



Antidiabetic Activity of Phytochemicals from the Jamun (*Syzygium cumini*): A Review

Dashpute PS, Sawant KS, Pagar AS, Surana KR*, Sonavane DD and Mahajan SK

Shreeshakti Shaikshanik Sanstha, Divine College of Pharmacy, Satana, India

***Corresponding author:** Khemchand R Surana, Department of Pharmaceutical Chemistry, Shreeshakti Shaikshanik Sansthas, Divine College of Pharmacy, Satana, Nashik, Affiliated to Savitribai Phule Pune University, Pune, Maharashtra 423301, and India, Tel: +91 7972232972; Email: Khemchandsurana772@gmail.com

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Abstract

The seeds of *Syzygium cumini* (Linn), a member of the Myrtaceae family, are responsible for the activity. Traditional Indian medicine widely uses *S. cumini* to treat diabetes. The point of this study was to look at the phytochemical bioactive parts of the extract from *Syzygium cumini* seeds and see how well they work against diabetes in a lab setting. Numerous components of the extract possess anti-inflammatory, anti-pyretic, anti-microbial, anti-cancer, protective layer, and anti-TB qualities. People have used *Syzygium cumini* for a long time because of its high nutritional value and potential therapeutic benefits. It has a range of pharmacological actions. Medicine has used fruit, leaves, bark, seeds, and other plant components to treat a wide range of ailments. Studies have shown that *Syzygium cumini* seeds have antibacterial, anti-inflammatory, anti-dysenteric, and antioxidant properties. The antibacterial, inflammatory-reducing, anti-diabetic, and antioxidant properties of *Syzygium cumini* seeds have led to their use. People have used the antibacterial and anti-dysentery qualities of *Syzygium cumini* leaves. People use jamun seed powder to treat diarrhea, dysentery, and diabetes. It is believed that the anti-diabetic properties of seeds cause their own effects.

Keywords: *Syzygium cumini* Seeds; Anti-Diabetic; Jamun; *Syzygium* Genus

Abbreviations

DM: Diabetes Mellitus; WHO: World Health Organization; GAE/g: Gallic Acid Equivalents/Gram; NBT: Nitro Blue Tetrazolium; ESBL: Extended Spectrum Beta Lactamases.

Introduction

With around 1200 species, the *Syzygium* genus is believed to be the largest in the Myrtle family (Myrtaceae). People frequently cultivate some of its economically important species due to their delicious fruits and medicinal properties. Tropical and subtropical areas cultivate the Indo-Malaysian tree *Litsea cumini* L., often known as Jambul rather than

Jambolana, for its many uses. Food, lumber, gardening, dye, and medicine are some of these applications [1]. This species of *Syzygium* holds significant economic value. Located in the Indian subcontinent, it is a massive, evergreen fruit tree that belongs to the tropical evergreen flowering plant family Myrtaceae [2]. This native Indian fruit crop is considered one of the most important fruit trees for medicinal purposes, despite the fact that not much is known about it. It is indigenous to the Indian subcontinent and the regions of China, Southeast Asia, and Queensland that surround it. Phenolic compounds, including tannins, lignans, phenols, and phenolic acids, are abundant in the tree. Studies from scientists have shown that some types of jambul have powerful biological effects, including the ability to fight bacteria, fungi, viruses, allergies,

inflammation, diarrhea, cancer, chemoradiation, and diabetes [3]. Diabetes is an endocrine condition characterized by persistently high blood glucose levels and impaired insulin sensitivity. These elements cause inflammatory diseases and changes in metabolism, which ultimately affect all bodily tissues [4]. An excess of glucose generated by tissues and a decrease in its use are the main causes of hyperglycemia in people with diabetes mellitus (DM). The extra production may be due to increased rates of glycogenolysis and hepatic gluconeogenesis [5]. Asian Indians have one of the highest incidences of diabetes among all major ethnic groups, and they rapidly progress from diabetes to pre-diabetes and beyond [6]. The South Asian Center for Cardio-metabolic Risk Reduction conducted a study that revealed the highest diabetes prevalence in Chennai, one of India's two major cities, at 25.2% (23.6–26.8%), and in Delhi, North India, at 22.8% (21.5–24.1%). Studies show that the rate of increase in diabetes prevalence is higher in men ($3.33 \times 1000/\text{year}$)

