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REVIEW PAPER

BIOACTIVE COMPOUNDS AND ETHNOMEDICINAL USES OF *Syzygium cumini* (L.) SKEELS – A COMPREHENSIVE REVIEW

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Abstract
Syzygium cumini (*S. cumini*) is an underutilized fruit of tropical and subtropical regions with various bioactive compounds distributed in all parts of the plant. The fruit and its by-products, such as seeds, have both nutritional and medicinal value. However, fruit and seeds have not been fully considered as potential functional food ingredients to develop foods with promising health benefits. Based on the available information in the literature, fruit and seed are rich in phytochemicals, such as myricetin, oxalic acid, gallic acid, citronellol, cyanidin diglucoside, hotrienol, phytosterols, flavonoids, carotenoids and polyphenols as well as micronutrients. In addition, they were reported to possess several beneficial health properties. Further, research in this area would provide valuable information for their potential utilization as functional food ingredients. This review presents comprehensive information about the bioactive compounds and nutraceutical properties of *S. cumini* fruit and seeds, as well as the potential of using them as functional food ingredients

Keywords: *Syzygium cumini*, fruits, Seeds, bioactive compounds, health benefit, functional food

Introduction

The genus *Syzygium* is derived from the Greek word *Syzygos* meaning yoked together (Janick and Paull, 2008). It is mainly distributed in the Old-World tropics from Africa to the West Pacific with a major concentration in Malaysia (Parnell *et al*., 2007). Till date, around 55 taxa of *Syzygium* have been reported in India (Shareef *et al*., 2012) with the highest concentration of 49 taxa in the Western Ghats (Shareef *et al*., 2010). *Syzygium cumini* is one among the species and belongs to the family Myrtaceae, which includes 150 genera and above 3600 species (Saleem *et al*., 2016). Global production of *Syzygium cumini* is about 13.5

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million tons per annum (Chhikara et al., 2018) out of which India contributes about 5.4% (Raza *et al*., 2015). It is an underutilized fruit of tropical and subtropical regions and contains phytoconstituents e.g. anthocyanins, flavonoids, steroids, polyphenols, terpenoids etc. in worthy amounts. Other associated species of the plant are *Syzygium cumini* (L.) Druce, *Eugenia jambolana* Lam., *Syzygium jambolanum* DC. It is commonly known by the name of jambolan, java plum, Jamun, Indian blackberry, kalajam, mahajambu, jambul, purple plum. The fruit is an oval-shaped berry and has been considered as "Fruit of Gods" in Hindu myths (Jagetia, 2017). The original home of *Syzygium cumini* is India, distributed throughout India, in the forest up to 1800m height. Today, these trees are found throughout the Asian subcontinent, Eastern Africa, South America, Madagascar, Java, Florida and Hawaii (USA). It is well known for its medicinal and curative properties like antidiuretic, antimicrobial, hepatoprotective, antifungal, antioxidant and various other properties. The nutritional and phytochemical content of fruits depends on the maturity level, variety, climatic conditions, agricultural practices, and post-harvest handling and processing. The purple to black colour of the fruit is due to the presence of anthocyanin and is responsible for high antioxidant potential (Panghal *et al*., 2018). The active principles present in medicinal plants are used for the healing purpose against a variety of diseases from the beginning of civilization. In Unani medicine, *Syzygium cumini* is used as a liver tonic, strengthens the teeth and gums, enrich the blood, and deworm against ringworm infection of the head (Damasceno *et al*., 2002). Stem bark, dried seeds and root bark decoction are used to treat diarrohea, dysentery and dyspepsia and further to cure asthma and bronchitis (Ranjan *et al*., 2011). The decoction of *Syzygium cumini* seeds relieves fatigue and strain. The fruit pulp is used to treat gingivitis, and haemorrhoids. Examples for the traditional use of *Syzygium cumini* in different regions of the world are given in Table 1. In Indian Ayurveda medicine, the aerial parts of Jamun have been used to cure sores in the mouth, colic, digestive illnesses, diarrhoea, dysentery, diabetes, pimples, piles, stomach ache, cancer (Jain, 1991) and act as a blood purifier. Fruit pulp with honey is administered to keep the body healthy, while its seed powder helps in clearing the skin blemishes and acne. The leaf juice is effective in the treatment of dysentery and skin disorders. Phytochemical constituents present in *Syzygium cumini* seed are used to treat diabetes, pharyngitis, spleenopathy, urethrorrhea due to the presence of gallic acid, ellagic acid, corilagin, 3, 6-hexahydroxy diphenoylglucose,1-galloylglucose, 3galloylglucose, quercetin, β-sitoterol,4,6-hexahydroxydiphenoyl glucose (Kumawat *et al*., 2018). The aim of this review is to provide literature covering botanical, phytochemical, pharmacological and health aspects of *Syzygium cumini* along with its utilization as a food fortification tool.

Morphology characteristics

Syzygium cumini is a perennial tree with a 30 meter height and stems up to 15 meters (Singh and Navneet, 2018) and is a foliaceous tree with greyish-brown bark. It is a cross-pollinated tree and bears fruits up to 100 years. Brown dyes and a gum

Kino are obtained from the wood which is whitish and durable. The leaves are 5-25 cm long and 2.5-10 cm wide with a turpentine smell and are leathery, oblongovate.

Table 1. Traditional uses of *Syzygium cumini* (Region- wise).

