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Antidiabetic potential and related activity of Jamun (*Syzygium cumini* Linn.) and its utilization in Unani medicine: An overview

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Abstract
Diabetes, a rampant disease is now a big concern for the humanity. *Syzygium cumini* Linn., commonly known as "Jamun" or black plum is an important medicinal plant in Unani system of medicine (USM) used commonly for the treatment of diabetes mellitus and other ailments. In USM the pharmacological actions of Jamun are *Nafe ziabetus* (Antidiabetic), *Qabiz wa habis Dam* (Astringent and Haemostatic), *Dafe salasal bawl* (Helpful in urinary incontinence), *Muquwie bah* (Sexual tonic) etc. Different parts of the Jamun were reported for its antidiabetic, antioxidant, hypolipidemic, neuropsycho-pharmacological, anti-ulcerogenic, free radical scavenging, nitric oxide scavenging and radio-protective activities. Both *in-vivo* and *in-vitro* anti diabetic activity are reported from the drug. The chemical constituents responsible for the inhibition of glucose are terpenoids, glycosides, saponins, flavanoids, phenols etc. Jamun contains an important glycoside namely Jambolin which prevents the conversion of starch into sugar thereby helps in controlling the blood sugar. This review helps to overcome the gap between traditional therapeutic and modern contemporary medication for providing better understanding. Overview of photochemistry / constituents and pharmacological activities of both classical and reported can update the information regarding the drug for better utilization in therapeutics of diabetes mellitus.

Keywords: *Syzygium cumini*, Jamun, Antidiabetic, USM Unani system of medicine

1. Introduction
Diabetes mellitus is a metabolic disorder complex in nature, resulting in either insulin insufficiency or insulin dysfunction with disturbance of carbohydrate, fat, and protein metabolism and classically characterized by hyperglycemia with other clinical presentations such as polyuria, polydipsia, polyphagia, fatigue and irritability. It is of two types viz. Type I diabetes (insulin dependent) and Type II diabetes (non insulin dependent), constituting 90% of the diabetic population [1, 2]. Diabetes is a leading cause of death [3]. The worldwide prevalence of diabetes for all age-groups was estimated to be 2.8% in 2000 and expected to be 4.4% in 2030. The total number of diabetic patients in India was 31.7 million in 2000 and is estimated to be 79.4 million in 2030. In developing countries the urban diabetic population is projected to double in 2000 to 2030 [4]. The pathophysiology of diabetes mellitus is not fully understood but experimental evidences suggest the involvement of free radicals in its pathogenesis and multiple abnormalities of lipoprotein metabolism in the development of diabetic complications [1].
Ibn Sina stated in his book of *Al qanoon fit tib* that the word diabetes is derived from Greek word, "*diabanein"* which means to "passing through" or "run through" or "siphon" in reference to the excessive urine produced as a symptom of this disease. It is not a new disease, ancient Greeks and Arabic physicians knew it well. They investigated it thoroughly and have prescribed various treatments for this disease. The causes of this disease are *sue e mizaj wa zauf e kulliya, masana wa jigar* (disordered temperament and weakness of kidney, bladder and liver) [5]. *Zakariya Razi* stated in his book of *Kitabul Havi* that the dribbling of urine is the only complaint of this disease because whatever enters to the bladder gets excreted immediately without being held. The patient feels excessive thirst, drinks plenty of water and whatever he drinks get expelled without any changes. In this disease the temperature of kidneys become hot due to which it absorbs water, but due to weakness of its retention power (*Quwat e masika*) it eliminate *rutubath* towards bladder i.e. the bladder does not absorbs water from kidney. Kidneys tend to suck fluid from vessels and absorb it. The vessels suck fluid from liver and the liver absorbs it from stomach and intestine. Consequently the patient feels excessive thirst and drinks plenty of water. But the fluid gets micturated and the problem persists as such and is difficult to treat [6]. There are various Unani single drugs used for the treatment of diabetes