than in women ($0.88 \times 1000/\text{year}$) [7]. The prevalence of diabetes has clearly increased over the past 40 years as a result of dietary changes. Clinical practice now uses oral hypoglycemic drugs, which have unique profiles of serious side effects [7]. People are increasingly turning to plant-based medicine, which has the ability to heal individuals as much as possible with little or no side effects, due to the detrimental effects of long-term synthetic medication use. People have been treating diabetes with plants and their extracts since ancient times. The World Health Organization (WHO) [8] provides a list of 21,000 plants used for medical purposes worldwide. The commercial sector uses about 150 of these species extensively. Empirical studies have used certain medicinal plants to treat diabetes and hyperlipidemia, and recent global reports have shown their benefits in managing diabetes. Most plants contain glycosides, alkaloids, terpenoids, flavonoids, carotenoids, etc., which are frequently associated with anti-diabetic properties [8] (Figure 1).



Figure 1: Various *S. cumini* stages include: flowering, fruiting, and mature fruit (a, b, c), and Seeds (d).

Nutritional Composition of Jamun Seed

Carbohydrates: Carbohydrates make up the majority of the nutritional value of jamun seeds. Starch, which ranges from 23 to 60 grams per 100 grams of seed DM, is the most prevalent type of digestible carbohydrate. Starch provides the organism with the energy it needs to sustain its many metabolic functions [9]. Jamun seeds are a well-known dietary fiber source. A nutrient-dense, health-promoting food component is lignin, one of the indigestible polysaccharides. The study revealed that the jamun seeds had a total dietary

fiber content of 27.7 g/100 g, with 2.8 g/100 g of soluble fiber and 24.9 g/100 g of insoluble fiber. We found significantly higher percentages of soluble and insoluble dietary fiber, with respective measurements of 24.9 and 2.8 g/100 g. With 40 grams of fresh matter per 100 grams and 5.9 grams of moisture per 100 grams of content, water-soluble gums make up the majority of the nondigestible carbohydrates in jamun seeds. The second nondigestible seed carbohydrate fraction was neutral detergent fiber, which is insoluble in water and weighs 15g/100 gm. It contains 6.9 g/100g fm of

cellulose, 5g/100 gm of hemicellulose, 100g/1.0gm of lignin, 100g/0.76 g of cutin, and also 0.44 g/100gm of silica. Food fiber's benefits for wellbeing may vary depending on its composition [10].

Proteins: Jamun seeds contain up to 8% protein. However, certain literature sources report a significantly higher protein content of 19.96 g/100 g FM. We found free amino acids in *S. cumini* seeds in addition to crude peptide. Although a profile analysis of cumini seeds is missing, their contents range from 4.84 to 9.90mg/100 g [11]. Recently, researchers used time-of-flight mass spectrometry based on matrix and two-dimensional gel electrophoresis with assisted laser desorption/ionization to determine the protein composition of jamun seeds. The data identified fifteen functional proteins involved in critical metabolic, transport, and defense processes in plants [12]. These proteins include the phosphate-binding protein, lactoferrin, chitinase 1, G protein-coupled receptor, pectate lyases, β -tubulin, ABC transporter, 1-aminocyclopropane-1-carboxylate oxidase, and ADP-pyrophosphorylase of glucose.

Lipids: Jamun seeds contain less than 1.5g/100 g of total fat. Nevertheless, the fatty acid composition of lipids is well-balanced. Saturated fatty acids make up half. Given the current global problem of human obesity and overweight, one may view the low nutritional value (267kcal/100 g) of jamun seeds as nutritionally advantageous. This is because jamun seeds are abundant in dietary fiber and low in fat [13].

Micronutrients: Jamun seeds contain a considerable amount of ascorbic acid. This product's mineral composition appeals to dietitians. Nine dietary macro- and micro-elements affect the mineral content of jamun seeds. Also highly sought after were iron, manganese, potassium, and chromium. Researchers found substantial levels of magnesium, zinc, and sodium, but only minimal amounts of copper and calcium [14]. The components were different, and the contents were declining for the following minerals. The concentration of iron was 4 mg/100 g, while the concentration of copper was 2.13 mg. There are 20 grams of iron per 100 milligrams, 0.46 grams of zinc, 0.40 grams of manganese, 1.40 grams of chromium, 606 grams of potassium, 112 grams of magnesium, 43.9 grams of sodium, and 136 grams of calcium. Various environmental conditions can cause changes in the mineral composition. Researchers found that the ripening process directly influences the minerals of *S. cumini* as the plant matures, its adaptation to soil and weather, varietal differences, and harvest time. Calcium and potassium levels were significantly higher in ripe fruits and cumini fruit pulp than in intermediately ripe fruits [15]. Ascorbic acid was the sole vitamin or provitamin present in jamun seeds. Its content ranged from 90 to 137 mg/100 g, surpassing each

genotype's fruit pulp and being higher than that of other genotypes. A study found that the only known β -sitosterol is in the part of jamun seed oil that can't be returned. The study also found that jamun seeds have slightly lower levels of ascorbic acid (49.8 mg/100 g) [16].

