IJPSR (2023), Volume 14, Issue 4 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 10 January 2023; received in revised form, 19 March 2023; accepted 28 March 2023; published 01 April 2023

EVALUATION OF ANTIDIABETIC ACTIVITY OF POLYHERBAL FORMULATION AGAINST STREPTOZOCIN –NICOTINAMIDE INDUCED DIABETES IN RATS

Monika Pandey * and Mahesh Kumar Gupta

School of Pharmacy, Career Point University, Kota - 324005, Rajasthan, India.

Keywords:

Gymnema sylvestre, Momordica charantia Curcuma longa, Eugenia jambolana, Embilica officinalis, Polyherbal Formulation

Correspondence to Author:
Monika Pandey

Ph.D Scholar,
School of Pharmacy, Career Point University, Kota - 324005, Rajasthan, India.

E-mail: monika.mpharma@gmail.com

ABSTRACT: 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 Streptozocin -nicotinamide 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 streptozocin -nicotinamide 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.

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.

QUICK RESPONSE CODE

DOI:
10.13040/IJPSR.0975-8232.14(4).2002-10

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.14(4).2002-10

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* and *Trigonella 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*.

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 Dec 2021 to March 2021 from the in and around local areas of Jaipur & authenticated by Mr. Bhima Ram Choudhary, Head Deputy Conservator of forest Sikar, dated 18/12/2022. were deposited in Laboratory, Voucher specimen No. DCF/2021/12 for leaves of *Gymnema sylvestre*, DCF/2021/12 for fruits of *Embilica officinalis*, DCF/2021/12 for fruits of *Momordica charantia*, DCF/2021/12 for seeds of *Eugenia jambolana* and DCF/2021/12 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 Accuprac Research lab Ahemdabad., 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*. The study was approved by the Institute Animal Ethics Committee of Accuprac Research lab Ahemdabad(ARLP/13/IAEC/P-230)., India, India and all the animal experiments were carried out according to the Committee for the Purpose of Control and Experiments on Animals (CPCSEA) guidelines.

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: Diabetes was induced in overnight-fasted rats by administering single intra peritoneal (i.p.) injection of freshly prepared streptozotocin (STZ) 50 mg/kg b.w. followed by 120 mg/kg of nicotimanide (NIC) in 0.1 M citrate buffer (pH 4.5) in a volume of 0.5 ml/kg b.wt. Diabetes was confirmed in the STZ + NIC treated rats by measuring fasting blood glucose levels after 48 h of induction. After 24 h of STZ + NIC injection, the rats were given 5% w/v of glucose solution (2 ml/kg b.w.) to prevent hypoglycemic mortality. Rats with fasting blood glucose of more than 200 mg/dl were considered as diabetics and they were divided randomly into four different groups. The standard (glibenclamide) and herbal formulation were suspended in 1% w/v carboxymethyl cellulose (CMC) and administered once daily through oral gavage for 21 consecutive days. The blood samples were collected on 1st, 7th, 14th, and 21st days of the treatment, through the tail vein of rats by pricking and were immediately used for the estimation of blood glucose with a glucometer. Weekly body weight variations were monitored for all the experimental animals. (Prasad *et al*, 2009)

At the end of the experiment, the blood sample was withdrawn from all the experimental animals through retro-orbital plexus puncture/posterior vena cava in plain and sodium ethylene diamine tetra acetic acid (EDTA) tubes for biochemical analysis (Parasuraman S *et al.*, 2010). Finally the animals were sacrificed by diethyl ether anesthesia and liver and pancreatic tissues were excised and used for biochemical and pathological analysis. Part of the tissue sample was preserved in an ice-cold container for biochemical analysis and the remaining was stored in 10% formalin solution for histo-pathologic analysis. The male Wistar rats were divided into five different groups of six animals each as follows.

