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Anti-Diabetic Action of Syzygium cumini

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Abstract: *Recently with the changes in population lifestyle, prediabetes is constantly on the rise. Management of prediabetes currently is with lifestyle modifications like weight loss, exercise and diet control. Better drugs with acceptable safety profile are needed for better control of prediabetes. This study was thus designed to evaluate the antihyperglycemic effect of one such potential compound Syzygium cumini (SC) (Jamun) in comparison to conventional antidiabetic drug Metformin. Plants have provided mankind with herbal remedies for many diseases for many centuries and even today. They continue to play a major role in primary healthcare as therapeutic remedies in developing countries. In India herbal medicines have been the bases of treatment and cure for various diseases in traditional methods practiced such as Ayurveda, Unani and Sidha. Syzygium cumini (syn.Eugenia Jambolana) commonly known as a " Jamun " having promising therapeutic value with its various phytoconstituents such as Tannins, Alkaloids, Steroids, Flavonoids, Terpenoids, Fatty acids, Phenols, Minerals, Carbohydrates and Vitamins. Its pharmacological actions like hypoglycaemic, diuretics, analgesic, anti-inflammatory, antiplaque, antimicrobial, antidiarrheal, antioxidant, Astro-protective and astringent to bowels proven on animal models. Most importantly the studies have shown that it protects against the radiation induced DNA damage and it has significantly decreased the fertilizing capacity of the male albino rats, some clinical trial reports are also available for its antidiabetic activity.*

Keywords: Prediabeties, Syzygiumcumini, Ayurveda, Unani, Sidha, Jamun, etc.

I. INTRODUCTION

Diabetes mellitus is a group of metabolic disorders arising from myriad pathogenic mechanisms, all resulting in hyperglycaemia. Genetic and environmental factors contribute to the pathogenesis and involves insufficient secretion of insulin, decreased response to insulin either endogenous or exogenous, raised glucose production, with or without abnormalities in fat and protein metabolism. The resultant hyperglycaemia might lead to acute symptoms and metabolic abnormalities. Diabetes mellitus is a group of syndromes characterized by hyperglycemia, altered metabolism of lipids, carbohydrates and proteins, and an increased risk of complications from vascular disease1More than 400 plant species have been reported to have hypoglycemic properties, although just a few have been studied. 2 NIDDM (non-insulin dependent diabetes mellitus) accounts for more than 85% of all diabetes cases globally.

Syzygium cumini belongs to the Myrtaceae family and is called in Tamil as 'Naaval' and in India as Jamun, Jambul, and Jambool. India is where Syzygium cumini originated. Thailand, the Philippines, Madagascar, and a few more countries have it. Many other tropical countries, including the West Indies, East and West Africa, and even subtropical regions, such as Florida, California, Algeria, and Israel, have successfully introduced the plant. 9 The fruits are rectangular berries with a pinkish content and a deep purple or bluish colour., and in chronic diarrhea and enlargement of spleen. In alloxan-induced diabetic rats, S. cumini seed extract significantly reduced blood glucose, blood urea, serum cholesterol, and serum triglyceride levels12. S. cumini fruit is widely used for the treatment of chronic diarrhoea and other enteric problems, as well as as an antibiotic. In cultured human peripheral blood lymphocytes14, the leaves were found to prevent radiation-induced DNA damage. S. cumini seeds have been shown to help diabetic patients with a variety of issues, including reducing blood glucose levels and delaying diabetes consequences including neuropathy and cataracts.