Plant Chemicals: In actuality, jamun seeds contain a wide range of phytochemicals, such as sterols, phenolic compounds, saponins, terpenes, and other terpenoids. We have only provided a qualitative description of the phytochemicals present in jamun seeds. Researchers have identified jamboline, ellagic acid, corilagin, gallic acid, quercetin, sitotol, 3, 6-hexahydroxydiphenoyl glucose, and 4, 6-hexahydroxydiphenoyl glucose in the seed [16]. Fats, including myristic, oleic, and linoleic acids, are also the primary components of *S. cumini* seeds. However, researchers found trace levels of stearic acid, palmitic acid, lauric acid, vernolic acid, and malic acid. Various studies revealed that the alcoholic seed extract included triterpenoids, alkaloids, flavonoids, glycosides, saponins, tannins, and phytosterol [17].

Phenolic Compounds: Phenolic compounds are the most prevalent and often recognized class of bioactive compounds in jamun seeds. Jamun seeds exhibited gallic acid equivalents/gram (GAE/g) of 55.54 mg, 62.25 g/100 g moisture content, and 22.59 mg GAE/g of fresh seed phenols. Researchers discovered that the lowest TPC of dry ground-up seeds was 26.9 mg/g of GAE [18]. We have documented higher levels ranging from 79.89 to 108.7 mg GAE/g for drained seeds. The phenolic profile of jamun seeds is composed of flavonoids and phenolic acids, including fumes, dihydrochalcones, and 3-ols of flavan, stilbenoids, coumarins, lignans, hydrolyzing tannins, and their phloroglucinol derivatives. Ellagitannins and gallotannins, respectively, are the polymeric forms of the basic derivatives most frequently identified and tested [19]. Researchers used nuclear magnetic resonance spectroscopy and liquid chromatography with mass spectrometry in tandem to identify nine gallotannins and seventeen ellagitannins in jamun seeds, along with other ellagic acid derivatives [20]. Hydrolyzable tannins are widely known for their potent antibacterial and antioxidant properties. They could also impact the functioning of the digestive system. Researchers found that the percentage rich in jamun seed ellagitannins blocked the major Wnt signaling pathway in the human cell line 293T, suggesting their potential to prevent colon cancer [21]. Additionally, studies have shown that the percentage of jamun seeds, rich in ellagic acid and ellagitannins, exhibits a higher antioxidative ability compared to the pulp, primarily composed of anthocyanins [22]. Jamun seeds primarily contain myricetin and its derivatives, including dihydroxy derivatives (dihydromyricetin), O-methylated forms (syringetin, syringetin 3-Oglucoside, lacintrin), and myricetin

3-Oglucoside [23]. The standardized extracts of flavonoid-rich jamun seeds had special bioactivity because they had kaempferol, quercetin, and rutin in them. Researchers found hypoglycemic, hypolipidemic, and anti-atherogenic properties in the extracts. Jamun seeds have also been found to contain swertisin, schaftoside, and apigenin (6, 8-di-C are instances of flavone C-glycosides-dglucopyranoside), which are rare in natural sources [24].

Terpenes and Terpenoids: Terpenoids and terpenes categorize forty-five seeds. Jamun seeds are known to include monoterpenes, triterpenoids, norsesquiterpenoids, and sesquiterpenes. Sesquiterpenoids derived from various jamun seeds exhibit biological action. Humulene and E-caryophyllene, two sesquiterpene hydrocarbons, constituted 22.2% and 42.5% of the total essential oil extracted from fresh jamun seeds, respectively [18].

Additional Phytochemicals: A pentacyclic triterpene glycoside is referred to as a vital boside. Saponin was quantified using NMR. Researchers have documented the presence of B-sitosterol, a bioactive phytochemical, in *S. cumini* seeds. A sterol with an unidentified structure was identified in the Sephadex LH-20 fractions of the ethanolic jamun seed extract, located in the part of jamun seed oil that is not sponorable [22].

