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Phytochemistry, traditional uses and pharmacology of *Eugenia jambolana* Lam. (black plum): A review

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ABSTRACT

Eugenia jambolana Lam. (syn. *Syzigium cumini* (L.) SKEELS; *S. jambolana* DC; Family: Myrtaceae), commonly known as black plum or Jamun is a plant native to India. Annually the trees produce oblong or ellipsoid fruits (berries). They are green when raw and purplish black when fully ripe. The ripe fruits are sweetish sour to taste and are used to prepare health drinks, squashes, juices, jellies and wine. Studies have shown that the berries contain carbohydrates, minerals and the pharmacologically active phytochemicals like flavonoids, terpenes, and anthocyanins. Jamun is a plant with known ethnomedicinal uses. Before the discovery of insulin, Jamun was useful in the treatment of diabetes and is an integral part in the various alternative systems of medicine. Scientific studies have shown that the various extracts of Jamun possess a range of pharmacological properties such as antibacterial, antifungal, antiviral, anti-genotoxic, anti-inflammatory, anti-ulcerogenic, cardioprotective, anti-allergic, anticancer, chemopreventive, radioprotective, free radical scavenging, antioxidant, hepatoprotective, anti-diarrheal, hypoglycemic and antidiabetic effects. The present paper reviews these aspects and also addresses the lacunas in the existing knowledge.

1. Introduction

Eugenia jambolana Lam. (Syn. *Syzygium cumini* Skeels or Syzygium jambolana Dc or *Eugenia cuminii* Druce.) (Fig. 1) belonging to the family Myrtaceae is a large evergreen tree indigenous to the Indian subcontinent. However today these trees are found growing throughout the Asian subcontinent, Eastern Africa, South America, Madagascar and have also naturalized to the warmer regions of the United States of America (in Florida and Hawaii) (Li et al. 2009; Warrier, Nambiar, & Ramankutty 1996). The trees are famous for their fruits and their colloquial names, which include Java plum, Portuguese plum, Malabar plum, black plum, Indian blackberry, jaman, jambu, jambul and jambool are attributed to the fruits (Warrier et al. 1996). The other colloquial names are enlisted in Table 1.

Botanical studies have shown that in the Indian subcontinent there are two main morphotypes of Jamun and this is based on the morphological and organoleptic features, the *Kaatha jamun* which are small and acidic to taste, and the *Ras Jaman*, that are oblong, dark-purple or bluish, with pink, sweet fleshy pulp and small seeds (Jabbar, Khan, & Jazuddin 1994; Morton 1987). The trees grow up to a height of 50 ft and have large canopy. The young bark is pale brown in color, while the mature are darkish brown and scaly. The leaves are elliptic to broadly oblong, smooth, glossy, leathery and fibrous in nature. The trees flowers once in a year and in the Indian subcontinent it is mostly during the month of June–July. The flowers are sessile, small (7–12 mm), white in color and with thin membranous petals. They are arranged mostly in threes and appear usually from the scars of the fallen leaves (Warrier et al. 1996).

The fruits are found in clusters of four to twenty and do not ripen simultaneously. Each fruit is round or oblong or ellipsoid, 1/2 to 2 in. long with a centrally placed large seed. The process of fruit development takes about two months during which a lot of changes in the proximate composition and in the phytochemical constituents

Abbreviations: 5-HT, 5-hydroxytryptamine; ALP, Alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CAT, Catalase; CCl4, Carbon tetrachloride; CPK, Creatine phosphokinase; DMBA, 7, 12, dimethyl benz (a) anthracene; Glut-4, Glucose transporter 4; GPx, Glutathione peroxidase; GST, Glutathione S-transferase; HbA_{1C}, haemoglobin A1C; HDL, High-density lipoprotein; LDH, Lactate dehydrogenase; LDL, Low-density lipoprotein; LPO, Lipid peroxides; NIDDM, non-insulin-dependent diabetes mellitus; PGE2, prostaglandin E2; PPARα, Peroxisome proliferator-activated receptor alpha; PPARγ, Peroxisome proliferator-activated receptor gamma; PPBS, post parandial blood sugar; SOD, Superoxide dismutases; ABTS, 2,2′-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid); DMBA, 7,12-dimethylbenz[α]anthracene; DPPH, 1,1-diphenyl-2-picrylhydrazyl.

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Fig. 1. Photograph of Jamun fruits.

occurs. The raw fruits are green in color and as they mature turn to light-magenta and finally to dark purple or black when fully ripe. The completely ripe fruit has a combination of sweet, mildly sour and astringent flavor and imparts purple color to the tongue. If not harvested, the ripe fruits drop off or are eaten by bats, squirrels and monkeys (Warrier et al. 1996). The fruits are of dietary importance and are considered a delicacy. The deseeded fruits are dried and marketed in the USA and other European countries. The ripe fruits are also used in the production of health drinks, squashes, juices and jellies. The Catholic community of Goa Karwar and Mangalore, India use the fully ripe fruits to prepare wine (Veigas, Narayan, Laxman, & Neelwarne 2007).

Table 1
The different vernacular names of *Eugenia jambolana* in India and other Southeast Asian countries (CHEMEXCIL, 1992).

Language	Names
Scientific name	*Syzygium jambolanum*, *Eugenia cumini*, *Syzygium cumini*, *Eugenia jambolana.*
English	Jaman, black plum, damson plum, duhat plum, Indian blackberry, jambolan, jambolan plum, Java plum, Malabar plum, Portuguese plum, black plum, black plum tree, Indian blackberry, jambolan, jambolan-plum, Java plum, malabar plum, Portuguese plum
Indian languages	
Assamese	Jamu, kala jamu
Bengali	Kala jam
Gijrati	Jambu, jaambu
Hindi	Jamun, duhat, jam, jaman
Kannada	Nerale hannu
Konkani	Jambul
Malayalam	Kaattucaampa, njaaval, njaara, perinjaara
Manipuri	Gulamchat, jam
Marathi	Jambool
Mizo	Hmuipui
Nepalese	Jamunu, phanrir
Oriya	Jamkoli
Pali	Jambu
Prakrit	Jambulo, jammulo
Punjabi	Jaman
Sanskrit	Jambu, jambulah, meghamodini
Tamil	Kottai-nakam, naval
Telugu	Neredu
Urdu	Jaman
Other languages	
Burmese	Thabyay-hypyoo
Filipino	Duhat, lomboi
French	Jamélongue
Javanese	Duwet, jamblang
Khmer	Pring bai
Malay	Jambolan, jambulana, jiwat, obah
Nepali	Jamun
Sinhala	Jambu, jambul, madan, naval
Swahili	Msambarau, mzambarau
Thai	Hakhiphae, wa
Tibetan	Dzam-bu
Vietnamese	Trâm môc, vôi rung

1.1. Proximate composition of Jamun

Studies have shown that the pulp of Jamun is highly nutritive and contains important minerals like sodium, potassium, calcium, phosphorous, iron and zinc; water soluble vitamins like ascorbic acid, thiamine and niacin; carbohydrates like glucose, mannose, sucrose, maltose, fructose, galactose and mannose; free amino acids like alanine, asparagine, tyrosine, glutamine and cysteine (Noomrio & Dahot 1996; Paul & Shaha 2004). The exact compositions of some of the ingredients are enlisted in Table 2.

1.2. Phytochemistry of Jamun

Jamun plant is known to possess diverse phytochemicals, most of which are observed to be of health benefits. The leaves are known to contain β-sitosterol, betulinic acid, mycaminose, crategolic (maslinic) acid, n-hepatcosane, n-nonacosane, n-hentriacontane, noctacosanol, n-triacontanol, n-dotricontanol, quercetin, myricetin, myricitrin and the flavonol glycosides myricetin 3-O-(4″-acetyl)-α-L-rhamnopyranosides, acylated flavonol glycosides (Mahmoud, Marzouk, Moharram, El-Gindi, & Hassan 2001; Sagrawat, Mann, & Kharya 2006).

The essential oil from the leaves is shown to contain the phytochemicals pinocarveol, α-terpeneol, myrtenol, eucarvone, muurolol, α-myrtenal, cineole, geranyl acetone, α-cadinol and pinocarvone (Shafi, Rosamma, Jamil, & Reddy 2002). The stem bark is reported to possess friedelin, friedelan-3-α-ol, betulinic acid, β-sitosterol, kaempferol, β-sitosterol-D-glucoside, gallic acid, ellagic

Table 2
Nutrient, vitamin and mineral content of Jamun fruit pulp.

Composition	Content	Reference
Moisture	85.9 ± 1.4 g/100 g	(Paul & Shaha, 2004)
Protein	1.4 ± 0.7 g/100 g	(Paul & Shaha, 2004)
Fat	0.6 ± 0.2 g/100 g	(Paul & Shaha, 2004)
Fibre	0.6 ± 0.06 g/100 g	(Paul & Shaha, 2004)
Carbohydrates	16.6 ± 1.2 g/100 g	(Paul & Shaha, 2004)
Maltose	210 mg/g	(Noomrio & Dahot, 1996)
Sucrose	95.5 mg/g	(Noomrio & Dahot, 1996)
Fructose	57.50 mg/g	(Noomrio & Dahot, 1996)
Galactose	52.50 mg/g	(Noomrio & Dahot, 1996)
Glucose	20 mg/g	(Noomrio & Dahot, 1996)
Vitamin		
B-Carotene	50 ± 5.9 mg/100 g	(Paul & Shaha, 2004)
Thiamine	0.12 ± 0.6 mg/100 g	(Paul & Shaha, 2004)
Riboflavin	0.06 ± 0.02 mg/100 g	(Paul & Shaha, 2004)
Ascorbic acid	30 ± 6.9 mg/100 g	(Paul & Shaha, 2004)
Minerals		
Mg	49.8 ± 1.2 mg/100 g	(Paul & Shaha, 2004)
Na	3.5 ± 0.8 mg/100 g	(Paul & Shaha, 2004)
Ca	21.5 ± 1.5 mg/100 g	(Paul & Shaha, 2004)
P	18.5 ± 2.8 mg/100 g	(Paul & Shaha, 2004)
K	130 ± 8 mg/100 g	(Paul & Shaha, 2004)
Fe	0.15 ± 0.01 mg/100 g	(Paul & Shaha, 2004)
Zn	0.28 ± 0.03 mg/100 g	(Paul & Shaha, 2004)
Cu	0.07 ± 0.02 mg/100 g	(Paul & Shaha, 2004)

acid, gallotannin and ellagitannin and myricetine (Rastogi & Mehrotra 1990; Sagrawat et al. 2006).