Region	Parts used	Mode of Use	References
Paraja tribe (Odisha, India)	Bark	Paste is used to cure dysentery when taken orally with water	Tikadar *et al*., 2017
India	Root	Used to cure dysentery and diarrhoea when taken twice daily with empty stomach	Sen and Behra, 2008
Brazil	Leaves	Tea prepared from infusion/decoction of leaves (taken orally) for treatment of diabetes	Ayyanar *et al*., 2008
Southern Brazil	Leaves	Daily intake of 2.5 g/L of leaves are used for treatment of diabetes	Ayyanar and Babu, 2012
Madagascar	Seeds	Seeds are taken as an effective remedy for stabilizing the impacts of diabetes	Ayyanar and Babu, 2012
Sinhal (Sri lanka)	Bark	Bark decoction is used in treating diabetes mellitus in Ayurveda medicine	Perera *et al*., 2017
-	Leaves	Used as a cleaning agent that effectively strengthens teeth and gingiva	Kumar *et al*., 2009
Kani(Tamil nadu, India)	Leaf juice	Leaf juice is mixed with honey or cow milk	Ayyanar *et al*., 2008
Surinam	Leaves	Women's use leaves to contract the vagina after delivery	Ramya *et al*., 2012
Pawi, Lakher (Northeast India)	Leaves juice	Juice of leaves is used as an antidote in Opium poisoning	Ayyanar *et al*., 2013
Maharashtra tribe (India)	Leaves	Oral intake of leaves for 2-3 days for jaundice treatment among adults and children	Ayyanar *et al*., 2013
-	Leaf ash	For strengthening teeth and gums leaf ash is used	Ramya *et a*l., 2012
-	Fruit	Jamun is used as semen-producer and is hematinic and is used as thermos regulant in Siddha medication	Ramya *et al*., 2012
Philippines	Bark	The bark is utilized for diabetes	Bandiola *et al*., 2017
Goa (India) and Philippines	Fruit	Wine is produced which resembles Port	Swami *et al*., 2012
Jhabua District (Madhya Pradesh, India)	Bark	The bark is used for dysentery and diarrhoea	Rout and Panda, 2017

Flowering starts in the month of March to April and the fruit develops in May or June and is initially green in color, then turns pink and finally purple in color. Flowers are scented, greenish-white, round or oblong in shape and are in clusters of just a few or 10 to 40. The fruits are dark purple, black, luscious, fleshy with edible berries weighing individually 2-5 g at the time of maturity, 1.5 to 3.5cm long and contains a large single, oblong, green or brown seed upto 4 cm long and some seedless. The skin of the fruit is glossy and smooth with purple or white pulp, discolored bark, rough and cracked on the lower part of the trunk (Bijauliya *et al.,* 2017). Fresh seeds contain 20-80% of the total fruit weight with 6% seed coat and 94% cotyledons (Sivasubramaniam and Selvarani, 2012). Depending on the fruit size there are two varieties of *Syzygium cumini*; small and big, the smaller variety is round and has sweet flesh with low content of acids, tannins and anthocyanins. The large seed is oval and has acidic flesh with a high content of acids, tannins and anthocyanins (Roy *et al*., 2013). The different varieties of *Syzygium cumini* grown in the Indian subcontinent are represented in Table 2.

Table 2. Different varieties of *Syzygium cumini* and their characteristics

Variety	Characteristics
Ra Jamun	Oblong, large, juicy, sweet, deep purple with a small seed, ripens in June-July
Badama	Large and juicy
Kaatha	Small, Acidic, ripens in the middle of June
Jathi	Ripens in May-June
Ashada	Ripens in June-July
Bhado	Ripens in August
Goma Priyanka	Ripens in fourth week of May
GJ – 8	Ripens in second week of June
GJ – 19	Ripens in first week of June
GJ – 23	Ripens in middle of June
GJ – 40	Ripens in fourth week of June
Narendra Jamun 6	Oblong
Krian Duat	Purple and white flesh
Paras	Large sized sweet and juicy fruits.
Konkan Bahdoli	Bold, small seeds

Source: Adapted from Potential of commercial cultivation of Jamun (Anonymous, 2013)

Phytochemical constituents of *Syzygium cumini*

Syzygium cumini (L.) is one of the fruits with high nutritive value. In the fruit processing industry, edible portions of the fruits are processed into valuable products such as puree, canned slices, juice, jam, pickles and results in high amounts of waste materials such as peels, seeds, stones, and oilseed meals which are discarded as waste (El-Safy *et al*., 2012). But seeds are also a promising source

of useful components because of their biochemical characteristics (Table 3). Different researchers have evaluated biochemical components present in fruit and found these to be of high medicinal value due to the presence of glycosides, flavonoids, terpenoids, alkaloids and phenols.

Table 3. Biochemical composition of *Syzygium cumini* seed

Component	Quantity	Reference
Moisture (%)	3.21-53	Dagadkhair *et al*., 2017; Ghosh *et al*., 2016; Harine and Janapriya, 2018; Ayya *et al*., 2015; Raza *et al*., 2015; Mathur, 2015; Kaur *et al*., 2018
Protein (%)	1.97-8.5	Dagadkhair *et al*., 2017; Ghosh *et al*., 2016; Harine and Janapriya, 2018; Ayya *et al*., 2015; Raza *et al*., 2015; Prajatka *et al*., 2016; Mathur, 2015; Kaur *et al*., 2018; Anjali *et al*., 2017; Ranjan *et al*., 2011; Binita *et al*., 2017
Fat (%)	0.65-4.86	Dagadkhair *et al*., 2017; Ghosh *et al*., 2016; Harine and Janapriya, 2018; Ayya *et al*., 2015; Raza *et al*., 2015; Prajatka *et al*., 2016; Kaur *et al*., 2018; Anjali *et al*., 2017
Ash (%)	1.5-21.72	Dagadkhair *et al*., 2017; Ghosh *et al*., 2016; Harine and Janapriya, 2018; Ayya *et al*., 2015; Raza *et al*., 2015; Prajatka *et al*., 2016; Kaur *et al*., 2018
Fibre (%)	1.21-16.9	Ghosh *et al*., 2016; Harine and Janapriya, 2018; Ayya *et al*., 2015; Raza *et al*., 2015; Prajatka *et al*., 2016; Kaur *et al*., 2018; Anjali *et al*., 2017; Ranjan *et al*., 2011; Binita *et al*., 2017
Carbohydrates (%)	6.05-89.68	Dagadkhair *et al*., 2017; Ghosh *et al*., 2016; Harine and Janapriya, 2018; Ayya *et al*., 2015; Kaur *et al*., 2018
Ascorbic acid (%)	1.84-35.75	Dagadkhair *et al*., 2017; Ghosh *et al*., 2016
Iron (mg)	1.25-18.62	Ghosh *et al*., 2016; Harine and Janapriya, 2018; Ayya *et al*., 2015
Total flavonoids (TF) (mg/g)	6.00	Prajatka *et al*., 2016; Hossain *et al*., 2017
Total phenolic content (TPC) (mg/g)	78.29	Prajatka *et al*., 2016; Hossain *et al*., 2017
(2,2'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid)) (ABTS) (μM/g)	118.61	Prajatka *et al*., 2016