Jamun Benefits & Medicinal Uses

Many medicinal ailments utilize Jamun fruits. The pulp, leaves, barks, seeds with the seed coat, and kernel, as well as the kernel alone, is utilized. We explore the benefits and potential therapeutic uses of the various parts of the jamun plant. These are few prevalent advantages (Figure 2) [25].



Figure 2: Different activities of various parts of Jamun, *Syzygium cumini*.

Additional Benefits of Jamun

Shields against Infections: Since ancient times, people have used jamun, which contains biological substances, to protect the body from diseases and viruses. Jamun extracts and formulations use their strong antiviral, antibacterial, and antifungal properties to treat and cure wounds, as well as to eradicate bacteria and germs from the body. Furthermore, the bioactive ingredients improve the body's vitality while reducing overall weakness, fatigue, and weakness [26].

Aids in Digestion: This wonderful fruit, with its exceptional carminative and digestive properties, serves as a comprehensive solution for all digestive issues. By reducing gas production in the gastrointestinal system, the anti-flatulent property reduces abdominal distension, bloating, constipation, and flatulence. Jamun extract's antacid qualities assist in treating gastritis, ulcers, and indigestion by reducing stomach acid production and promoting better nutrient absorption [27].

Fights Respiratory Issues: The fruit of the gods is a well-known folk remedy for a number of respiratory conditions. Fruit extract has strong anti-inflammatory, antibacterial, and anti-asthmatic properties, making it a typical treatment for cold, cough, and flu conditions. It also helps the body remove mucus and makes breathing easier by thinning and releasing carbon particles from the chest and nasal cavities. It also helps in the treatment of asthma and bronchitis [28].

Enhances Libido: Jamun offers men a one-time application of a traditional cure that boosts fertility and libido. It has strong aphrodisiac properties that increase testosterone production, which increases libido. It also helps to ease worry and tension in the mind. It increases the synthesis of male hormones such as luteinizing hormone and testosterone, which in turn improves men's sperm motility and quality. Additionally, it boosts men's virility and endurance [29].

Jamun in Ayurveda and Supplements: According to Ayurveda, jamun is essential to the treatment of the majority of ailments. Several ancient Ayurvedic scriptures even call India a "land of Jambu," or Jambudweep, because of the large number of jamun trees that thrive there. Because of its numerous therapeutic uses, which include the bark in addition to the leaves, fruits, and roots, Jamun is considered a magic tree. The pulp and seeds are crucial in the treatment of diabetes, even if the tree's leaves are good for teeth and gum disease. The bark of the tree is effective in preventing gingivitis and worm infection in the body [30].

Jamun Churna Powder: The powder from the seeds of the jamun plant is highly beneficial for lowering blood

sugar levels. It helps with digestion and is beneficial for a healthy liver and heart. Additionally, it aids in preventing bilious diarrhea, hoarseness, blood dysentery, bedwetting in children, excessive urine in adults, and maintaining bone health [31].

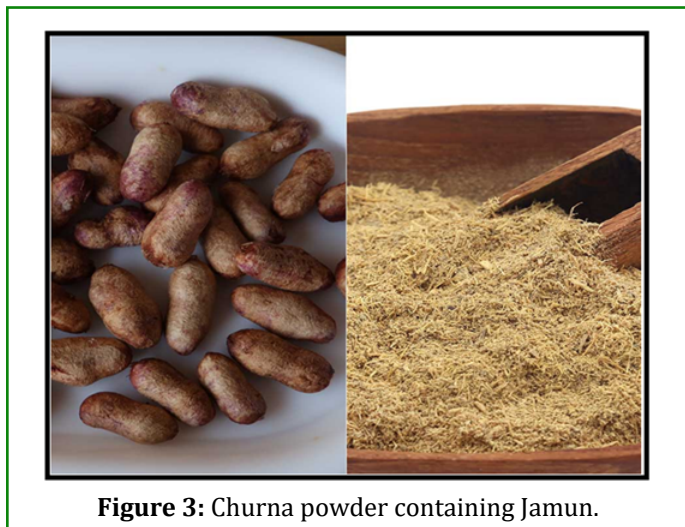


Figure 3: Churna powder containing Jamun.

Antidiabetic Engagement

Brito, et al. [32] says that the allergic pleurisy model stops eosinophils from accumulating because of a problem with the production of IL-5 and CCL11/eotaxin. On the other hand, the skeletal parts of *Syzygium cumini* show anti-diabetic properties and may also help people feel empathy by stopping the breakdown of histamine, serotonin, and mast cells.

