PRETREATMENT OF ALBINO RATS WITH POLY HERBAL EXTRACT OF *ANDROGRAPHIS PANICULATA, BOUGAINVILLEA SPECTABILIS AND CINNAMOMUM TAMALA* FOR PROTECTION AGAINST STREPTOZOTOCIN INDUCED DIABETES MELLITUS

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ABSTRACT

Phytomedicine is said to be less harmful and devoid of adverse effects than synthetic medicine. Therefore, the present study is an effort to study antihyperglycemic activity of polyherbal formulation of selected plants against streptozotocin encouraged diabetes. Orally administration of polyherbal formulation in the dose of 300 & 500 milli gram/kilo gram of body weight shows major antihyperglycemic activity at the end of 21th day. Anti-diabetic effect of it at both the dose is comparable to that of herbal control as well as Glibenclamide at 10mg/Kg dose. Because each individual medication in this polyherbal combination extract has been found to have anti-diabetic effects, the anti-diabetic impact of polyherbal formulation could be attributable to the presence of more least 1 antihyperglycemic component and their combinatorial characteristics.

KEY WORD: Phytomedicine, Antihyperglycemic activity, polyherbal formulation

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INTRODUCTION

Diabetes mellitus is a metabolic disease characterized by hyperglycemia that affecting people all over the world.It is causedby changes in theinsulin production, action produced by insulin and can be both. Chronic hyperglycemia, a typical complication by untreated diabetes, damages, malfunctions, and eventually fails a variety of organs, like the kidneys, heart, nerves, blood vessels and eyes. Type I and type II diabetes are the two most common kinds of diabetes.[1]

Insulin-dependent diabetes, also referred as type I diabetes, is characterized by low insulin production and the requirement of daily insulin injections. The pancreatic beta cells were killed as a result of autoimmune injury of the pancreatic cell.

Type-II diabetes, commonly known as non-insulin-dependent diabetes, is characterized by the body's inefficient insulin use. Obesity, poor diet, insufficient physical exercise, advanced age, hypertension, as well as other risk factors are all associated to type II diabetes. [2-3] Gestational diabetes, which is caused by glucose intolerance and occurs during pregnancy, is another kind of diabetes that has been found. This is a temporary state, but it has the potential to lead to diabetes4 in the long run. By the World Health

Organization, diabetes affect 422 million of people worldwide (WHO).

It killed 1.5 million individuals in 2012, with type-II diabetes afflicting the bulk of the population. Type-II diabetes was formerly solely diagnosed in adults; however, it increasingly affects children and teenagers as well. The state of oxidative stress is well-known. Effective diabetes treatment, on the other hand, is still a work in progress [9]. Alternatives are being investigated right now.

As medicinal plants are usually an excellent supply of drugs, they played a significant part in this study. [5] Many plants are shown to be useful in the diabetes treatment in India. Approximately 800 plants have been identified as having antidiabetic potential based on ethnobotanical data10. We may be able to identify novel medications that are both therapeutically active and less expensive based on our expertise and extensive survey of medicinal plants. Herbs provide a number of benefits, like being readily available, having few adverse effects, and so forth. This paper provides an overview of anti-diabetic medicinal plants that have been found to be effective. A comprehensive literature review revealed therapeutic activity[6].

DESCRIPTION OF PLANTS

Andrographis paniculata

Family: *Acanthaceae*

Synonyms: Green chirata, king of bitters (english); Kirayat (hindi)

Parts used: Aerial parts

Botanical description: *Andrographis paniculata* grows erect shady places. The dark green stem has longitudinal grooves and wings along the sides and is squared in cross-section. The little blooms are borne in racemes that stretch outward. The fruit is in the shape of a capsule. It has a lot of yellow-brown seeds.

Uses: Antityphoid and antifungal properties of the plant extract, as well as antihepatotoxic, antibiotic, antimalarial, antihepatitic, antithrombogenic, and anti-inflammatory properties. In vitro growth of numerous tumor cell lines representing diverse kinds of malignancies was suppressed by andrographolide therapy [7-8].

