green or brown seed, up to 4 cm long, though some fruits have 2-5 seeds tightly compressed within a leathery coat, and some are seedless. The fruit is usually astringent, sometimes unpalatably so, and the flavour varies from acid to fairly sweet. [16]

FIG. 5: *SYGZIUM CUMINI* FRUITS

4. Phytochemistry: Photochemical studies have identified gallic acid, cyanidin glycoside, glycoside jamboline, triterpenoids, tannins, gallitanins, essential oils, myricetine, β-sitosterol, myricyl alcohol etc. Compounds isolated from the leaf, fruit, seed, flower, stem bark and edible pulp of the plant has been discussed below.

4.1 Stem Bark: Stem bark of *Syzygium cumini* contain betulinic acid, ß-sitosterol, friedeanol, epi-friedeanol and eugenin. It also contains ß-sitosterol-D-glucoside, Kamepferol-3-0- glucoside, quercetin, myricetin, astragalin, and gallic acid. [17-18]

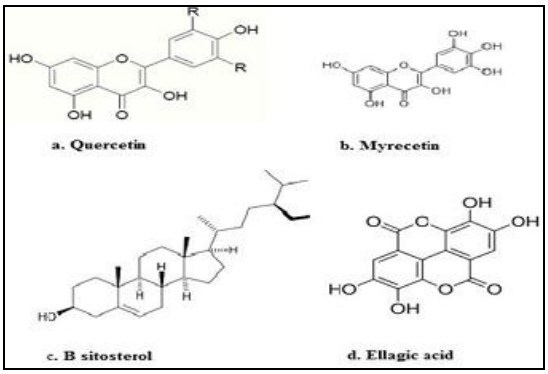

FIG. 6: CHIEF ACTIVE CONSTITUENTS OF STEM BARK OF *SYZYGIUM CUMINI* (L.)

4.2 Fruit: Fruit of *Syzygium cumini* contains malic acid and a small quantity of oxalic acid as its acid constituent. Gallic acid and tannins present in the fruit account for its astringency. The presence of Cyanidine and diglycoside (**Fig. 3**) imparts purple color to the fruit. It further contains glucose, fructose, mannose, and galactose as the principal sugar moieties. The mineral constituents are also reported to present which includes Ca, Mg, Na, K, Cu and vitamins such as thiamine, riboflavin, nicotinic acid etc. [19-20]

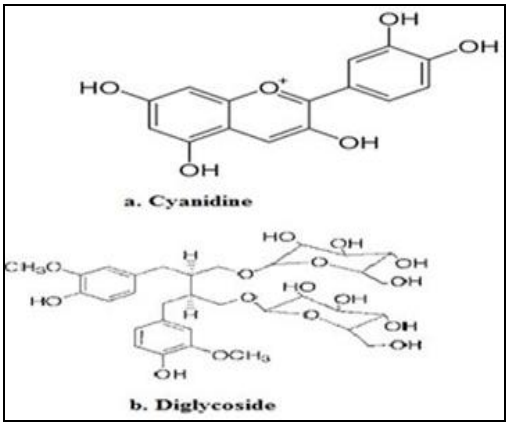

FIG. 7: CHIEF ACTIVE CONSTITUENTS OF FRUIT OF *SYZYGIUM CUMINI* (L.)

4.3 Seed: It contains a glucoside jamboline, a new phenolic substance, a trace pale yellow essential oil, chlorophyll, fat, resin, gallic acid, ferulic acid guaicol, resorcinol, dimethyl ether and corilaginin. The seeds are fairly rich in the protein, and calcium. [21-22]

4.4 Leaves: They contain gallitanins, essential oil (terpenes, 1-limonene and dipentene), monoterpenoid terpinene, terpenolene, borbeneol, terpineol and eugenol, complicated mixture of polyphenol such as gallic acid, methylgallate, kaempferol, ellagic acid, ellagitannin, nilocitin, myrecetin 3-0-D- glucaronopyranoside, 3-0-ß D-glucuronopyranoside and two flavanol glycosides such as mearsetin 2-0-(4"-0-acetyl)-a-L rhamnopyranoside, and myricetin 4"-0-acetyl"-2-0-gallate. [23-25]

4.5 Flowers: They contain kaempferol, quercetin, myricetin, isoquercetin (quercetin-3- glucoside), myricetin- 3 - L - arabinoside, quercetin-3-D-galactoside, dihydromyricetin, oleanolic acid, acetyl oleanolic acid, eugenol-triterpenoid A and eugenol-triterpenoid B. [26]