mentioned in the old classical Unani texts i.e. *Gymnema sylvestre, Azadirachta indica, Aloe vera, Momordica charantia, Acacia arabica, Aegle marmelos, Allium cepa, Allium sativum, Althaea officinalis, Caesalpinia bonducella, Cinnamomum zeylanicum, Emblica officinalis, E. jambolana, Ficus racemosa, Plantago ovate, Trigonella foenum graecum, Tinospora cordifolia, Punica granatum, Syzygium cumini* etc. [7]. Jamun (*Syzygium cumini* Linn.) is the one of them and is being claimed in having good effect for decreasing the plasma blood sugar level in diabetes patients and also can be utilized in conditions / complications related to diabetes and as a supportive in diabetes [8]. Jamun (*Syzygium cumini* Linn.) is an important medicinal plant in Unani systems of medicine. The trees have fruits once in a year and the berries are sweetish sour to taste. The ripe fruits are used for jellies, health drinks, squashes and wine [9]. The fruits and seeds are generally used in antidiabetic formulations in USM. The Jamun tree resembles like the walnut tree having 50-90 meters long. Its branching are distributed all around the tree. The tree is quite long, greenish black in color, branches are white in color and fruits look like black grapes but quite long, violet in color. The color of fresh woody endocarp (pit) is light pink but becomes brown on drying. The woody endocarp (pit) is divided into two parts [10, 11]. This pit contains the kernel which remains efficient upto two years [12]. The leaves of this plant are moreen, smooth, short and deep green in color [13]. The bark of this tree is one and a half inch in thickness and deep brown in color [14]. The Jamun tree is of three types *viz*. Bastani, Saharie and Bahri. The fruits of Jamun tree from Arkut and karnataka are sweetish in taste. Daryawe Jamun is also known as Jal Jamun Arjaljambu. Badiya or Badawu Jamun is one which is growing in Bahdou. As per Hkm. Shareef Khan Delhvi, the sweet Jamun is one which is not having the inner pit and is also known as Behdana [13, 14]. Traditionally the fruits, leaves, seeds, and bark of Jamun tree are all used in Unani System of medicine. The trees of Jamun is found in large numbers throughout the India [15]. The fruit of Jamun is considered as one of the important fruits of India [14].

2. Afa'al (Pharmacological actions) as per Unani literature

Qabiz wa habis Dam (Astringent and Haemostatic), *Habis ishal* (Astringent of diarrhoea), *Nafe litha wa damiya* (Helpful in bleeding gums), *Nafe ziabetus* (Antidiabetic), *Mujli dandan*, *Kaiser riyah* (Carminative) [13-16], *Mumsik-i-mani* (Retentive of semen), *Nafe ziabetis* (Anti diabetic) [17], *Habis ishal safrawi* (Astrigent of bilious diarrhoea), *Muquawie meda* (Stomachic), *Muquawie kabid har* (Liver tonic) [18, 19], *Muharik ishteha* (Appetite stimulant), *Musakin hararat* (Antipyretic) [14, 16, 20], *Dafe salasal bawl* (Helpful in urinary incontinence), *Hazim* (Digestive), *Muquwie lisha* (Tonic for gingiva) [12, 14], *Muquwie bah* (Sexual tonic), *Muquwie teehal* (Spleen tonic) [14, 21].

3. Istemal (Uses) as per Unani literature

Ishal (Diarrhea), *Litha damiya* (Bleeding gums), *Warm lisha* (Gingivitis) [15, 22], *Safrai ishal* (Bilious diarrhoea), *Ziabetis* (Diabetes), *Bhalgemi ishal* (Phelgemtic diarrhoea), *Dama* (Bronchial asthma), *Khansi* (Cough), *Amraz halq* (Diseases of throat), *Khafqan* (Palpatation), *Qay* (Emesis), *Jildi amraz* (Skin diseases), *Amraz dandan wa lisha* (Diseases of teeth and gingiva), *Amraz meda wa jigar* (Diseases of stomach and liver) [12, 14, 20], *Zofe bah* (Loss of libido) [21], *Warme tehal* (Spleenomegaly) [16], *Riyah* (Flatus), *Humma* (Fever), *Thakaan* (Fatigue) [13].

4. Murakkabat (Compound Formulations) of Jamun used in Diabeties

Safoof Ziyabetus, *Qurs Ziyabetus*, *Safoof khasta* [11], *Sharbat Jamun* [23], *Sirka Jamun*, *Safoof Jamun* [15].

5. Hissa Mustamela (Part used)

Bark [22], Seed [14, 22, 23], Leaves [13, 14, 23], Fruit [23], Root [23] and Flowers [13, 14].

Fig 1: Seeds of Jamun (*Syzygium cuminii* Linn.)

6. Reported Pharmacological activity

6.1 Antidiabetic activity

Kumar in their study described the antidiabetic activity of seed kernels of *Syzygium cumini* Linn. and its isolated extracted compound (Mycaminose) against the streptozotocin-induced diabetic rats. The Mycaminose at the dose of 50 mg / kg, ethyl acetate and methanol extracted compounds of *Syzygium cumini* Linn. seeds at the dose of 200 mg/kg and 400 mg/kg respectively was administered to streptozotocin-induced diabetic rats and found that Mycaminose and ethyl acetate and methanol extracts of *Syzygium cumini* Linn. Produced significant reduction in blood glucose level. This indicates the isolated compound "Mycaminose" and ethyl acetate and methanol extracts possess antidiabetic effects against streptozotocin- induced diabetic rats [24].

