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Medicinal and therapeutic properties of Jamun (*Syzygium cumini*) – A Comprehensive Review

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ABSTRACT:

Hepatocellular carcinoma (HCC) is the seventh most common cancer and the third leading cause of cancer-related death globally. It has a poor prognosis and is resistant to the majority of chemotherapeutics. The present review aimed to highlight studies into the tumor cycle and its prevention by appropriate herbal (Ayurvedic/Unani) medicine that is essential to reduce the effects of the deadly disease. There are few treatment options for end-stage liver cancer, which forces patients to undergo expensive liver transplantation, which is not an option in the majority of nations. Herbal medicine has experienced exponential growth in recent years, and due to its natural origins and limited side effects, these medications are becoming more and more popular in both developed and developing nations. The anti-diabetic function of *S. cumini* has the most potential nutraceutical value among these advantageous physiological effects. The numerous phytoconstituents included in the fruit, including tannins, alkaloids, steroids, flavonoids, terpenoids, fatty acids, phenols, minerals, carbohydrates, and vitamins, are primarily responsible for *S. cumini*'s favourable benefits on health. An overview of the scientific data supporting *S. cumini*'s pharmacological potential is provided in this review.

Introduction:

People all around the world have been using medicinal plants as alternative treatments for a variety of illnesses, especially when their positive effects have been supported by scientific research¹. Hepatocellular carcinoma (HCC) is one of the most common types of solid tumour, currently More than 800,000 cases are diagnosed with this cancer each year worldwide². It is highly aggressive, as currently evidenced by the annual mortality rate of 700,000, which is approximately equal to the incidence of this tumour type³. Hepatocellular carcinoma (malignant hepatoma; HCC) is an advanced form of liver cancer that causes skin discoloration, fluid accumulation in the abdomen, blood clotting irregularities, severe abdominal pain, vomiting/nausea, and restlessness⁴. The progressive destruction and regeneration of liver parenchyma are pathological processes that lead to numerous chronic liver disorders. Viral hepatitis, alcoholic or non-alcoholic fatty liver disease, autoimmune hepatitis, cirrhosis, and hepatocellular carcinoma are the most common chronic liver illnesses⁵.

In severe liver damage conditions, the most of the cells either die or transition to a fibrotic condition. In these cases, treatment options include both therapeutic medications and drugs that promote the proliferation of liver cells. Human liver cell lines, either from malignant tissue or produced by genetic engineering of primary liver cells, are commonly employed in in vitro research because they are more readily available. Because of their stable metabolism and increased proliferation potential, these cells are suited for in vitro study under repeated and standardized settings. The hepatoma cell line HepG2 is used in the majority of in vitro research for the development of cancer therapies. Cell lines, according to reports, are critical for investigating metabolic pathways or evaluating new cancer treatments alone or in combination^{6,7}.

Liver diseases

The liver plays an important role in the control of several physiological functions. It participates in a variety of critical activities, including metabolism, secretion, and storage. A wide range of xenobiotics and medications can be detoxified by the liver. Bile acid produced by the liver, along with a few other components, regulates how food is digested. One of the most serious conditions is liver disease. Cirrhosis

(which leads to liver fibrosis), hepatizes, and chronic or acute (inflammatory illness) are the three types (non-inflammatory ailment). They are typically caused by a combination of risk factors that generate oxidative stress in the liver, which leads to lipid peroxidation and other oxidative damage to the liver cells. Increased lipid peroxidation during the liver's microsomal ethanol processing can cause hepatitis and cirrhosis⁸.

Risk factors for liver cancer

Chronic infection with the Hepatitis C and B viruses has been identified as the common component producing liver cirrhosis⁹. The hepatitis C and B viruses can transfer from one person to another through the use of contaminated needles and the sharing of blood. A blood test before a blood transfusion can help to reduce the likelihood of transmission¹⁰. Another risk factor is alcoholism, which causes liver cirrhosis and hepatic cancer¹¹. Smoking, being overweight, having diabetes, and using tobacco all raise the risk of developing liver cancer¹². Furthermore, long-term exposure to thorium dioxide (an X-ray chemical), vinyl chloride, and aflatoxin can raise the chance of developing cirrhosis and liver cancer¹³.