Bougainvillea spectabilis

Synonym: Bougainvillea spectabilis Comm. ex Juss. , Bougainvilla (english); Booganbel (hindi)

Parts used: Leaves, stems, flowers

Botanical description: *Bougainvillea spectabilis* Comm. ex Juss. Large prickly stem and long dangling branches characterize this woody climber. Petiole leaves are alternating, oval, and petiole leaves are petiole leaves. Flowers are grouped in threes and are surrounded by three large, purple bracts on each side.

Constituents and properties: B. glabra have been found to contain pinitol, beta cyanine, flavonoids, tannins, and alkaloids. The leaves are supposed to have anti-inflammatory qualities. B. spectabilis contains pinnitol, which is supposed to help people with non-insulin diabetes [11].

Uses: Anti-ulcer, Anti-diarrheal, Anti-microbial [9-10].

Cinnamomum tamala

Family: Lauraceae

Synonym: Laurus tamala Buch-Ham., Indian cassia lignea (english), Tamalapatra, Tejpat (hindi)

Parts used: Leaves

Botanical description: *Cinnamomum tamala Nees & Eberm.* seems to be an evergreen tree with lanceolate, glabrous leaves that are alternately arranged, opposite, and short stalked. 3-nerved from the ground up Cinnamomum is a genus of tropical tree and shrubs species with over 250 species.

Chemical constituents: Monoterpenoids were detected in abundance by extraction of essential oil from the leaves: Linalool (50%) is most abundant component, with -pinene, p-cymene, -pinene, and limonene each accounting for 5 to 10%. Only tiny amounts of phenylpropanoids are found: newer research claims 1% cinnamic aldehyde and no eugenol, whereas previous research claims traces of both chemicals.

Uses: C. tamala leaves are useful in the treatment of colic and diarrhoea. C. tamala essential oils were hydro distilled and tested for antifungal activity. Many ayurvedic remedies, such as sudarshan, choorna, and chanderprabhavati, use plant components [12-13].

MATERIAL AND METHODS

The plant materials required for preparation of a polyherbal formulation included the fresh leaves of *Cinnamomum tamala*, *Bougainvillea spectabilis*and aerial plant parts of *Andrographis paniculata* were collected in the month of November from the herbal garden of Uttaranchal university, and authenticated by Department of Botany, FRI, Dehradun.

Preparation of polyherbal extract for activity

Plant Material in a semi-dried was made free from all foreign impurities. After duration of 3 days, when plant material gets properly dried it was followed by coarse grinding with the help of miller. The grinded material will be sieved by 18 mesh size sieves in order to ensure uniform size for the preparation of aqueous extract of polyherbal plant mixture reduced to proper size. 200 gm of each of dried coarsely powdered leaves of *Bougainvillea spectabilis* dried arial parts of *Andrographis paniculata* & leaves of *Cinnamonium tamala* were dipped in 1.5 liters of distilled water and regularly shaken for a time period of nearly 48 hrs. till the plant materials got completely exhausted. Solvent was removed by filtering it through muslin cloth & freely extractable substances was removed and extract concentrated with the help of rotatory evaporator pressure of 72mm bar and temperature of 45ºC for approximately 6 hrs. It was then dried over the electric water bath at the bath temperature of 35ºC and stored at 4ºC. It was then reduced to powdered form and preserved in a glass reagent bottle in the refrigerator at 2-4ºC till experimentation.

Preparation of the extracts for TLC

50grams of coarsely powdered plant materials of *Bougainvillea spectabilis, Cinnamomum tamala* and *Andrographis paniculata* were separately macerated with 200ml of water. It was oncentrated using rotavapour and dried and dissolved in sufficient volume of ethanol needed to dissolve the extracts in separate eppendroffs Precoated silica gel-G TLC plates were used applied through fine capillary carefully corresponding to individual extracts and polyherbal extract. Dipped in a chamber containing mobile phase (solvent systems) in two different concentrations as solvent A: Hexane: Ethyl Acetate (80:20) and solvent B: hexane: ethyl acetate (70:30). The spots were visualized and RF was calculated

Animal used for the experiment

Adult albino rats (CF Strain) of both sexes 3-4 weeks old weighed from 150-250 grams were obtained from animal house named as *in-vivo* testing facility from department of pharmacology, Shidhartha Institute of Pharmacy. The animal ethical committee of the concerned institution gave its approval to the study protocol.