Earlier studies revealed that the extracts also play a great role in the extraction of phytochemicals from seed, leaves, bark, flower, fruit and even roots. Different phytochemicals such as 1-galloylglucose, 3-galloylglucose, gallic acid, 3,6-hexahydroxy diphenoyl glucose, ellagic acid, corilagin, quercetin, β-sitoterol, 4,6-hexahydroxydiphenoyl glucose, ferulic acid, guaicol, resorcinol, *p*-coumaric acid, catechin, epicatechin, quercetin, caffeic acid, tannic acid were reported from seed (Kumawat *et al.,* 2018; Balyan and Sarkar, 2017; Mathur, 2015).

The leaves are reported to contain mearsetin, quercetin, myricetin, gallitanins, essential oil (terpenes, 1-limonene and dipentene), monoterpenoid terpinene, terpenolene, borbeneol, polyphenol (gallic acid, methylgallate, kaempferol, ellagic acid, ellagitannin, nilocitin, myrecetin 3-0-D- glucaronopyranoside, 3-0-ß Dglucuronopyranoside, myricetin 3-O-4-Acetyl-L-rhamnopyranoside), terpineol and eugenol (Satpute and Vanmare, 2018). The root extract showed the presence of flavonoid glycosides, isorhamnetin 3-O-rutinoside). Malvidin-3-laminaribioside, citric acid, mallic acid, gallic acid, anthocyanins delphinidin-3-gentiobioside, petunidin-3 gentiobioside, cyanidin diglycoside, petunidin and malvidin are reported from the fruit extract (Bijauliya *et al*., 2017). Myricetin-3-L-arabinoside, quercetin-3-D-galactoside, kaempferol, quercetin, myricetin, isoquercetin, dihydromyricetin, oleanolic acid, acetyl oleanolic acid, eugenol-triterpenoid A, eugenol-triterpenoid B are reported in the flower extract (Sehwag and Das, 2014). The bark extract contains β-sitosterol, eugenin and fatty acid ester of epi-friedelanol, betulinic acid, friedelin, epi-friedelanol, quercetin kaempferol, myricetin, gallic acid and ellagic acid bergenins, flavonoids and tannins (Sehwag and Das, 2014). The various bioactive chemicals along with their structure are presented in Figure 1.

Pharmacological activities of *Syzygium cumini* fruit and seeds

The extracts of different plant parts and the isolated compounds of *Syzygium cumini* have been evaluated for antimicrobial, antibacterial, anticancer, antimicrobial, antidiabetic, hepatoprotective, antifungal, anti-diuretic and antioxidant activities. The health benefits of *Syzygium cumini* (L.) Skeels seed extracts are represented in Table 4.

Antimicrobial Activity

The methanolic extracts of *Syzygium cumini* (Linn.) seeds show 20.03 mm zone of inhibition against MTCC 2413 *Bacillus subtilis* at a concentration of 25 mg/ml using agar well diffusion method (Yadav *et al*., 2017). The antimicrobial activity of *Syzygium cumini* seed powder with 4 different formulations such as sample A (collected from a local manufacturer), sample B (polyherbal formulation with *Syzygium cumini* seed powder), sample C and D (formulations from diverse manufacturers) were determined. The results revealed that *Syzygium cumini* seed powder from a local manufacturer and formulation with powder from other manufacturers had good activity against *Candida albicans* (Chitnis *et al.,* 2012). The methanol, ethanol and acetone extracts of *Eugenia jambolana* (Lam.) seeds have significant antimicrobial activities *against Streptococcus aureus, Shigella, Pseudomonas* and *Salmonella* isolates with an inhibition zone of 11 to 35 mm (Ogato *et al*., 2015).

Antibacterial Activity

Antibacterial activity is the ability of a substance to inhibit or kill bacterial cells. Medicinal plants such as *Allium sativum, Azadirachta indica, Cordia dichotoma, Holoptelea integrifolia, Ocimum sanctum, Syzigium cumini,* Wild Himalayan fig and *Trigonella foenum graecum* possess antibacterial properties (Imran *et al*.,

2017; Kumari *et al*., 2017). Aqueous extract of *Syzygium cumini* leaf showed lowest minimum inhibitory concentration (MIC) of 10µL in the case of *Proteus mirabilis* and *Shigella flexneri* and highest minimum inhibitory concentration (MIC) of 50 µL in case of *Staphylococcus aureus, Shigella sonnei* (Satish *et al*., 2008). Crude methanol and aqueous extracts of the leaves of *Syzygium cumini* were assessed against Gram positive and negative bacterial strains using the disc diffusion method and the maximum zone of inhibition 22m was obtained using methanol extract against Gram negative bacteria (Gowri and Vasantha, 2010). In another study methanol extract of *Syzygium cumini* leaf showed an inhibition zone of 32mm against *Staphylococcus aureus* as a comparison to standard drug Chloramphenicol which is 26mm (Kumar *et al*., 2014).