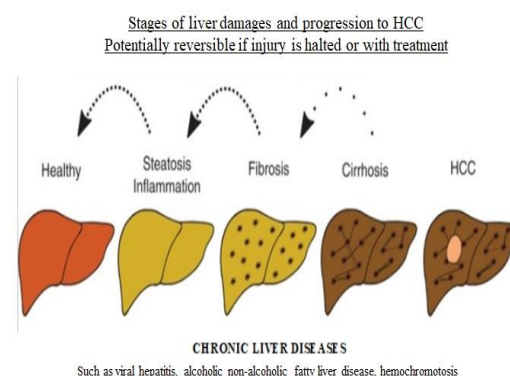


Fig.1. Progressive stages of liver disease to hepatocellular carcinoma development.¹⁴

Jamun (*S. cumini*) is one of the known herbal medicinal plants in the Unani system of medicine (USM). In India and several nearby nations, the Unani System of Medicine (USM) is practised as a kind of complementary, alternative, and traditional medicine. This plant, which has 2,800 species and 90 genera, is a sizable tropical evergreen glabrous tree. Ibn Batuta, who traveled to India in 1332 AD, named it one of Delhi's fruits. Since ancient times, it has been

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discovered all across India, as well as other nations like Nepal, Myanmar, Sri Lanka, Indonesia, Pakistan, Bangladesh, Malaysia, Thailand, and other tropical areas of the globe ¹⁵. India is one of the nations that has been gifted with a rich history of conventional medical practises and a rich biodiversity to support the herbal needs of conventional medical practises' treatments. Ayurveda, Yoga, and Unani are the accepted Indian medical systems. Siddha and Unani, whose compositions include plants and minerals. India, which has 15 agro-climatic zones and 47000 plant species, is said to have 15000 of them with varied degrees of medicinal characteristics. The World Health Organization (1980) also advised assessing the efficacy of plants in situations where there are no safe synthetic medications available ¹⁶.



Fig.2. Therapeutic activities of Jamun (*S. cumini*)

Botanical description:

a smooth, 4–15-meter-tall member of the Myrtaceae family tree. Leaves are 6-12 cm long, leathery, oblong-ovate to elliptical or obovate, and have a broad, pointy tip. The panicles, which are often axillary or terminal and 4-6 cm long, are borne largely from the branchlets beneath the leaves. Numerous, fragrant, pink or almost white, stalkless, and borne in dense fascicles at the tips of the branchlets are the flowers. The calyx has four teeth, is funnel-shaped, and is around 4 mm. The petals stick together and drop as a single tiny disc. The calyx and the stamens are both equally long and abundant. Fruit is 1.5-3.5 cm long, oblong to elliptical, dark purple or almost black, luscious, juicy, and tasty. It contains one huge seed ¹⁷.

Vernaculars names and Scientific Classification¹⁸

It is a very popular herbal medicine but it is known by various names in different languages and Scientific Classification such as:

Table – 1: Vernaculars names and taxonomy

(<i>Syzygium cumini</i>) Vernaculars names	Kingdom	Plantae
Hindi	Jam, Jamun, Jaman, Phalanda, Phalinda	Division SubKingdom
		Tracheophyta Viridiaeplante
English	Black plum, Black Berry	Infrakingdom Subdivision
		Streptophyta Spermatophytina
Urdu	Jaman, Phalenda	Class
		Magnoliopsida
Sanskrit	Jambula, Jambu	Order
		Myrtales
Telugu	Neereedu, Neredu, Jambuvu, Naeraedu, Nesedu	Family Genus
		Myrtaceae Syzygium
Punjabi	Jaamun	Species
		cumini
Tamil	Naval	Superorder
		Rosanae

Phytochemistry of Jamun

Jamun contains phytochemicals in all of its parts: leaves, fruit, seed, and bark. Various studies have revealed the presence of phenols, flavonoids, alkaloids, glycosides, steroids, cardiac glycosides, saponins, terpenoid, and tannins in Jamun leaf extract as demonstrated by ^{19,20}. α -pinene (32.32%), β -pinene (12.44%), transcaryophyllene (11.19%), 1, 3, 6-octatriene (8.41%), delta-3-carene (5.55%), α -caryophyllene (4.36%) and α -limonene (3.42%) are the most abundant elements of the oils in Jamun leaves.