The flowers are observed to contain oleanolic acid, ellagic acids, isoquercetin, quercetin, kampferol and myricetin (Sagrawat et al. 2006). Studies have shown that the pulp of Jamun contains the anthocyanins, delphinidin, petunidin, malvidin-diglucosides, and these compounds are responsible for their bright purple color (Li, Zhang, & Seeram 2009; Sagrawat et al. 2006; Veigas et al. 2007; Sharma, Viswanath, Salunke, & Roy 2008; Sharma, Balomajumder, & Roy 2008). The seeds are the most studied plant part and are reported to contain jambosine, gallic acid, ellagic acid, corilagin, 3,6-hexahydroxy diphenoylglucose, 4,6-hexahydroxydiphenoyl-glucose, 1-galloylglucose, 3-galloylglucose, quercetin, β-sitoterol (Rastogi & Mehrotra 1990; Sagrawat et al. 2006). Some of the phytochemicals present in Jamun are depicted in Fig. 2.

1.3. Traditional uses

All parts of the tree and the seeds in particular, have a long history of medicinal use in the various folk systems of medicine in countries where Jamun is reported to grow (Bhandary, Chandrashekar, & Kaveriappa 1999). Jamun is also used extensively in the various traditional systems of medicine like in the Ayurveda, Unani, Siddha, in the Srilankan, in the Tibetan and in the Homeopathy systems of alternative and complementary medicine (Warrier et al. 1996). Before the discovery of insulin, Jamun was

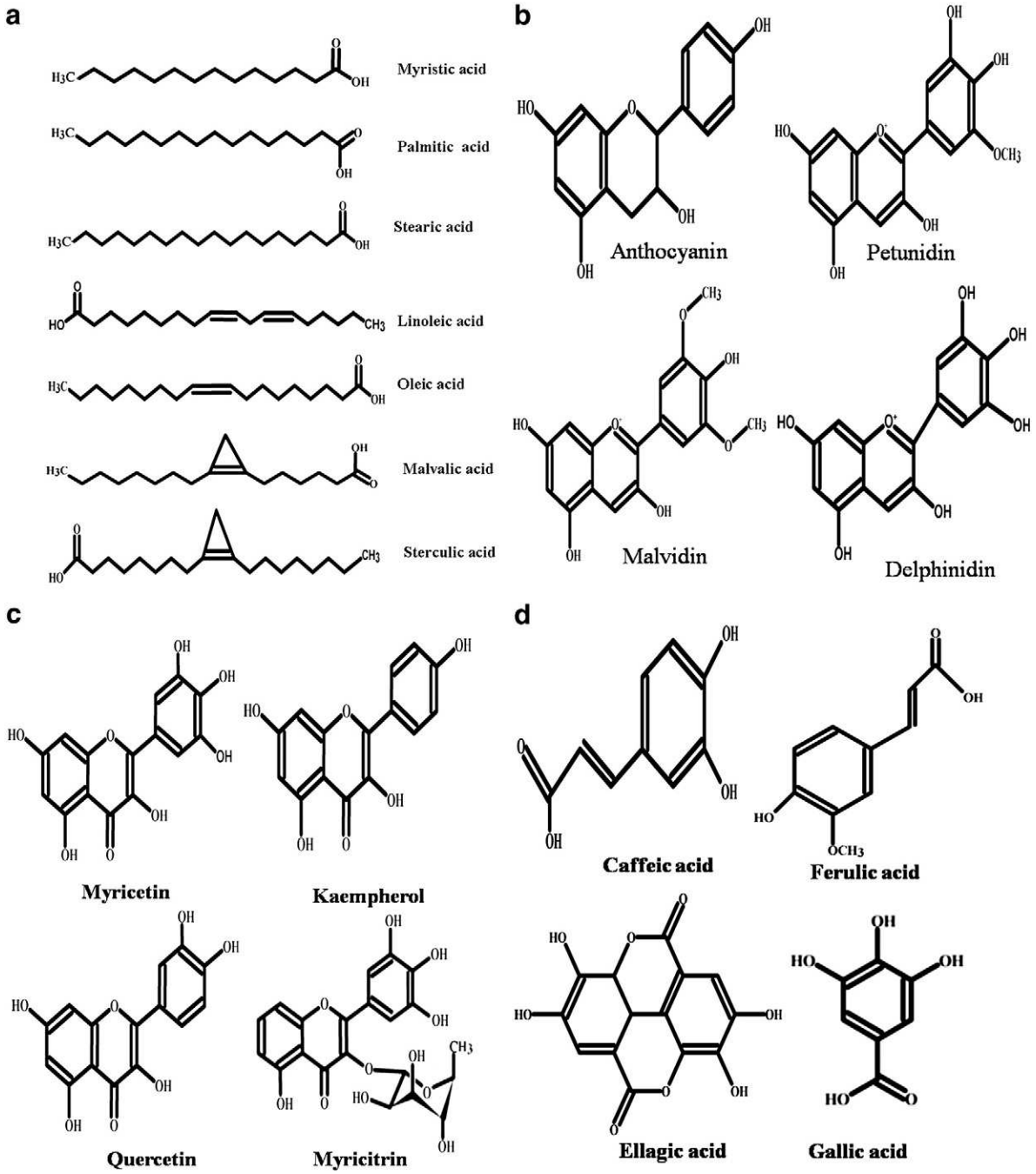

Fig. 2. a. Aliphatic acids present in Jamun. b. Anthocyanins presents in Jamun. c. Flavonoids present in Jamun. d. Important phenolics in Jamun. e. Phytosterols present in Jamun, Terpenes present in Jamun.

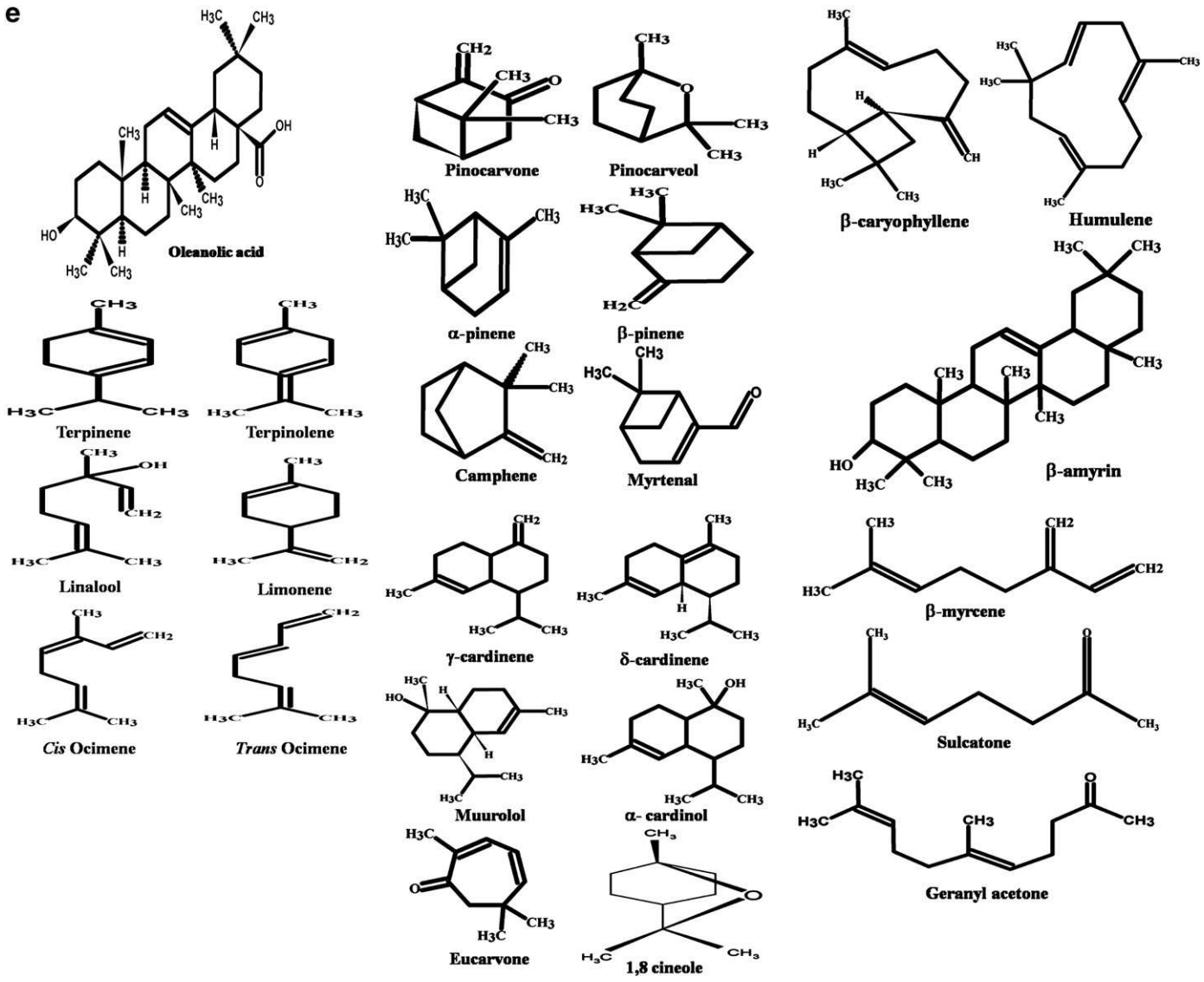

Fig. 2 (*continued*).

useful in the treatment of diabetes and was used either alone or in combination with other hypoglycemic plants even in Europe (Helmstädter, 2007).

