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ANTI HYPERGLYCAEMIC ACTIVITY OF *EUGENIA JAMBOLANA*- A REVIEW

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ABSTRACT

Objective: The aim of present review article is to briefly discuss the pharmacological and clinical studies of *Eugenia jambolana* in the context of its anti hyperglycaemic activity. **Methods:** The data was collected from libraries of various institute, journals and different available online sources on the above topic and thoroughly studied. Results of these pharmacological and clinical studies were keenly observed and compared by keeping in view the various parameters used in it. The impact of different dosage and their forms with different parameters are evaluated. Also, it was tried to explore the possible mechanism of action of *Eugenia jambolana* as hypoglycaemic agent.

Results: The comparative review shows that *Eugenia jambolana* has significant impact on controlling blood sugar. And it has good potential for the management of diabetes mellitus as described in traditional systems of medicine, that too without any major side effect.

KEYWORDS- Diabetes mellitus, *Eugenia jambolana*, Hyperglycemia, Aqueous extract, Efficacy, Unani medicine.

INTRODUCTION

Diabetes is a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disturbance of carbohydrate, fat and protein metabolism, resulting from defects in insulin secretion, insulin action or both.[1] The world is facing an explosive increase in the incidence of diabetes mellitus. It is known that diabetes is possibly the world's fastest growing metabolic disease.[2] Diabetes is growing alarmingly in India, more than 65,1 million

people with the disease, compared to 50.8 million in 2010.[3] Currently, India has the highest number of diabetic patients, and India is being called the diabetic capital of the world.[4] Diabetes caused 5.1 million deaths in 2013. Every six seconds a person dies from diabetes.[5] It causes premature morbidity and mortality, particularly from cardiovascular disease (CVD), adult blindness, non traumatic lower extremity amputations and end stage renal diseases.[6] The treatment of Diabetes mellitus is based on oral hypoglycaemic agents and insulin. The oral hypoglycaemic agents currently used in clinical practice have characteristic profiles of serious side effects.[7] These drugs cause insulin resistance, lose their efficacy and give rise to various side effects (such as; hypoglycaemia, weight gain, anorexia, diarrhoea, flatulence, abdominal distension and metallic taste in mouth etc).[8] Diabetes mellitus is also treated in Indian traditional medicine by different parts of medicinal plants having anti-diabetic activity. Plant derivatives with purported hypoglycaemic properties are used in folk medicine and traditional healing systems around the world.

Substantial efforts have been made in recent years to identify natural drugs; *Eugenia jambolana* (Jamun) is foremost common among them. *Eugenia jambolana* (Jamun) is a plant with known ethno-medicinal uses. Before the discovery of insulin, it was useful in the treatment of diabetes and is an integral part in the various alternative systems of medicine.[9]
The *Eugenia jambolana* or *Syzygium cumini* belongs to the Myrtaceae family. Other common names are Jambul, Black Plum, Java Plum, Indian Blackberry, Jamblang, Jamun etc. Scientific classification of *Eugenia jambolana* is.

Kingdom	:	Plantae
Division	:	Magnoliophyta
Class	:	Magnoliosida
Family	:	Myrtaceae
Genus	:	*Eugenia*
Species	:	*jambolana* Lam.[10]

Trees of Jamun are found growing throughout the Asian subcontinent, Eastern Africa, South America, Madagascar and have also naturalized to Florida and Hawaii in the United States of America. The ripe fruits are used for health drinks, making preserves, squashes, jellies and wine. In association to its dietary use, all parts of the tree and, importantly the seeds are used to treat a range of ailments, the most important being diabetes mellitus.[11]

Decoction of *Eugenia*

jambolana (*E. jambolana*) seed kernel is used as a domestic preparatin for diabetes and it also forms a key ingredient of several anti-diabetic herbal formulations.[12]

ANTI-DIABETIC ACTIVITY OF EUGENIA JAMBOLANA

Eugenia jambolana has been reported to have hypoglycaemic effects both in pre clinical and clinical studies. Some of pharmacological studies that have been conducted for anti-diabetic effect of *Eugenia jambolana* are as follows- Study conducted by Bhavana Srivastava on hypoglycaemic and hypolipidemic activity of *Eugenia jambolana* (*EJ*) pulp and seed extract in Streptozotocin induced diabetic albino rats that *EJ* pulp extract 200mg/kg/day (Group III) reduced the hyperglycaemia significantly as compared to the diabetic group II , it failed to restore the level to that of the control group and same finding was seen with *E. Jambolana* pulp extract (group IV).[13]