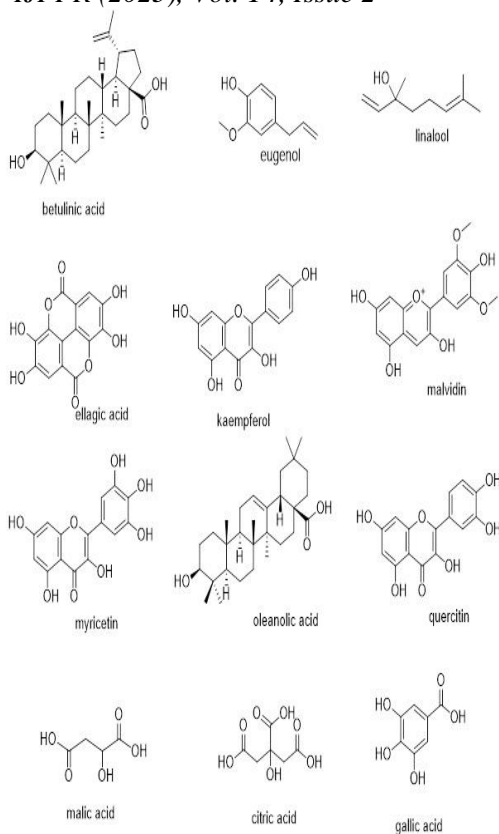


Fig. 3. Chemical structures of some important phytochemicals found in various parts of the Jamun, *Syzygium cumini*.

Table-2 Summary of *Syzygium cumini*³⁶

S. No	Plant part	Metabolic class	Active Constituents	Uses
1.	Seeds	Polyphenols including Flavonoids, alkaloids, glycosides and phenolic compound, fatty oils.	Quercetin, Rutin, 3,5,7,4-tetrahydroxy flavones, caffeic acid, ellagic acid, ferullic acid, albumen, fat, jambosine, ellagic acid, lauric, myristic, palmitic, stearic, oleic acid, linoleic, malvalic and vernolic acid and phytosterols	Diabetes (Leaf, Bark, Seed, Pulp), Anti allergic (Leaf), Antioxidant (Leaf, Fruit, Seed), Anti-Viral (Leaf), Anti-bacterial (Leaf, Seed), Anti-cancer (Fruit), Anti-inflammatory (Seed,

			such as β -sitosterol.	Leaf), Gastric ulcer (Seed), Antihyperlipidemic (Fruit), DNA damage (Leaf).
2.	Leaves	phenolic content and acetylated flavonol glycosides	Ferrullic acid, catechin, cretegolic acid, n-dotricontanol, myrcetin, mycaminose, quercetin, tannic acid, BHA, Tocopherol.	
3.	Fruit	Tannins, Glycosides, Vitamin A, C	Oxalic acid, malic acid, gallic acid cyanidine diglycosides, thiamine, riboflavin, nicotinic acid, folic acid	
4.	Fruit pulp	Anthocyanins, volatile oils, terpenes	Petunidin, α -pinene, β -pinene, malvidin, peonidin, cyanidin, delphinidin, pelargonidin	
5.	Stem bark	Triterpenoids, Resin, Resin, Phytosterol	Oleanolic acid Eugenia-triterpenoid-A Eugenia-triterpenoid-B Ellagic acid, Pentacyclic triterpenoid-Betulinic acid, Pentacyclic triterpenoid Friedelin, Myricetin, β -sitosterol, Myricyl alcohol	