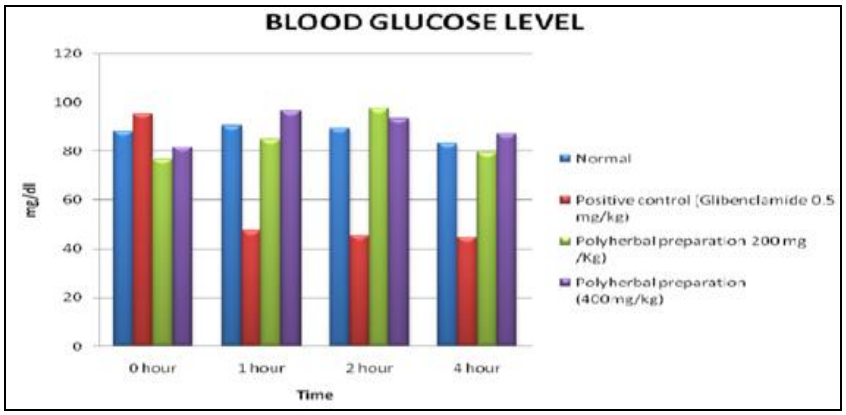
Group I	Normal control
Group II	Diabetic control
Group III	Diabetic rats treated with polyherbal preparation (Capsule) (200mg/kg)
Group IV	Diabetic rats treated with polyherbal preparation (Capsule) (400mg/kg)
Group V	Diabetic rats treated with polyherbal preparation (Vati) (200mg/kg)
Group VI	Diabetic rats treated with polyherbal preparation (Vati) (400mg/kg)
Group VII	Diabetic rats treated with glibenclamide (0.5 mg/kg).

Biochemical Analysis: The whole blood sample was used for the estimation of glucose (One-Touch Horizon glucometer; Ortho-Clinical Diagnostics, Johnson and Johnson Company, USA), hemoglobin and glycosylated hemoglobin (HbA1c). The plasma sample was used for the estimation of insulin (radioimmunoassay kit; Diasorin, Italy). The serum was used for the estimation of biochemical markers such as creatinine, urea, protein, liver glycogen, total serum cholesterol, serum triglyceride, high density lipoprotein (HDL)-cholesterol, serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT). The biochemical markers were measured using a Prietest Easylab - Biochemistry Analyser (Robonik [India] Private Limited) and the LAB-KITS enzymatic kits. The liver tissue homogenate was used for the estimation of protein and glycogen.

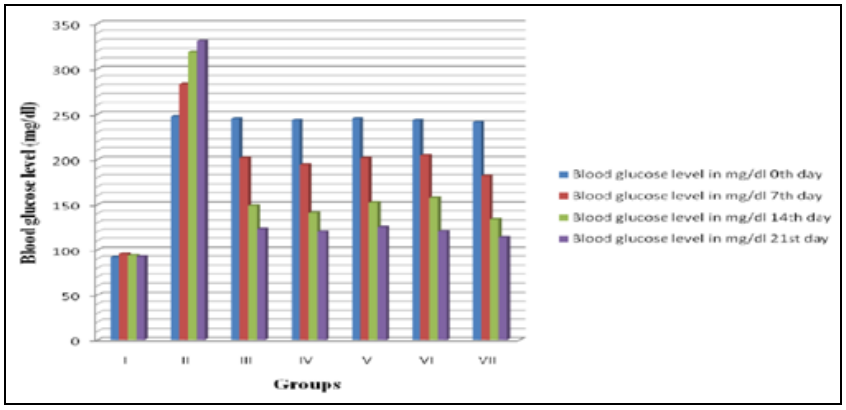
Statistical Analysis: The data were expressed as mean ± SEM. The data of hypoglycemic activity, oral glucose tolerance test (OGTT) and antidiabetic activity were analyzed by one-way analysis of variance (ANOVA) followed by Dunnett's ttest for multiple comparisons. Values with $P < 0.05$ were considered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

RESULTS AND DISCUSSION: 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 400mg/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**.



GRAPH 1: GRAPH SHOWING EFFECT OF ORAL GLUCOSE TOLERANCE TEST OF POLYHERBAL PREPARATION



GRAPH 2: GRAPH SHOWING EFFECT OF POLYHERBAL FORMULATION ON FASTING BLOOD GLUCOSE LEVELS (mg/dL) IN STZ-AND NIC-INDUCED DIABETICRATS

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.