4.6 Roots: of *syzygium cumini* contain myricetin 3-o-glucoside and the new flavanoid myricetin 3-o-robinoside.[27]

5. Phytochemical Screenings: The leaf extracts of *Syzygium cumini* were analysed for the presence of flavonoids, alkaloids, glycosides, steroids, phenols, saponins, terpenoid, cardiac glycosides and tannins according to standard methods.[28]

5.1 Alkaloids [Mayer's test]: 1.36gm of mercuric chloride dissolved in 60ml and 5gm of potassium iodide were dissolved in 10 ml of distilled water respectively. These two solvents were mixed and diluted to 100ml using distilled water. To 1ml of acidic aqueous solution of samples few drops of reagent was added. Formation of white or pale precipitate showed the presence of alkaloids.

5.2 Flavonoids: In a test tube containing 0.5ml of alcoholic extract of the samples, 5 to 10 drops of diluted HCl and small amount of Zn or Mg were added and the solution was boiled for few minutes. Appearance of reddish pink or dirty brown colour indicated the presence of flavonoids.

5.3 Glycosides: A small amount of alcoholic extract of samples was dissolved in 1ml water and then aqueous sodium hydroxide was added. Formation of a yellow colour indicated the presence of glycosides.

5.4 Steroids [Salkowski's test]: About 100 mg of dried extract was dissolved in 2 ml of chloroform. Sulphuric acid was carefully added to form a lower layer. A reddish brown colour at the interface was an indicative of the presence of steroidal ring.

5.5 Cardiac glycosides [Keller killiani's test]: About 100mg of extract was dissolved in 1ml of glacial acetic acid containing one drop of ferric chloride solution and 1ml of concentrated sulphuric acid was added. A brown ring obtained at the interface indicated the presence of a de oxy sugar characteristic of cardenolides.

5.6 Saponins: A drop of sodium bicarbonate was added in a test tube containing about 50 ml of an aqueous extract of sample. The mixture was shaken vigorously and kept for 3min. A honey comb like froth was formed and it showed the presence of saponins.

5.7 Resins: To 2 ml of chloroform or ethanolic extract 5 to 10 ml of acetic anhydrite was added and dissolved by gentle heating. After cooling, 0.5 ml of H_2SO_4 was added. Bright purple colour was produced. It indicated the presence of resins.

5.8 Phenols [Ferric Chloride Test]: To 1ml of alcoholic solution of sample, 2 ml of distilled water followed by a few drops of 10% aqueous ferric chloride solution were added. Formation of blue or green colour indicated the presence of phenols.

5.9 Tannins [Lead acetate test]: In a test tube containing about 5 ml of an aqueous extract, a few drops of 1% solution of lead acetate was added. Formation of a yellow or red precipitate indicated the presence of tannins.

5.10 $FeCl_3$ test: A 2ml filtrate [200 mg of plant material in 10ml distilled water, filtered], and 2ml of $FeCl_3$ were mixed. A blue or black precipitate indicated the presence of tannins. [29]

6. Pharmacological activity:

6.1 Anti- Diabetic activity: Diabetes is becoming the third „killer" of mankind, after cancer and cardiovascular diseases, because of its high prevalence, morbidity and mortality. [30] The oral hypoglycaemic agents currently used in antidiabetic therapy are associated with serious side effects. So, there is an utmost requirement to explore newer anti-diabetic agents that hold therapeutic efficacy and are free of such side effects.[31] In this regard antidiabetic potential of various parts of *Syzygium cumini* (L.) has been explored by different researchers.

Singh and Gupta 2007, investigated the effects of ethanolic extract of *Syzygium cumini* (L.) (Linn) seed powder on pancreatic islets of alloxan diabetic rats. They reported that ethanolic extract of seeds of *Syzygium cumini* (L.) significantly decreased blood sugar level in alloxan diabetic albino rats. Further the histological studies showed definite improvement in the histopathology of islets. They also reported that the blood sugar level once dropped to normal levels after extract feeding was not elevated when extract feeding was discontinued for 15 days. [32]