S.B Sridhar concludes that the anti-diabetic effect of *E. jambolana* seed powder was better with 500 mg/kg body weight in Streptozotocin diabetic female albino wistar rats weighing 150-200 g. Blood glucose levels decreased only by 11-15% *vs* the normal controls after the GTT, this shows that *E. jambolana* possibly acts as a hypoglycemic agent by rising insulin levels rather than just as an anti-hyperglycemic agent.[14]

In a study on anti-diabetic and antiulcer effects of extract of *Eugenia jambolana* seed in mild diabetic rats: study on gastric mucosal offensive acid-pepsin secretion by Chaturvedi et al showed seed kernel of *Eugenia.*

jambolana (EJE) dose-dependent decrease in blood glucose level in mild diabetes rats. Blood glucose level remained stable in mild diabetic rats from 3rd day onwards after streptozotocin administration (taken as 1st day for treatment) and EJE (200 mg/kg) showed anti-hyperglycemic effect on 10th day of its administration. Glycosylated haemoglobin level in mild diabetic rats was decreased significantly after treatment with EJE for 30 days. EJ has been reported to show significant antihyperglycemic activity in mild diabetes rats which have functioning pancreatic beta cells. This indicates that it may alter insulin release which was observed with an increase in insulin level with EJ treatment.[15]

Ethyl acetate fraction of seed of *Eugenia jambolana* at genomic level in streptozotocin induced diabetic male albino rat showed significant anti-diabetic effect in both short and long

duration treatment schedule in study conducted by Kishalya et al.[2] This effect may be due to high solubility of bioactive phytomolecules i. e. gallic acid and polyphenolic compounds present of this solvent fraction. The administration of this fraction at a dose level of 200 mg/Kg of body weight of rat for single time attenuates FBG level effectively up to 8 hrs. It may be due to stimulation of pancreatic β–cells for short duration insulin release against high blood glucose level likewise produced by other synthetic oral drugs such as glibenclamide, which is responsible to increase in sensitization and stimulation of β- cells against blood glucose.[2,16]

The isolated compound mycaminose (50 mg/kg) and ethyl acetate [EA] and methanol [ME] extracted compounds of *S. cumini* seed (200 and 400 mg/kg) was undertaken to evaluate the anti-diabetic activity against streptozotocin (STZ) induced diabetic rates which produced significant ($p<0.05$) reduction in blood glucose level in a trial conducted by Kumar et al. The possible mechanism behind antihyperglycemic property of compound of *syzgium cumini* by which seed brings about decrease in blood sugar level may be due to potentiation of the insulin effect of plasma by increasing either the pancreatic secretion of insulin from beta cells of the islets of Langerhans or its release from the bound form.[7]

Pandey and Khan conducted a study in alloxan diabetic rats which demonstrates that feeding for 21 days of the diets containing 15% powdered unextracted seeds containing water soluble gummy fibre, 15% powdered defatted seeds from which lipid and saponins were removed only and 6% water soluble gummy fibre isolated from *S. cumini* seeds significantly lowered blood glucose levels and improved oral glucose tolerance.[17]

Significant blood glucose lowering activity was observed in fasted (at 1 h $P<0.01$, 3 h $P<0.001$ & 4 h $P<0.001$), fed (at 3 h $P<0.05$), glucose loaded (at 1 & 3 h $P<0.05$) and diabetic (at 3 & 4 h $P<0.01$) rats feeded with 95% ethanolic extract of whole fruit of *S. Cumini* in a single oral dose of 250mg/kg body weight in study by Gupta and Saxena. Also marked degranulation of beta cells of treated rats were noticed which suggests that rate of extract stimulated insulin is probably greater which further favours the insulin secretagogue effect of *S. cumini*.[18]

Saravanan et al showed that oral administration of aqueous extract of the bark of *Syzgium cumini* in the dose of 300 mg/kg body weight led to significantly decreased levels of blood glucose and urine sugar in diabetic rats. Also, during oral glucose tolerance test, long term

administration of *Syzgium cumini* aqueous extract was able to significantly decreased blood sugar concentration in streptozotocin diabetic rats.[19]

A study by Singh and Gupta shows that the alcoholic extract of *S. cumini* produced a fall in blood glucose level of 13, 23 and 28% after 30 days with 25, 50 and 75mg doses respectively in alloxan diabetic albino rats. The blood sugar once dropped to normal level after extract feeding, did not increase again after discontinuation of extract feeding up to 15 days. The possible mechanism of action for hypoglycaemic effect is due to regeneration of beta cells in alloxan induced diabetic albino rats and probably due to presence of alkaloid in alcohol extract of *S. cumini* which causes improvement in beta cells.[20]