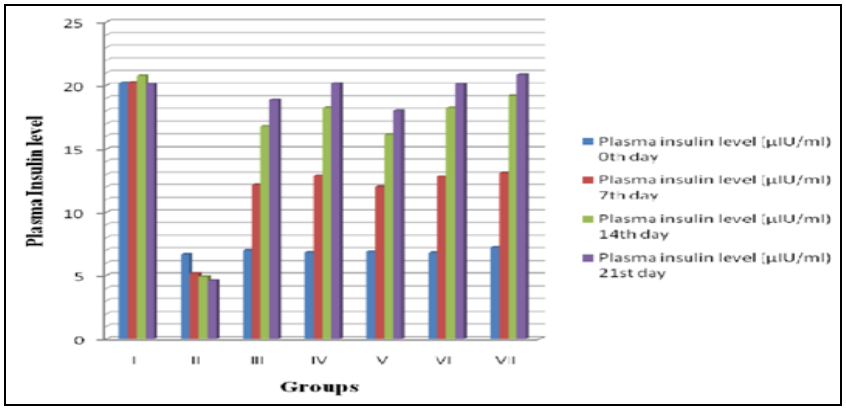
TABLE 2: EFFECT OF POLYHERBAL FORMULATION ON FASTING BLOOD GLUCOSE LEVELS (MG/DL) IN STZ-AND NIC-INDUCED DIABETIC RATS

Groups	Treatments	Blood glucose level in mg/dl			
		0^{th} day	7^{th} day	14^{th} day	21^{st} day
I	Normal control 0.2ml of 2% gum acacia	91.43±0.59	95.12±1.23	93.42±1.19	92.07±1.05
II	Diabetic controlSTZ	247.53±2.10	282.87±2.19	318.61±1.03	330.51±1.23
III	STZ+ PHF (Capsule) (200mg/kg)	245.03±2.01***	201.62±2.29***	148.81±1.78***	123.20±1.98***
IV	STZ + PHF (Capsule) (400mg/kg)	243.43±2.10***	194.29±2.23***	140.51±1.90***	119.82±2.10***
V	STZ + PHF (Vati) (200mg/kg)	245.12±2.83***	201.43±2.18***	152.20±2.65***	125.23±2.13***
VI	STZ + PHF (Vati) (400mg/kg)	243.39±2.19***	204.31±2.43***	157.40±2.09***	120.31±1.98***
VII	STZ + Std drug - Glibenclamide (0.5 mg/kg)	241.32±2.10***	181.37±2.78***	133.43±2.15***	113.44±1.98***

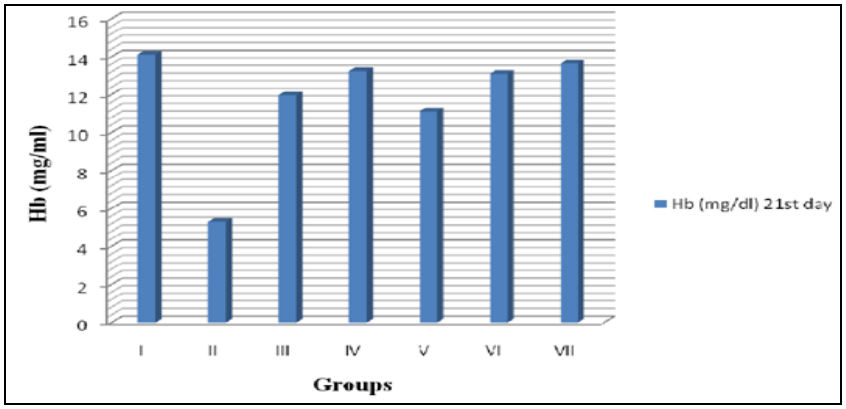
n=6 *p < 0.05, **p < 0.01 vs. Negative control (ANOVA followed by Dunnet's test) Value expressed in mean ± SEM (mg/dl) of normal rats.

Diabetic control animals showed severe hyperglycemia compared to normal animals. The mean blood glucose level in the diabetic control group on day 0 was 247.53 ± 2.10 mg/dl and on day 21 was 330.51 ± 1.23 mg/dl. It was observed that the standard drug glibenclamide lowered the blood glucose level significantly, bringing it back to near normal level, whereas the polyherbal capsule at 200 mg/kg and 400 mg/kg significantly (P<0.001) decreased the fasting blood serum glucose level in the diabetic rats on 7th, 14th and 21st days, as compared to the diabetic control group. The results are presented in **Table 2** and graph 2.