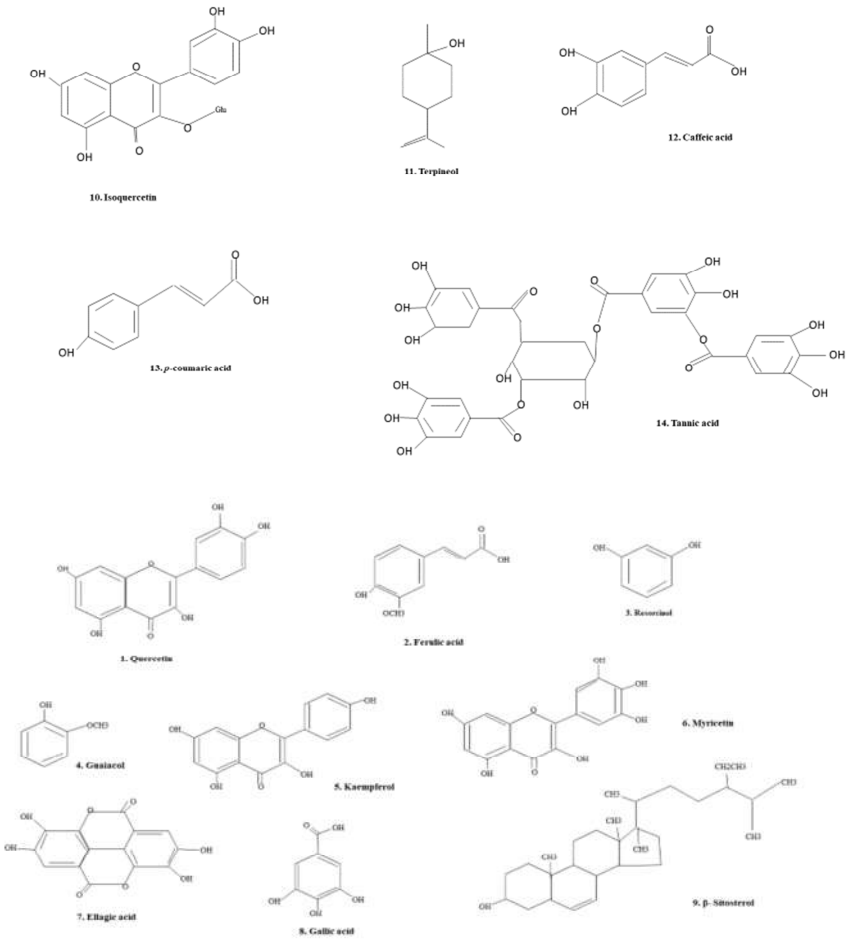

Figure 1. Biologically active compounds reported from *Syzygium cumini*

The Acetylsalicylic acid extract of *Syzygium cumini* leaves showed a 24 mm zone of inhibition against Gram negative bacteria *Vibrio parahimolyticus* (Julie *et al*., 2017). Petroleum and ethanolic extracts of leaves showed a maximum zone of inhibition (8-25mm) against the drug resistant strains of *Streptococcus aureus* and *E. coli* (Imran *et al*., 2017). Antibacterial activity of the aqueous and alcoholic extracts of stems was observed against two Gram-positive bacteria (*Bacillus amyloliquefaciens* and *Staphylococcus aureus*) and two Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) by agar well diffusion method and the results revealed that the alcoholic extract showed maximum antibacterial activity (Sharma *et al*., 2017). The fruit juice of *Syzygium cumini* showed inhibition of 1 to 6 logs against enteric pathogens *Salmonella typhimurium*, *Shigella Flexneri* and *Staphylococcus aureus* (Haque *et al*., 2017). Hence, from the earlier results, it can be concluded that every part of the plant has antibacterial activity when extracted with different solvents. Therefore, the plant has the potential to be used in nano-composite forms for application in different fields of applied sciences.

Table 4. Health benefits of *Syzygium cumini* (L.) Skeels seed extracts prepared using different solvents on living organism

No	Activity	Extract type	*in vitro*/ animal model	Reference
1.	Antidiabetic	Methanol, Ethyl acetate	Mice	Kumar, 2008
		Ethanol	Rat	Chaturvedi *et al*., 2009
		Chloroform	Mice	Dusane *et al*., 2011
		Methanol	Rat	Mastan *et al*., 2009
		Ethanol	Rat	Kasiappan *et al*., 2005
2.	Analgesic	Methanol, Ethyl acetate	Mice	Kumar, 2008
3.	Anti-inflammatory activity	Methanol, Ethyl acetate	Mice	Kumar, 2008
		Methanol, Ethyl acetate	Rats	Kumar *et al*., 2008
		Aqueous	Human	Ezekiel and Heuertz, 2015
4.	Cardioprotective	Aqueous	Rat	Patel *et al*., 2010
		Methanol	Rat	Mastan *et al*., 2009
5.	Chemopreventive	Acetone	Mice	Parmar *et al*., 2010
		Aqueous, ethanol	pBR322	Arun *et al*., 2011

No	Activity	Extract type	*in vitro*/ animal model	Reference
			DNA	
		Double distilled water	Mice	Goyal *et al*., 2010
6.	Neuro-psychopharmacological activity	Methanol/Ethyl acetate	Mice	Kumar, 2008
		Ethyl acetate/ methanol	Mice	Kumar *et al*., 2007
		Chloroform	Rat	Sehwag and Das, 2014
		Hydro-alcohol	Rat	Sehwag and Das, 2014
7.	Gastroprotective	Ethanol	Rat	Jonnalagadda *et al*., 2013
8.	Heptoprotective	Methanol	Rat	Sisodia and Bhatnagar, 2009
		Ethanol	Rat	Islam *et al*., 2015
9.	Antipyretic activity	Methanol, Chloroform extract	Rat	Sehwag and Das, 2014
10.	Anticancer	Ethyl acetate, Methanol	MCF-7 breast cancer cells	Ruthurusamy *et al*., 2015
11.	Radioprotective	Hydro-alcohol	Mice	Jagetia *et al*., 2005
12.	Immunomodulatory	Aqueous	Human lymphocytes	Borges *et al*., 2017
		Methanol	Mice	Barh and Vishwanathan 2008
13.	Antimicrobial	Methanol	*Bacillus subtilis*	Yadav *et al*., 2017
		Acetone, methanol, ethanol	*S. aureus, Pseudomonas species and Salmonella species*	Ogato *et al*., 2015
		Methanol, ethyl acetate	Gram positive and negative bacteria	Sehwag and Das (2014), Kumawat *et al*., 2018
		Ethyl acetate	Mice	Bag *et al*., 2012