According to Ayurveda, their barks are acrid, digestive and astringent. They are supposed to be useful for treating sore throat, bronchitis, asthma, thirst, biliousness, dysentery and ulcers (Warrier et al. 1996). The ash of the leaves is used as a dentrificant and is effective at strengthening the teeth and the gums. The bark is also known to possess wound healing properties. In the Siddha system of medicine, Jamun is considered to be a haematinic, semen promoting and to decrease excessive heat of the body (Warrier et al. 1996). According to the Unani system of medicine, they are supposed to be a liver tonic, to enrich blood, strengthen teeth and gums. The decoction is supposed to be a good lotion for removing ringworm infection of the head (Warrier et al. 1996).

2. Validated pharmacological properties of Jamun (Table 3)

2.1. Antibacterial activity

Indiscriminate use of antibiotics has led to the development of drug resistance in many strains of pathogenic bacteria and studies are ongoing to discover novel agents that are effective and safe for human consumption. With regard to Jamun, studies have shown that the hydroalcoholic extract of the leaf (De Oliveira et al. 2007), petroleum ether, methanolic and ethyl acetate extract of the leaf (Kaneria, Baravalia, Vaghasiya, & Chanda 2009), the aqueous extract of the leaf (Satish, Raghavendra, & Raveesha 2008), the methanolic and ethyl acetate extracts of seed (Bhuiyan, Mia, & Rashid 1996), the methanolic extract of the seed (Acharyya, Patra, & Bag 2009), the aqueous, ethanolic and acetone extracts of the bark (Sharma, Patel, & Chaturvedi 2009) and the essential oil (Shafi et al. 2002) have all been shown to possess antibacterial effects.

Additionally, studies have also shown that the aqueous, methanolic and hydromethanolic extracts are also effective against the cariogenic bacteria, *Streptococcus mutans* and to inhibit/suppress the plaque formation *in vitro* (Namba, Tsunezuka, Dissanayake, & Hattori 1985). The details of the study have been enlisted in Table 3. Together all these observations clearly indicate that the Jamun possess antibacterial compounds in the extract and warranty detailed investigation, especially with the isolated phytochemicals.

2.2. Antifungal activity

The indiscriminate use of antifungal agents has also resulted in some fungal strains developing resistance to the clinically used drugs

Table 3
Validated pharmacological properties of *Eugenia jambolana.*

Pharmacological properties	Observations and references
Antibacterial activity	The hydroalcoholic extract of jamun leaf is shown to possess antibacterial effects against *Enterococcus faecalis, Escherichia coli, Kocuria rhizophila, Neisseria gonorrhoeae, Pseudomonas aeruginosa, Shigella flexneri, Staphylococcus aureus* and the multi-resistant *Klebsiella pneumoniae, Pseudomonas aeruginosa and Staphylococcus aureus in vitro* (De Oliveira et al., 2007). Petroleum ether, methanolic and ethyl acetate extract of the leaf shown to possess antibacterial effects on *Bacillus subtilis, Staphylococcus aureus, Pseudomonas aeruginosa, Salmonella typhimurium* and *Enterobacter aerogenes*. Methanolic extract was better than other extracts and more effective on gram positive organisms (Kaneria et al., 2009). Aqueous extract of leaf shown to be effective against the clinical isolates of Citrobacter sp., *Escherichia coli*, Klebsiella sp., *Proteus mirabilis, Pseudomonas aeruginosa, Salmonella typhi, Salmonella typhimurium, Salmonella paratyphi A, Salmonella paratyphi B, Shigella boydii, Shigella flexneri, Shigella sonnei, Staphylococcus aureus* and *Streptococcus faecalis* (Satish et al., 2008). Methanolic and ethyl acetate extracts of seed shown to be effective against *Bacillus cerus, B. subtalis, B. megateriun, Steptococcus beta haemolyticus, S. aureus, Shigella dysenteriae, Sh. Shiga, Sh. boydii, Sh. flexneriae, Sh. sonnei, E. coli, S. typhi B, S. typhi B*-56 and *Klebsiella* species (Bhuiyan et al., 1996). Methanolic extract of seed was effective against *V. cholerae* (serotypes O1, O139, and non-O1, non-O139) *Klebsiella pneumoniae, A. hydrophila, Escherichia coli*, Enterotoxigenic *Escherichia coli*, *Pseudomonas aeruginosa* and *Bacillus subtilis*, but was ineffective against Enterohaemorrhagic *E. coli* strain VT3 (Acharyya et al., 2009). The aqueous, ethanolic and acetone extracts of the bark was studied for its antibacterial effects on twelve strains of *Vibrio cholerae*. The ethanolic extract was the most effective while the aqueous and acetone extracts were less effective (Sharma et al., 2009). Aqueous, methanolic and hydromethanolic extracts also effective against the cariogenic bacteria, *Streptococcus mutans* and to inhibit/suppress the plaque formation *in vitro* (Namba et al., 1985). The essential oil of Jamun shown to possess antibacterial effects on *Basillus sphaericus, Basillus subtilis, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa* and *Samonella typhimurium.* The effect was profound for *Samonella typhimurium* and least for *Escherichia coli* (Shafi et al., 2002).
Antifungal activity	The hydroalcoholic extract of leaf is shown to possess antifungal effects against *Candida albicans* and *Candida krusei* (De Oliveira et al., 2007). The aqueous and methanolic extracts inhibited growth of dermatophytic fungi *C. albicans*, *T. rubrum, T. mentagrophytes* and *M. gypseum* (Chandrasekaran and Venkatesalu 2004). The aqueous, ethanol and *n*-hexane extracts from the leaves, fruit, root-bark and stem-bark possess growth inhibitory effects on *Ascochyta rabiei*, the causative agent of blight disease in chickpea (*Cicer arietinum* L.). The aqueous extracts of all the four plant parts showed significant antifungal activity (Jabeen and Javaid, 2010). The aqueous, petroleum ether, benzene, chloroform, methanol and ethanol of the leaf were studied on *Aspergillus candidus*, *Aspergillus columnaris*, *Aspergillus flavipes, Aspergillus flavus*, *Aspergillus fumigatus, Aspergillus niger, Aspergillus ochraceus* and *Aspergillus tamari.* The methanolic extract was more effective than the other extracts (Satish et al., 2008).
Antiviral activity	Aqueous extract of the Jamun leaves were effective in inhibiting the replication of the buffalopox virus (Bhanuprakash et al., 2007) and goatpox virus (Bhanuprakash et al., 2008).
Free radical scavenging	The ethanolic extract of the fruit pulp, kernel and seed coat evaluated with gallic acid, quercetin and trolox as reference molecules. The kernel extract was observed to be better than the seed coat and pulp extract in DPPH, superoxide radical scavenging and hydroxyl radical scavenging assays (Benherlal and Arumughan (2007). The methanol-formic acid (9:1) extract of the fruit (Reynertson et al., 2008), the hydroethanolic extract of the seed (Raquibul-Hasan et al., 2009), methanolic extracts of stem (Kshirsagar and Upadhyay, 2009) and the methanolic extract of the leaves (Kshirsagar and Upadhyay, 2009; Nahar et al., 2009) have all been reported to be potent free radical scavengers in the DPPH$^{\bullet}$ scavenging assay. The hydrolysable and condensed tannins in the fruit possess antioxidant activity in the DPPH and FRAP assays (Zhang and Lin, 2009). The organic extract of leaf (methanol:dichloromethane extract) as well as the hydroethanolic extract of the seed shown to be effective scavenger of nitric oxide *in vitro* (Jagetia & Baliga, 2004). Various fractions (viz water, ethyl acetate, chloroform and *n*-hexane) of the methanolic extract were studied for their free radical scavenging effects in the DPPH and FRAP assays. The ethyl acetate fraction was observed to be more effective (Ruan et al., 2008). The fruit skin also possess antioxidant effects as confirmed by results from the hydroxyl radical-scavenging assay, superoxide radical-scavenging assay, DPPH radical-scavenging assay and lipid peroxidation assay with egg yolk as the lipid-rich source (Banerjee et al., 2005). The anthocyanin-rich fruit peel extract shown to be a effective as a reducing agent and scavenger of DPPH free radicals (Veigas et al., 2007). The hydromethanolic extract of the Jamun seed was effective in scavenging free radicals in the auto-oxidation of β-carotene and linoleic acid assay (Bajpai et al., 2005).
Free radical scavenging	The anthocyanin rich pulp extract shown to inhibit the iron ($FeSO_4$)-induced lipid peroxidation in the rat brain, liver, liver mitochondria, testes and human erythrocyte ghost cells *in vitro* (Veigas et al., 2007). It was also effective in decreasing the levels of CCl_4-induced LPx in the primary rat hepatocytes *in vitro* (Veigas et al., 2008). The 80% methanolic, ethanolic and acetone (solvent:water, 80:20 v/v) extract of the bark were studied for anti lipidperoxidative effects in the linoleic acid system *in vitro*. The results showed that the Ethanolic extract was more effective than butylated hydroxytoluene, BHA, and PG in inhibition of peroxidation in the linoleic acid peroxidation system (Sultana et al., 2007). The ethanolic extract of the fruit pulp, kernel and seed coat inhibits lipid peroxidation but the effect was less than that of the reference molecules gallic acid, quercetin and trolox (Benherlal and Arumughan, 2007). Administering Jamun decreased the levels of lipid peroxides in the stomachs of animals subjected to ulcerogenic treatments (Chaturvedi et al., 2009a, 2009b, 2007) and in the brain, liver, kidneys and serums of diabetes animals (Prince et al., 1998; Ravi et al., 2004a, 2004b, 2004c, 2004d; Chaturvedi et al., 2009a, 2009b; Krishnamoorthy et al., 2006).
Anti-inflammatory effects	Ethanolic extract of the bark possess anti-inflammatory effects in both acute (carrageenan, kaolin–carrageenin, and formaldehyde-induced) and chronic (cotton pellet granuloma) models in rats (Muruganandan et al., 2001).
Gastroprotective effects	Tannins isolated from Jamun were effective against the HCl/ethanol-induced gastric ulceration in rats (Ramirez and Roa, 2003). Fruits shown to be effective in preventing ulcerations in both normal and streptozotocin-induced diabetic rats (Chaturvedi et al., 2009a, 2009b, 2007).
Hepatoprotective effects	Pulp extract was effective in preventing paracetamol-induced hepatotoxicity in rats (Das and Sarma, 2009). Aqueous extract of the leaf (Moresco et al., 2007) and methanolic extract of the seed (Sisodia and Bhatnagar, 2009) were effective against CCl_4-induced hepatotoxicity in rats.
Antidiabetic activities	Jamun has been thoroughly investigated for its antidiabetic effects and the seed, pulp and bark have been found to have effective antidiabetic action (Sharma et al., 2009; Gohil et al., 2010; Saravanan and Leelavinothan, 2006; Saravanan and Pari, 2007; Sharma et al., 2006; Pepato et al., 2005), while the leaf was ineffective (Pepato et al., 2001). The seed is the most studied and the effective in causing anti-hyperglycemic effects in different experimental models of study (Achrekar et al., 1991; Panda et al., 2009; Rathi et al., 2002; Ravi et al., 2005, 2004a, 2004b, 2004c, 2004d; Sharma, Balomajumder and Roy, 2008b; Sharma, Viswanath, et al., 2008a; Sharma et al., 2003; Sridhar et al., 2005).