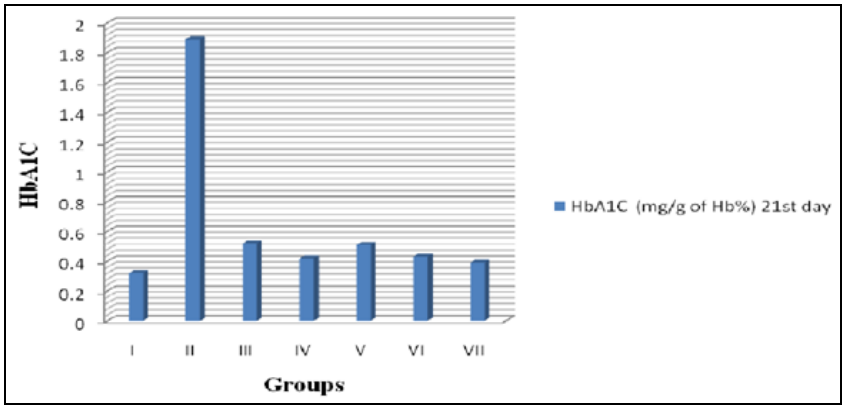
Biochemical Analysis: Diabetic animals showed significant decrease in plasma insulin, hemoglobin, and HbA1c levels when compared with control animals. Herbal formulation and glibenclamide reversed the insulin depletion in diabetic condition and also brought back the hemoglobin and HbA1c levels to normal. The results were given in **Table 3** and graph 3, 4, 5.



GRAPH 3: GRAPH SHOWING EFFECT OF POLYHERBAL FORMULATION ON PLASMA INSULIN LEVEL IN STZ-AND NIC-INDUCED DIABETIC RATS



GRAPH 4: GRAPH SHOWING EFFECT OF POLYHERBAL FORMULATION ON HB LEVEL IN STZ-AND NIC-INDUCED DIABETIC RATS



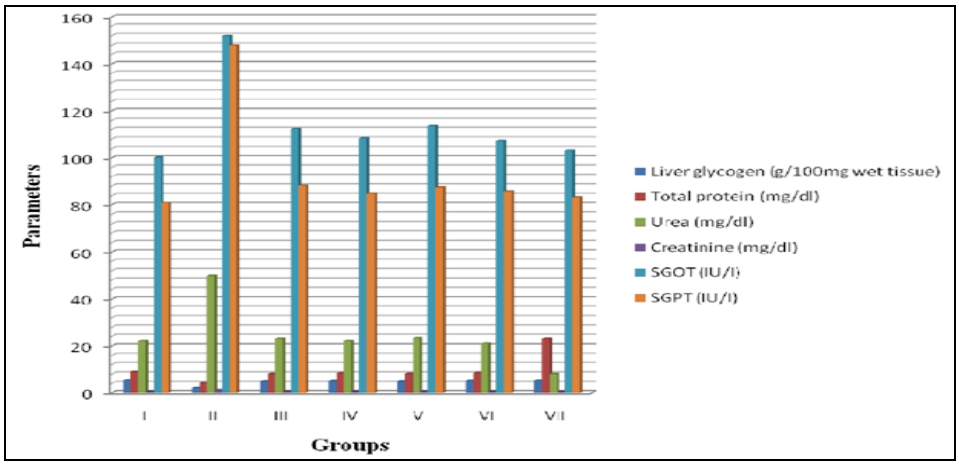
GRAPH 5: GRAPH SHOWING EFFECT OF POLYHERBAL FORMULATION ON HBA1C LEVEL IN STZ-AND NIC-INDUCED DIABETIC RATS