No	Activity	Extract type	*in vitro*/ animal model	Reference
		Dichloromethane methanol	*Candida*	Hofling *et al*., 2010
14.	Antibacterial	Methanol	*Vibrio cholera, Aeromonas hydrphila, Bacillus subtilis*	Jadhav *et al*., 2009
		Methanol	*Proteus vulgaris/ Pseudomonas aeruginosa*	Mathur *et al*., 2011
		Methanol/ ethanol	Gram positive/ Gram negative bacteria	Sharma *et al*., 2012
		Alcohol	*E. coli*	Meshram *et al*., 2011
		Ethanol	*E. coli, B. subtilis, P. aeruginosa and S. aureus*	Bhusari, 2014

Antifungal activity

Antimycotic activity of plants remains largely unexplored and these days' interest has grown in studying antifungal activity from plant sources (Singh *et al*., 2017). The aqueous and methanolic extract of *Eugenia jambolana* (Lam.) seeds possesses antifungal activity against dermatophytic fungi *Candida albicans* and *Tricophyton rubrum* using agar diffusion method (Chandrasekaran and Venkatasalu, 2004). Kharat *et al*., 2005 also reported the plant effectiveness against the standard fungal culture of *Fusarium oxysporum* and *Alternaria alternata* which are responsible for various diseases in agriculture crops. Pant *et al*., 2014 administered that methanolic fruit extract of *Syzygium cumini* has excellent antifungal action against various pathogenic fungi *Fusarium oxysporium, Rhizoctonia solani and Sclerotium rolfsii*. Methanolic bark extract at a concentration of 5% was highly effective against fungal species and was reported to reduce the fungal growth by 43% (Khan *et al*., 2016).

Anti-arthiritic activity

Arthritis is a chronic inflammatory disease in joints. The oral administration of petroleum ether extract of the plant stem bark in rats with a dose of 1000 mg/kg on

complete freund's adjuvant induced arthritis showed high anti-rheumatic effect (Venkataramanan *et al*., 2016). Similarly, methanolic extract of the plant seeds showed anti-arthritis effect on adjuvant induced arthritis in rats when given at a dosage of 500mg/kg (Kumar *et al*., 2008; Arya *et al*., 2011).

Chemopreventive activity

In vitro anti breast cancer activity of methanol extract of *Syzygium cumini* fruit pulp against MCF-7 cell line was evaluated using the method of microculture tetrazolium (MTT) assay to evaluate the reduction of viability of cell cultures. The results showed that the cell viability was inhibited to different extents due to the presence of flavonoids, alkaloids, steroids in the extract (Tripathy and Pradhan, 2015). Hydro-alcoholic extract of *Syzygium cumini* seed (125mg/kg body weight) possesses chemopreventive properties in the DMBA-induced and croton oil promoted skin carcinogenesis in Swiss albino mice by a significant reduction in cumulative numbers of papillomas and tumor incidence (75%) (Parmar *et al*., 2010). The aqueous extract of *Syzygium cumin* seed (25 mg/kg body weight/day) was effective in preventing benzo-a-pyrene (BaP)-induced forestomach carcinogenesis in swiss albino mice and had reduced the tumour incidence, tumour burden and the cumulative number of gastric carcinomas (Goyal *et al*., 2010). Oral administration of 125 mg extract/kg body weight/day of *Syzygium cumini* seeds during pre-initiation or post initiation reduced the aggregate numbers of papillomas, the tumour incidence and increased the average latency period when compared with the control group and it was concluded that extract has the potential to modulate biochemical and histopathological status during skin carcinogenesis. Further, there was a significant reduction in lipid peroxidation and elevation in the activities of enzymatic antioxidants, non-enzymatic antioxidants and protein levels (Parmar *et al*., 2011). In- *vitro* inhibitory effect of *Syzygium cumini* extract on two cervical cell lines (HeLa and SiHa) was also observed. The crude extract was reported to be more effective in growth inhibition and apoptosis with growth inhibition of 33.7 % and 24.4% in HeLa and SiHa cells at its highest concentration (100%) in MTT assay and the methanolic extract (80% v/v) showed an apoptotic index of 20.5% and 16.1% (Barh and Vishwanath, 2008).

Antianaemic activity

Anemia is the most common blood disorder as it decreases the total amount of red blood cells or haemoglobin in the blood. Aqueous extract of *Syzygium cumini* seed was reported to increase the total haemoglobin, preventing and lowering the bodyweight and free radical formation in tissue (Sah and Verma, 2011).