Table 3 *(continued)*

Pharmacological properties	Observations and references
Antidiabetic activities	Jamun seeds prevent the diabetes-induced secondary complications like nephropathy (Grover et al., 2002), neuropathy (Grover et al., 2002), gastropathy (Grover et al., 2002), diabetic cataract (Rathi et al., 2002) and also decreased peptic ulceration (Chaturvedi et al., 2009). Human studies have shown that Jamun possess promising anti-hyperglycemic effects (Kohli and Singh 1993; Sahana et al., 2010).
Hypolipidemic effect	Feeding ethanolic extract of the seeds to allaxon-induced (Sharma et al., 2003), seed kernel (100 mg/kg body weight) to streptozotocin-induced (Ravi et al., 2005) and flavonoid enriched extract from seeds (Sharma, Viswanath, et al., 2008a; Sharma, Balomajumder and Roy, 2008b) to diabetic rats caused hypolipidemic effect.
Cardioprotective effects	The methanolic extract of the seeds is reported to possess cardioprotective effects in the isoproterenol-induced Myocardial Infarction model in rats (Mastan et al., 2009).
Anti-diarrheal effects	Ethanolic extract of the Jamun tree bark was effective in preventing castor oil-induced diarrhea, PGE_2-induced enteropooling and to reduce gastrointestinal motility (Mukherjee et al., 1998).
Antifertility activity	Chronic administering of oleanolic acid, a constituent of the jamun flowers shown to possess antifertility activities in the male albino rats (Rajasekaran et al., 1988).
Anti-allergic effects	Aqueous extract of leaf shown to possess antiallergic effects in mice (Brito et al., 2007).
Antipyretic effects	Jamun possess significant anti-pyretic action against the yeast-induced pyrexia in mice (Chaudhuri et al., 1990).
Neuropsychopharmacological effects	Administering chloroform extract of seeds caused CNS depressant action (Chakraborty et al., 1986). The ethyl acetate and methanolic extract of the seed also shown to modulate CNS activity (Kumar et al., 2007).
Antineoplastic effects	Jamun extract induced cytotoxic effects against the human cervical cancer cells the HeLa and SiHa (Barh and Viswanathan, 2008). The fruit extract caused selective cytotoxity to the MCF-7aro and MDA-MB-231 but not to the normal/nontumorigenic MCF-10A cells (Li, Adams, et al., 2009; Li, Zhang and Seeram, 2009). Ellagitannins obtained from jamun inhibited Wnt signaling in a human 293 T cell line (Sharma et al., 2010).
Chemopreventive effects	The hydroethanolic extract of the seed prevented the DMBA-induced croton oil promoted skin (Parmar, Sharma, Verma and Goyal, 2010; Parmar, Sharma, Verma, Sharma, et al., 2010b) and benzo a pyrene-induced gastric carcinogenesis in mice (Goyal et al., 2010).
Radioprotective effects	Administration of the hydroalcoholic extract of the seed and the dichloromethane extract of leaf possess radioprotective effects (Jagetia and Baliga, 2003; Jagetia et al., 2005). The dichloromethane extract of leaf also afforded enteroprotective effects against the radiation-induced damage to the GIT in mice (Jagetia et al., 2008).
Anticlastogenic effects	The methanol:dichloromethane extract reduces the radiation-induced DNA damage in the cultured human peripheral blood lymphocytes (Jagetia and Baliga, 2002). Aqueous and ethanolic extracts of Jamun seed reduced the hydroxyl radical-induced strand breaks in pBR322 DNA *in vitro* (Arun et al., 2010). Aqueous extract also reduced the genotoxic of the carcinogens urethane and DMBA in mice (Arun et al., 2010).

and this has necessitated the need for developing newer agents (De Oliveira et al. 2007). Preclinical studies have shown that the hydroalcoholic extract (De Oliveira et al. 2007), aqueous, petroleum ether, benzene, chloroform, methanolic and ethanolic extract of leaf (Satish et al. 2008) and aqueous and methanolic extracts of seeds (Chandrasekaran & Venkatesalu, 2004), are all reported to possess antifungal action *in vitro* (Table 3).

Additionally the aqueous, ethanol and *n*-hexane extracts from the leaves, fruit, root-bark and stem-bark were effective in inhibiting the growth of *Ascochyta rabiei*, the causative agent of the blight disease in chickpea (*Cicer arietinum* L.) suggesting its use as a non toxic agent effective in preventing food infestation by fungi (Jabeen & Javaid 2010).

2.3. Antiviral activity

Globally, viral diseases are increasing and the discovery of newer antiviral agents that are non toxic and safe for human consumption has been a priority. *In vitro* studies have shown that the aqueous extract of the Jamun leaves was effective in inhibiting the replication of the buffalopox (Bhanuprakash, Hosamani, Balamurugan, Singh, & Swarup 2007) and goatpox virus (Bhanuprakash et al. 2008). The results showed that the extract caused a 98.52% inhibition of the buffalopox virus at its maximum non toxic concentration (of approximately 2000 μg/ml), and that the EC_{50} was 134 μg/ml (Bhanuprakash et al. 2007). In the cytopathic effect inhibition assay, studies with the goatpox virus also showed that Jamun extract had a 99.92% inhibition at their maximum non toxic concentration (1999.73 μg/ml) in vero cells (Bhanuprakash et al. 2008). The extract also possessed inhibitory effects on both buffalopox and goatpox virus suggesting its effectiveness (Bhanuprakash et al., 2008, 2007). With regard to virus causing pathogenesis in humans, experiments have shown that the aqueous and methanolic extracts of the bark inhibited the HIV type 1 protease activity by more than 70% at a concentration of 0.2 mg/mL (Kusumoto et al. 1995). Together these observations clearly suggest that Jamun could be a useful antiviral agent and further studies are warranted with the isolated compounds.

2.4. Free radical scavenging effects and antioxidant effects

Superfluous generation of the free radicals is proved to initiate/aggravate important human ailments like arthritis, cancer, Alzheimer, Parkinson's disease, AIDS and diabetic complications. Reports indicate that plants rich in anthocyanins, flavonoids and polyphenols are observed to be effective in scavenging the free radicals (Alia et al. 2008; Rufino et al. in press; Sánchez-Moreno, Larrauri, & Saura-Calixto 1999). With regard to Jamun, Benherlal and Arumughan (2007), evaluated the antioxidant effects of the ethanolic extract of fruit pulp, kernel and seed coat in various *in vitro* assays (DPPH•, OH• and $O_2•^{-}$) with gallic acid, quercetin and trolox as reference molecules. In the DPPH scavenging assay the kernel extract was better than the seed coat and pulp extract, but less than the reference molecules. However in the superoxide radical scavenging activity the kernel extract was six times more effective than trolox and three times than catechin. In the hydroxyl radical scavenging assay, the kernel extract was comparable to the effect of catechin (Benherlal & Arumughan 2007).