TABLE 3: EFFECT OF POLYHERBAL FORMULATION ON PLASMA INSULIN LEVEL IN STZ-AND NIC-INDUCED DIABETIC RATS

Groups	Treatments	Plasma insulin level (µIU/ml)				Hb (mg/dl)	HbA1C (mg/g of Hb%)
		0th day	7th day	14th day	21st day	21st day	21st day
I	Normal control	20.21± 0.01	20.24± 0.29	20.78± 0.54	20.13± 0.02	14.12± 0.99	0.32± 0.01
II	Diabetic control	6.68± 0.01	5.15± 1.87	4.91± 0.56	4.62± 0.39	5.30± 0.31	1.89± 0.50
III	PHF (Capsule) (200 mg/kg)	6.98± 1.48**	12.16± 0.65***	16.79± 0.52***	18.87± 0.40***	11.96± 0.41***	0.52± 0.05***
IV	PHF (Capsule) (400 mg/kg)	6.82± 1.20**	12.89± 1.43***	18.23± 1.02***	20.18± 0.27***	13.23± 0.58***	0.42± 0.06***
V	PHF (Vati) (200 mg/kg)	6.87± 1.28**	12.02± 1.50***	16.12± 1.08***	18.01± 0.69***	11.12± 0.81***	0.51± 0.02***
VI	PHF (Vati) (400 mg/kg)	6.80± 1.01**	12.82± 1.20***	18.21± 1.03***	20.12± 0.89***	13.09± 0.65***	0.43± 0.04***
VII	Glibenclamide (0.5 mg/kg)	7.21± 0.40**	13.12± 0.45***	19.20± 0.62***	20.87± 0.10***	13.63± 0.83***	0.39± 0.02***

PHF: Polyherbal Formulation, Hb: Hemoglobin, HbAIC: Glycosylated hemoglobin. Values are expressed as Mean±SEM (n=6). ** p<0.01, ***p<0.001 compared to diabetic control (one-way ANOVA followed by a Dunnett's t test) STZ: Streptozotocin, NIC: Nicotinamide

Diabetic animals showed significant reduction in liver glycogen and total protein levels when compared to the control animals, whereas herbal formulation and glibenclamide treated animals showed normal liver glycogen and total protein levels. The prevention of depletion of glycogen in the liver tissue was possibly due to stimulation of insulin release from the β cells that activates the glycogen synthase system. Effects of herbal formulation and glibenclamide on the liver and renal markers of diabetic animals are presented in **Table 4** and graph 6.



GRAPH 6: GRAPH SHOWING EFFECT OF POLYHERBAL FORMULATION ON SERUM CREATININE, PROTEIN, UREA, AND LIVER GLYCOGEN LEVELS IN STZ-AND NIC-INDUCED DIABETIC RATS

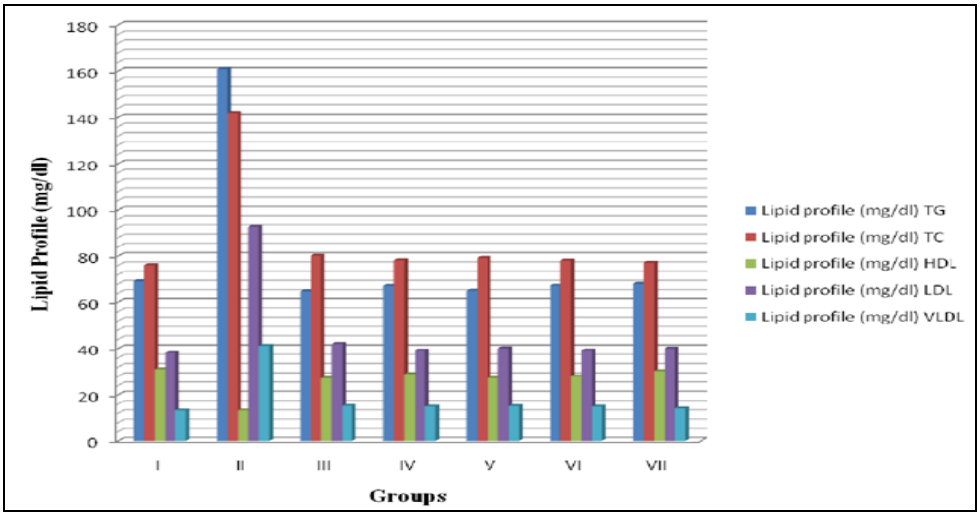
TABLE 4: EFFECT OF POLYHERBAL FORMULATION ON SERUM CREATININE, PROTEIN, UREA, AND LIVER GLYCOGEN LEVELS IN STZ-AND NIC- INDUCED DIABETIC RATS