Antidiabetic activity

Diabetes mellitus is a silent killer disease and other than insulin, this disorder can be controlled with the plant sources. The seeds of *Syzygium cumini* (L.) are recommended widely in many medical systems for controlling diabetes. Anti-diabetic effect of seeds has also been proved by many pharmacological studies and their mode of action is represented in Figure 2. Acute *in-vivo* studies of ethanol extract (100 mg/kg p.o.) of *Syzygium cumini* seeds in alloxan-induced diabetic rats

showed a decrease in serum glucose level by 88mg/dl as compared to Gibenclamide (97mg/dl) (Bansode *et al*., 2017). In another study, in-vivo anti-diabetic activity of chloroform, methanol and aqueous extracts of *Syzygium cumini* seeds were assessed histologically in streptozotocin (STZ) induced diabetic mice and the results revealed restoration of normoglycemia, increase in G6PD, Plasma insulin and C-Peptide levels in the chloroform extract (Dusane and Joshi, 2011). Mycaminose, a deoxy-amino sugar isolated from the aerial parts of *Syzygium cumini* were evaluated for antidiabetic activity and alcoholic extract of seed powder was also reported to show hypoglycemic effect in Streptozotocin induced diabetic rats at a dosage level of 50mg/kg body weight (Kumar *et al*., 2008). Inorganic metals of the alcoholic extract of *Eugenia jambolana* (Lam.) flower showed a decrease in the blood glucose level in nicotinamide-streptozotocin-induced diabetic rabbits by 78.2 mg/dl after 30 days supplementation at a dosage of 100 mg/kg of body weight (Nisa and Malik, 2010). Ethanolic extract of *Eugenia jambolana* (Lam.) seed stimulated the pancreatic B cells to secrete more insulin and increased the insulin sensitivity in peripheral tissues i.e. adipose tissue, muscle, and liver, to clear blood glucose at a faster rate due to presence of 12% flavonoids (Yadav *et al*., 2010).

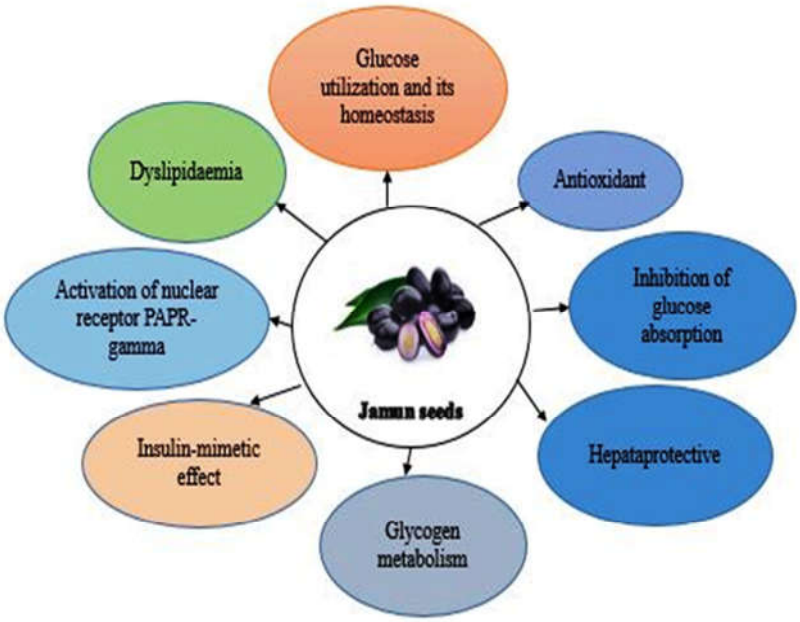

Figure 2. Mode of action of *Syzygium cumini* seeds as anti-diabetic agent

Anti-diarrheal activity

Antidiarrheal, antimotility and antisecretory activity of aqueous extract of *Syzygium cumini* seed was also studied by using the method of castor oil, charcoal meal test and castor oil induced intestinal secretions in mice and the extract showed

antidiarrheal activity with inhibition of 42.85% at a dose level of 500mg/kg, antimotility activity with inhibition of 38.89% at a dose level of 500mg/kg and antisecretory activity with inhibition of 51.61% at a dose level of 500mg/kg (Shamkuwar *et al*., 2012). In another study, the ethanol extract of *Syzygium cumini* bark reduced diarrhoea in rats when given an oral dose of 400 mg/kg by inhibiting gastrointestinal motility (45.1%) (Mukherjee *et al*., 1998). Seed powder prepared by mixing *Eugenia jambolana* (Lam.) seed with jaggery helps to get relief from diarrhoea and dysentery (Bhowmik *et al*., 2013).

Antioxidant activity

Oxidative stress is characterized by increased lipid peroxidation and a number of chronic complications of diabetes. Further, it occurs due to the depletion of antioxidant scavenger which creates an imbalance between free radical generation (Binita *et al*., 2017). Further, quercetin modifies the antioxidant defense pathways and inhibits lipid peroxidation either by directly scavenging free radicals or by inhibiting biomolecule oxidation. Antioxidants prevent free-radicals (O_2 and H_2O_2) and generate hydroxyl radicals for the acceleration of lipid peroxidation and decrease the activities of superoxide dismutase (SOD) and catalase (CAT) which further are responsible for several diseases and accelerate aging. Activities of these enzymes in diabetic brain increases after oral administration of aqueous extract of *Syzygium cumini* seed and alcoholic extract helped to restore them to the normal level. Further, more superoxide dismutase helped to reduce the toxic effects of superoxide radicals whereas CAT protected tissues from highly reactive hydroxyl radicals. The methanolic extract of *Syzygium cumini* showed total phenolic content of 17.6mg/g in leaf, 16.1.mg/g in seed and 8.7mg/g in pulp and flavonoid content of 43.24mg/g in leaf, 19.1/g in seed and 12.27mg/g in pulp (Margaret *et al*., 2015). Methanolic extract of leaves possesses an antioxidant property at a concentration of 106.34 ug/mL with IC_{50} value of 0.584 ± 4.0 µg/mL of DPPH assay (Kumar and Kalakoti, 2015). In-vitro antioxidant activity of methanolic extract of the bark and fruit skin using 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging assay, lipid peroxidation, ABTS assay, hydrogen peroxide scavenging assay, and ferric reducing antioxidant power (FRAP) assay has also been reported (Haroon *et al*., 2015).