Gastroprotective Activities

Chaturvedi, et al. [8] investigated the impact of *E. jambolana* ethanolic extract seed on stomach ulcers in rats induced by aspirin, ethanol-pylorus ligation, and two hours of cold restraint stress. Because *Eugenia jambolana* impacts both defensive and offensive aspects, it may have an ulcer-preventive effect. *Eugenia jambolana* is active in part because of its antioxidant properties [33].

Antioxidant Activity

Antioxidant-rich foods are essential for avoiding disease. This method uses riboflavin light to reduce nitro blue Tetrazolium (NBT) in the context of DPPH radical scavenging, lipid peroxidation, and a riboflavin light-NBT system. During the screening process, different tests are used, such as finding hydroxyl radicals, which are superoxide radicals made by the benzoic acid hydroxylation method Ion method. Researchers used a variety of experiments to report the antioxidant capacity of fruit skin. Zhi Ping Runa, et al. studied the antioxidative properties of *Syzygium cumini* leaves using FRA tests to measure their iron content and DPPH tests to assess

their ability to eliminate free radicals. Antioxidant-rich foods are essential for avoiding disease. Ackerman et al. reported the antioxidant activity of fruit skin using a range of assays, such as the superoxide radical and the hydroxyl radical sca The screening analysis relied on the photocatalytic degradation of nitro blue tetrazolium (NBT) within an NBT system under riboflavin light. Since egg yolks are a good source of fat for testing DPPH radical scavenging and lipid peroxidation, it's possible that the vitamin antioxidants, phenolic or anthocynins, and tannins in the fruit also help it be an antioxidant. We measured the antioxidant content of the four ethanolic extract fractions—water, n-hexane, ethyl acetate, and chloroform. The antioxidant activity of the ethyl acetate fraction was higher than that of the other fractions. This leaf extract of *Syzygium cumini* had phenolic parts, like catechin and ferulic acid, that are what makes the antioxidant effect happen, according to HLCC data [27,34].

CNS Activity

Researchers led by De Lima and others looked into how keels seeds might calm and stop seizures in mice to find out if they are extracts, fractions, or subfractions from *Syzygium cumini* Linn. The oral administration of the hydroalcoholic extract not only made the animals cold, but it also stopped seizures caused by pentylene tetrazol and maximum electroshock. The latency-causing effect of the first seizure caused by pentylene tetrazol was made stronger by the fraction of ethyl acetate and its parts being present for a longer time. Certain dynamic principles of *S. minors* possess central depressive properties, while others exhibit anticonvulsant properties. The prolonged presence of ethyl acetate and its constituent parts enhanced the latency-producing nature of the initial seizures caused by pentylene tetrazol. Certain dynamic principles of *S. diminuis* exhibit central depressive properties, whereas others have anticonvulsant properties [35,36].

Reducing Inflammation

Muruganandan, et al. [37] investigated the ethanolic bark sample of *S. cumini*'s inflammatory-reducing qualities. At doses up to 10-125 g/kg i.p., the extract showed no toxicity in mice. According to research, *S. cumini* extract from bark has potent anti-arthritis qualities that prevent different stages of swelling without putting the stomach mucosa at risk.

Antihyperlipidemic Activity

Diabetes mellitus affects about 40% of diabetics, and lipid profile abnormalities are actually one of the most common problems. Kasiappan, et al. demonstrated the most common issues using an extract from the ethanol of a *Jambolana*, *E. kernel* (100 mg/kg body weight). Glibenclamide was the usual drug with antihyperlipidemic effects in diabetic rats produced by streptozotocin [38].

Antifertility Activity

Researchers led by Rajasekaran and others found that oleanolic acid from the flowers of *E. jambolana* made it much harder for male albino rats to get pregnant, but it didn't have a big effect on their body or reproductive organ weights. Early meiosis stops spermatogenesis, which reduces the amount of sperm with no defects to leydig interstitial cells, sertoli cells, and spermatogenic cells, as well as the spermatocytes' capacity to transform into spermatids [39].

Antidiarrheal Properties

The Mukherjee group evaluated the antidiarrheal qualities of an ethanol extract of *Syzygium cumini* using a number of rat models for diarrheal investigations. In experiments involving charcoal meals, it dramatically decreased the amount of gastrointestinal motility in rats and inhibited entero-pooling and diarrhea caused by castor oil [40].