Designing of experimental protocol and in-vivo studies

21 days experimental protocol was designed for the study. For estimation of blood glucose, tail bleeding technique was used. Readings were taken for blood glucose by blood glucose test strips on the day after overnight fasting or fasting and then after 24 hrs, 3rd, 7th and 21st day after induction. Readings were also taken for blood glucose by GOD-POD kit at the duration of 0 day (after overnight fasting) and then 7th and 21st day of induction. All of the rats are randomly separated into the six groups of five rats.

Group 1 served as vehicle control which received 1ml distilled water only daily for 3 weeks. **Group 2** served as herbal control which received Diabecon at the dose concentration of 1gram/kilogrambody weight daily for 3 weeks.
Group 3 served as treatment group receiving polyherbal extract at the dose of 500milli gram/kilo gram of body weight. daily for 3 weeks.
Group 4 served as positive control group receiving Diaonil (Glibenclamide) at the dose concentration of 10 milligram/kilo gram body weight for 3 weeks.
Group 5 served as negative control which contains only STZ induced diabetic rats not receiving any drug.
Group 6 served as treatment group receiving polyherbal extract at the dose concentration of 300mg/kg body wt. daily for 21 weeks.

In-vivo study protocol includes the standardization of dose of STZ in rats (60mg/kg body wt.), and induction by streptozotocin as as single intra peritoneal parenteral dose of (60 milligram/kilogram of body wt.). The study comprised rats with a blood sugar level of less than of 200 mg/dl. After 1st day, the blood glucose levels were measured and it was confirmed that the induction was successful in all the animals of all the groups The dosing started after 48 hrs. of induction that is on the 2nd day till then the diabetes remained stable and no mortality was observed and was done once a day daily for 21 days. Next sampling was done on a day after termination of last dosing and serum was isolated from the whole blood and preserved in -20ºC for biochemical analysis. For biochemical analysis**,** blood sample was collected using Retro-orbital plexus puncture method.

RESULTS AND DISCUSSION

Table 1: Effects of polyherbal extract on albino rats by body weight on normal and standardized triggered diabetic

GROUPS	DAYS AFTER DOSING			
	0	3	7	21
GROUP 1 (Vehicle)	172.2 ± 3.9	176.2 ± 3.2	176 ± 1.9	185 ± 6.0
GROUP 2 (Herbal Control)	194.8 ± 5.5	182.8 ± 10.7	190 ± 13.8	173.2 ±15.7
GROUP 3 (500 mg/kg b. wt)	186.8 ± 5.4	170.4 ± 8.4	161 ± 6.0	161 ± 6.1
GROUP 4 (Positive control)	200 ± 2.0	183.2 ± 6.0	177 ± 10.4	170.8 ± 5.0
GROUP 5 (Negative control)	200.4 ± 7.9	197.2 ± 6.4	180 ± 5.2	174 ± 2.9
GROUP 6 (300 mg/kg b. wt)	193.6 ± 3.6	189.6 ± 4.8	189 ± 4.8	183 ± 4.9

Table 2: Effects of polyherbal extract on blood glucose (by GOD-POD Kit) on normal and standardized triggered diabetic albino rat

GROUPS	DAYS AFTER DOSING		
	0	7	21
GROUP 1 (Vehicle)	75.29±4.2	78.51±7.2	68.70±4.8
GROUP 2 (Herbal Control)	86.48 ± 2.9	537.06±15.460^{NS}	375.29±30.228*
GROUP 3 (500 mg/kg b. wt)	76.719±4.5	270.88±10.7*	183.759±8.2**

GROUP 4 (Positive control)	124.99±9.9	180.33±11.5 *	65.53±3.7 *
GROUP 5 (Negative control)	81.63±6.5	521.595±19.0 #	247.73±9.6 #
GROUP 6 (300 mg/kg b. wt)	101.24±3.0	451.90±15.69 ***	157.487±6.4 *