Hepatoprotective activity

Hepatoprotective activity of methanol extract of *Syzygium cumini* seeds was investigated in rats at different doses for 14 consecutive days with group-I (control), group-II (silymarin treated; 1.0 mg/kg BW), group-III (extract of *Syzygium cumini* seeds treated; 250 mg/kg), group-IV (extract treated; 500 mg/kg) and group-V (CCl_4 treated; 1.5 mg/kg). An oral dose of CCl_4 (1.5 mg/kg, 1:1 in olive oil) was administered to all the groups, except animals in the control group and after 24h blood samples and liver tissues were collected for biochemical analysis. The values of liver function were found to be significantly lower while serum protein level was significantly higher in control and treated groups as compared to that of the CCl_4 treated group (Islam *et al*., 2015). The alcoholic extract of the pulp of *Eugenia jambolana (Lam.)* exhibited a significant

hepatoprotective action on paracetamol (PCM)-induced hepatotoxicity in albino rats when given at a dose level of 100 and 200mg/kg/day. The results showed a decrease in the serum levels of ALT (alanine aminotransferase), AST (aspartate aminotransferase), ALP (alkaline phosphatase) and a reduction in fibrosis and necrosis (Das and Sarma, 2009). The fruit of the plant is a rich source of anthocyanins. The *Syzygium cumini* peel extract was reported to suppress CCl(4)-induced LDH (Lactate dehydrogenase) leakage by 54% at 50ppm in rats and further, improving the cell viability by 39% (Veigas *et al*., 2008). Aqueous leaf extract (Moresco *et al*., 2007) and methanolic seed extract of *Eugenia jambolana* (Lam.) were also reported to show hepatoprotective effects through biochemical estimations and histopathological studies (Sisodia and Bhatnagar, 2009). Sidana *et al*., 2016 noticed significant reduction in the cholesterol levels from 220±33.60mg/dl to 199±30.85mg/dl and 190±28.81mg/dl and a reduction in triglyceride levels from baseline of 183±39.19mg/dl to 169±36.08mg/dl and 161±34.71mg/dl after 60 and 90 days of supplementation with *Syzygium cumini* seed powder and a percentage reduction by 8.28% and 13.66% respectively.

Immunomodulatory activity

The expression immune-modulatory means regulation of the immune system by suppression and stimulation of cells and organs of the immune system. Immunomodulatory therapy could be used as an alternative to conventional chemotherapy towards a variety of diseases. In- *vitro* study on the immunomodulatory effects on AAPH-induced damage in lymphocytes was conducted using the aqueous extracts of leaves and seeds of *Syzygium cumini* and the extracts are extracts were reported to exhibit antioxidant activity, prevent the increase of ectonucleotidase and adenosine deaminase (ADA) activities, inhibit acetylcholinesterase (AChE) activity, decrease lipoperoxidation and improvement in the cellular viability (Borges *et al*., 2017).

Neuro-psychopharmacological activity

Neuropharmacology is the methodology to study the effect of the functional component on the central nervous system with respect to biochemical and behavioral changes. Depressants are often prescribed by doctors to patients suffering from anxiety. The aqueous and ethanol extract of *Syzygium cumini* stem were observed by Sharma *et al*., (2017) on rat pheochromocytoma (PC)-12 cell line, by giving neurotoxic shock to Rat PC-12 cells using 6-hydroxydopamine. The ethanolic extract (75%) showed the maximum number of viable cells as compared to aqueous extract (50%). The chloroform extract of the seeds was also reported to possess central nervous system depressant action on rats by exhibiting variation in the general behavior pattern, reduction in spontaneous motility, hypothermia, muscle relaxation and suppression of aggressive behavior (Chakraborty *et al*., 1986). Oral treatment of hydro alcoholic extract showed anticonvulsant activity in pentylenetetrazol and maximum electroshock-induced convulsions besides a hypothermic effect due to the presence of active compounds present in the *Syzygium cumini* (Lima *et al*., 1998). Ethyl acetate and methanol extracts of the seeds at the dose level of 200mg/kg and 400mg/kg were reported to exhibit central

nervous system depressant action in Albino mice due to the presence of saponins (Kumar *et al*., 2007).

Anti-diuretic activity

Diuretics are drugs that increase the excretion of water and sodium ions. The frequently occurring side effects by using diuretics drugs are headache, nausea, dizziness, loss of appetite, gout, rheumatoid arthritis and joint pain in severe cases (Chandrasekar and Sivagami, 2017). The diuretic activity and mechanism of action were evaluated using the methanolic extract of *Syzygium cumini* seeds in male Wistar albino rats and it was reported that the oral administration of methanolic extract (300 mg/kg) in association with Lornoxicam (3 mg/kg) reduced the urinary sodium, potassium, and chlorine excretion as when compared to the methanol extract (Venkateshwarlu *et al*., 2015). Different extracts prepared using chloroform, methanol and aqueous extracts were used to study the diuretic activity of *Syzygium cumini* and were administered orally at a dose of 500 mg/kg. The methanol and aqueous extract possess the diuretic activity and showed an increase in total urine output and excretion of the electrolyte concentrations of sodium and potassium ions as compared to standard drug furosemide which was administered at a dose of 10 mg/kg body weight (Chandravarkar and Desai, 2014).

Radioprotective activity

Intraperitoneal administration of 80mg hydro alcoholic extract of *Syzygium cumini* seed/kg body weight in mice showed a reduction in the symptoms of radiation sickness (Jagetia *et al*., 2005). Histological examination of *mouse jejunum* exposed to 7, 10, 15 Gy gamma radiation was studied using leaf extract (50mg/kg body weight) of *Syzygium cumini* and the results revealed that the extract had provided protection against radiation induced intestinal mucosal damage in the small intestine and gastrointestinal damage (Jagetia *et al*., 2008).