The Antiplatelet Action

Namba, et al. [41] demonstrated that methanolic, aqueous, and methanol-water (1:1) extracts of bark prevent plaque formation in vitro. 260, 120, and 380 µg milliliters, respectively, all showed anti-Streptococcus mutans activity.

Antispasmodic Properties

Dhawan, et al. discovered that histones and acetylcholine did cause spasms in the ileum of simian pigs, but the ethanol-water (1:1) extract of aerial parts did not. According to a study by Mokkhasmit, et al. [42] the intestinal tract of Guinean sprig was impacted by 0.01 gm of dried bark water ethanol (1:1).

Antihistamine Activity

Mahapatra and others discovered that pedal edema, which is caused by histamine, is not the same as pedal edema. Rats responded favorably to the intraperitoneal administration of dried seed methanol extract [43].

Antiviral Activity

Rana, et al. [44] found that a one-milligram/ml water-ethanol (1:1) preparation of the dried entire plant was ineffective against the Ranikhet and vaccinia viruses in cell culture. For the Ranikhet infection, the viral titre of the chorioallantoic membrane infection decreased by 10%, while for the vaccinia virus, it decreased by 0%. When given to chick embryos at an animal dose of 1.0 mg, the extract had no effect on the vaccinia and Ranikhet viruses. Infected chick embryos showed a 10% and 0% decrease in viral titre, respectively. Dhawan & Co. claim that an ethanol/water (1:1) extract of aerial parts at a concentration of 50.0 mcg/ml in a cell culture had no effect on vaccinia or Ranikhet pathogens. The water extract from

the bark demonstrated its beneficial effects.

Antibacterial Activity

Researchers led by Shaikh have looked into how well ethanol-based *Eugenia jambolana* extracts kill both gram-positive and gram-negative bacteria. By employing the disc diffusion approach, Bhuiyan et al. [45] reported that methanol and ethyl acetate extracts had antibacterial properties. *E. jambolana* plants inhibit nine Gram-negative bacteria (*S. typhi* B, *S. typhi* B-56, *Shigella*, *boydii*, *flexneriae*, *sonnei*, *E. coli*, and *Klebsicella* species) and five Gram-positive bacteria (*Bacillus creus*, *B. subtilis*, *B. magisterium*, *S. aureus*, and *Streptococcus β-haemolyticus*). Shafi, et al. claimed that the essential oil from *E. jambolana* leaves has strong antibacterial qualities. Researchers led by Pitchai Daisy and others used the disc diffusion method to test how well *Syzygium cumini* extract kills bacteria that make extended spectrum beta lactamases (ESBL). The researchers tested the antibacterial activity of methanol, acetone, and hexane extracted from *Syzygium cumini* seeds against the following bacteria: *Aeromonas hydrophila pneumonia*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Enterobacter aerogenes*, *Klebsiella*, *E. coli*, *Acinetobacter baumannii*, and *Citrobacter freundii*. Methanol extract from *Syzygium cumini* seeds showed potent antibacterial and antibacterial properties [45,46].

Conclusion

Traditional healers have been using *Syzygium cumini* for centuries to treat diabetes and its related conditions. Numerous clinical and experimental studies have demonstrated the tremendous efficacy of *S. cumini* and its many parts, especially the seed, in the management of type 2 diabetes. The active compounds in the seeds target the pathways involved in the hyperglycemia process and regulate glucose balance through a variety of modalities and actions. Because of their insulin-tropic and insulin-mimetic qualities, *S. cumini* seeds exhibit hypoglycemic behavior, making them a common option for treating type II diabetes. As a diabetes drug, it raises insulin sensitivity by improving glucose absorption and utilization in the periphery, activating PPAR-γ nuclear receptors, and releasing insulin from beta cells. It does this by lowering the amount of glucose absorbed in the gut and hepatic glucose production. Additionally, these glucose-maintaining practices balance the incidence of other diabetes-related complications. Consequently, it can be utilized as a therapeutic agent that is both cost-effective and beneficial with an improved safety profile. To demonstrate their effect on hypoglycemia, further research is necessary to determine the exact mechanism of action. This can be achieved through consistent extract, large sample sizes, arbitrary double-blind medical trials, and other suitable methods. The identification of novel proteins from *S. cumini* seeds suggests that these substances have a wide

variety of applications. It also provides a platform for further investigation into their potential as antidiabetic drugs and other health benefits.

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