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Mini-Review

A Review on Zizyphus as Antidiabetic

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ABSTRACT

The present review paper aims to highlight the effects of extracts of genus zizyphus for the treatment of Diabetes clinically throughout the world. The basic aim is to study the hyperglycemic effect of this genus and its use. So as the effect of herbal medicine is more friendly than synthetic medicines. The effects of three species Ziziphus spinacristi, Zizyphus jojoba, and Zizyphus vulgaris have been studied clinically and have great effect on insulin secretion. While work on Zizyphus maritiana have also been done. It is concluded that genus zizyphus have potential of antidiabetic activity. Many species of Zizyphus grow widely. As natural drugs are with no or less side effects and safe for human health so they can greatly replace synthetic drugs in the forth coming future.

Keywords: Ziziphus spinacristi, Zizyphus jojoba, Zizyphus maritiana and Zizyphus vulgaris.

INTRODUCTION

Diabetes is a heterogeneous group of metabolic disorders characterized physiologically by deficiency in insulin or insulin activity and clinically by hyperglycemia or impaired glucose tolerance and other manifest able disorders (WHO, 1994). Hyperglycemia is due to deficiency of insulin secretion or resistance of the body cells to the action of insulin, often associated with carbohydrate, protein and lipid metabolism. These metabolic disturbances result in acute and long term diabetic complications, which are responsible for premature death and disability. According to World health organization, approximately more than 100 million peoples were reported to have diabetes mellitus worldwide (Zimmet, 1999). Attention to diabetes mellitus is necessary because number of diabetic patients is increasing and diabetes has various side effects (Jodeph and Smith, 2003; Barnett and Braunstein, 2001). Use of medicinal plants in medicine is increasing because of their widespread use and for their curing various diseases. Recent studies have indicated that some herbal extracts have anti-diabetic effects, thus can be used in diabetic patients in order to reduce blood glucose. (Hussain *et al.*, 2004).

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A survey of the literature revealed that a number of cyclopeptide and isoquinoline alkaloids flavonoids, terpenoids and their glycosides have been found to occur in various amounts in most *Zizyphus* species. The leaves of plants of this genus contain betulic and ceanothic acids, various flavonoids, saponins, erols, and triterpenes (Ali and Hammed, 2006; Glombitza *et al.*, 1994)

Zizyphus spinachristi

The butanol extract of *Zizyphus spinachristi* fruit or its main saponins glycoside, christinin-A, improved glucose utilization in diabetic rats, but not in normal rats after 1 and 4 weeks of treatment. Serum insulin levels showed a significant increase in diabetic rats treated for a period of 4 weeks with the butanol extract. The antidiabetic effect of butanol extract was more pronounced than that of christinin-A. (Glombitza *et al.*, 1994; Adzu *et al.*, 2002).

Clinical trials were done on Root extracts of *Zizyphus spinachristi*. 100mg/kg extract was used to treat diabetic rats orally. Fasting serum glucose was measured every week and the period of the treatment continued for 2 weeks. Serum insulin, lipid profiles, liver and kidney functions were measured at the end of the experiment. In diabetic rats extract significantly reduced fasting serum glucose levels ($p < 0.001$) and markedly increase serum insulin level ($p < 0.001$). The data revealed that extract of ZSC have beneficial effects on diabetic rats. It reduce hyperglycemia, hyperlipidemia and peroxidates that associate diabetes. Its save towards liver and kidney function also. (Hussein *et al.*, 2006).

10 days oral administration of *Z. spinachristi* fruit hydro alcoholic extract (500 mg/kg) was carried out. The results showed that treatment with glibenclamide nonsignificantly reduced the blood glucose level ($p > 0.05$) and significantly increased the serum insulin level of diabetic dogs ($p < 0.05$). In contrast to glibenclamide, the hydroalcoholic extract of *Z. spina-christi* resulted in a significant decrease in the level of blood glucose, with a concomitant significant increase in the serum insulin level, in diabetic dogs ($p < 0.05$). The extract had a mild, but significant, blood glucose lowering effect and the longterm use of this agent may be advantageous over chemical drugs in alleviating some of the chronic diseases and complications caused by diabetes. (Avizeh, R. *et al.*, 2010).