Vasim Khan et al stated that the increased serum insulin levels and inhibition of insulinase activity from the kidneys was observed on oral administration of the extract of *Eugenia jambolana* in diabetic rats.[12]

Ethanolic extract of *Eugenia seed kernel* also established its antioxidant potential along with hypoglycaemic effect in streptozotocin-diabetic rats in a study conducted by Ravi and Sivagnanam. Combination treatment of lower dose of glimepride together with *ethanolic eugenia seed* extract showed potent hypoglycaemic as well as antihyperglycemic activities without stern hypoglycaemia in normal rats. It concludes that it may be possible to use for considerable dose reduction of standard drugs. Potentiation of the insulin effect of plasma by increasing either the pancreatic secretion of insulin from beta cells of the islets of Langerhans or its sensitivity by *Eugenia seed kernel*. As administration of *Eugenia jambolana* leads to decrease in blood glucose as discussed in the present study.[21]

In a study, conducted by Deepika Yadav, better positive response was found after administration of 50% methanolic extract of *Syzgium cumini* in alloaxan induced diabetic rats. Results in test group treated by *Syzgium cumini* exhibits better response than control group. Study indicates that methanolic extracts of *Syzygium cumini* exhibited significant anti-hyperglycemic activities in alloxan-induced hyperglycemic rats through the regeneration of cells of pancreas.[22]

Clinical studies

Beside the pharmacological studies certain clinical trials conducted with *Eugenia jambolana* as test drug have also indicated similar findings in human as well such as.

G Shivaprakash *et al.* conducted open labeled, randomized trial in DM patients: fifteen in group1 received *Eugenia jambolana* seed powder 10 gm orally per day along with diet and exercise shows the antihyperglycemic and antioxidant action with use of *Eugenia jambolana* seed powder. Significant reduction observed only in FBS, maintenance of PPBS values at the baseline level throughout the study period and no increase in serum insulin levels at any visits suggest that *EJ* seed powder also exhibits an extrapancreatic action, besides the pancreatic action as suggested by previous studies.[23] This extrapancreatic action could be due to its action on the liver to decrease blood glucose levels by enhancing glycogenesis or by restoring carbohydrate enzyme activity.[24,25]

In a study conducted by Akbar et al. 10 patients of type-2 diabetes mellitus with no previous medication, 10 patients of type-2 diabetes mellitus taking oral hypoglycemic agents with history of inadequate control and six control subjects were given low (2 gm thrice daily) and high (4gm thrice daily) doses of powdered part, aqueous extract and alcoholic extract of seeds of *Eugenia jambolana* for 14 days. It was found that *Eugenia jambolana* has significant hypoglycemic activity both in low and high doses.[26] The possible mechanism of action of supports that alkaloid named as glycoside present in jambul fruit is believed to have the power to check the pathological conversion of starch into sugar in cases of increased production of glucose.[27]

LIKELY MECHANISM OF ACTION: Exact mechanism of action is not established regarding the hypoglycaemic action of *Eugenia jambolana*, although different studies explore about its mechanism of action. Pharmacological studies shows that the plant is rich in compounds containing anthocyanins, glucoside, ellagic acid, isoquercetin, kaemferol and myrecetin. The seeds are claimed to contain alkaloid, jambosine, and glycoside jambolin or antimellin, which halts the diastatic conversion of starch into sugar.[11]

The jambolin, a glycoside present in seed of *Eugenia jambolana* is believed to have the power to check the pathological conversion of starch into sugar in cases of increased production of glucose.[26]

The ethanolic extracts of seeds of *Eugenia jambolana* contain saponins which also have the anti-diabetic effect and appear to be involved in stimulation of pancreatic β-cells and subsequent secretion of insulin.[25] Various pharmacological studies favours the insulin secretogogue effect of *Eugenia jambolana* and it also improved the insulin

responsiveness.[12,18,20,21,22] Some studies also favours the extra-pancreatic effect of *Eugenia jambolana* in context of it anti-diabetic action.[14]

CONCLUSION

The results of various studies confirm and justify the use of *Eugenia jambolana* seeds in traditional system of medicine to manage Diabetes mellitus. And has also opened avenues for the further research specially with reference to development of potent phytomedicine for the the treatment of Diabetes mellitus from *Eugenia jambolana*. Advance comprehensive studies are needed to make clear the exact mechanism of the antihyperglycaemic action of *Eugenia jambolana*.

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