The results represent the mean SEM of five rats. There was a substantial change in normal control and diabetic control on successive days.: #P< 0.001. On the respective days, there was a major change between the diabetic control and treated groups: **P< 0.05; On the respective days, there was a major change between the diabetic control group and treated groups:***P< 0.01;
On the corresponding days, there was a major change between the diabetic control and treated groups: *P< 0.001; on the corresponding days, there was a major change between the diabetic control and treated groups: *P< 0.001: non-significant change between the diabetic control and treated groups: NS

Table 3: Effects of polyherbal extract on blood glucose (by blood glucose Strip method) on normal and standardized triggered diabetic albino rats

GROUPS	DAYS AFTER DOSING				
	0 DAY		3 DAY	7 DAY	21 DAY
	Pre-induction	Post-induction			
GROUP 1 (Vehicle)	92.4 ± 2.4	95.2 ± 3.0	97.2 ± 2.3	110.6 ± 2.5	111.4 ± 3.0
GROUP 2 (Herbal Control)	133.2 ± 1.4	389.4 ± 11.0	538.4 ± 33 NS	363.4 ± 21.2 *	103 ± 6.4 *
GROUP 3 (500 mg/kg b. wt)	97.2 ± 2.3	355.2 ± 12.1	593.4 ± 3.9 NS	331 ± 14.3 *	106 ± 1.8 *
GROUP 4 (Positive control)	132.2 ± 5.7	528.4 ± 4.9	522 ± 17 NS	226.4 ± 5 *	106.6 ± 5.6 *
GROUP 5 (Negative control)	115.6 ± 10.2 $	372.4 ± 24.4 #	593 ± 26.8 #	577 ± 23.3 #	337.2 ± 6.1 #
GROUP 6 (300 mg/kg b. wt)	121 ± 8	508 ± 4.4	574 ± 13.1 NS	526.6 ±19.2 NS	99.6 ± 3.1 *

Prior to induction, there was no major change between the diabetic control *and normal control. #Majorchange between the normal and diabetic control on successive days: P < 0.001*
**Major change between the diabetic control and treated groups on the corresponding days: P < 0.001. NS Treatment groups differed from diabetes control groups in a non-significant way.*

Table 4: Effects of Polyherbal extract on lipid profile (serum levels of cholesterol) on normal and standardized triggered diabetic albino rats

GROUP	DAYS AFTER DOSING		
	0	7	21
GROUP 1 (Vehicle)	85.59 ± 2.3	88.68 ± 3.3	80.90 ± 1.2
GROUP 2 (Herbal Control)	79.53 ± 3.6	69.90 ± 1.6 *	82.86 ± 3.4 *

GROUP 3 (500 mg/kg b. wt)	96.39 ± 2.3	88.65 ± 3.6 NS	136.16 ± 2.8 *
GROUP 4 (Positive control)	72.69 ± 2.9	68.74 ± 0.6 *	111.72 ± 1.7 *
GROUP 5 (Negative control)	97.48 ± 1.3	91.93 ± 0.7 NS	196 ± 2.3 #
GROUP 6 (300 mg/kg b. wt)	90.65 ± 3.8	78.47 ± 2.6 **	118.98 ± 3.4 *

*On consecutive days, there was a major change between normal control and diabetic control: # P < 0.001.On the respective days, there was a major change between the diabetic control group and treated groups: *P < 0.001; **P < 0.05; Major change between the diabetic control group and treated groups on the respective days. Non-significant change between diabetic control groups and treated group: NS.*

Table 5: Effects of polyherbal plant aqueous extract on lipid profile (serum levels of triglyceride) on normal and standardized triggered diabetic albino rat

GROUPS	DAYS AFTER DOSING		
	0	7	21
GROUP 1 (Vehicle)	38.07 ± 1.6	34.01 ± 1.3	27.85 ± 2.1
GROUP 2 (Herbal Control)	35.13 ± 1.4	82.35 ± 1.8 *	47.48 ± 1.8 *
GROUP 3 (500 mg/kg b. wt)	47.66 ± 3.1	91.66 ± 3.2 *	57.74 ± 1.7 *
GROUP 4 (Positive control)	34.56 ±1.4	91.84 ± 1.7 *	57.53 ± 1.9 *
GROUP 5 (Negative control)	34.09 ± 3.3 NS	109.80 ± 2.0 #	91.66 ± 1.4 #
GROUP 6 (300 mg/kg b. wt)	68.81 ± 3.22	70.85 ± 5.2 *	63.75 ± 1.9 *