6.	Flo wer	Flavonoid s, tannins, triterpenoi ds	Eratogenic acid, isoquercetin, quercetin, Kaempferol Oleanolic acid
7.	Ro ots	Flavonoid s, glycosides	Isorhamine 3- o-rutinoside, myricetin 3- o- robinoside

Table 3: List of phytochemicals present in *Syzygium cumini* ³⁷

Sr . No	Pla nt part	Chemicals present
I.	Lea ves	Mycaminose, crategolic (Maslinic) acid, β -sitosterol, Betulinic acid, heptacosane, n-dotricontanol, quercetin, n-nonacosane, n-hentriacontane, n-octacosanol, ntriacontanol, myricetin, myricitrin and the flavonols glycosides myricetin 3-O-(400-acetyl)- α L-rhamnopyranosides
II.	Flo wer s	Oleanolic acid, Ellagic acids, isoquercetin, quercetin, Kaempferol, and myricetin
III.	Ste m	Fried Elin, Betulinic acid, friedelan-3- α -ol, β -sitosterol, gallic acid, Kaempferol, β -sitosterol-D-glucoside, ellagic acid, Gallotannin and myricetin and ellagitannin.
IV.	Fru it pulp	Anthocyanins, delphinidin, petunidin, malvidin-diglucosides
V.	See ds	Jambosine, gallic acid, ellagic acid, corilagin, 3,6-hexahydroxydiphenoylglucose, 1-galloylglucose, 3-galloylglucose, quercetin, β -sitosterol, 4,6 hexahydroxy diphenoy lglucose
VI.	Esse ntial oils	α -Terpineol, eucarvone, myrtenol, muurolol, geranyl acetone, α -myrtenal, 1, 8-cineole, pinocarvone and α -cadinol.

MEDICINAL PROPERTIES:

Syzygium cumini having pharmacological activity like Anti-Hepatocellular carcinoma, Anti-cancer, Antiallergic, Antioxidant, Gastroprotective, Anti-inflammatory, Anti-diabetic, Immunomodulatory, Central nervous system (CNS) activity etc.

Jamun and its antioxidant properties:

Antioxidant-rich foods have an important role in disease prevention. The fruit's antioxidant activity has been reported skin using several assays such as the hydroxyl radical scavenging assay, which is based on the benzoic acid hydroxylation method, and the superoxide radical - scavenging assay, which is based on photochemical reduction of nitroblue tetrazolium (NBT) in the presence of a riboflavin light-NBT system, DPPH radical scavenging assay, and lipid peroxidation assay The antioxidant potential of the egg yolk is enhanced by using it as a lipid-rich source. Fruit skin may contain antioxidant vitamins, phenolics, or both. tannins and anthocyanins found in fruit ²¹. Antioxidant activity against DPPH free radicals and reduction of ferric (FRAP) were used to assess the antioxidant property of *Syzygium cumini* leaves. The methanolic extract and its four fractions (water, ethyl acetate, chloroform, and n-hexane) were produced and tested for antioxidant activity. The antioxidant activity of the ethyl acetate fraction was higher than that of the other fractions. HPLC analysis revealed that *Syzygium cumini* leaf extract contained antioxidant-active phenolic components such as ferulic acid and catechin ²². Presented a thorough and succinct analysis of clinical trials of antioxidative natural compounds derived from jamun seeds They determined that products derived from jamun seed extracts are generally thought to be safer, less expensive, more readily available, and occasionally more effective than fully synthetic medications. Blackberries are regarded natural antioxidant sources, and the seeds contain significant antioxidants that promote health and prevent disease ²³. Several more investigations have discovered that jamun Seeds include antioxidant characteristics that are useful to human health and the treatment of numerous ailments such as diabetes, cancer, stroke risk, and cardiovascular disease. Jamun are known to be high in natural antioxidants and so have an essential role in disease and ageing prevention.