Groups	Treatments	Liver glycogen (g/100mg wet tissue)	Total protein (mg/dl)	Urea (mg/dl)	Creatinine (mg/dl)	SGOT (IU/I)	SGPT (IU/I)
I	Normal control	5.52± 1.03	8.98± 0.12	22.10± 0.11	0.42± 0.11	100.12± 2.81	80.89± 0.09
II	Diabetic control	2.10± 0.05	4.12± 10.08	49.92± 0.59	1.10± 0.06	151.90± 1.39	148.00± 2.01
III	PHF (Capsule) (200 mg/kg)	5.02± 1.04***	8.20± 0.07*	23.01± 0.61***	0.53± 0.76*	112.21± 2.36***	88.21± 1.21***
IV	PHF (Capsule) (400 mg/kg)	5.21± 0.71***	8.44± 0.71**	22.10± 0.48***	0.49± 0.02**	108.29± 2.22***	84.81± 1.91***

V	PHF (Vati) (200 mg/kg)	5.03± 1.06***	8.24± 0.09*	23.2± 0.62***	0.52± 0.64**	113.49± 2.39***	87.38± 1.20***
VI	PHF (Vati) (400 mg/kg)	5.29± 0.88***	8.54± 0.81**	21.02± 0.51***	0.48± 0.05**	107.23± 2.36***	85.71± 1.90***
VII	Glibenclamide (0.5 mg/kg)	5.41± 0.52***	23.01± 0.57***	8.12± 0.68**	0.40± 0.08**	103.21± 2.14***	83.24± 1.41***

PHF: Polyherbal Formulation. Values are expressed as Mean±SEM (n=6). ** p<0.01, ** p<0.01, ***p<0.001 compared to diabetic control (one-way ANOVA followed by a Dunnett's t test) STZ: Streptozotocin, NIC: Nicotinamide

The diabetic rats showed significant (P < 0.001) increase in serum lipid profiles except HDL when compared to the control animals, whereas the levels in the treatment group remained within normal limits at the end of the study. Effects of herbal formulation and glibenclamide on the lipid profile of diabetic animals are presented in **Table 5** and graph 7.



GRAPH 7: GRAPH SHOWING EFFECT OF ETHANOLIC EXTRACTS OF THE POLYHERBAL FORMULATION ON SERUM LIPIDS

TABLE 5: EFFECT OF ETHANOLIC EXTRACTS OF THE POLYHERBAL FORMULATION ON SERUM LIPIDS

Groups	Treatments	Lipid profile (mg/dl)				
		TG	TC	HDL	LDL	VLDL
I	Normal control	69.10±0/28	76.10±1.89	31.01±0.92	38.09±1.56	13.18±0.62
II	Diabetic control	160.87±0.61	141.90±0.59	13.18±0.18	92.59±0.21	41.16±0.25
III	PHF (Capsule) (200 mg/kg)	64.89±0.48***	80.10±0.49***	27.12±0.98***	41.90±0.07***	15.16±0.87***
IV	PHF (Capsule) (400 mg/kg)	67.12±1.03***	78.16±1.03***	28.91±0.82***	39.10±0.92***	14.82±0.45***
V	PHF (Vati) (200 mg/kg)	65.12±0.44***	79.16±0.50***	27.22±0.96***	40.12±0.06***	15.05±0.86***
VI	PHF (Vati) (400 mg/kg)	67.23±1.09***	78.01±1.01***	27.88±0.80***	39.14±0.90***	14.81±0.44***
VII	Glibenclamide (0.5 mg/kg)	68.01±0.09***	77.09±0.46***	30.21±0.36***	39.97±1.05***	14.00±0.16***