The methanol-formic acid (9:1) extract of the fruit (Reynertson, Yang, Jiang, Basile, & Kennelly 2008), the hydroethanolic extract of the seed (Raquibul-Hasan et al. 2009), methanolic extract of the stem (Kshirsagar & Upadhyay 2009), anthocyanin-rich fruit peel extract (Veigas et al. 2007), the methanolic extract of the leaves (Kshirsagar & Upadhyay 2009; Nahar, Alam Ripa, Rokonuzzaman, & Al-Bari 2009) and the hydrolysable and condensed tannins present in the fruits (Zhang & Lin 2009) have also been reported to be effective in the *in vitro* DPPH• assay. The organic extract of the leaf (methanol: dichloromethane extract) as well as the hydroethanolic extract of the seed are reported to be a scavenger of nitric oxide *in vitro* (Jagetia & Baliga, 2004). The hydrolysable tannins are also observed to be effective in the FRAP assay (Zhang & Lin 2009).

Ruan et al. (2008) subjected the methanolic extract to fractionation with water, ethyl acetate, chloroform and *n*-hexane, and studied their free radical scavenging effects in the DPPH and FRAP assays. It was observed that in the DPPH assay, the efficacy was as follows ethyl acetate fraction ≈ methanolic extract > chloroform fraction ≈ water fraction > *n*-hexane. However the antioxidant activity of ethyl acetate fraction (IC50 = 112.79 μg/mL) was lower than that of Vit. C (IC50 = 71.30 μg/mL), but not significantly different from that of BHA (114.69 μg/mL). In the FRAP assays similar observations were observed and except for the hexane fraction, all other fractions showed high ferric reducing power at high concentrations (Ruan, Zhang, & Lin 2008).

Studies by Banerjee et al. (2005) have shown that the fruit skin of Jamun possess antioxidant effects as confirmed by results from the hydroxyl radical-scavenging assay, superoxide radical-scavenging and DPPH radical-scavenging assay *in vitro*. The anthocyanin-rich fruit peel extract is also observed to be effective as a reducing agent (Veigas et al. 2007). Recently, Bajpai et al. (2005), have also observed that the hydromethanolic extract of the Jamun seed was effective in scavenging (90.6%) free radicals as evaluated in the auto-oxidation of β-carotene and linoleic acid assays. Together all these observations clearly indicate that the Jamun possess free radical activity and warranties detailed investigation, especially with the isolated phytochemicals.

2.5. Inhibition of lipid peroxidation

Lipid peroxidation which can occur through enzymatic or nonenzymatic reactions is associated with cellular damage and mutagenesis. Sultana et al. (2007) evaluated the antioxidant activity of the 80% methanol, ethanol and acetone (solvent:water, 80:20 v/v) extract of the bark by measuring the reducing power, inhibition of peroxidation using linoleic acid system and DPPH scavenging activity. The results showed that the ethanolic extract was more effective than the butylated hydroxytoluene (BHT), butylated Hydroxyanisole (BHA), and propyl gallate (PG) in the linoleic acid peroxidation system. The methanolic and acetone extract were comparable to that of BHA, BHT, but, greater than PG (Sultana, Anwar, & Przybylski 2007). Benherlal and Arumughan (2007) evaluated the inhibition of lipid peroxidation of the ethanolic extract of the fruit pulp, kernel and seed coat *in vitro*, and observed that the kernel extract was better than the seed coat and pulp extract, but less than the reference molecules (gallic acid, quercetin and trolox).

Veigas et al. (2007) studied the ability of anthocyanin rich pulp extract for its efficacy to inhibit the iron ($FeSO_4$)-induced lipid peroxidation in the various organs (rat brain, liver, liver mitochondria, testes and human erythrocyte ghost cells) *in vitro*, and observed it to be effective in all the organs but with differential degree. At the lowest concentration of 5 ppm the anti-lipid peroxidative effects were high in the rat brain (68.3%) followed by rat liver (83%), mitochondria (86%) testes (72%), and the erythrocyte ghost cells (48%) (Veigas et al. 2007).

The extract was also observed to decrease the levels of CCl4-induced LPx in the primary rat hepatocytes *in vitro* (Veigas, Shrivasthava, & Neelwarne 2008). Animal studies have also shown that administering Jamun decreased the levels of lipid peroxides in the stomachs of animals subjected to ulcerogenic treatments (Chaturvedi et al. 2009a, 2009b, 2007), in the brain, liver, kidneys and serum of diabetic animals, suggesting its usefulness in amelioration of diseases (Chaturvedi et al. 2009a, 2009b; Prince, Kamalakkannan, & Menon 2004; Prince, Menon, & Pari 1998, Ravi, Rajasekaran, & Subramanian 2005; Ravi et al. 2004a, 2004b; Ravi, Sekar, & Subramanian 2004c; Ravi, Sivagnanam, & Subramanian 2004d; Ravi, Ramachandran, & Subramanian, 2004a, b).

2.6. Anti-inflammatory effects

Excess production of free radicals from the activated inflammatory leukocytes, especially under conditions of chronic inflammation, may have an important role in various pathogenesis. Several reports have suggested that diseases associated with inflammation may be ameliorated by plants. With respect to Jamun, preclinical studies have shown that the chloroform fraction of the seed inhibited the carrageenin, kaolin and other inflammatory mediator-induced edema in rats (Chaudhuri, Pal, Gomes, & Bhattacharya 1990). The extract inhibited exudation of protein, leakage of dye in peritoneal inflammation and migration of leucocytes. It also caused inhibition of granuloma formation, experimental arthritis and turpentine-induced edema of the joints (Chaudhuri et al. 1990). The ethyl acetate and methanol extracts of seed (200 and 400 mg/kg orally) are also reported to possess anti-inflammatory activities in the carrageenan-induced paw edema in Wistar rats (Kumar et al. 2008).

The ethanolic extract of the tree bark has also been demonstrated to possess anti-inflammatory effects. Muruganandan et al. (2001) observed that administering the extract (100, 300 and 1000 mg/kg, p.o.) caused a significant decrease in the inflammatory reactions initiated by the inflammogens carrageenin, combination of kaolin–carrageenin, and formaldehyde in the rat paw edema model of acute inflammation. The extract was also effective in the cotton pellet granuloma model in rats, suggesting its usefulness in ameliorating chronic inflammation. Studies with individual autacoids have also shown that the bark extract was effective in inhibiting the histamine, 5-HT and PGE2-induced rat paw edema (Muruganandan et al. 2002). Together all these observations clearly suggest that the non polar compounds present in the seed and bark possess anti-inflammatory effects and merit detail investigations.

2.7. Gastroprotective effects

Peptic ulcer is one of the most common gastrointestinal ailments and affects considerable amount of the world's population. Preclinical studies have shown that Jamun fruits possess gastroprotective effect in both normal (Chaturvedi et al. 2007) as well as in the streptozotocin-induced diabetic rats (Chaturvedi et al., 2009a, b), against various ulcerogens like cold restraint stress, aspirin, 95% ethanol and pylorus ligation-induced (Chaturvedi et al. 2007). The effective dose was observed to be 200 mg/kg b. wt. when administered orally for 10 days. Mechanistic studies showed that administering Jamun, before treatment with the ulcerogens decreased the acid-pepsin secretion, the levels of LPO and concomitantly increased the levels of GSH in gastric mucosa. The extract also enhanced the levels of mucin and mucosal glycoprotein and decreased the cell shedding (Chaturvedi et al., 2009a, b, 2007).

Administering the quantified tannins isolated from the Jamun seed protected rats against the HCl/ethanol-induced gastric ulceration (Ramirez & Roa 2003). The authors observed that macroscopically there was no significant difference in the number, size and surface area of macroscopic lesions between the tannin and omeprazole (positive control) group. However, when microscopically evaluated (using Best's Ulcer Staging Index), the tannin treatment offered better protection and significantly by decreasing the gastric mucosal damage. When compared to the cohorts receiving only the ulcerogen, administering tannins reduced the levels of free radicals in the stomach suggesting that the observed gastroprotection may be partly due to this property (Ramirez & Roa 2003). Together, all these observations clearly indicate that jamun fruits and seed possess gastro-protective effects and that this effect was brought about by increasing the mucosal defensive factors, the gastric antioxidants and by concomitantly decreased lipid peroxidation (Chaturvedi et al. 2007; Chaturvedi et al., 2009a, b; Ramirez & Roa 2003).

2.8. Anti-diarrheal effects

Diarrhea which may be observed as a mild and inopportune illness, at times in its severe state causes malnutrition, particularly among the children. According to the world health organization (WHO), annually diarrhea causes 1.87 million deaths, especially in the underdeveloped countries and its prevention is a priority for both international and national agencies (Boschi-Pinto, Velebit, & Shibuya 2008). Mukherjee et al. (1998) in their investigative studies for the first time validated the traditional use of these plants as anti-diarrheal agents. The authors observed that administering the ethanolic extract of the Jamun tree bark was effective against different experimental models of diarrhea in rats. The extract showed significant inhibitory activity against the castor oil-induced diarrhea, PGE_2-induced enteropooling and also caused reduction in the gastrointestinal motility in charcoal meal studies (Mukherjee et al. 1998). Together, all these observations emphasize the usefulness of Jamun as anti-diarrheal agent.