Hepatoprotective activity:

The ethanolic extract of the pulp of *E. jambolana* (EPEJ) was tested for its ability to protect the liver

against paracetamol (PCM)-induced hepatotoxicity in albino rats. When compared to control rats, paracetamol significantly increased the levels of blood marker enzymes aspartate aminotransferase (ALT), alanine aminotransferase (AST), and ALP, while decreasing total protein and albumin content. Pre-treatment of rats with two dosages (0.1 and 0.2 g/kg body weight) of *E.jambolana* and the conventional medication silymarin resulted in a drop in enzyme levels and an increase in total protein and albumin content. The most commonly used markers of hepatocellular damage are serum levels of AST, ALT, and ALP ²⁴.

Elevated levels of these blood enzymes were indicative of cellular leakage and loss of cell membrane functional integrity in the liver ²⁵. Total protein and albumin levels were lower, indicating a loss of hepatocyte biosynthetic function, whereas bilirubin levels were higher, indicating a failure of hepatocellular absorption, conjugation, and excretion of bilirubin due to hepatic cell function ²⁴. The reduced rise in serum enzymes, as well as the reduced decrease in total protein and albumin levels in the extract (EPEJ)-treated groups, was a clear expression of the extract's hepatoprotective action. EPEJ administration also restored the liver's histological structure to near normal. EPEJ likely stabilised hepatocyte plasma membranes and repaired damaged hepatic tissues by boosting hepatocellular protein production and accelerated hepatocyte regeneration. The main mechanism behind all of these benefits was most likely the reduction of oxidative stress caused by paracetamol, which was caused by EPEJ's antioxidant activity. The flavonoids, gallic acid, and anthocyanins found in *E.jambolana* pulp served as natural antioxidants ²⁶.

Thus, EPEJ protected against paracetamol-induced liver damage by boosting reduced glutathione concentration and the activity of antioxidant enzymes such as superoxide dismutase, scavenging free radicals and avoiding oxidative stress-mediated cellular damage. According to the literature, it has hepatoprotective properties. In rats given hepatotoxic paracetamol, the Ethanolic Extract of The Pulp of *Eugenia Jambolana Lam.* at doses of 100 mg/kg and 200 mg/kg exhibited considerable hepatoprotective action ²⁷. It was discovered that the methanolic extract of *Eugenia Jambolana Lam.* was effective at an oral

dose of 400mg/kg/day against the hepatotoxicity produced by carbon tetrachloride (CCL4) ²⁸.

Jamun and its anti-inflammatory properties:

The property of a chemical or medicine that lowers inflammation is known as anti-inflammatory. Anti-inflammatory medications alleviate pain by lowering inflammation. These medications can be used to treat pain, stiffness, edoema, and fever. The property of a chemical or medicine that lowers inflammation is known as anti-inflammatory. Anti-inflammatory medications alleviate pain by lowering inflammation. These medications can be used to treat pain, stiffness, edoema, and fever.

It has been claimed that the seeds of *S. cumini* exhibit anti-inflammatory effect, which has the same chemical structure as cholesterol and is particularly useful in lowering blood cholesterol. Jamun contains polyphenols, which have been shown to have anti-inflammatory properties in humans. Anthocyanins, which give blackberries their distinctive colours of red, blue, and purple, are among the most famous polyphenols found in them. Thus, it was discovered that jamun seeds include anti-inflammatory qualities that are good for preserving human health and treating heart disease, reducing inflammation, boosting immunity, and counteracting discomfort, stiffness, and lowering cholesterol. Jamun seeds have been extensively researched for their antioxidant qualities; nonetheless, preliminary findings indicate significant impacts on inflammatory pathways ²⁹.

Jamun and its Anti-diabetic properties:

Diabetes Mellitus is one of the most common endocrine illnesses, and it is associated with a variety of metabolic abnormalities. The World Health Organization recommends using traditional medicine to treat diabetes. Alternative approaches including conventional medicinal compounds are being considered in order to obtain lower blood glucose levels with little side effects and at a reasonable cost ³⁰.

According to researcher, after 1 hour in excess glucose, an ethanolic extract of *S. cumini* reduced blood sugar levels by 20% in rabbits. Several further animal investigations have shown the role of jambul in diabetes treatment. As a result, it was discovered that many authors extracted the seeds of *S. cumini* and conducted research to determine the anti-diabetic effect of jamun ³¹.