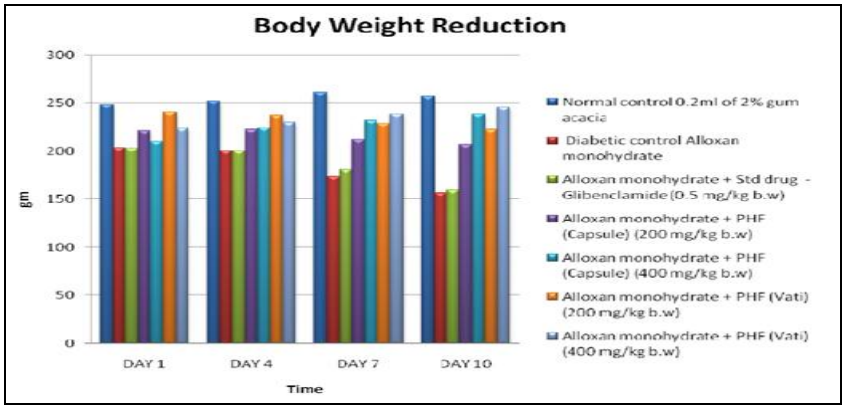
PHF: Polyherbal Formulation. Values are expressed as Mean±SEM (n=6). ** p<0.01, ** p<0.01, ***p<0.001 compared to diabetic control (one-way ANOVA followed by a Dunnett's t test) STZ: Streptozotocin, NIC: Nicotinamide, TG: Triglycerides, TC: Total Cholesterol, HDL: High density lipoprotein, LDL: Low density lipoprotein, VLDL: Very low density lipoprotein.

Average Body Weight: The rats of group I showed an average weight of while the rats of group II which received only STZ showed a very highly significant decrease in average body weight. The rats of the groups receiving Poly herbal formulation showed a dose dependent increase in average body weight. During the course of these studies average body weight were recorded on day 0, day 7, day 14 and day 21 Effect of Poly herbal formulation (capsule & Vati) on Average Body Weight (gms) against Streptozotocin induced diabetes mellitus in rats are presented in **Table 6** and graph 8.

TABLE 6: EFFECT OF POLY HERBAL FORMULATION (CAPSULE & VATI) ON AVERAGE BODY WEIGHT (GMS) AGAINST STREPTOZOTOCIN INDUCED DIABETES MELLITUS IN RATS

Groups	Treatments	Average Body weight (in gms)			
		1th day	7th day	14th day	21st day
I	Normal control 0.2ml of 2% gum acacia	248.48±8.11	251.90±9.83	261.12±10.37(NS)	257.23±11.09(NS)
II	Diabetic controlSTZ	203.83±7.54	200.16±6.51	173.56±6.67**	156.8±7.61**
III	STZ+ PHF (Capsule) (200 mg/kg)	220.82±9.49	222.17±10.75	212.30±10.82*	207.18±11.12**
IV	STZ + PHF (Capsule) (400 mg/kg)	210.17±12.18	223.98±12.03	232.20±11.14*	238.78±10.12**
V	STZ + PHF (Vati) (200 mg/kg)	240.13±9.15	237.13±9.17	228.80±12.58*	222.12±13.83**
VI	STZ + PHF (Vati) (400 mg/kg)	223.87±6.71	230.42±5.76	238.80±4.76*	245.50±4.27**
VII	STZ + Std drug - Glibenclamide (0.5mg/kg)	203.17±4.91	200.67±4.94	180.92±7.63*	160.00±8.69**

N = 6 (Number of animals in each group) DAY 1 compared with DAY 21*p< 0.05 significant; **p<0.01 highly significant; ***p< 0.001 very highly significant; p> 0.05 non-significant (NS).



GRAPH 8: GRAPH SHOWING EFFECT OF POLY HERBAL FORMULATION (CAPSULE & VATI) ON AVERAGE BODY WEIGHT (GMS) AGAINST STREPTOZOTOCIN INDUCED DIABETES MELLITUS IN RATS

CONCLUSION: In conclusion, these formulations showed significant anti-diabetic effect in diabetic rats after oral administration. Thus the claim made by the traditional Indian systems of medicine regarding the use of these plants in the treatment of diabetes stands confirms. STZ is toxic glycoside obtained from Streptomyces achromogenes, a gram-positive bacterium. It accumulates in pancreatic β cells via the glucose transporter 2 (GLUT2) and reduces their expression.

The alkylating properties of the STZ modify the biological macromolecules, fragment DNA and destroy the β cells, causing insulin-dependent diabetes. In the diabetic control group, severe body weight loss was observed, which may be due to increased muscle wasting and loss of tissue proteins. In the present study, the treatment groups showed significant improvement in body weight, which indicates that polyherbal formulation and glibenclamide prevent the hyperglycemia-induced muscle wastage. The reduction in glucose levels may be due to increase in plasma insulin levels or enhanced transport of blood glucose in the peripheral tissue. The study gives evidence that the polyherbal formulation increases the plasma insulin levels and has promising antidiabetic activity. Diabetic animals showed enhanced levels of HbA1c due to excessive production of glucose in blood, which further reacts with blood hemoglobin and produces HbA1c. The diabetic hyperglycemia induced by STZ and NIC causes elevation of plasma levels of SGPT, SGOT, urea and creatinine, which are considered as significant markers of liver and renal dysfunction.