Kumar *et al.*, 2008 isolated and identify the supposed antidiabetic compound from the *Syzygium cumini* (L.) [SC] seed. They isolated mycaminose from SC seed extract and investigated anti-diabetic activity against streptozotocin (STZ)-induced diabetic rats. They reported that mycaminose exhibited significant ($p<0.05$) reduction in blood glucose level. Glibenclamide the standard drug (1.25 mg/kg) also produced significant ($p<0.05$) reduction in blood glucose level against STZ-induced diabetic rats. Conclusively they demonstrated that isolated compound mycaminose possess anti-diabetic activity against STZ-induced diabetic rats.[33]

Tripathi and Kohli 2014, studied antidiabetic activity of bark extract of *Syzygium cumini* (L.) on streptozotocin (STZ)-induced diabetic Wistar albino rats. They reported that 30 minutes prior administration of *Syzygium cumini* (L.) extracts before oral glucose loading significantly decreased ($p<0.001$) the rise in postprandial blood glucose levels in treated rats as compared to control rats however the result was less significant than glibenclamide. Every day, continuous oral treatment of STZ-induced diabetic with various *Syzygium cumini* (L.) extract for 3 weeks lead to significant reductions in fasting blood glucose levels as compared to diabetic controls. [34]

6.2 Anticancer activity: Cancer is a public health problem all around the world. Exploration for anticancer agents from plant origin dates back to 1947, when the cytotoxic properties of podophyllotoxin from *Podophyllum peltatum* (Berberidaceae) were detected. [35] The discovery of the antileukemic properties of vinblastine and vincristine from *Catharanthus roseus* (Apocynaceae) shortly went behind [36] and offered the desire for broad investigations of plant extracts and plant-derived compounds for possible anticancer activity.

In the case of human cancers, thus far, nine plant-derived compounds have been approved for clinical use in the United States. They include vinblastine, vincristine, the campothecin derivatives-topotecan and irinotecan, and paclitaxel. Numerous agents such as betulinic acid, roscovitine and silvestrol are in clinical or preclinical stage of development. Few reports have indicated potential of *Syzygium cumini* (L.) fruits to combat cancer.

Nazim, 2007 isolated four anthocyanins pelargonidin-3-O-glucoside, pelargonidin-3,5 Odiglucoside, cyanidin-3-O-malonyl glucoside, and delphenidin-3-O-glucoside from the acidic alcoholic extract of *Syzygium cumini* (L.) fruits. They performed cytotoxic activity of total alcoholic extract of the fruits against various tumor cell lines using the SRB assay. Results revealed that they showed significant cytotoxic activity for MCF7 (breast carcinoma cell line) (IC_{50} = 5.9 µg/mL), while the IC_{50} was > 10 µg/mL for both Hela (Cervix carcinoma cell line), HEPG2 (liver carcinoma cell line), H460 (Lung carcinoma cell line) and U251 (Brain carcinoma cell line). [37]

Afify *et al.,* 2011 investigated anticancer activitiy of *Syzygium cumini* (L.) fruit extracts using cell viability assay of leukemia cancer cell line. They prepared successive extracts of hexane, chloroform, ether, ethyl acetate, ethanol, and water and evaluated for anticancer activity. They reported that the ethanol extract exhibited stronger anti-leukemia activity as compared to other ones. Spectroscopic findings of active ingredients separated from ethanol extract showed that fruit extract of *Syzygium cumini* (L.) contained phenolic compounds namely Kaempferol 7-O-methylether and sterols such as γ-Sitosterol was responsible for their anticancer activity. [38]

6.3 Antioxidant: Generation of free radicals initiates/aggravates various diseases like cancer, AIDS, arthiritis, Alzheimer and diabetic complications. Thus, there is a requirement of safer drugs that have property of scavenging the free radicals. With regard to SC fruit, polyphenols have shown outstanding antioxidant capacity when compared to the standard polyphenols. [39]

The methanolic extract of leaves, bark and seeds of SC were fractionated in different solvents: n-hexane, chloroform, ethyl acetate, butanol and water. These fractions were studied for their antioxidant and free radical scavenging activities. Of all the fractions, the polar ones *i.e.,* ethyl acetate and water fractions showed excellent results. [40]

The leaf and seed extract of SC exhibited a significant antioxidant activity when they were assessed by various in vitro methods such as Ferric reducing antioxidant power (FRAP) assay, 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging assay, Nitric oxide radical scavenging, ABTS Assay, Total Reducing antioxidant potential, Total antioxidant activity, Reducing power and Hydroxyl radical scavenging activity. [41]

