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Antidiabetic Activity of a Polyherbal Preparation in Alloxan Induced Diabetic Rats

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A B S T R A C T

The present work was executed to evaluate the anti-diabetic potency of a polyherbal preparation. The objective of this study is to induce experimental diabetes mellitus using Alloxan in normal Albino wistar rats and study the antidiabetic activity of polyherbal formulation by comparison of changes in body weight and levels of glucose between normal and diabetic rats. Hypoglycemic agents from natural and synthetic sources are available for treatment of diabetes. Indian medicinal plants have been found to be useful to successfully manage diabetes. The effect of alcoholic extract of poly herbal preparation containing leaves of *Gymnema sylvestre*, fruits of *Momordica charantia*, rhizomes of *Curcuma longa*, seeds of *Eugenia jambolana* and fruits of *Embilica officinalis* was investigated in normal, glucose load conditions and alloxan induced diabetic rats. Significant anti diabetic activity was exhibited by the poly herbal formulation. Treatment with the polyherbal Preparation 200 mg/kg body wt and 400 mg/kg body wt for 10 days in diabetic animals has shown significant decrease in serum glucose levels in comparison to control animals.

Keywords: *Gymnema sylvestre, Momordica charantia Curcuma longa, Eugenia jambolana, Embilica officinalis,* Polyherbal Formulation.

A R T I C L E I N F O

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1. Introduction

Diabetes mellitus is a heterogeneous metabolic disorder characterized by altered carbohydrate, lipid and protein metabolism [1]. The management of diabetes mellitus is considered a global problem and successful treatment is yet to be discovered. The modern drugs, including insulin and oral hypoglycemic agents, control the blood sugar level as long as they are regularly administered and they also produce a number of undesirable effects [2, 3].

The treatment of diabetes mellitus has been attempted with different indigenous plants and polyherbal formulations [2, 4, 5]. Traditional medicines all over the world have advocated the use of herbs to treat diabetes since time immemorial. Many Indian plants have been investigated for their beneficial use in different types of diabetes and reports occur in numerous scientific journals [6]. In the Ayurvedic system of medicine, as mentioned in ancient Indian books like Charak, Samhita, Mahdhav Nidan and Astang Sanghra, there are about 600 plants, which are stated to have antidiabetic property [7].

Wide arrays of plant derived active principles representing numerous phytochemicals have demonstrated consistent hypoglycemic activity and their possible use in the treatment of diabetes mellitus. Indian plants which are most effective and commonly studeed in relation to diabetes and its associated complications are :Allium cepa, Allium sativum, Aloevera, Cajanus cajan, Coccinia indica, Caesalpinia bonducella, Ficus bengalenesis, Gymnema sylvestre, Momordica charantia, Ocimum sanctum, Pterocarpusmarsupium, Swertia chirayita, Syzigium cumini, Tinospora cordifolia, graecum andTrigonella foenum [8, 9].

Keeping the above information in view, an indigenous polyherbal preparation was developed containing the extracts of *Gymnema sylvestre*, *Momordica charantia Curcuma longa*, *Eugenia jambolana*, *Embilica officinalis*

2. Materials and Methods

Plant material

The different fresh plant parts viz., leaves of *Gymnema sylvestre*, fruits of *Momordica charantia*, rhizomes of *Curcuma longa*, seeds of *Eugenia jambolana* and fruits of *Embilica officinalis* were collected in the months Jan 2014 to March 2014 from the in and around local areas of Bhopal District of M.P. and identified & authenticated by Dr Zia Ul Hasan, Professor, Head Dept. of Botany, Safia College of science, Bhopal, M.P., dated 22/04/2014. M.P. and were deposited in Laboratory, Voucher specimen No. 470/Bot/Safia /2014 for leaves of *Gymnema sylvestre*, 469/Bot/Safia /2014 for fruits of *Embilica officinalis*, 468/Bot/Safia /2014 for fruits of *Momordica charantia*, 467/Bo/Safia /2014 for seeds of *Eugenia jambolana* and 466/Bot/Safia /2014 for rhizomes of *Curcuma longa*

Extraction

Leaves of *Gymnema sylvestre*, fruits of *Momordica charantia*, rhizomes of *Curcuma longa*, seeds of *Eugenia jambolana* and fruits of *Embilica officinalis* were coarsely powdered and extracted with ethanol in a soxhlet apparatus exhaustively. *Gymnema sylvestre*, *Momordica charantia Curcuma longa*, *Eugenia jambolana*, *Embilica officinalis* were mixed properly in capsule (1:1:1:1:1) & (1:1:1:1:1) in Vati to get the polyherbal formulation.