*On successive days, there was a major change between normal control and diabetes control group: # P < 0.001. On the following days, there was a majorchange between normal control and diabetes control group: *P < 0.001. Non-significant changes between thediabetic control groups and treated group: NS*

Table 6: Effects of Polyherbal extract on Liver function test serum levels of (SGOT) on normal and standardized triggered diabetic albino rat

GROUPS	DAYS AFTER DOSING		
	0	7	21
GROUP 1 (Vehicle)	10.7±1.0	8.62±0.6	11.39±0.6
GROUP 2 (Herbal Control)	9.8±0.5	8.8±0.3 *	11.03±0.5 *
GROUP 3 (500 mg/kg b. wt)	10.7±0.5	12.8±1.2 NS	7.3±0.3 *
GROUP 4 (Positive control)	13.2±0.5	18.8±0.6 NS	9.7±0.4 *
GROUP 5 (Negative control)	12.00±0.5 NS	15.5 ± 2.05 #	24.04 ± 2.3 #
GROUP 6 (300 mg/kg b. wt)	11.6±0.3	7.8±0.2 *	12.5±0.4 *

*On successive days, there was a major change between the normal control and diabetes control group: # P < 0.001. On the following days, there was a majorchange between normal control and diabetes control group: *P < 0.001. Non-significant change between diabetic control groups and treated group: NS.*

Table 7: Effects of Polyherbal extract on Liver function test (serum levels of SGPT) on normal and standardized triggered diabetic albino rat:

GROUPS	DAYS AFTER DOSING		
	0	7	21
GROUP 1 (Vehicle)	15.16 ± 0.3	10.4± 0.5	14.28 ± 1.7
GROUP 2 (Herbal Control)	17.04±0.3	26.69±0.5 NS	18.19±0.2 *
GROUP 3 (500 mg/kg b. wt)	18.12± 1.9	41.94± 3.2 *	68.23± 3.3 NS
GROUP 4 (Positive control)	17.4± 3.2	19.69 ± 1.9 NS	27.17± 4.3 *
GROUP 5 (Negative control)	26.15±2.7 NS	20.33± 2.5 NS	62.06± 1.2 #
GROUP 6 (300 mg/kg b. wt)	20.93±0.5	25.04± 1.3 NS	78.01 ± 3.8 *

*On successive days, there was a major change between diabetes and non-diabetic control: # P < 0.001. On the following days, there was a major change between the diabetic group and treated group: *P < 0.001. Changes between diabetic control groups and treated group are not significant: NS*

Table 8: Effects of polyherbal extract on ALP on normal and standardized triggered diabetic albino rats

GROUPS	DAYS AFTER DOSING		
	0	7	21
GROUP 1 (Vehicle)	15.45 ± 6.3	36.33 ± 12.6	47.24 ± 3.4
GROUP 2 (Herbal Control)	23.54 ± 2.9	128.16 ± 4.8 ns	58.29 ± 2.1 *
GROUP 3 (500 mg/kg b. wt)	26.77 ± 2.7	40.34 ± 7.5 *	57.0 ± 2.5 *
GROUP 4 (Positive control)	23.96 ± 1.3	191.65 ± 4.1 @	180.58 ± 8.5 @
GROUP 5 (Negative control)	28.90 ± 8.2 ns	101.99 ± 0.8 *	111.32 ± 3.2 *
GROUP 6 (300 mg/kg b. wt)	28.97 ± 3.2	62.94 ± 5.2 **	126.45 ± 4.4 NS

*On successive days, there was major changes between normal control and diabetes control: # P < 0.001 On the respective days, there was major changes between the diabetic control group and treated groups: *P < 0.001; **P < 0.01 non-significant changes between diabetic control group &treated group: NS*