Botanical Description:

An easy tree of the Myrtaceae family, four-15 meters in height. Leaves leathery oblong-ovate to elliptical or obovate and 6-12 cm long, the top being vast and soon pointed. The panicles are borne by and large from the branchlets under the leaves, frequently being axillary or terminal and four-6 cm long. The vegetation are severa, scented,crimson or almost white, without stalks, and borne in crowed fascicles at the ends of the branchlets. The calyx is funnel shaped,

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approximately four mm long, and four toothed. The petals cohere and fall collectively as a small disk. The stamens are very severa and so long as the calyx. Fruit is oval to elliptic;1. five-3. five cm long, darkish red or almost black, luscious, fleshy and edible; it consists of unmarried big seed

Scientific Classification:

Kingdom	: Plantae
Unranked	: Angisperms
Unranked	: Eudicots
Unranked	: Rosids
Order	: Myrtales
Family	: Myrtaceae
Genus	: Syzygium
Species	: Cumini
Binomial Name	: Syzygium cumini (L) Skeels
Parts Used	: Seeds, Leaves, Fruits, Bark
Ayurvedic Properties	: 3-6
Rasa	: Kasaya, Madhura, Amla
Virya	: Sita
Guna	: Laghu, Ruksa
Vipala	: Madhura, Katu
Karma	: Vatala, Pittahara, Kaphahara, Vistambhi, Grahi

Phytochemistry:

Phyto' is the Greek phrase for plant. There are many households of phytochemicals and that they assist the human frame in quite a few ways. Phytochemicals can also additionally guard human from a bunch of diseases. Phytochemicals are non-nutritive plant chemical substances which have protecting or disorder preventive properties. Fruit of Syzygium cumini consists of Malic acid is the most important acid (0. fifty-nine of the wt of fruit), a small amount of oxalic acid is likewise mentioned to be present. Gallic acid and tannins account for astringency of the fruit. The crimson color of the fruit is because of presence of cyaniding diglycosides.7 Fruit incorporate sugar (eight.09%), nonreducing sugar (9.26%) and sulfuric acid (1.21%). eight Glucose, Fructose, mannose and galactose are the fundamental sugars. The mineral components mentioned to be present (mg/100g of suitable for eating pulp) are Ca, 15, Mg, 35: P,15 (phytin P,2); Fe, 1.2 (ionisable Fe, o.1); Na, 26.2; K 55; Cu, 0.23; S,thirteen and Cl,eight. The nutrients present (in 100g. suitable for eating pulp) are vit.A, eighty IU; thiamine,0.03 mg, riboflavin,0.01mg; nicotinic acid ,0.2 mg; vit.C, 18 mg; choline,7 mg; Folic acid, three µg.

Cardiometabolic Properties and Potential Mechanisms of Action:

Antihyperlipidemic Activity

Flavonoid-wealthy extract of S. cumini seed (three hundred mg/kg/day, 15 days) changed into defined to lessen general ldl cholesterol, LDL-ldl cholesterol, and triacylglycerol in addition to enhance HDL-ldl cholesterol levels. Similar outcomes have been discovered for aqueous extract of fruit at doses of one hundred and two hundred mg/kg, for hydroalcoholic extract of seed kernel (one hundred mg/kg/day, 30 days) and for management of Dihar (one hundred mg/kg/day, 6 weeks), an Indian combination of herbs containing S. cumini. In all of the above cited studies, dyslipidemia secondary to streptozotocin-caused diabetes changed into used as animal version to evaluate S. cumini antihyperlipidemic activity, that have been especially ascribed to the inhibition of 3-hydroxy-3-methyl-glutaryl-CoA (HMG-CoA) reductase, the enzyme accountable for ldl cholesterol synthesis. Flavonoids discovered in S. cumini are predicted to account for this activity, because it has been defined that this magnificence of compounds will increase the expression of cAMP-based phosphokinase, enzyme accountable for 5-hydroxy-3-methylglutaryl-coenzyme a reductase inhibition.