Immunomodulatory Activity:

The immunomodulatory effect of *S. cumini* seed extract was investigated. In rats, it was found to have a dose-dependent effect on the humoral antibody levels and the delayed-type hypersensitivity (DTH) reaction. The medication caused an increase in the total quantity of white blood cells, lymphocytes and neutrophils in rats. According to the findings of this investigation, *S. Cumini* seed extract showed the ability to boost the body's hematological system, suggesting that the plant has the potential to treat immune-deficient disorders brought on by radiotherapy or chemotherapy³².

Anti-cancer Activity:

Cancer is the unchecked expansion of aberrant cells in the body, which results in the formation of tumours, or masses of tissues. When the body's regular regulating mechanism breaks down, the old cells proliferate out of control and give rise to new, aberrant cells rather than dying. The second leading cause of death in humans, behind cardiovascular disease, is a non-communicable killer called cancer. Surgery, radiation, chemotherapy, or a combination of these methods are used to treat cancer (or all).³³, stated that A higher risk of developing cancer has been associated with environmental, nutritional, or lifestyle variables. In order to prevent and treat cancer, many scientists are looking for alternatives that are efficient, non-toxic, and economical. Due to the abundance of bioactive phyto-chemicals found in blackberries/jamun, such as anthocyanins and poly-phenols, the anti-cancer potential of these fruits is receiving a lot of attention these days. According to epidemiological evidence, consuming more dark-coloured fruits like jamun can help reduce your chance of developing some malignancies by increasing your antioxidant intake.

Central nervous system (CNS) activity

At dose levels of 200 mg/kg and 400 mg/kg, the Central Nervous System Activity of ethyl acetate and methanol extracts of jamun (*Syzygium cumini*) seed on Albino mice was examined using a rota rod and an actophotometer, respectively. They discovered that the safe dose for animals was 2000 mg/kg body weight, and both extracts considerably reduced spontaneous loco-motor activity in mice, indicating a central depressive action³⁴.

Antiallergic activity

According to HPLC analysis, the extract's main components include hydrolyzable tannins and flavonoids. The antiallergic activity of jamun (*Syzygium cumini*) aqueous extract implies that its antiedematogenic effect is related to mast cell degranulation inhibition as well as serotonin and histamine effects, whereas the inhibition of eosinophil accumulation in the allergic pleurisy model is likely due to an impairment of CCL11/eotaxin and IL-5 production, as demonstrated by³⁵.

CONCLUSION:

Through literature review specifically on the liver-protective and antioxidant properties of Jamun was carried out and the data has been compiled and presented here This information will be useful to researchers involved in liver carcinoma and free radical scavenging studies. This review provides a scientific foundation for the rational discovery, development, and application of Jamun (*Syzygium cumini*), in future treatment practice. Furthermore, pre-clinical studies are required to improve our understanding of phytoconstituents' anti-HCC and antioxidant activity. Thus, a more specific evaluation of natural sources is required. These herbs have anticancer potential due to their hepatocellular carcinoma and antioxidant capabilities. Knowledge of anticancer medicinal plants used by people from around the world from different countries is also included in this article. Utilizing cutting-edge anticancer medications made from therapeutic plants is also essential.

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ABBREVIATIONS:

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(CCL4): Carbon tetrachloride, **(EPEJ):** Ethanolic extract of the pulp of *E. jambolana*, **(HCC):** Hepatocellular carcinoma, **(FRAP):** Ferric-reducing antioxidant power, **(DPPH):** 2,2-Diphenyl-1-picrylhydrazyl, **(AST, ALT, and ALP):** Alkaline Phosphatase, Alanine Transaminase, Aspartate Aminotransferase, **(HPLC):** High-pressure liquid chromatography, **(NBT):** Nitro-blue tetrazolium, **(CNS):** Central nervous system, **(PCM):** paracetamol, **(CCL11):** C-C motif chemokine ligand 11, **(IL-5):** Interleukin-5.

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