Biochemical studies on hypoglycemic effect of 
Aavirai Kudineer : A herbal formulation in alloxan diabetic rats

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Aavirai Kudineer (AK) is an herbal decoction of seven botanical drugs, cited in the Gunapadam; a Tamil Siddha medical text. The anti-diabetic efficacy of this formulation was evaluated using alloxan-induced diabetic and normal rats. Glucose tolerance was observed within 1 hr in AK-treated rats (10ml/kg body) as compared to control. A significant decrease in the severe hyperglycemia characteristic of alloxan diabetes was noted after 15 days of AK treatment. Further AK treatment reversed the elevated area, creatinine, cholesterol and decreased protein values to near normal levels. Assay of glycogen content and chief carbohydrate-metabolizing enzymes, viz. hexokinase, glucose-6-phosphatase and fructose 1,6 diphosphatase in the liver of diabetic and AK-treated diabetic rats clearly ascertains the hypoglycemic efficacy of this formulation.

The mode of action of this herbal formulation remains to be elucidated.

Plants have been used by man, from time immemorial for their extraordinary healing abilities and pain relieving properties. Most of the plant parts used are important sources of tannins, which are important pharmacological and therapeutic agents. Presently, the medical fraternity has increasingly started using plants to overcome various illnesses and sufferings, mainly to obviate the profound side effects encountered in usage of modern drugs.

Aavirai Kudineer (AK), a herbal formulation cited in the Tamil Siddha medical text 'Gunapadam' is suggested as panacea for diabetes. AK is composed of seven herbs, viz. Cassia auriculata (bark), Cassia fistula (bark), Cyperus rotundus (tubers), Saussurea lappa (tubers), Salacia prinoides (roots), Eugenia Jambolina (bark) and Terminalia arjuna (bark).

Tablets prepared from root bark of Salacia prinoides have been clinically demonstrated to have significant hypoglycemic activity. Leaves of Cassia fistula significantly reduced hyperglycemia in experimental diabetic mice. Decoctions prepared from fruit pulp, kernel and seeds of Eugenia jambolana exhibit marked anti-diabetic effect in humans, rabbits, and rats. Alcoholic extracts of roots of Saussurea lappa elicited significant hypoglycemic response in normal albino rats.

In spite of the above reported studies on some of the individual plants of Aavirai kudineer, no data are available on the collective hypoglycemic effect of this herbal formulation. The present study is a pilot attempt to evaluate the anti-diabetic effect of this formulation, following biochemical analysis in experimental animal models.

Male Wistar albino rats (150-180g) procured from the Centre for Animal health studies, TANUVAS, Madhavaram, Chennai, were used for the study. They were housed in well-ventilated polyurethane cages at normal room temperature and had free access to tap water and laboratory pellet feed.

The herbs purchased from the local market, duly authenticated by Dr. S. Usman Ali, Central Research Institute for Siddha, Arumbakkam, Chennai, was used for study.

A powdered mixture (100g) of equal portions of all the 7 ingredients mentioned above was boiled in 800ml of distilled water, until the volume was reduced to approximately 100ml. The filtered decoction called Aavirai Kudineer (AK) was used to treat the diabetic and normal animals. They were given a daily oral dose of 10ml/kg body weight, by gastric intubation, for a period of 15 days. The dose was empirically based on that given in the Siddha text.

Effect of AK on glucose tolerance was determined by dividing the fasted rats into two groups (A and B).
of six rats in each group. Group A (control) rats were given distilled water. Group B rats were given AK. The rats of both group A & B were given glucose (2g/kg body weight), 30 min after administration of the drug. Blood samples were collected from the tail vein just prior to glucose administration and at 30 and 90 min after the glucose loading and blood glucose levels were measured immediately.

Diabetes was induced by an i.p. injection of freshly prepared alloxan (120mg/kg-body wt. Sigma Chemicals, USA) and was confirmed by testing for glucosuria, using glucose indicator sticks. The rats were then divided into four groups such as controls, AK-treated normals, diabetics and AK-treated diabetics.

After 15 days of AK treatment, the animals were fasted overnight and then sacrificed by decapitation. Blood was collected for determining glucose, urea, creatinine, protein, cholesterol, and creatine levels showing its positive effect on renal function.

Reduced glucose utilization and lipogenesis are typical of insulinopenic diabetes produced by alloxan. This explains the severe hyperglycemia and hypercholesterolemia encountered in diabetic rats. AK treatment achieved glucose tolerance within a short time and lower dose as compared to individual use of Cassia fistula. Further chronic AK treatment for 15 days normalized the blood glucose levels suggesting enhanced glucose uptake and utilization by the body.

Renal disease is one of the most common and severe complications of diabetes. Distinct metabolic renal alterations are demonstrable in experimental diabetes leading to a negative nitrogen balance, enhanced proteolysis and lowered protein synthesis. AK treatment has appreciably normalized urea and creatinine levels showing its positive effect on renal function.

Liver is the candidate organ for glucose metabolism. Glycolysis and gluconeogenesis are the two prime complementary events balancing the glucose load in our body. The activity of the key glycolytic enzyme hexokinase is lowered during diabetes leading to reduced disposal of glucose as glucose-6-phosphate. On the contrary the activities of the gluconeogenic enzymes, viz. glucose-6-phosphatase and fructose 1,6-biphosphatase are enhanced during diabetes. Glycogen synthesis in the rat liver and skeletal muscles was impaired during diabetes. All these derangement in carbohydrate metabolism result in impaired glucose homeostasis leading hyperglycemia.

AK treatment has reversed the diabetic status. It increased hexokinase activity up to 82% as compared to Eugenia jambolana which increased hexokinase activity by 72.7% when used singly, replenished liver glycogen stores and suppressed the hepatic gluconeogenesis by reducing activities of Fructose 1,6-biphosphatase and glucose-6-phosphatase significantly with P<0.001.

Thus this study indicates that AK treatment can normalize many of the metabolic abnormalities due to
diabetes and can be safely concluded that Aavirai Kudineer is potently hypoglycemic. The anti-diabetic effect of AK seems superior as compared to similar effect of the individual plants used in this formulation. Its hypoglycemic efficacy could be attributed to the synchronicity and the additive effects of the constituents, reducing the possibility of side effects. The mechanism by which hypoglycemia is achieved by this herbal formulation needs to be further investigated. Estimation of insulin level and insulin receptor may give more insight into its mechanism of action.

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