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ANTI DIABETIC ACTIVITY OF NAVARKOTTAI MATHIRAI IN WISTAR ALBINO RATS

P. Benazeer Malhiya[1], A. Kingsly[2]

[1] PG Scholar, Department Of Gunapadam, Gsmc, Palayamkottai.

[2] HOD, Department Of Gunapadam, Gsmc, Palayamkottai.

ABSTRACT

Diabetes Mellitus is one of the most dreaded ailments affecting the mankind today. It is a metabolic disorder of carbohydrate, fat and protein metabolism caused due to insufficient production of insulin or due to its inhibitory action. In *siddha* Diabetes Mellitus (DM) may be correlated with *Madhumeham* or *Neerizhivu.* The global figure of people with diabetes set rise from the current estimate of 150-220 million in 2010 and 300 million in 2025. Incidence in India: Type 1: 5-10%,Type :90-95%,Gestational diabetes-2-5% & Other specific types-2%. It is a deteriorating diseased condition weakens the immune system and predisposes human beings for greater health hazards and mortality due to clinical complications such as microvascular (retinopathy, neuropathy, and nephropathy) and macrovascular (heart attack, stroke and peripheral vascular disease) complications.] In spite of the presence of known allopathic anti-diabetic medicine in the pharmaceutical market, remedies from medicinal plant are used to treat this disease. Many traditional herbal treatments for diabetes are used throughout the world and there is an increasing demand by patients to use the natural products with anti-diabetic activity. So there is a need of a effective standard herbal formulation which is affordable and fulfil the preclinical standards. The present study is undertaken to the evaluate the effect of *Navarkottai Mathirai* on changes in Body weight and blood glucose level of Wistar albino rats.

BACKGROUND

In *Siddha* system of medicine diseases are classified into 4448 types according to the *Siddhar* Yugimuni among them *Mega neer Noigal* is further classified into 21 types which include *Madhu megam. Mathumegam* is one of the challenging diseases in our modern life.

As per the literature *Siddha maruthuvam (podhu)* by the author k. M. Kuppusamy Mudhaliar the disease *Madhumegam* is defined as it is a condition characterized by frequent profuse urination, often flies and ants are stacked to the urine and on heating it smells like sugar which is followed by emaciation of the body day by day. [1] The trial drug ***Navarkottai Mathirai*** in the literature of Pharmacopoeia of Siddha Research Medicines by the Authors Dr.M. Shanmuga velu L.I.M., H.P.I.M. and DR.G.D. Naidu, Page no 201.

Ingredients of Navarkottai Mathirai

Tamil Name	**Botanical Name**	**Family**	**Parts Used**
Naval	*Syzygium cumini*	Myrtaceae	Seed
Aavarai	*Cassia auriculata*	Caesalpiniaceae	Root bark
Adu theendapalai	*Aristolochia bracteolata*	Aristolochiaceae	Leaf

METHOD OF PREPARATION

These two powders are placed in a mortar. Mixed together and rubbed with the juice of *Adu theenda palai* leaves for 3 or 4 days, rounded into pill up to 2 kundries size 260 mg or 5 grains each when the mass is of waxy consistancy dried in the shade and preserved in a bottle. To avoid fungus formation the pills must be very well dried.

DRUG DOSAGE

1 – 2 pill twice a day

SHELF LIFE

One year

INDICATION OF TRIAL MEDICINES

Adhi moothira noi (Poly urea), *Madhumegam* (Diabetes mellitus),

Adhi thaagam (Poly dypsia) [2]

EXPERIMENTAL MODELS

For the study of anti-diabetic an experimental model is selected in such a way that it would satisfy the following:

- The animal should develop hyperglycemia rapidly.
- Pathological changes in the site of induction should result from pancreatitis or damage of β-cells.
- The symptoms should be ameliorated or prevented by a drug treatment effective in human beings.

MATERIALS AND METHODS

Materials:

Animals : Male wistar albino rats (180-220gm)

Drugs : *Naval Kottai Mathirai*

Chemical: Streptozotocin (S. D Fine. Chem. Ltd, Mumbai)

Selection & acclimatization of animals

Wistar strains of male albino rats weighing between 180-220gm are used for this study. The animals were housed in large spacious cages and they were fed with commercial pellets and access to water *ad libitum*. The animals were well acclimatized to the standard environmental condition of temperature (22^0c ± 5^0c) and humidity (55 ±5%) and 12 hour light dark cycles throughout the experimental period.

INDUCTION OF DIABETES MELLITUS

Diabetes mellitus is induced in wistar albino rats by single intra peritoneal injection of freshly prepared solution of Streptozotocin (25mg/kg BW) in physiological saline after overnight fasting for 12hrs.[1]

Streptozotocin is commonly used to produce diabetes mellitus in experimental animals due to its ability to destroy the β-cells of pancreas possibly by generating the excess reactive

oxygen species such as H_20_2, 0_2 and $H0^-$. The development of hyperglycemia in rats is confirmed by plasma glucose estimation 72 hours post Streptozotocin injection. The rats with fasting plasma glucose level of >180-220mg/dl were used for this experiment.

Experimental procedure

In the experiment a total of 30 rats (24 diabetic surviving rats & 6 normal rats) were used. Diabetes was induced in rats 3 days before starting the experiment. The rats were divided into 5 groups after the induction of Streptozotocin diabetes. In the experiment 6 rats were used in each group.