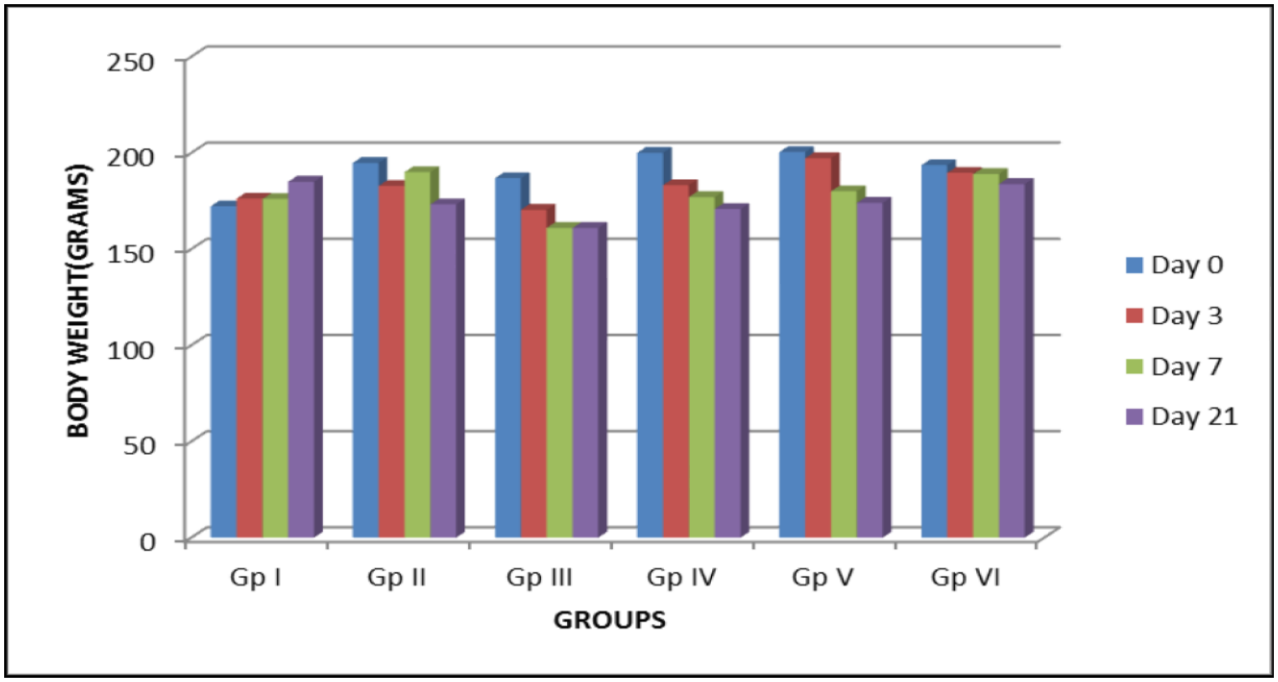

Figure 1: Effects of polyherbal extract on the body weight of common and standardized triggered diabetic albino rats