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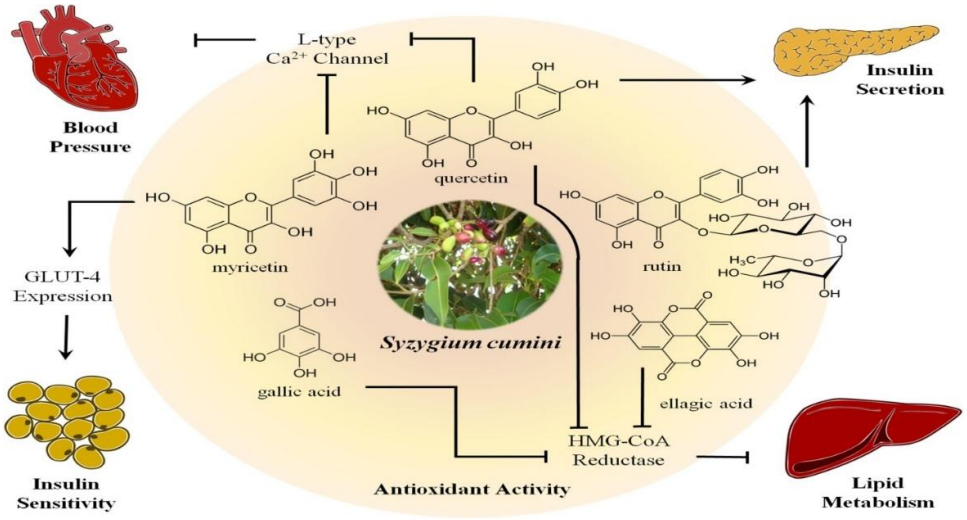

Figure 1: Biological properties and main mechanisms of action described for the most prevalent polyphenolic compounds identified in Syzygium cumini.

Anti-inflammatory Activity

Inflammatory strategies are at once concerned withinside the improvement of cardiometabolic sicknesses together with atherosclerosis, kind 2 diabetes, and cancer. Methanolic and ethyl acetate extracts of S. cumini leaf (two hundred and four hundred mg/kg) decreased carrageenan-brought on paw edema in rats (Jain et al., 2011). Methanolic extract of seed (250 and 500 mg/kg, 21 days) additionally decreased paw edema extent and leukocyte migration in rats with adjuvant-brought on arthritis. Ethanolic extract of the bark (one hundred, 300, and one thousand mg/kg) decreased the manufacturing of prostaglandin E2, serotonin, and histamine. Similarly, pre-remedy of mice with ethanolic extract of leaf (25, 50, and one hundred mg/kg) decreased systemic manufacturing of pro-inflammatory factors, consisting of interleukin-five, while TNF-α and NO• manufacturing changed into reduced at doses of five or 50 mg/kg administered 6-h preceding to infection induction.

Antioxidant Activity

Polyphenolic and associated antioxidant compounds are diagnosed as crucial cardiometabolic retailers due to the fact that they scavenge reactive oxygen/nitrogen species and stimulate antioxidant defenses, which can be concerned in all of the aforementioned sports of S. cumini. Oral management of aqueous extract of seed (500, one thousand, and1500 mg/kg/day, five days) to mice dealt with with urethane 7,12- dimethyl benzanthracene ended in decreased chromosomal damage, appreciably inhibited hepatic lipid peroxidation, which changed into related to appreciably improved pastime of glutathione S-transferase, superoxide dismutase, and catalase.

Antihyperglycemic Activity

Use of S. cumini withinside the combat towards diabetes has been studied with the aid of using western medication because greater than one hundred thirty years. In latest years, severa preclinical research have evaluated extracts of numerous parts, particularly seeds, of this plant speciesfor anti-hyperglycemic hobby. Blood and urine glucose tiers of streptozotocin-brought about diabetic rats had been reduced upon 30-days remedy with ethanolic extract of seed at doses of a hundred mg/kg/day. In addition to blood glucose reducing impact, flavonoid-wealthy extract of seed changed into additionally proven to get better peripheral glucose tolerance in streptozotocin- brought about diabetic rats (500 mg/kg/day, 21 days) and mice (three hundred mg/kg/day, 15 days). Those results had been ascribed to improved hobby of peroxisome proliferator-activated receptors (PPAR) alpha and gamma, which changed into assessed in 3T3-L1 preadipocytes incubated for twenty-four h with growing concentrations (1–a hundred mg/mL) of flavonoid-wealthy extract of seed.