TREATMENT PROTOCOL

- Group-I: (Normal control) consist of normal rats given with 10ml/Kg of normal saline, orally.
- Group-II: (Toxic control) Diabetic control received 25mg/Kg of Streptozotocin through I.P.
- Group-III: Diabetic control received Glipizide at a dose of (10mg/Kg orally) for 28 days.
- Group-IV: Diabetic control received NKM at a dose of (100mg/Kg orally) for 28 days.
- Group-V: Diabetic control received NKM at a dose of (200mg/Kg orally) for 28 days.

METHODOLOGY

Sample collection

After 28 days of treatment, body weight, blood glucose, haemoglobin, glycosylated haemoglobin, plasma insulin, total cholesterol, triglycerides, HDL-cholesterol and phospholipids and glycogen content and antioxidant enzymes level were determined. Blood was collected from the eyes (venous pool) by sino-ocularpuncture. [2] In EDTA coating plasma tubes for the estimation of blood parameters.

BIOCHEMICAL ANALYSIS

Estimation of blood glucose

Blood glucose was estimated by commercially available glucose kit (One Touch Ultra) Johnson Johnson based on glucose oxidase method. [3]

Statistical analysis

The data for various biochemical parameters were analyzed using analysis of variance (ANOVA), and the group means were compared by Newman-Keul's multiple range test (NKMRT). Values were considered statistically significant at $p<0.01$.

Table No: 1

- **Effect of Navakottai Mathirai on initial and final body weight and blood glucose in normal and treated animals.**

GROUP	Body weight (g)		Blood glucose (mg / 100ml)	Blood glucose (mg / 100ml)
	Initial	Final	Initial	Final
G1 Normal control	239 ± 6.12	243 ± 6.15	88.62 ± 4.38	90.80 ± 3.15
G2 Diabetic control	228 ± 5.58	172 ± 7.30**(a)	89.25 ± 3.72	218.45 ± 5.80**(a)
G3 Std control	235 ± 7.48	239 ± 7.32	91.65 ± 4.32	125.48 ± 4.40**(b)
G4 Test Drug 100 mg	231 ± 7.25	241 ± 7.37	89.76 ± 3.70	132.35 ± 7.30**(b)
G5 Test Drug 200mg	235 ± 7.37	241 ± 7.42	90.45 ± 3.80	128.42 ± 4.65**(b)

Values are expressed as mean ± SEM.

- Values were compared by using analysis of variance (ANOVA) followed by Newman-Keul's multiple range tests.
- ** (a) Values are significantly different from normal control G1 at P<0.001.

** (b) Values are significantly different from Diabetic control G2 at P<0.01.

RESULTS

Table no: 1 illustrates the levels of initial and final blood glucose, and change in body weight, in normal rat, and treatment control animals in each group. The mean body weight of diabetic rats (G2) was significantly decreased as compared to normal control rats. The body weight of diabetic control rats treated with ***Navarkottai Mathirai*** at a dose of 100mg/kg and 200mg/kg (NKM) was increased the body weight non-significantly as compared to normal control animals.

Fasting blood glucose level was significantly increased 218.45 ± 5.80 in diabetic animals as compared to normal animals. However the level of fasting blood glucose, returned to near normal range in diabetic rats treated with ***Navarkottai Mathirai*** at a dose of 100mg/kg and 200mg/kg (NKM).

DISCUSSION

Streptozocin causes massive reduction in insulin release, through the destruction of β-cells of the islets of Langerhans. The mechanism of Streptozocin action was fully described elsewhere (Lazarow, 1964; Colca et al., 1983).[4,5] In our study, we have observed a significant increase in the plasma insulin level when Streptozocin induced diabetic rats were treated with ***Navarkottai Mathirai*** at a dose of 100mg/kg and 200mg/kg (NKM) this could be due to potentiation of the insulin effect of plasma by increasing the pancreatic secretion of insulin from existing β- cells of islets of Langerhans or its release from bound insulin.

In uncontrolled or poorly controlled diabetes there is an increased glycosylation of a number of proteins including haemoglobin and α-crystalline of lens (Alberti and Press, 1982). [6] Glycosylated haemoglobin (HbA_1C) was found to increase in patients with diabetes mellitus to approximately 16% (Koenig et al., 1976) [7] and the amount of increase is directly proportional to the fasting blood glucose level (Jackson et al., 1979). [8] During diabetes the

excess glucose present in blood reacts with haemoglobin. Therefore, the total haemoglobin level is decreased in Streptozocin induced diabetic rats (Sheela and Augusti, 1992).[9] Administration of ***Navarkottai Mathirai*** at a dose of 100mg/kg and 200mg/kg (NKM) for 28 days prevents a significant elevation in glycosylated haemoglobin thereby increasing the level of total haemoglobin in diabetic rats. This could be due to the result of improved glycaemic control produced by ***Navarkottai Mathirai*** at a dose of 100mg/kg and 200mg/kg (NKM).

The body weight was decreased in Streptozocin diabetic rats. ***Navarkottai Mathirai*** at a dose of 100mg/kg and 200mg/kg (NKM) increases the body weight in Streptozocin induced diabetic rats. The ability of ***Navarkottai Mathirai*** at a dose of 100mg/kg and 200mg/kg (NKM) to protect massive body weight loss seems to be due to its ability to reduce hyperglycemia.

CONCLUSION

The result shows the level of fasting blood glucose decreased from 218.45 to 132.35 mg/dl. However, the level of fasting blood glucose returned to near normal range with the dose of 100mg of test drug NKM and in the dose of 200mg/dl NKM is further decreased the blood glucose level to 128mg/dl. So, that the test drug "*Navarkottai Mathirai*" are responsible for Anti-diabetic activity.

IAEC NO: 321 K. M college of pharmacy, Madurai.

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