RSC (Radical Scavenger Capacity) of *SC* was determined by using DPPH (2, 2-diphenyl-1-picrylhydrazyl radical) assay. The second order rate constants-k2 was evaluated to determine RSC and then these were compared to natural and synthetic antioxidants. The k_2 value of SC was determined to be 15.60 L/mol g s in methanol at 25 °C proving that it has a excellent antioxidant potential. [42]

6.4 Anti microbial activity: Following the rebellion in the "golden era", while about all groups of vital antibiotics (tetracyclines, cephalosporins, aminoglycosides and macrolides) were discovered and now a days and these exciting compounds are in danger of losing their efficacy because of the increase in microbial resistance. For such motive, discovery of new antibiotics is an utterly vital objective. Nowadays natural products remain one of the key sources of new drug molecules. Plants and other natural sources can provide a huge range of complex and structurally diverse compounds. Recently, researchers are being focusing on investigating plant and essential oils, microbial extracts, pure secondary metabolites and novel synthesized molecules as budding antimicrobial agents. [43]

Gawri and Vasantha, 2010 examined antibacterial activity of crude methanol and aqueous extracts of the leaves of *Syzygium cumini* (L.) against standard strains and clinical isolates of some bacteria using the disc diffusion method. The extracts exhibited inhibitory activity against clinical isolates of gram negative bacteria such as *Salmonella enteritidis*, *Salmonella typhi*, *Salmonella typhi A, Salmonella paratyphi A, Salmonella paratyphi B, Pseudomonas aeruginosa* and *Escherichia coli* and gram positive bacteria such as *Bacillus subtilis*, and *Staphylococcus aureus.* They reported that the methanol extracts was more potent than the aqueous extracts. [44]

Prateek *et al.,* 2015 studied antimicrobial activity of *Syzygium cumini* (L.) fruit and leaf extract against bacterial stains such as *Staphylococcus*

aureus, Staphylococcus saprophyticus, Escherichia coli, Pseudomonas aeurioginosa, Roultella plantikola, Proteus vulgaris and fungal stains namely *Aspergillus niger* MTCC 282, *Penicillium chrysogenum* MTCC 161, *Candida albicans* MTCC 183, *Fusarium solani* MTCC 9667. They reported antibacterial activity against all used bacteria. Maximum zone of inhibition was observed for *Roultella plantikola* (25 mm) and minimum zone of inhibition was observed against *Pseudomonas aeruginosa* by using fruit extract (14 mm). The plant extract showed maximum zone of inhibition (18 mm) against fungal strains *Penicillium chrysogenum* and minimum (7mm) against *Candida albicans*. Conclusively they demonstrated that *Syzygium cumini* (L.) extract possess potential antibacterial and antifungal activity.[45]

6.5 Anti-inflammatory activity: Inflammation can be defined as a generalized, nonspecific but beneficial tissue response against injury. It comprises a complex array of adaptive responses to tissue injury which are both local and systemic. The local responses lead to staffing of phagocytic cells and removal of endogenous or foreign material. The systemic responses may alter the environment interior to permit these processes to occur more proficiently. [46]

Natural products have long been recognized as an important source of therapeutically effective medicines. In this regard *Syzygium cumini* (L.) has also been reported to possess anti-inflammatory activity.

Muruganandan *et al.,* 2001 evaluated ethanolic bark extract of *Syzygium cumini* (L.) was for its anti-inflammatory activity in animal models. The extract did not exhibit any toxicity up to a dose of 10.125 g/kg, p.o. in mice. Significant anti-inflammatory activity was found in carrageenin (acute), kaolin-carrageenin (subacute), formaldehyde (subacute)-induced paw oedema and cotton pellet granuloma (chronic) tests in rats. The extract did not stimulate any gastric lesion in both acute and chronic ulcerogenic tests in rats. Overall they concluded that *Syzygium cumini* (L.) bark extract possess a potent anti-inflammatory action against different phases of inflammation without any side effect on gastric mucosa.[47]

Kumar *et al.,* 2008 evaluated anti-inflammatory activity of ethyl acetate and methanol extracts of *Syzygium cumini* (L.) seed in carrageenan induced paw oedema in wistar rats at the oral dose level of 200 and 400 mg/kg. Both the extracts presented significant anti-inflammatory activity supporting anti-inflammatory activity of the seed of *Syzygium cumini* (L.). [48]