2.9. Hepatoprotective effects

Liver diseases remain one of the most serious health problems and with satisfactory protective drugs unavailable in the allopathic system of medicine people rely on the complementary and alternative medicines. *In vitro* studies with the rat hepatocytes have shown that the anthocyanins rich (230 mg/100 g dry weight) pulp extract of Jamun was effective in preventing the CCl4-induced liver damage. Treating hepatocytes with the extract (50 to 500 ppm) suppressed the CCl4-induced release of LDH, decreased the lipid peroxidation, reversed the toxicant-induced changes in cellular glutathione level and increased the activity of the antioxidant enzyme GPx (Veigas et al. 2008).

Studies have also shown that the hepatoprotective effects of the pulp also extended against the paracetamol-induced hepatotoxicity in rats (Das & Sarma 2009). Administering the pulp extract to the animals (100 or 200 mg/kg/day for ten consecutive days) resulted in a concentration dependent decrease in the serum levels of ALT, AST, AP and total bilirubin that were elevated in the paracetamol alone cohorts (Das & Sarma 2009). The histopathological findings showed a reduction in necrosis and fibrosis (Das & Sarma 2009).

Experiments have also confirmed that the aqueous extract of the leaf when given either as a single dose or consecutively for seven days prevented the CCl_4-induced hepatotoxicity in rats. Administering the extract for seven consecutive days caused a significant decrease in the levels of AST and ALT, while single dose administration was ineffective (Moresco, Sperotto, Bernardi, Cardoso, & Gomes 2007). Recently, Sisodia and Bhatnagar (2009) have also observed that the administration of methanolic extract of the seed (doses 100, 200 and 400 mg/kg p. o.) also possess hepatoprotective effects against the CCl4-induced damage as observed from both biochemical and histopathological observations (Sisodia & Bhatnagar 2009). Collectively all these observations emphasize the usefulness of Jamun as a hepatoprotective agent and emphasizes the need for detail investigations.

2.10. Antidiabetic activities

The world's leading endocrine disorder today is diabetes and estimates are that it affects almost 5% of the global population (Achrekar, Kaklij, Pote, & Kelkar 1991; Sharma, Nasir, Prabhu, Murthy, & Dev 2003). Historical reports indicate that before the discovery of insulin, Jamun was used in the treatment of diabetes both in India and other countries. Even today Jamun seeds are an important constitute in many of the polyherbal antidiabetic formulations in the Ayurveda, Siddha, Unani, Srilankan and Homeopathy (Helmstädter, 2007; Rathi, Grover, Vikrant, & Biswas 2002; Sridhar, Sheetal, Pai, & Shastri 2005).

Jamun has been thoroughly investigated for its antidiabetic effects both in preclinical and human studies (Helmstädter, 2008). Many studies in the past two decades have shown that the seed (Achrekar et al. 1991; Panda et al., 2009; Rathi et al. 2002; Ravi et al., 2005, 2004a, 2004b, 2004c, 2004d; Sharma, Balomajumder and Roy, 2008b; Sharma, Balomajumder and Roy, 2008b; Sharma, Viswanath, et al., 2008a; Sharma, Viswanath, et al., 2008a; Sharma et al. 2003; Sridhar et al. 2005), the fruit pulp (Achrekar et al., 1991; Pepato et al., 2005; Sharma et al., 2006; Sundaram et al., 2009) and bark (Villasenor and Lamadrid, 2006) possess antihyperglycemic effects, while the leaf was ineffective and devoid of this pharmacological effects (Pepato et al., 2001). The seed has been subjected to detailed investigations and observations suggest that it is effective when given as powder (Sridhar et al., 2005) or as an extract (Achrekar et al., 1991; Panda et al., 2009; Ravi et al., 2005, 2004a, 2004b, 2004c, 2004d; Sharma, Balomajumder and Roy, 2008; Sharma, Viswanath, et al., 2008; Sharma et al., 2003; Sundaram et al., 2009) in reducing both hyperglycemia and diabetic complications in the experimental animals.

Jamun is shown to be effective in streptozotocin (Panda et al., 2009; Ravi et al., 2005, 2004a, b, c, d; Sharma, Viswanath, et al., 2008a; Sharma, Balomajumder and Roy, 2008b;Sridhar et al., 2005; Sundaram et al., 2009), and alloxan (Kar et al., 2003; Rathi et al., 2002; Sharma et al., 2006, 2003) induced models of Type 1 diabetes as well as in the fructose-induced model (Suganthi et al., 2007; Vikrant et al., 2001) for type 2 diabetes. The efficacy of Jamun has also been observed with both rabbits (Sharma et al., 2003) and rats Kar et al., 2003; Panda et al., 2009; Rathi et al., 2002; Ravi et al., 2005, 2004a, 2004b, 2004c, 2004d; Sharma, Viswanath, et al., 2008; Sharma, Balomajumder and Roy, 2008; (Sridhar et al., 2005; Sundaram et al., 2009; Sharma et al., 2006, 2003) and the observations also extended to humans (Kohli and Singh, 1993; Sahana et al., 2010; Srivastava et al. 1983).

Studies with alloxan-induced diabetic rabbits have shown that the ethanolic extract of the seeds was effective in decreasing hyperglycemia (Sharma et al., 2003). The extract also decreased the peak blood glucose level in the glucose tolerance test in sub-diabetic and mildly diabetic rabbits but was ineffective against the severely diabetic rabbits (Sharma et al., 2003). Administering the extract (100 mg/kg body weight), orally to the sub-diabetic rats for 1 day, mildly diabetic for seven days and severely diabetic rabbits for 15 consecutive days showed significant decrease in the fasting blood glucose at 90 min and peak blood glucose levels during glucose tolerance test. When administered daily for 15 days to the mildly diabetic and severely diabetic rabbits, a significant decrease in the fasting blood glucose and glycosylated hemoglobin levels and a concomitant increase in the concentration of serum insulin and glycogen in the liver and muscle of diabetic animals were seen. The histopathological studies of liver, pancreas and aorta of the diabetic animals administered with the extract revealed almost normal appearance confirming its protective effects (Sharma et al., 2003).

Administration of different doses of alcoholic and aqueous extracts of Jamun seed to rats fed with fructose diets (to induce type 2 diabetes) was observed to induce concentration dependent, beneficial effects. Feeding fructose for 15 days marginally increased the serum glucose, insulin levels and the triglycerides levels when compared with the normal controls (Vikrant et al., 2001). Treatment with 400 mg per day of aqueous extract of Jamun for 15 days substantially prevented hyperglycemia and hyperinsulinemia suggesting it to be of use in Type 2 diabetes (Vikrant et al., 2001).

Studies by Sharma, Viswanath, et al. (2008a); Sharma, Balomajumder and Roy (2008b) have shown that the flavonoid rich extract obtained from the seed was effective in reducing hyperglycemic in the streptozotocin-induced diabetic rats. *In vitro* studies have also shown that culturing pancreatic cells with flavonoids stimulated 16% release in insulin, thereby confirming its secretagogue effects. The extract also caused hypolipidemic action and decreased the levels of LDL, triglycerides and increased the HDL levels in the treated diabetic

animals. When compared with the diabetic cohorts, the levels of glycogen biosynthesis, glucose homeostatic enzyme (glucose-6-phosphatase, hexokinase) were also enhanced. At a molecular level these effects were observed to be mediated through the up regulation of peroxisome proliferators-activated receptors (PPARα and PPARγ) and their capacity to differentiate 3T3-L1 preadipocytes (Sharma, Balomajumder and Roy, 2008b; Sharma, Viswanath, et al., 2008a). Studies have also shown that mycaminose (50 mg/kg), isolated from the seeds of Jamun also possess anti-hyperglycemic effects in the streptozotocin-induced diabetes in rats (Kumar, Ilavarasan, Jayachandran, Deecaraman, Mohan Kumar, et al., 2008).

Feeding Jamun has also been shown to enhance the levels of serum insulin levels in both normoglycemic and diabetic rats (Achrekar et al., 1991; Chaturvedi et al., 2007; Panda et al., 2009; Ravi et al., 2004c; Sharma et al., 2006, 2003), to protect pancreatic β-cells (Ravi et al., 2004d), stimulate synthesis of insulin from the residual beta cells (Grover et al. 2000; Ravi et al. 2004d; Sharma et al. 2006; Sridhar et al. 2005), inhibit insulinase in the liver and kidney and to trigger the development of insulin positive cells from the epithelial cells of the pancreatic duct (Helmstädter 2008; Schossler et al. 2004).

In vitro studies have also shown that Jamun seed possess inhibitory effect on both pancreatic amylase (Ponnusamy, Ravindran, Zinjarde, Bhargava and Ravi Kumar, 2010) and α-amylase (Karthic et al., 2008). The Jamun seed extract fraction is also reported to activate glucose transport in a phosphatidylinositol 3′kinase-dependent fashion in a cell culture model (Anadharajan et al. 2006). Jamun extract up-regulated the glucose transporter Glut-4 and activated the peroxisome proliferator-activated receptor gamma (Anadharajan et al. 2006; Rau et al. 2006).

Jamun seed and pulp extract stimulated the release of insulin from the cultured Langerhans cells from both normal and diabetic rats, with better effects being observed in the cells isolated from the normoglycemic animals (Achrekar et al. 1991). The pulp and seed extracts inhibited the hepatic and renal insulinase activity and in a concentration-dependent manner (Achrekar et al., 1991). Both aqueous and methanolic extracts inhibited glucose utilization (Khan et al. 2005), with the results being better in the neutral and basic than in the acidic media (Arayne et al. 2007).