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In this equal study, seed extract changed into proven to own insulinotropic hobby, which can be worried withinside the abovementioned results. Considering flavonoids already diagnosed in S. cumini seed antihyperglycemic impact of rutin changed into attributed to inhibition of glucose metabolism enzymes hexokinase and glucose-6-phosphatase. As highlighted in Figure 1, rutin (0.5–eight mM) additionally improved insulin secretion in streptozotocin-handled pancreatic islets of rats. On the alternative hand, 20 µM quercetin inspired insulin secretion with the aid of using activation of L-kind calcium channels in remoted rat beta cells. Nevertheless, quercetin has additionally been defined to boom insulin sensitivity with the aid of using enhancing the manufacturing of the adipocyte-derived factors, like adiponectin and leptin.

II. MATERIALS AND METHODS

Materials:

- **Chemicals:** All the chemical substances and reagents used inmthis take a look at have been bought from Sigma Aldrich Inc. L6 cells procured from ATCC [CL-173], á- MEM & Insulin from Sigma, Horse serum & Antimycotic from Invitrogen, DMEM from GIBCO, BSA, and Insulin from GE Amersham, UK.
- **Plant Material:** The standardized hydro-ethanolic extract of SCE became procured from Natural remedies, Bangalore (Batch number; FSCEX/2015090001). The extract became standardized to incorporate polyphenols (29.4% with the aid of using spectrophotometry) and ellagic acid (2.8 % with the aid of using excessive overall performance liquid chromatography). The ranges of heavy metallic content, microbial counts, aflatoxin, and residual solvents have been in compliance with British Pharmacopeia (BP) / United states pharmacopoeia standards (USP).

Acute Toxicity Studies:

The SCE became assessed for the extreme toxicity take a look at in albino Wistar rats in step with ICH guidelines.10

In-vivo Assessment for Anti-diabetic Activity:

Induction of diabetes in rats became done primarily based totally at the approach observed with the aid of using Srinivasan etal., which became modified. The rats have been divided into ordinary and excessive-fats food regimen (HFD) groups. The ordinary institution obtained ordinary chow food regimen, while the others have been placed on HFD. The HFD consisted of Vanaspati ghee and coconut oil, the contents of that are proven in Table. The have been jumbled together a percentage of 3:1 and administered at a dose of 3ml/kg frame weight orally in step with day for 12 weeks. After 12 weeks, the animals on HFD have been fasted and given the freshly organized answer of Streptozotocin (STZ, 35mg/kg, procured from Sigma Aldrich Lot #WXBC726V) in citrate buffer with pH 4. five with the aid of using intraperitoneal route.

The animals have been administered 10% glucose and 1% saline withinside the water on 1st day and five% glucose and 1% saline in water for the following consecutive days to save you unexpected hypoglycemic shock. The animals have been determined for one week submit diabetic induction for the stabilization of glucose ranges.

The blood samples have been accumulated at the 8th day following STZ injection via retro-orbital puncture for fasting blood glucose (FBG), serum insulin and lipid profiles. The animals certified as diabetic with FBG above 200mg/dl have been decided on and used for the take a look at.

Determination of Diabetic Profile:

FBG (Contour TS Clinical Glucose meter), serum insulin (ELISA package from KINESISDx, LA, USA (catalogue number: K11-0708, Lot number: RI0118) and, Serum lipids ((Agappe diagnostics Ltd. Ernakulum, India) specifically cholesterol (TC), triglycerides (TG), excessive-density lipoprotein (HDL) and low-density lipoprotein (LDL) have been expected the usage of the process mentioned in industrial kits. Insulin resistance (IR) and b mobileular characteristic: Caculation of IR and b mobileular characteristic became performed the usage of the homeostasis version evaluation approach (HOMA). The following equations have been used: IR (HOMA-IR) = [Fasting glucose (mM) × Fasting insulin (µIU/ml)] / 22. five b Cell characteristic (HOMA- B) = [20 × Fasting insulin (µIU/ml)] / [Fasting glucose (mM) “3.5].