Siani *et al.,* 2013 examined the anti-inflammatory activity of the essential oils from the leaves of *S. cumini* of their terpene-enriched fractions (+V = more volatile and −V = less volatile) obtained by vacuum distillation. Anti-inflammatory activity was accessed in the lipopolysaccharide-induced pleurisy model, by measuring the inhibition of total leukocyte, neutrophil and eosinophil migration in the mice pleural lavage, after oil treatment with the oils at 100 mg/kg. Results revealed that eosinophil migration was inhibited by SC (67%), SC (+V) (63%), PG (76%), PG (+V) (67%) and PG (−V) (74%). Conclusively they demonstrated that essential oils from *S. cumini* may be useful to treat inflammatory diseases by mechanisms that include the inhibition of eosinophil migration.[49]

6.6 Anti-diarrhoeal activity: Diarrheal diseases are a key problem in Third World countries and are responsible for the death of millions of people each year. Diarrheoa refers to an alteration in normal bowel movement and is characterized by an increase in the water content, volume, or frequency of stools. Plants have long been a vital foundation of novel drugs. Several plant species have been screened for presence of compounds having therapeutic activity. For achieving success in this area, international organizations including the World Health Organization (WHO) have encouraged studies concerning the treatment and prevention of diarrheal diseases using traditional medicinal plants.

In this context Shamkuwar *et al.,* 2012 evaluated anti-diarrhoeal activity of aqueous extract of *Syzygium cumini* (L.) seed in mice. They tested antidiarrhoeal, antimotility and antisecretory activity *Syzygium cumini* (L.) seed extract. The method of castor oil induced diarrhoea was performed for investigating antidiarrhoeal activity; whereas charcoal meal test and castor oil induced intestinal secretions were used for testing

antimotility and antisecretory activity in mice. They reported that aqueous *Syzygium cumini* (L.) extract (ASC) exhibited a significant and dose dependent antidiarrhoeal, antimotility, and antisecretory effect. Overall they concluded that antidiarrhoeal effect of ASC might be because of its antimotility and antisecretory effect.[50]

6.7 Antiviral: With the changing environment, new viral diseases are being identified, so there is a demand for a safer, non-toxic remedy. The cold and hot aqueous extracts of leaves and barks of SC were evaluated for their antiviral potential against H5N1 (avian influenza virus which causes a highly contagious disease of poultry) using CPE reduction assay to establish virucidal, pre-exposure and post-exposure potential of these extracts. With hot and cold aqueous bark extracts and hot aqueous leaf extracts, 100% inhibition of the virus was observed in virus yield reduction assay and in egg based in ovo assay. CC_{50}/EC_{50} (selective index) for cold aqueous extract (43.5) and hot aqueous extract (248) of bark exhibited their potency against H5N1 virus.[51] The aqueous extract of leaves was also found to inhibit the goatpox virus [52] and the buffalo pox virus.[53]

6.8 Cardioprotective: In case of SC, the hydroalcoholic extract of leaves was evaluated in spontaneously hypertensive and normotensive wistar rats. The findings of the research investigation revealed that the extract decreased the blood pressure as well as the heart rate. Extracellular calcium influx and inhibition of arterial tone were suggested as the most probable mechanism of action.[54]

The hydroalcoholic extract of SC was evaluated for its antihypertensive, and vasorelaxant effect. Polyethylene catheters were inserted into the inferior vena cava and lower abdominal aorta in the anaesthetized rats for dosing and measuring blood pressure. The extract at the doses of 0.5; 1; 5; 10; 20 and 30 mg/kg, i.v. was able to induce hypotension (due to reduction in endothelium mediated peripheral resistance) and bradycardia (due to meandering cardiac muscarinic activation).[55]

The elevated serum levels of alanine transaminase (ALT), serum creatine phosphokinase (CPK), aspartate transaminase (AST), lactate dehydrogenase (LDH), HDL-cholesterol due to Doxorubicin(1.5 mg / kg/b.w., 15 days) induced cardiotoxicity were brought to normal range after the administration of aqueous suspension of SC seed extract (100 mg/kg/b.w. for 15 days).[56]

The oral administration of the methanolic extract of SC at the doses of 250 mg/kg and 500 mg/kg consecutively for 30 days reversed and retained the activity of AST, ALT, LDH and CPK to normal levels against the isoproterenol- induced myocardial infarction. [57]