Ravi founded in their study that administration of the ethanolic extract of different parts of *Eugenia jambolana* seeds such as whole seed, kernel, and seed coat100 mg/kg of body weight on streptozotocin-induced diabetic rats decreases significantly the levels of blood glucose, blood urea, and cholesterol, increased glucose tolerance and levels of total proteins and liver glycogen, and decreased the activities of glutamate oxaloacetate transaminase and glutamate pyruvate transaminase in experimental diabetic rats. The hypoglycemic efficacy was compared with that of glibenclamide, a standard hypoglycemic drug [25].

Chattu conducted a study to evaluate the anti diabetic potency of *Syzygium cumini* leaf on the blood glucose level in alloxan induced diabetic rats. Diabetic Wistar strain rats were treated with standard drug Glibenclamide and test drug *Syzygium cumini* at 100mg, 200mg and the hypoglycemic effect was determined in the rats and the efficacy of the test drug was compared to the standard drug Glibenclamide. *Syzygium cumini* leaf was orally administered for 14 days in alloxan induced diabetic rats [26].

Jana K in their study aimed to investigate the antidiabetic effect of the ethyl acetate fraction of the seed of *Eugenia jambolana* in streptozotocin-induced diabetic male albino rats.

The diabetic rats were treated with this fraction at a dose of 200 mg/kg/d for 35 days and the potential antidiabetic mechanisms were investigated with blood glucose (short-term and long-term model). The result suggests a significant antihyperglycemic action in both short-term and long-term treatment schedules [27].

Chatterjee K conducted a study to evaluate the anti diabetic potency of ethyl acetate fraction of hydromethanolic (40:60) extract of seed of *Eugenia jambolana* was investigated following *in-vivo* models in experimental diabetic rat. Oral administration of 20 mg ethyl acetate fraction or 0.6 mg glibenclamide in 0.5 ml water/100 g body weight/rat for twice a day at fasting state to diabetic rats for 28 days significantly ($p< 0.05$) resulting in carbohydrate metabolic towards the control levels. Two separate spots of ethyl acetate fraction were recorded after scanning of HPTLC fingerprinting. RP-HPLC study also shows two completely resolved peaks. Its biosafety profle was established following guidelines [28].

Prabakaran K reveals in their study that the extract exhibits the dose-dependent increase in the inhibitory effect on alpha amylase enzyme upto 95.4%. The result suggested that significant amount of flavonoid in *Syzygium cumini* seed is responsible for antidiabetic properties and it is further confirmed by higher intensity of alpha amylase inhibitory effect [29].

Achrekar S concluded in their study that the extract of jaman pulp from fruit of *Eugenia jambolana* showed hypoplycemic activity. This report is the first evidence of such activity in relation to pulp. The effect of pulp was seen in 30 min, while the seeds of the same fruit required 24 hr [30].

Villasenor suggested that the dried bark of *Syzygium cumini* (Linn.) Skeels (Myrtaceae) exhibited anti-hyperglycemic activities when fed simultaneously with glucose. At the same dosages of 5 mg/20 g mouse, *Syzygium cumini*-treated mice showed a significant decrease in blood glucose levels (BGLs) at 30 min (alpha=0.10) and from 45 min onwards at alpha=0.05 [31].

Schossler in their study verified the effect of *Syzygium cumini* upon the regeneration of insulin producing cells in the pancreatic duct wall. For this purpose the animals were divided into four groups, control (C), treated control (TC), diabetic control (DC) and treated diabetic (TD). An aqueous extract from *Syzygium cumini* bark was given by gavage in a daily dose of 1g/kg of body weight. After a thirty day period the animals were euthanized and the pancreas taken to immunohistochemical analysis. it was observed the positive staining for insulin on cells of the pancreatic duct and connective tissue in the pancreas of TD and TC animals. These results indicate that *Syzygium cumini* bark extract stimulates development of insulin positive cells from the pancreatic duct epithelial cells [32].

6.2 Nephroprotective activity

Baig MA suggested in their study that the effect of a herbomineral formulation (HMF) containing Jamun on early diabetic nephropathy was investigated. In Wistar rats the diabetes was induced by administering streptozotocin (55 mg/kg, intraperitoneally) and occurrence of early diabetic nephropathy in rats was revealed by high plasma glucose and depleted liver glycogen, decreased glucose uptake by peripheral tissue, impaired renal function, increased antioxidants and lipid peroxidation in kidney. The treatment with this herbomineral formulation shows significantly lowered blood glucose, glycosylated hemoglobin, creatinine, blood urea nitrogen, triglycerides, total cholesterol, serum albumin level, total urine volume, urinary albumin excretion rate, urinary albumin to creatinine ratio and relative kidney weight, and increased urinary creatinine and GFR [33].