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III. EXPERIMENT DESIGN

The animals have been randomly divided into six groups, as illustrated below.

Group I: Normal manage institution, animals on a ordinary food regimen that obtained the car. five riboxymethylcellulose (CMC), in water.

Group II: Diabetic manage institution, excessive fats food regimen +STZ that obtained best CMC,

Group III: Pioglitazone institution, diabetic animals dealt with with pioglitazone 10 mg/kg frame weight in CMC

Group IV, V, VI: SCE groups, diabetic animals dealt with with SCE at doses of 100,2 hundred and four hundred mg in step with kg every day dose in CMC

Administration of Drugs:

The 100, 2 hundred, four hundred mg/kg doses of SCE extracts and fashionable drug pioglitazone (10/ kg) have been organized as a suspension the usage of five riboxymethylcellulose (CMC) as a car and administered with the aid of using oral gavage for 21 days. The ordinary manage and diabetic manage institution obtained the car best.

Table 1: Composition of high fat diet administered to Wistar albino rats in addition to the standard chow

Components	Indian Vanaspati	Coconut Oil
Ratio	Three parts	One part
% of fatty acid	>20%	9%
% of saturated fatty acid	>60%	90%

Table 2. Effect of SCE on fasting blood glucose and serum insulin levels in long term high fat diet and low dose Streptozotocin induced Type 2DM in Wistar albino rats. The values are expressed as mean± standard deviation (n=6). *p<0.01 and **p<0.05 compared to the diabetic control.

Study group	Fasting blood glucose before treatment (mg/dl)	Fasting blood glucose after treatment (mg/dl)	Serum insulin before treatment (m IU/L)	Serum insulin after treatment (m IU/L)
I Normal Control	73.5 ± 12.5	78.33 ± 6.53	14.35±3.05	16.28±4.49
II Diabetic control	419.50 ± 131.38	414.83 ± 129.16	6.47± 4.14	7.13± 3.74
III SCE 100mg/kg	268.83 ± 63.87	98.00 ± 24.69*	6.47±4.26	8.90±1.27
IV SCE 200mg/kg	306.17 ± 108.69	96.00 ± 8.32*	7.99±5.15	12.00± 1.57
V SCE 400mg/kg	332.17 ± 128.12	235.50 ± 121.10*	7.55± 4.84	12.50± 3.41*
VI Pioglitazone, 10mg/kg	293.00 ± 143.46	121.50 ± 53.10*	6.80± 2.55	15.70± 5.4

IV. RESULT AND DISCUSSION

Based on its effectiveness as an anti-hyperglycemia, oral management of Jamblang has a good-sized impact on decreasing fasting blood glucose ranges in rat, while as in comparison to bad controls (DM organization). If primarily based totally at the chemical ingredients contained in each Jamblang leaf extract, consisting of alkaloids, saponins, tannins, phenols, flavonoids, steroids, and additionally glycosides, there are numerous mechanisms that can be concerned with inside the procedure of decreasing GDP. Based at the studies that has been done, those ingredients have the capacity

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for antidiabetic activity. Alkaloid compounds characteristic to facilitate glucose uptake, boom insulin secretion and assist regenerate pancreatic β-cells19.

Effect of SCE on fasting blood glucose and serum insulin ranges:

The 100mg/kg and 200mg/kg dose organization of SCE confirmed a good-sized discount in FBG ranges, and the impact became similar to traditional drug pioglitazone (Table 2). However, at a dose of four hundred mg/kg SCE has proven handiest slight activity. All the remedy corporations advanced serum insulin ranges notably compared to diabetic control, and pioglitazone had the exceptional impact in improving the serum insulin ranges.

V. CONCLUSION

Oral management of Jamblang has a good-sized impact on decreasing fasting blood glucose ranges in rat, while as in comparison to bad controls (DM organization). However, the mechanism that takes place withinside the phenomenon of the decline in GDP on this examine want in addition examine.

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