Toxicity

The acute toxicity is the toxicity produced by a substance when administered in one or more doses during a period not exceeding 24hours. The hydro-alcoholic seed extract of *Syzygium cumini* and its phytosome formulation were evaluated against streptozotocin-induced diabetic rats for the acute toxicity, oral glucose tolerance test (OGTT) and anti-diabetic activity and the results showed no mortality and morbidity at a dose of 2000mg/kg of body weight and also control in blood sugar level in comparison with standard drug Glibenclamide (Amudha *et al*., 2018). 70% methanolic extract of leaf and stem bark of *Syzygium cumini* was evaluated for their acute toxicity studies in mice and the leaf extract was reported to produce a lower LD_{50} of 3,873 mg/kg compared to the stem bark which was 5000 mg/kg (Ugbabe *et al*., 2010). In another study, anti-diabetic potential of albino mice was evaluated for acute toxicity using methanol and aqueous extracts of leaves, seeds, barks, and roots of *Syzygium cumini*. The results revealed a significant reduction in blood glucose levels in mice when orally administered at a level of 50 and 100 mg/kg (Deb *et al*., 2013). The phytochemical analysis and oral acute toxicity of aqueous extract of stem and bark

were investigated. The phytochemical screening revealed the presence of flavonoids, tannins, carbohydrates, sterols and amino acids. However, no signs of toxicity and mortality were detected while examining the oral acute toxicity during the study period of 14 days at a dose level of 5000 mg/kg body weight and no significant alteration in body weight, organ weight and hematological parameters were reported when compared to control group (Prasad *et al*., 2016).

Use of *Syzygium cumini* as a functional ingredient in food products

Seed, a waste obtained in excess amounts from *Syzygium cumini* processing is a rich source of nutrients. The fruits are processed to form various fermented, non-fermented beverages, jams etc. Besides that, good quality products can be prepared by incorporating seed powder. Different products are prepared using seed powder. Biscuits are a form of confectionery and are very convenient and inexpensive food products. In recent years, the consumption is increasing among rural and urban populations especially among children as well as aged persons at around 8-10% annually. Incorporation of jamun seed powder into biscuits reduces the rise in the blood glucose level and improves glycemic control (Kannan and Puraikalan, 2015). Patil *et al*., (2014) studied the sensory evaluation of biscuits supplemented with soy flour and jamun seed powder and found that biscuits prepared with 32% soy flour and 8% jamun seed powder gave the highest overall acceptability and was found significantly superior to other formulations. Similarly, Kalse *et al*., 2016 prepared biscuits using 81% wheat flour, 9% jamun seed powder, 10% finger millet had gain overall acceptability, with a density of 0.347 g/cc, calorific value of 482.68 kcal/100g and hardness value of 4535 g by textural analysis. The effect of fortification of seed powder in cookies at the concentration of 0, 5, 10, 15% were studied by Desai *et al*., 2018 using 15% finger millet flour. Cookies were subjected to organoleptic and nutritional quality analysis. The cookies prepared by the addition of 10% seed powder and 15% finger millet flour attained the highest acceptability with moisture (4.87%), fat (13.49%), fiber (1.73%), protein (9.47%), ash (1.11%) and carbohydrate (69.25%). Kannan and Puraikalan, (2015) formulated the cookies by incorporating seed powder at different levels 5%, 10% and 15%. The results obtained revealed that cookies incorporated with 10% jamun seed powder showed higher acceptability. Noodle is a form of pasta that is becoming extremely popular in India and has become internationally recognized food. (Sood *et al*., 2018) prepared noodles by blending seed powder in 2%, 4%, 6%, 8%,10% level and the studied cooking attributes such as optimum cooking time, volume increase, weight increase, cooking loss and sensory properties. The cooking time decreased with the increase in the addition of seed powder. The weight increase of 141.42 to 174.52% was reported with the highest in control noodles. There is an increase in the volume of cooked noodles from 140 to 210 %. The highest cooking loss of 7.03 % was observed in control sample and lowest was observed in 10% seed powder blended noodles. Noodles incorporated with 8% jamun seed powder were highly acceptable. Harine and Janapriya, (2018) prepared dhal adai mix powder as represented in using ingredients such as parboiled rice(75 g), Bengal gram dhal (5 g), green gram dhal (5 g), red dhal (5 g), red chilli with

varying proportions of seed powder (2 %, 4 % and 6 %). The results of the study revealed that dhal adai mix powders incorporated with 4 % of seed powder is mostly acceptable by the panel members and the nutritive value was also high when compared with the control with a protein content (9.76g), carbohydrates (72.42 g), fiber content (1.21 g) and iron content (1.8mg). Further, the development of dhal adai mix powder contributes to the reduction of blood glucose levels when consumed by diabetic patients. Kasthuri *et al*., (2017) used Jamun seed powder and drumstick leaf powder which are a source of natural antioxidant and natural preservative with added health benefits for the development of functional chicken chips at different levels of (1, 2 and 3%). The results showed that chicken chips containing 1% drumstick leaf powder and 1% jamun seed powders were highly acceptable.

Conclusion

Plants are the most exclusive source of drugs for a majority of the population as they provide efficient, safe and cheap medications for rural areas. *Syzygium cumini* is widely distributed and is used as a traditional medicine in different regions of the world. A high number of constituents have been extracted both from the aerial as well as underground parts of the plant using various solvents. The presence of numerous phytochemicals (anthocyanins, ellagic acid, citric acid, quercetin etc.) gives this plant various pharmacological properties such as antidiabetic, antioxidant, anti-inflammatory, anticancer, antifungal, antibacterial, antimicrobial, antipyretic, and antiulcer. The extracts of the plants are also used in the treatment of diarrhoea and dysentery, cancer, diabetes, alzheimer, stress etc. Most of the biological effects can be explained by the high amounts of tannins present in them such as antiviral, antimicrobial, hepatoprotective and anti-inflammatory effects. Further, fortification of the food with the various parts of the plant can also be one of the alternatives to utilize the plant along with increasing the medicinal properties of these foods. Hence, in the present review, the literature pertaining to phytochemical, pharmacological activities and medicinal uses has been given comprehensively.

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