A bioactivity guided fractionation of the leaves of *Zizyphus spina-christi* (L.) Wild extracted with different solvents revealed that the ethanol 70% extract possessed the highest antihyperglycemic activity when compared to metformin ($P < 0.01$). LD50 of the extract was found to be 10 g/kg. B.wt Thus indicating the safety of the extract. Long term administration revealed that the ethanol 70% extract had no toxic effect on cholesterol, triglycerides, creatinine, urea and liver enzymes (AST and ALT). (D.I.Nesseem.2008)

Zizyphus jujoba

Ethanol leaf extract of *Zizyphus jujoba* was used to treat alloxan induced diabetic rats. 100mg/kg of extract was given to diabetic rats for five days alternately. The analysis variance

results indicated significant reduction ($P = 0.001$) of glucose–triglyceride– cholesterol and VLDL levels in diabetic in comparison with no diabetic. *Z. Jujoba* also increased HDL levels significantly ($P=0.001$). Also, the extract reduced diabetic rats LDL level, but it wasn't significant ($P=0.12$). According to the results obtained, it was concluded that, *Z. Jujoba* leaves can be used in diabetics for the purpose of glucose and lipid reduction. (Shirdil Z.2009).

Clinical trials were done on Root extracts of *Zizyphus jujoba*. 100mg/kg extract was used to treat diabetic rats orally. Fasting serum glucose was measured every week and the period of the treatment continued for 2 weeks. Serum insulin lipid profiles, liver and kidney functions were measured at the end of the experiment. In diabetic rats extract significantly reduced fasting serum glucose levels ($p < 0.001$) and markedly increase serum insulin level ($p < 0.001$). The data revealed that extract of *Z. Jajoba* have beneficial effects on diabetic rats. It reduce hyperglycemia, hyperlipidemia and peroxidates that associate diabetes. Its save towards liver and kidney function also. (Hussein *et al.*, 2006)

Zizyphus vulgaris

Zizyphus vulgaris L. are widely used for the treatment of diseases such as diabetes mellitus. The effects of water extracts of *Zizyphus vulgaris* Laws investigated. The effect of fruit on serum glucose, triglycerides, LDL-cholesterol, HDL cholesterol and activities of aminotransferase enzymes in streptozocin-induced diabetic adult male rats. Continuous supplementation of this water extract by gavage at doses of 0.25, 0.5, 1, 1.5 and 2 g/kg in 0.5 ml distilled water in diabetic rats resulted in a significant decrease of fasting blood glucose and LDL-cholesterol and triglyceride levels after 14 days. The levels of HDL-cholesterol and insulin, and activities of serum aminotransaminase enzymes, alanine aminotransferase and aspartate aminotransferase were not changed significantly in the extract-supplemented group compared to the control group. (Sulati and Soleimani 2009).

Zizyphus mauritiana

Various extracts, petroleum ether, chloroform, acetone, ethanol, aqueous, and crude aqueous, of fruits of *Zizyphus mauritiana* Lam. (Rhamnaceae) and the fractions of petroleum ether and aqueous extracts were tested for antihyperglycemic activity in glucose overloaded hyperglycemic rats. The effective antihyperglycemic extracts and fraction were tested for their hypoglycemic activity at two dose levels, 200 and 400 mg/kg, respectively. To confirm their utility in a higher model, the effective extracts and fraction of *Z. mauritiana* were also subjected to an antidiabetic study in the alloxan-induced diabetic model at two dose levels, 200 and 400 mg/kg. The aqueous extract and the non-polysaccharide fraction of the aqueous extract of *Z. mauritiana* were found to exhibit significant antihyperglycemic and hypoglycemic activities. The petroleum ether extract was found to exhibit only an antihyperglycemic effect. Treatment of diabetic rats with petroleum ether extract, aqueous extract, and non-polysaccharide fraction of this plant restored the elevated biochemical parameters, glucose, urea, creatinine, serum

cholesterol, serum triglyceride, HDL, LDL, hemoglobin, and glycosylated hemoglobin significantly to the near normal level. The activity of the non-polysaccharide fraction was comparable to that of the standard drug glibenclamide (E.E.Jarlad et al., 2009).

The aqueous extract from the leaves of *Zizyphus Mauritiana* Lam (Rhamnaceae) was studied. It was observed a striking decrease of the hyperglycemic arrow ($p < 0.05$), with 300 mg/kg administrated 90 minutes before starting the test. The results obtained with a dose of 300 mg/kg once or twice a day were identical as those with glibenclamide at 0.2 mg/kg per day. So, the antidiabetic activity of *Zizyphus Mauritiana* Lam was experimentally born out but it has to be standardized for common use. (Criss, et al., 2000). Hypoglycemic effect of seed extract of *Zizyphus maritiana* in alloxan-induced diabetic mice was assessed. Seed extract was administered orally at doses of 100, 400, and 800 mg/kg body weight and also in combination with glyburide (800 mg/kg seed extract and 10 mg/kg glyburide). Their blood glucose level (in acute and sub-acute study), body weight, and mortality rate were monitored. Administration of the extract reduced the weight loss and mortality rate during the sub-acute study. The extract also augmented the glucose tolerance in both normal and diabetic mice. These results suggest that the extract possesses synergistic hypoglycemic activity (Bhatia et al., 2010).

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