In addition to decreasing hyperglycemia and hyperinsulinemia, animal studies have also shown that Jamun seeds prevent the diabetes-induced secondary complications like damage to kidneys (Grover, Rathi and Vats, 2002; Grover, Vats, Rathi and Dawar, 2001a, 2001b; Tanwar et al., 2010), neuropathy (Grover et al., 2002), gastropathy (Grover et al., 2002), diabetic cataract (Rathi et al., 2002) and to decrease peptic ulceration (Chaturvedi et al., 2009a, 2009b). These observations ascertain the usefulness of Jamun in the management of the hyperglycemia-induced secondary complications. Jamun is reported to stimulate myriad protective mechanisms that ultimately contribute towards reduction of diabetes and its complications. In diabetes, glycogen is depleted in both liver and muscles, and administering Jamun is shown to reverse these changes and to restore the levels of glycogen (Achrekar et al. 1991; Grover et al. 2000; Ravi et al., 2005, 2004b; Sharma et al. 2003).

Hyperglycemia induces oxidative stress and contributes towards the life threatening secondary complications. Studies have shown that Jamun reduces hyperglycemia-induced oxidative stress by restoring the levels of glutathione, increasing the activities of SOD, CAT, GPx, GST and concomitantly decreasing the levels of lipid peroxides (Kar et al. 2003; Prince et al., 2004, 1998; Ravi et al. 2004c; Stanely Mainzen Prince et al. 2003). Some of the other protective mechanisms observed to be operating are the inhibition of carbohydrate cleaving enzymes (Helmstädter 2008), inhibition of the human peroxisome proliferator-activated receptor gamma (Helmstädter 2008; Rau et al. 2006), up-regulation of the glucose transporter Glut-4 (Anandharajan, Jaiganesh, Shankernarayanan, Viswakarma and Balakrishnan, 2006), augmentation in the activity of cathepsin-B (Achrekar et al. 1991).

With respect to clinical studies, Srivastava et al. (1983) observed that administering 4 to 24 g of the seed powder to twenty eight diabetic patients caused a reduction in the mean fasting and post-prandial blood sugar levels. However five patients developed adverse drug reactions, including nausea, diarrhoea, and epigastric pain possibly due to the use of high doses of Jamun powder (Srivastava et al. 1983).

Subsequent studies by Kohli and Singh (1993) have shown that administering 12 g of the Jamun seed powder in three divided doses for three months to 30 patients with "uncomplicated" NIDDM caused a moderate hypoglycaemic effect. The effect of Jamun was comparable to that of chlorpropamide. Additionally, administering Jamun also provided considerable relief and reduced polyurea, polyphagia, weakness and weight loss. In this study no side effects were observed and this may be possibly due to the fact that the powder was administered thrice in a day (Kohli and Singh, 1993).

Recently, in an open labeled randomized parallel designed controlled study with freshly diagnosed type 2 diabetes mellitus patients Sahana et al. (2010) observed that administering the standardized Jamun seed powder caused a significant decrease in the fasting blood sugar, insulin resistance and increase in HDL cholesterol at the end of 3rd month (when compared to the baseline). However, when compared to the baseline, there was no significant reduction in the PPBS and HbA_{1C} at the end of the 3rd and 6th months. Additionally, there was no change in the triglyceride, total cholesterol and LDL levels (Sahana, et al., 2010). In conclusion, all these observations clearly indicate the usefulness of Jamun as a hypoglycemic agent but not as a hypolipidemic agent. Further studies are required to validate these observations with a larger number of patients with suitable controls. Studies should also be aimed at understand the phytochemical/s responsible for the antidiabetic effects and their mechanism of action.

2.11. Hypolipidemic effect

Alterations in lipid profile are one of the most common complications in diabetes mellitus and affects 40% of all diabetic patients (Ravi et al., 2005). Studies by Sharma et al. (2003) have shown that feeding the ethanolic extract of seeds to allaxon-induced diabetic rats caused a significant hypolipidemic effect and decreased the levels of total serum cholesterol (TC)/high density lipoprotein cholesterol (HDL-c) ratio, serum low density lipoprotein cholesterol (LDL-c) levels and the activity of HMG-CoA reductase (Sharma et al., 2003). Experiments have also shown that feeding ethanolic extract of the seed kernel (100 mg/kg body weight) to streptozotocin-induced diabetic rats also caused a decrease in the levels of cholesterol, phospholipids, triglycerides and free fatty acids and to near normal levels in both plasma and tissues. The plasma lipoproteins (HDL, LDL, VLDL-cholesterol) and fatty acid composition which were also altered in diabetic rats were restored back to normal levels after administering the extract (Ravi et al., 2005). Additionally, studies with the flavonoid enriched extract from the seeds have also shown that it decreases the levels of LDL, triglycerides and a concomitant increase in HDL levels over the untreated diabetic rats (Sharma, Balomajumder and Roy, 2008b; Sharma, Viswanath, et al., 2008a). Cumulatively all these observations suggest that usefulnes of Jamun as a hypolipidimic agent.

2.12. Cardioprotective effects

Cardiac ailments are the world's leading cause of death and the World Health Organization predicts that deaths due to diseases of the circulatory system are projected to double between 1985 and 2015 (Mastan et al., 2009). The methanolic extract of the seeds are shown to possess cardioprotective effects in the isoproterenol-induced myocardial infarction model in rats. Oral feeding of the extract (250 mg/kg and 500 mg/kg) for thirty consecutive days resulted in a concentration dependent protection against the isoproterenol-

induced myocardial infarction. Administration of isoproterenol caused a significant elevation in the levels of AST, ALT, LDH and CPK profiles and feeding the seed extract caused a reversal and retained the activity of these enzymes to near normal levels. Of the two doses studied, 250 mg/kg showed a marginal effect while the next higher dose of 500 mg/kg was effective (Mastan et al., 2009). Collectively all these observations emphasize the usefulness of Jamun as a cardio-protective agent.

2.13. Anti-fertility activity

Population explosion is a serious problem in many of the third world countries and search for an effective non toxic contraceptive agent of dietary source is preferred (Rajasekaran et al., 1988). Studies by Rajasekaran et al. (1988) have shown that administering oleanolic acid, a constituent of the jamun flowers possess antifertility activity in the male albino rats. Administering the compound for 60 consecutive days decreased the fertilizing capacity of the animals without affecting the body weight or the gross weight of the reproductive organs. Oleanolic acid arrested spermatogenesis but did not cause any abnormality to spermatogenic cells, leydig interstitial cells and sertoli cells indicating that the effect is selective to the process of spermatogenesis. These observations clearly suggest that oleanolic acid may be a promising and a safe non toxic antifertility agent (Rajasekaran et al., 1988).

2.14. Anti-allergic effects

Allergy, which is a heightened reactivity of the host on being exposed to an antigen, is an immediate reaction and includes anaphylaxis following contact with an antigen (Brito et al., 2007). Oral administration of the aqueous extract of the leaf (25–100 mg/kg) to Swiss albino mice inhibited the rat paw edema induced by the allergenic compound 48/80. The extract also inhibited histamine and 5-HT-induced edema but was ineffective against the platelet-aggregating factor-induced paw edema. The mast cell degranulation and the consequent histamine release were also inhibited in the rat peritoneal mast cells when stimulated by the compound 48/80. Pre-treatment of BALB/c mice also inhibited eosinophil by inhibiting IL-5 and CCL11/eotaxin in the pleural lavage fluid. Together these observations indicate that Jamun leaf extract possess anti-allergic effects and also that the anti-edematogenic effect was due to the inhibition of mast cell degranulation and by affecting both histamine and serotonin.

2.15. Neuropsychopharmacological effects

Studies have shown that the chloroform extract of seeds altered the general behavioral pattern, potentiated pentobaritone hypnosis, caused analgesia, reduced exploratory behavioral pattern, possess muscle relaxant action, suppressed aggressive behavior, reduced the spontaneous motility and caused hypothermia. The extract also caused suppression of conditioned avoidance response and showed antagonism to amphetamine group toxicity. Together these observations suggest that the organic extract of Jamun seeds possesses a potent CNS depressant action (Chakraborty et al., 1986). The ethyl acetate and methanolic extract of the seed, at a dose of 200 and 400 mg/kg were also observed to possess significant CNS activity, thereby suggesting its usefulness and need for detail investigations (Kumar et al., 2007). Pyrexia, which in colloquial term is known as fever is regulated by the hypothalamus and can have both beneficial and deleterious effects. Studies have shown that Jamun possesses significant anti-pyretic action against the yeast-induced pyrexia in mice (Chaudhuri et al., 1990). Together all these observations emphasize the usefulness of Jamun for these medical conditions.

2.16. Jamun in the treatment and prevention of cancer

2.16.1. Antineoplastic effects

Chemotherapy has been the mainstay of cancer treatment for the past 50 years. However, most of the chemotherapeutic drugs exhibit severe normal toxicity, resulting in undesirable side effects. The herbal drugs used in complementary and alternative systems of medicine provide a cheaper alternative to synthetic drugs and their screening provides a major avenue for new drug discovery (Barh and Viswanathan, 2008).

Experimental studies have shown that supplementing the human cervical cancer cells [HeLa (HPV-18 positive) and SiHa (HPV-16 positive)] with media containing Jamun extract caused a dose dependent cell death *in vitro*. At a 40% concentration of the extract, a 14.4% growth inhibition was observed in the HeLa cells while in the SiHa cells, at the same concentration, it was observed to be 11.8%. With increase in concentration to 80% the growth inhibition was observed to be 30.3% and 23.2% respectively for HeLa and SiHa cell lines (Barh and Viswanathan, 2008). Additionally, both crude as well as the methanolic extracts of the pulp at 80% concentration induces a time dependent apoptosis in both cells. The methanolic extract was observed to be less effective when compared to the crude extract in both the cell lines. Among the two cell lines, the Hela cells were observed to be more sensitive than the SiHa cells at all the time points assayed and this may be due to the difference in the cell proliferative kinetics and the intrensic sensetivity towards the induction of apoptosis (Barh and Viswanathan, 2008).