6.3 Antioxidant activity

Nair reveals in their study the *in-vitro* antioxidant activity of the seed and leaf extract of *Syzygium cumini* by various *in vitro* methods such as 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging assay, ABTS Assay, Total antioxidant activity (Phosphomolybdic acid method), Nitric oxide radical scavenging, Ferric reducing antioxidant power (FRAP) assay, Hydroxyl radical scavenging activity, Total Reducing antioxidant potential and Reducing power. The extract showed significant antioxidant activity in all antioxidant assays when compared to ascorbic acid [34].

Mohamed in their study found the antioxidant activities of all extracts were examined using two complementary methods, namely diphenylpicrylhydrazyl (DPPH) and ferric reducing power (FRAP). In both methods, the methanol extract exhibited a higher activity than methylene chloride and essential oil extracts [35].

Ravi in their study investigates the effect of ethanolic extract of *Eugenia jambolana* seed kernel on antioxidant defense systems of plasma and pancreas in streptozotocin-induced diabetes in rats. In this study the levels of glucose, vitamin-C, vitamin-E, ceruloplasmin, reduced glutathione and lipidperoxides were estimated in plasma of control and experimental groups of rats as well as the levels of lipidperoxides, reduced glutathione and activities of superoxide dismutase, catalase and glutathione peroxidase were assayed in pancreatic tissue of control and experimental groups of rats. A significant increase in the levels of plasma glucose, vitamin-E, ceruloplasmin, lipid peroxides and a concomitant decrease in the levels of vitamin-C, reduced glutathione were observed in diabetic rats. The activities of pancreatic antioxidant enzymes were altered in diabetic rats. These alterations were reverted back to near normal level after the treatment with *Eugenia jambolana* seed kernel and glibenclamide [36].

6.4 Hypolipidemic activity

Jadeja RN evaluate the anti-atherogenic potential of *Eugenia jambolana* seed extract (EJSE) against *in vitro* low-density lipoprotein (LDL) oxidation, foam cell formation, and atherogenic (ATH) diet-induced experimental atherosclerosis in rats. The EJSE was able to prevent *in vitro* LDL oxidation and oxidized LDL-induced macrophage foam cell formation and also, EJSE supplementation to ATH rats significantly minimized increment in serum markers of LDL oxidation. The ex vivo oxidation indices were also minimized in LDL of EJSE-treated animals [37].

Ravi K in their study found the anti-hyperlipidemic efficacy of *Eugenia jambolana* seed kernel in streptozotocin (STZ)-induced diabetic rats. The effect of oral administration of ethanolic extract of Eugenia Jambolana kernels (100 mg/kg body weight) was examined on the levels of cholesterol, phospholipids, triglycerides and free fatty acids in the plasma, liver and kidney tissues of STZ (55 mg/kg body weight)-induced diabetic rats. The plasma lipoproteins and tissues fatty acid composition were also monitored. STZ-induced diabetic rats, showed significant increase in the levels of

cholesterol, phospholipids, triglycerides and free fatty acids which were considerably restored to near normal in EJs-kernel or glibenclamide treated animals. The plasma lipoproteins (HDL, LDL, VLDL-cholesterol) and fatty acid composition were altered in STZ-induced diabetic rats and these levels were also reverted back to near normalcy by EJs-kernel or glibenclamide treatment [38].

6.5 Neuroprotective activity

Sharma Y concluded in their study that the neuroprotective ability of aqueous and ethanolic extract of stem of *S. cumini* were observed on Rat pheochromocytoma (PC)-12 cell line, by giving neurotoxic shock to Rat PC-12 cells using 6-hydroxydopamine [39].

7. Conclusion

In the present study it was concluded that the increasing side effects of conventional antidiabetic medicine are alarming the world, so there is an important and immense need of doing extensive research work towards the antidiabetic herbal drugs. Keeping in mind the complications of diabetes are very dangerous for humanity, the research of herbal medicine to treat the diabetes should be done in a multidimensional way. The approach of treating the diabetes by old Unani physicians was quite phenomenal as there was not that kind of research at that time but the drugs they use are now proving their not only antidiabetic activity but also those activities which will help in its complications. The Unani single drugs to be used in diabetes are astringent in nature. The astringency in herbal medicine is now proved that these medicines contain tannins and these tannins actually inhibit the alpha amylase and alpha glucosidase enzyme activity which is responsible for increased blood sugar levels. The reported activities of Jamun suggested that it acts by inhibiting the alpha amylase and alpha glucosidase enzyme activity because of having higher content of tannins. If this concept is compared with the Unani pharmacological action, we can say that old Unani classical text can help the present world in a descent and nice way of treating those diseases which still do not have medications for treatment.

8. Conflict of Interest

There are no conflicts of interest.

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