The polyherbal formulation treated animals reversed the effect of STZ and NIC on the liver and renal markers. This may be due to the hepatoprotective mechanism of the individual herbs present in the polyherbal formulation. STZ diabetic rat has increased levels of lipid peroxides and

reactive oxygen species, which cause hyperglycemia. Incessant generation of free radicals can lead to tissue damage through peroxidation of unsaturated fatty acids. The polyherbal formulation treated animals inhibited the hyperglycemia induced by STZ, which may be due to the free radical scavenging properties of the individual herbs present in it.

ACKNOWLEDGEMENT: NIL

CONFLICTS OF INTEREST: NIL

REFERENCES:

1. Reynolds JEF: editor. Martindale-The Extra Pharmacopoeia 30th Edition. The Pharmaceutical Press London 1997.
2. Deb L and Dutta A: Diabetes mellitus its possible pharmacological evaluation Techniques and naturopathy. Int J Green Pharmacy 2006; 1: 7-28.
3. Murray MT: Healing power of Herbs. 2nd Edition Gramercy Books 1995; 357.
4. Grover JK, Yadav S and Vats V: Medicinal plants of India with anti-diabetic potential, J Ethnopha 2002; 81-81.
5. Das AV, Padayutti PS and Paulose CS: Ind J Exp Biol 1996; 34: 341-45.
6. Shukla R, Sharma S B, Puri D, Prabhu KM & Murthy PS: Medicinal plants for treatment of diabetes mellitus, Indian Journal of Clinical Biochemistry 2000; 15: 169.
7. Ghosh MN: Fundamentals of experimental Pharmacology. Ed 3rd Hilton and Company 2005; 190–7.
8. Naik SR, mandlik RV and Desai SK: Antidiabetic activity of a polyherbal formulation. IJEB 2008; 46: 599-606.
9. Chattopadhyay RR: A comparative evaluation of some blood sugar lowering agents of plant origin. J Ethnopharmacol 1999; 67: 367-72.
10. Kuttan R and Joy KL: Anti-diabetic activity of Picrorrhiza kurroa extract, J. Ethnopharmacol 1999; 167: 143-8.
11. Shanmugasundaram K and Panneerselvam C: Enzyme changes and glucose utilisation in diabetic rabbits: the effect of Gymnema sylvestre, R.Br, Journal of Ethnopharmacology 1983; 7(2): 205–34.
12. Sharma PV: Dravyagun Vigyan, Chaukhamaba Sanskrit Series Varanasi 1956; 2.
13. Shirwaikar AA, Shirwaikar Annie, Aswatha Ram HN and Upadhyay DK: 2005.
14. Formulation and evaluation of *Boswella serrata* tablets. International J of Pharmaceutical Science 67(4): 427-431.
15. Shoback, David G. Gardner and Dolores: Edited by Greenspan's basic & clinical endocrinology 9th ed., New York, McGraw-Hill Medical 2011; 17.
16. Singh B, Saxena AK and Chandan BK: Adaptogenic activity of a novel, withanolide-free aqueous fraction from theroot of *Withania somnifera*. Phytother Res 2001; 15: 311-18.
17. Soni Himesh: Qualitative & Quantitative Profile of Curcumin from Ethanolic Extract of Curcuma Long, International Research J of Pharmacy 2011; 2(4): 180-184.
18. Srivastava Shikha, Vijay Kumar Lal and Kamlesh Kumar Pant: Polyherbal formulations based on Indian medicinal plants as antidiabetic phytotherapeutics, Phytopharmacology 2012; 2(1): 1-15.

How to cite this article:
Pandey M and Gupta MK: Evaluation of antidiabetic activity of polyherbal formulation against streptozocin –nicotinamide induced diabetes in rats. Int J Pharm Sci & Res 2023; 14(4): 2002-10. doi: 10.13040/IJPSR.0975-8232.14(4).2002-10.