Recently Li, Adams, et al. (2009); Li, Zhang and Seeram (2009) investigated the antiproliferative and pro-apoptotic effects of standardized Jamun fruit extract in the estrogen dependent/aromatase positive (MCF-7aro), and estrogen independent (MDA-MB-231) breast cancer cells, as well as in a normal/nontumorigenic (MCF-10A) breast cell line. The results clearly showed that the extract was selectively cytotoxic to the neoplastic cells and that at equivalent concentration was not toxic to the normal cells. The extract was highly effective against MCF-7aro (IC50 = 27 microg/mL), followed by MDA-MB-231 (IC50 = 40 microg/mL) breast cancer cells, while for the normal MCF-10A cells it was observed to be > 100 microg/mL. Additionally, the extract induced pro-apoptotic effects selectively in the MCF-7aro and the MDA-MB-231 cells, but not to the normal MCF-10A breast cells indicating its usefulness in cancer treatment (Li, Adams, et al., 2009; Li, Zhang and Seeram, 2009). Additionally, studies have also shown that the ellagitannins obtained from Jamun inhibited Wnt signaling in a transfected human 293T cell line (Sharma et al., 2010). Together these results clearly indicate that at supra dietary levels the fruit pulp extract possess selective antineoplastic effects against breast cancer and that its regular consumption may prevent the initiation, development and progression of colon cancer where Wnt signaling is deranged.

2.17. Radioprotective effects

The effective use of radiotherapy in cancer cure and palliation is compromised by the side effects resulting from the radio sensitivity of the bordering normal tissues, invariably exposed to the cytotoxic effects of ionizing radiation during treatment. In such situations, an agent that can render a therapeutic differential between the cancer and normal cell will be beneficial (Jagetia et al., 2005). Therapeutic differential may be achieved with chemical compounds that may selectively protect the normal cells from the deleterious effects of radiation termed as radioprotectors (Jagetia et al., 2005). Studies have shown that the intraperitoneal administration of the hydroalcoholic extract of the Jamun seed and the dichloromethane extract of Jamun leaf possess radioprotective effects (Jagetia and Baliga, 2003; Jagetia et al., 2005).

Pretreatment with hydroalcoholic extract of jamun seeds (5 to 160 mg/kg body weight) for five consecutive days before exposure to supralethal dose of radiation (10 Gy) protected mice against the radiation-induced sickness and mortality. The best effect was observed at 80 mg/kg but only when administered through the intraperitoneal route as 50% of the animals survived when compare to 22% in the oral route and none in the radiation alone cohorts. Administering 80 mg/kg of the seed extract before exposure to 6 to 11 Gy of radiation caused a significant increase in the animal survival when compared with the concurrent radiation alone cohorts and also resulted in a dose reduction factor of 1.24 (Jagetia et al., 2005).

Intraperitoneal administration of the organic extract of the leaves (5 to 80 mg/kg b. wt.) for five days before irradiation was also observed to be effective in preventing the radiation-induced sickness and mortality in mice. The optimal effects were observed for 30 mg/kg b. wt. cohorts as the number of survivors after 30 days post-irradiation was highest (41.66%) in this group (Jagetia and Baliga, 2003). Histopathological investigations showed that when compared with the concurrent irradiation control, administering Jamun leaf increased the villus height, the number of crypts and reduced the goblet and dead cells. The recovery and regeneration was faster in Jamun pretreated animals than the irradiation alone cohorts and this may have contributed towards the increased survival of mice (Jagetia et al., 2008).

2.18. Chemopreventive effects

Chemoprevention, a science that has emerged during the three last decades, presents an alternative approach to reducing mortality from cancer. It aims at blocking, reversing, or delaying carcinogenesis before the development of invasive disease by targeting key molecular derangements using pharmacological or nutritional agents. Chemopreventive interventions may be applied at any time during carcinogenesis, from the initial molecular defect through the accumulated molecular, cellular and histopathological alterations that characterize disease progression before an invasive and potentially metastatic stage (Parmar, Sharma, Verma and Goyal, 2010; Parmar, Sharma, Verma, Sharma and Goyal, 2010b).

Recently, Parmar, Sharma, Verma and Goyal (2010); Parmar, Sharma, Verma, Sharma, et al. (2010b) have reported that jamun possess cancer chemopreventive properties in the DMBA-induced croton oil promoted two stage skin carcinogenesis in Swiss albino mice. Feeding 125 and 250 mg/kg/b. wt./animal/day of the extract either during the peri-initiation (i.e. 7 days before and 7 days after the application of DMBA) or post-initiation (i.e. from the day of start of croton oil treatment and continued till the end of the experiment) phases reduced the cumulative numbers of papillomas, the tumor incidence and increased the average latency period when compared with the control group (carcinogen alone) (Parmar, Sharma, Verma and Goyal, 2010; Parmar, Sharma, Verma, Sharma, et al., 2010b). Studies have also shown that administration of the extract (25 mg/kg b.wt/day) was effective in reducing the tumor incidence, tumor burden and cumulative number of gastric carcinomas induced by benzo-a-pyrene indicating that Jamun possess broad spectrum chemopreventive effects (Goyal et al., 2010).

Recent studies have also shown that administration of the aqueous extract also reduced the genotoxic effects of the carcinogens urethane and DMBA in mice. The anti-genotoxic effects operating may have been responsible for the observed chemopreventive effects of the Jamun seeds, at least in part (Arun et al., 2010). Additionally, studies have also shown that Jamun seed possess free radical scavenging effects (Benherlal and Arumughan 2007; Reynertson et al., 2008; Raquibul-Hasan et al., 2009; Kshirsagar and Upadhyay, 2009; Veigas et al., 2007; Nahar et al., 2009; Zhang and Lin, 2009; Jagetia et al., 2005; Zhang and Lin, 2009; Ruan et al., 2008; Banerjee et al., 2005), inhibited lipid peroxidation, increase antioxidant biomolecule GSH, increase phase 2 detoxification (GST) and antioxidant enzymes (SOD and CAT), and they may have also contributed towards the observed chemoprevention (Arun et al., 2010; Goyal et al., 2010; (Parmar, Sharma, Verma and Goyal, 2010;Parmar, Sharma, Verma, Sharma, et al., 2010b).

2.19. Anticlastogenic effects

The process of carcinogenesis is extended and involves a complex series of events. The earliest event for any cancer to develop includes DNA damage and the fixation of mutations. Exposure to genotoxic chemicals causes mutations and ionizing radiation being one is proved to cause both DNA damage and cancer (Jagetia and Baliga, 2002). Accordingly prevention of DNA damage and mutagenesis is important to stall the initiation of possible carcinogenesis.

In vitro studies have shown that treatment of with human peripheral blood lymphocytes with various concentrations of Jamun (1.56 to 100 μg/ml) before exposure to 3 Gy of γ-irradiation resulted in a significant decline in the micronuclei-induction and that the optimal effects were seen at 12.5 μg/ml drug concentration (Jagetia and Baliga, 2002). Recent studies have also shown that the aqueous and ethanolic extracts of Jamun seed reduced the hydroxyl radical-induced strand breaks in pBR322 DNA *in vitro* and that the aqueous extract was also effective in decreasing the urethane and DMBA-induced chromosomal aberration in mice (Arun et al., 2010). Together these observations clearly indicate the usefulness of Jamun in preventing mutagenesis and initiation of carcinogenesis.

3. Conclusion

Studies carried out in the past indicate that jamun possesses diverse health benefits and are an important food. Studies have shown that various extracts of Jamun possess a range of pharmacological actions, such as antimicrobial, anti-inflammatory, anti-ulcerogenic, cardioprotective, anticancer, antiallergic, hepatoprotective, antidiarrhoeal, hypoglycemic and antidiabetic effects supporting its traditional use. However, the most prominent and the well studied effects are the antidiabetic effects of Jamun seed in different experimental models and in patients. The observed health benefits may be credited to the presence of the various phytochemicals like polyphenols, terpenes, anthocyanins and flavonoids. The presences of anthocyanins, fibers and ellagitannins which are present in the pulp are important in reducing the oxidative stress-induced diseases.

Jamun also contains minerals like potassium, sodium, calcium, phosphorous, iron and zinc; water soluble vitamins like ascorbic acid, thiamine and niacin and these may contribute for the myriad beneficial effects at least in part. Future studies should be on validating the mechanism of action responsible for the various beneficial effects and also on understanding which compound/s are responsible for the reported effects. The required information when available will enhance our knowledge and appreciation for the use of Jamun in our daily diet.

In parts of India, Jamun pulps are used to make wine and attempts should also be made to encourage research on optimizing the taste, aroma and color of the wine so that industrial scaling can be performed. Studies should also be on improving the quality and marketability of the various finished products of Jamun pulp (juice, jams etc.). Emphasis should also be on improving the quality and shelf life of the fruits and their products so that the potential of this plant can be realized.

Preliminary studies suggest that the Jamun plant possess antifungal effects and prevents spoilage of grains. Necessary studies should be undertaken towards developing Jamun as a non toxic and an easily affordable preservative of grains. Additionally attempts should also be made to publicize the various benefits of Jamun and the policy makers should render the necessary support to farmers to take up the

cultivation of Jamun either alone or with other plants (especially the climbers like *Piper beetle*, *Piper nigrum* and vanilla that need support and foliage for optimal growth) so that its optimal medicinal and industrial benefits may be realised.

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