Animals

Adult Wistar rats (180 ± 10 g) of either sex were procured from D Y Patil College of Pharmacy, Pune (Maharashtra.), India. The animals were housed in large, spacious polyacrylic cages at an ambient room temperature with 12-h light/12-h dark cycle. Rats had free access to rodent pellets diet (Hindustan Lever Ltd, Bangalore, India) and water ad libitum. Experimental protocols were approved by Institutional Ethics Committee.

Acute Toxicity Studies:

Acute oral toxicity of the polyherbal formulation was carried out as per the guidelines set by the Organization for Economic Co-operation and Development (OECD), revised draft guidelines 423. The principle involves a stepwise procedure with the use of a minimum number of animals per step to obtain sufficient information on the acute toxicity of the test substance to enable its classification. Healthy Wistar rats (3animals/dose) of either sex were used for the experiment. Overnight fasted rats were orally fed with the polyherbal formulation (Capsule & Vati) in increasing dose levels of 5, 50, 300, and 2000 mg/kg body weight, respectively.

The animals were observed for their behavioral (alertness, restlessness, irritability, and fearfulness), neurological (spontaneous activity, reactivity, touch response, pain response, and gait), and autonomic (defecation and urination) profiles continuously for 24 h. After a period of 24 h, the animals were observed for 14 days for mortality [10].

Selection of Doses:

For the assessment of Antidiabetic activity, two dose level were chosen in such a way that one dose was approximately one-tenth of the maximum dose during acute toxicity studies and the other high dose was twice that of one-tenth dose (200 mg/kg, 400 mg/kg body weight)

Preparation of dosing:

The dose of 200 and 400 mg/kg of polyherbal preparation was prepared by suspending appropriate quantity of capsule and Vati in 1 % w/v CMC.

Oral glucose tolerance test in normal rats animals and experimental setup:

Albino rats of either sex weighing 130 – 180 g were taken. The rats were kept fasting overnight with free access to water. During experiment the animals were divided into three groups of six animals in each group. The blood sample was taken by pricking the rat's tail. Polyherbal formulation was administered with glass syringe and microsuction canula no. 18.

Grouping of animals:

Group I Kept as negative control, i.e., neither treated with Polyherbal preparation nor standard.

Group II Treated with standard oral hypoglycemic drug, i.e., Glibenclamide (0.5 mg/kg)

Group III Treated orally with polyherbal preparation (400 mg/kg)

Determination of OGTT activity:
The blood glucose concentration of animals were measured at the beginning of the study. Then the rats were orally treated with 3 g/kg body weight glucose solution after 30 minutes of the product and drug treatment. The measurements were repeated after 30, 90 and 150 minutes after the glucose load [11, 13].

Antidiabetic activity:
In this study, Polyherbal Formulation (Capsule & Vati, 200 and 400 mg/kg b.w) were evaluated for antidiabetic activity against alloxan induced diabetes mellitus in rats. Rats were divided into 7 groups consisting of 6 rats in each group. The rats were acclimatized for a period of 7 days before starting the experiment. After overnight fasting, hyperglycaemia was induced by administering a single dose of alloxan monohydrate (125 mg/kg b.w) prepared in sterile saline to all the groups except group I which served as normal control. During this period, the animals were given free access to water. After 3 days of alloxan administration, fasting blood glucose levels of rats were checked by glucostrips. The animals having blood glucose levels > 250 mg/dl were separated and selected for further studies and then re-grouping of these hyperglycemic rats was done as per the following protocol, for studying the antidiabetic activity of Polyherbal Formulation.