6.9 CNS Activity: De Lima *et al.*, studied, different extracts, fractions and subfractions from the seeds of *Syzygium cuminii* Linn. Skeels, for behavioural effects in mice, particularly in relation to their sedative and anticonvulsant actions. Oral treatment with the hydroalcoholic extract showed an anticonvulsant activity in pentylenetetrazol- and maximal electroshock-induced convulsions, besides a hypothermic effect. The ethyl acetate fraction and its subfractions enhanced latency and duration of the first convulsion induced by pentylenetetrazol. *S. cuminii* has some active principles with central depressant properties, and some of them also present an anticonvulsant action.[58]

Kumar *et al.*, reported the seed extracted with ethyl acetate and methanol investigated on albino mice in rota rod and actophotometer at a dose of 200 mg/kg and 400 mg/kg exihibited significant CNS activity. The significant CNS activity due to the presence of saponins.[59]

6.10 Antinociceptive: Antinociceptive activity is a process of blocking the detection of a painful or injurious stimulus by sensory neurons. With SC, the hydro-alcoholic leaf extract was evaluated for its analgesic potential in rats. To assess the cutaneous nociception, hot plate and formalin tests were used while for muscular nociception, forelimb grip force was measured. The extract at the dose of 100–300 mg/kg i.p. exhibited a significant decrease in the pain scores in all the phases of the formalin test but extract even at the dose of 300 mg/kg was not able to modify the grip force in intact rats. Therefore, the extract exhibited an excellent analgesic activity (on cutaneous and deep muscle pain). [60]

6.11 Gastroprotective: Natural products provide a safer remedy to protect the gastric mucosa of aggressive or irritating agents. Seed kernel extract of SC (200 mg/kg) was evaluated for its antiulcer activity. First, the diabetes was induced using low dose streptozotocin (35 mg/kg) in combination with high fat diet. Then the gastric ulceration was produced in diabetic rat's ethanol and indomethacin models. It was observed that there was a significant decrease in the gastric ulcer index after the administration SC extract alone and as well as in combination with Acarbose (5mg/kg).[61]

In another research investigation, the hard liquor (48% ethanol- 1ml/150gm b.w.) and aspirin (200 mg/kg, orally) were used to induce gastric ulcer in rats. The aqueous extract of SC leaves at the doses of 200 and 400 mg/kg produced ulcer inhibition (%) of 32.17% and 61.09% respectively in hard liquor model and 23.01% and 70.33% respectively in aspirin model. [62] SC fruit extract at the dose of 200 mg/kg b.w. was administered orally for 10 days to streptozotocin induced diabetic and to rats exposed to ulcerogens (like aspirin, 95% ethanol, cold-resistant stress and pylorus-ligation). The observations of the study revealed that there was a decrease in acid-pepsin secretion, cell shedding and LPO while an increase in the GSH (in gastric mucosa), mucosal glycoprotein and mucin. [62-65]

6.12 Antifertility activity: Rajasekaran *et al.,* has revealed antifertility effect of oleanolic acid isolated from the flowers of *E. jambolana* significant decreased the fetilizing 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. [66]

6.13 Hepatoprotective: Hepatoprotective agents are those that provide protection to the liver (which performs important functions like metabolism, secretion, storage, and detoxification of endogenous and exogenous substances). The alcoholic extract of the pulp of SC (100 and 200 mg/kg/day) exhibited a significant hepatoprotective action on paracetamol (PCM)-induced hepatotoxicity in albino rats. The elevated serum levels of ALT, AST, AP were decreased and histopathological studies depicted a reduction in fibrosis and necrosis.[67]

The anthocyanins rich SC pulp extract (50 to 500 ppm) has shown its beneficial effects in preventing the CCl_4 induced liver damage by declining the lipid peroxidation, suppressing the CCl4-induced release of LDH, and elevating the GPx (antioxidant enzyme) activity. [68] Aqueous leaf extract [69] and methanolic seed extract [70] have also shown hepatoprtective effects through biochemical estimations and histopathological studies.