Group I Normal Control i.e., neither treated with polyherbal preparation nor with standard
Group II Diabetic Control treated with alloxan (125 mg/kg, i.p)
Group III Alloxan monohydrate + Glibenclamide 0.5 mg/kg,).after 3rd day of the treatment with alloxan (125 mg/kg, i.p)
Group IV Alloxan monohydrate + PHF Capsule (200 mg/kg b.w) after 3rd day of the treatment with alloxan (125 mg/kg, i.p)
Group V Alloxan monohydrate + PHF Capsule (400mg/kg b.w) after 3rd day of the treatment with alloxan (125 mg/kg, i.p)
Group VI Alloxan monohydrate + PHF Vati (200 mg/kg b.w) after 3rd day of the treatment with alloxan (125 mg/kg, i.p)
Group VII Alloxan monohydrate + PHF Vati (400 mg/kg b.w) after 3rd day of the treatment with alloxan (125 mg/kg, i.p)

The treatment was started from the same day except normal control and diabetic control groups for a period of 10 days orally. During this period, animals in all groups had free access to standard diet and water. Blood glucose levels were estimated on 1st, 4th, 7th and 10th day of the treatment. Besides this during this study the body weight of the rats were recorded on 1st, 4th, 7th and 10th day of the treatment.

Statistical analysis
The data were expressed as mean ± SEM. The data of hypoglycemic activity, oral glucose tolerance test (OGTT), and antidiabetic activity were analyzed by one-way analysis of variance (ANOVA) followed by Dunnett's ttest for multiple comparisons. Values with $P < 0.05$ were considered significant.

3. Results and discussions

Acute toxicity studies on female rats showed no mortality at a dose of 2000 mg/kg, during a time period of 14 days. During the study, no noticeable responses were seen in the rats. This helps to predict that it does not contain any type of toxicity and is safe. In the OGTT, polyherbal preparation at a dose of 400 mg/kg significantly reduced the blood glucose level at 30 minutes after glucose administration. Standard drug glibenclamide produced activity at all the time interval tested [Table 1].Polyherbal preparation showed significant antidiabetic activity at both 200 and 400 mg/kg dose levels [Table 2].

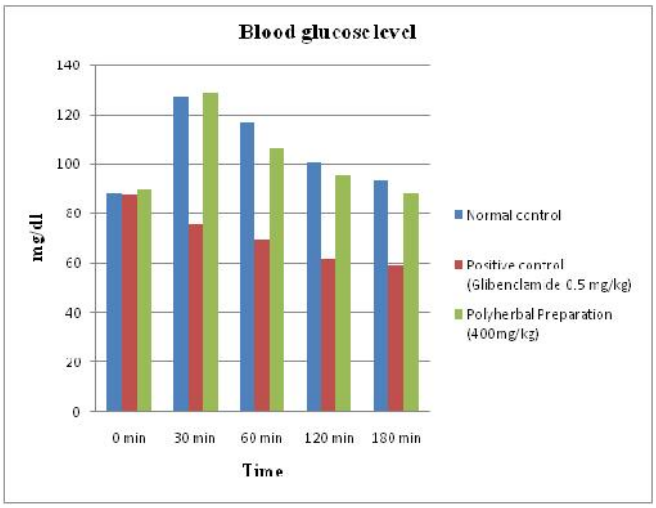

Figure 1: Graph showing effect of Oral glucose tolerance test of polyherbal preparation

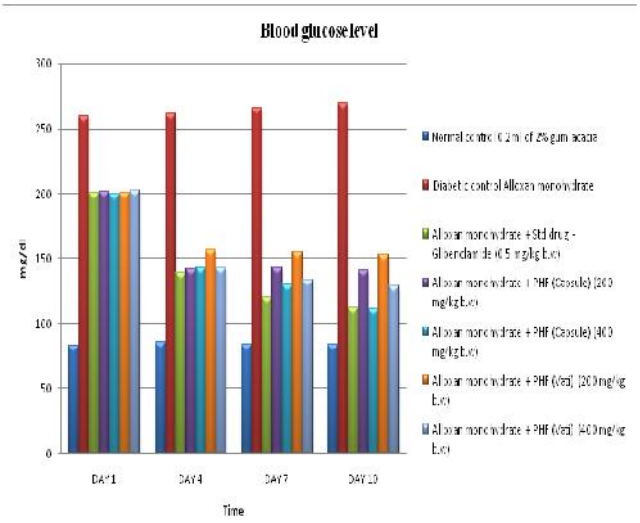

Figure 2: Graph showing Effect of ethanolic extract of Poly Herbal Formuation (Capsule), Poly Herbal Formuation (Vati) on Blood Glucose Levels (mg/dl) against alloxan induced diabetes mellitus in rats (10 days study)

Table 1: Oral glucose tolerance test of polyherbal preparation on blood glucose level (mg/dl) of normal rats

Group	Blood Glucose Level (mg/dl)				
	0 min	30 min	60 min	120 min	180 min
Normal control	88.00 ± 1.45	127.00 ± 1.58	116.30 ± 2.11	100.70 ± 1.91	93.50 ± 1.30
Positive control (Glibenclamide 0.5 mg/kg)	87.34 ±2.59	75.50 ±2.00**	69.33 ±1.13**	61.67 ±0.61**	59.11 ±1.11**
Polyherbal Preparation (400mg/kg)	89.6 ± 1.80	128.70 ± 1.53	106.50 ± 2.38*	95.40 ± 2.08*	87.83 ± 1.64 *

n=6 *p < 0.05, **p < 0.01 vs. Negative control (ANOVA followed by Dunnet's test)
Value expressed in mean ± SEM (mg/dl) of normal rats

Table 2: Effect of ethanolic extract of Poly Herbal Formuation (Capsule), Poly Herbal Formuation (Vati) on Blood Glucose Levels (mg/dl) against alloxan induced diabetes mellitus in rats (10 days study)

Groups	Treatment	Blood Glucose Levels (mg/dl)			
		DAY 1	DAY 4	DAY 7	DAY 10
I	Normal control 0.2ml of 2% gum acacia	83.05± 3.25	85.16±4.23	83.82±5.86(NS)	83.71±6.09 (NS)
II	Diabetic control Alloxan monohydrate	259.47±8.17	261.28±8.19	266.03±8.38 (NS)	269.33± 8.09 (NS)
III	Alloxan monohydrate + Std drug -Glibenclamide (0.5 mg/kg b.w)	200.17± 5.15	139.18± 2.13	120.52± 2.10**	111.84±3.10***
IV	Alloxan monohydrate + PHF (Capsule) (200 mg/kg b.w)	201.38±4.34	141.87± 2.10	142.56± 2.16**	140.82± 2.71***
V	Alloxan monohydrate + PHF (Capsule) (400 mg/kg b.w)	199.24± 4.80	142.29± 2.06	129.44± 1.77**	110.57± 2.17***
VI	Alloxan monohydrate + PHF (Vati) (200 mg/kg b.w)	200.17±4.65	156.48±2.63	154.76±2.51**	153.04±3.19***
VII	Alloxan monohydrate + PHF (Vati) (400 mg/kg b.w)	202.17±4.75	142.43±2.26	133.44±2.22**	128.64±1.51***

Alloxan monohydrate (120 mg/kg) was administered i.p, in sterile saline, single dose, 5 days before the administration of different ethanolic extracts. Standard drug, Glibenclamide and Poly Herbal Formulation (Capsule & Vati) given as ethanolic extracts in 2% gum acacia were administered orally for 10 days, in a single dose daily five days after confirmation of hyperglycemia. n=6 (No of animals in each group) DAY 10 compared with DAY 1; ***p< 0.001 very highly significant; p < 0.01 Highly Significant; p> 0.05 non-significant (NS)

4. Conclusion

Alloxan causes massive reduction in insulin release, through the destruction of ß-cells of the islets of Langerhans. In our study, we have observed a significant increase in the plasma insulin level when alloxan diabetic rats were treated with our polyherbal formulation. This could be due to Potentiation of the insulin effect of plasma by increasing the pancreatic secretion of insulin from existing ß-cells of islets of Langerhans or its release from bound insulin. The significant and consistent antidiabetic effect of polyherbal formulation in alloxan diabetic rats may also be due to enhanced glucose utilization by peripheral tissues. It can be concluded that this poly herbal formulation may be an ideal alternative for the existing synthetic formulation.

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