6.14 Antibacterial activity: Shaikh *et al.,* have investigated antibacterial activity of ethanolic extracts of *Eugenia jambolana* against gram positive and ngram negative organisms.[71]

Bhuiyan *et al.,* reported antibacterial activity of methanol and ethyl acetate extracts of the seeds of *E. jambolana* at a concentration of 200 µg/disc against five Gram positive bacteria (*Bacillus creus, B. subtalis, B.megateriun, Steptococcus ß–haemolyticus, S. aureus*) and nine Gram negative bacteria (*Shigella dysenteriae, S. Shiga, S. boydii, S. flexneriae, S. sonnei, E. coli, S. typhi B, S. typhi B- 56* and *Klebsicella species*) by disc diffusion method.[72]

Shafi *et al.,* has reported good antibacterial action from essential oil of *E. jambolana* leaves.[73]

Pitchai Daisy *et al*., have worked on the antibacterial activity of the extract of *Syzygium cumini* by disc diffusion method using extended spectrum beta lactamase (ESBL) producing bacteria. Methanol, acetone and hexane extract of *Syzygium cumini* seeds were examined for antibacterial activity on *Aeromonas hydrophila, Acinetobacter baumannii, Citrobacter freundii, E. coli, Enterobacter aerogenes, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis.* Methanol extract of *Syzygium cumini* seeds exhibited significant antibacterial activity against bacteria.[74]

6.15 Chemoprotective: Various herbal drugs have proved their beneficial effect in protecting healthy tissues from the toxic effects of anti-cancer drugs. The aqueous and ethanolic SC seed extracts have

shown chemoprotective action in the *in vivo* oxidative stress and genomic damage.[75]

It has been reported that SC extract in the doses of 125 and 250 mg/kg/b.w./animal/day exhibited the cancer chemopreventive properties in the DMBA-induced croton oil promoted two stage skin carcinogenesis in Swiss albino mice. It was found that the extract was able to decline the tumor incidence, cumulative number of papillomas and elevate the average latency time as compared to the control group. [76-77]

The tumor burden, tumor incidence and cumulative number of gastric carcinomas induced by benzo-a-pyrene were found to decrease after the treatment with 25 mg/kg b.w./day of the SC extract exhibiting its broad spectrum chemoprotective effects.[78]

6.16 Antiallergic Activity: According Brito *et al., Syzygium cumini* skeels shows antiallergic effect and indicate that its edematogenic effect is due to the inhibition of mast cell degranulation and of histamine and serotonin effects where as the inhibition of eosinophil accumulation in the allergic pleurisy model is probably due to an impairment of CCL11/ eotaxin and IL-5 production.[79]

6.17 Inhibits lipid peroxidation: Some enzymatic and non-enzymatic reactions lead to lipid peroxidation associated with mutagenesis and cellular damage. The fruit pulp, seed coat and kernel extracts were evaluated for their lipid peroxidation inhibition activity and was seen that the seed and coat and the pulp extracts were less active than the kernel. [80]

An research investigation utilized the pulp extract (enriched with anthocyanins) to study its potential to inhibit the iron ($FeSO_4$)-induced lipid peroxidation in different organs of rat (Liver, liver mitochondria, brain, testes etc.) *in vitro*. A concentration of 5ppm was found to show beneficial results with highest lipid peroxidation inhibition in liver mitochondria (86%), followed by liver (83%), testes (72%) and brain(68.3%). [81] SC seed extract when administered orally for 15 days to alloxan treated rats, exhibited an elevated antioxidant the enzyme level and declined lipid peroxidation activity. [82]

6.18 Antihistamine activity: Mahapatra *et al.*, found the methanol extract of dried seeds, administered intraperitoneally to rats was active vs. histamine induced pedal edema.[83]

6.19 Antipyretic activity: According to Chaudhari *et al.*, chloroform extracts of dried seeds showed antipyretic activity [84] and Mahapatra *et al.*, studied methanol extracts of dried seeds administered intraperitoneally to rats at doses of 50 mg per kg were active versus yeast induced pyrexia.[83]

6.20 Antiplaque activity: Namba *et al*., have studied aqueous, methanolic and methanol-water (1:1) extracts of the bark were able to suppress plaque formation *in vitro*. All were active against *Streptococcus mutans* at 260,120 and 380 µg per ml respectively.[84]

CONCLUSION: *Syzygium cumini* (L.), a traditional plant medicine having multiple pharmacological actions possess considerable potential value clinically. The plant has many imperative compounds which present the nearly all characteristics of the plant. Though many works on pharmacological activities of phytochemical constituents of *Syzygium cumini* (L.) has been carried out, still much more is remaining to work on the development of novel drug delivery systems of *Syzygium cumini* (L.) extract and its isolated compounds. Further more attention should be paid to the chemical and toxicity studies of *Syzygium cumini* (L.).

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