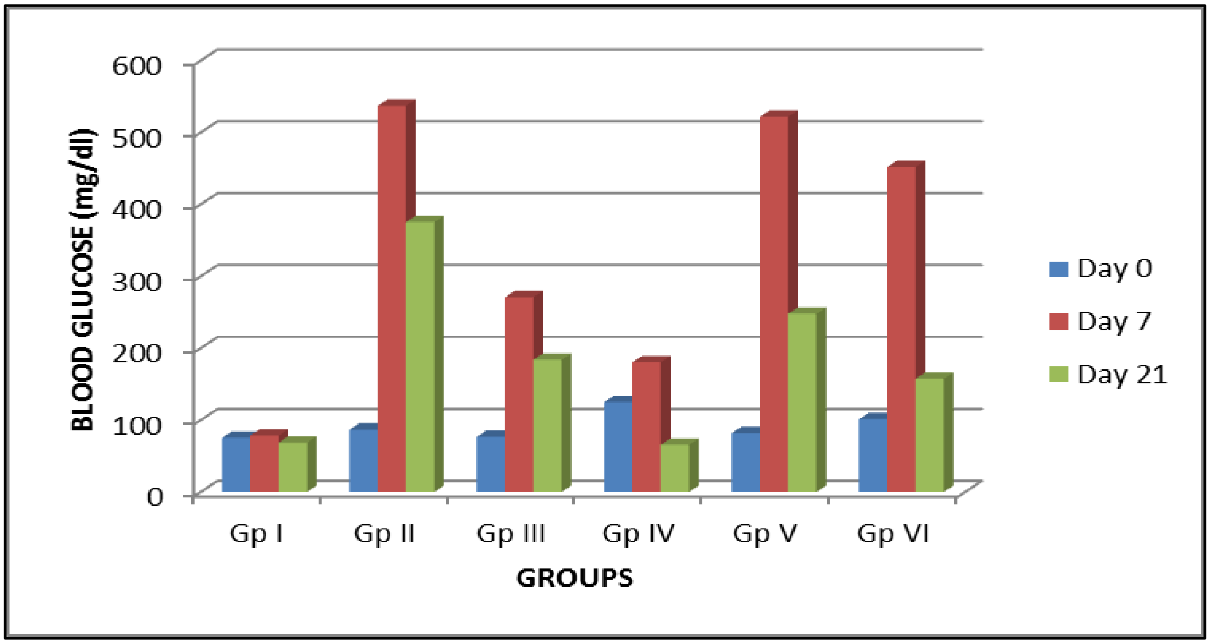

Figure 2: Effects of polyherbal extract on lipid profile (serum levels of cholesterol) on common and standardized triggered diabetic albino rats

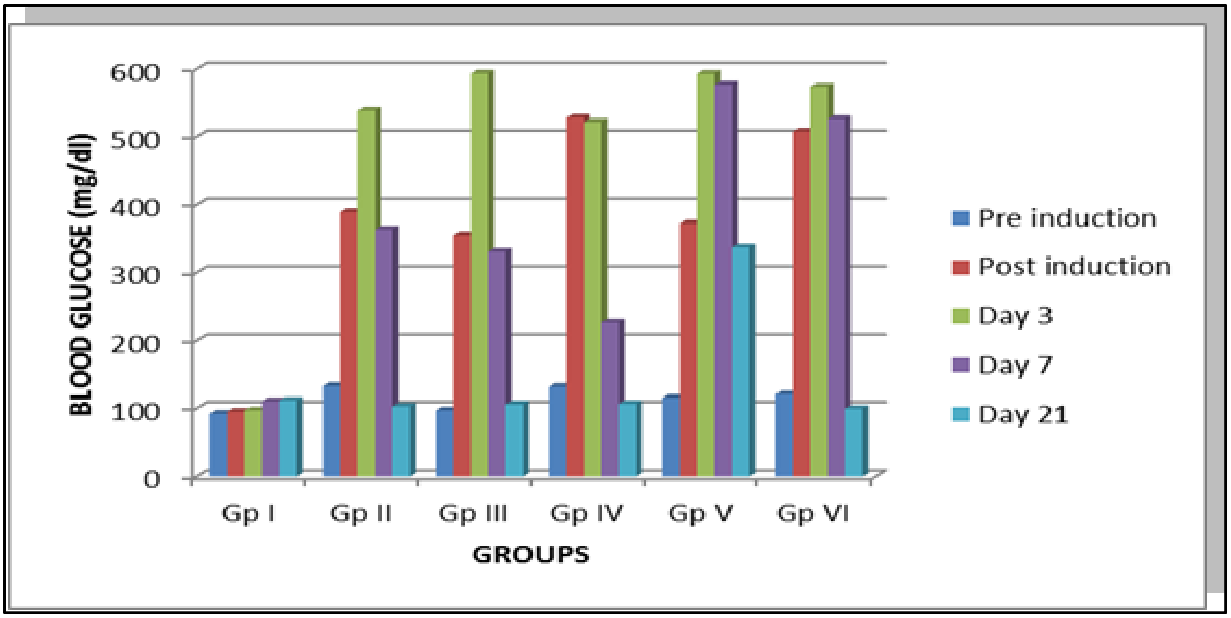

Figure 3: effects of polyherbal extract on blood glucose(by glucose strip method) on common and standardized triggered diabetic albino rats

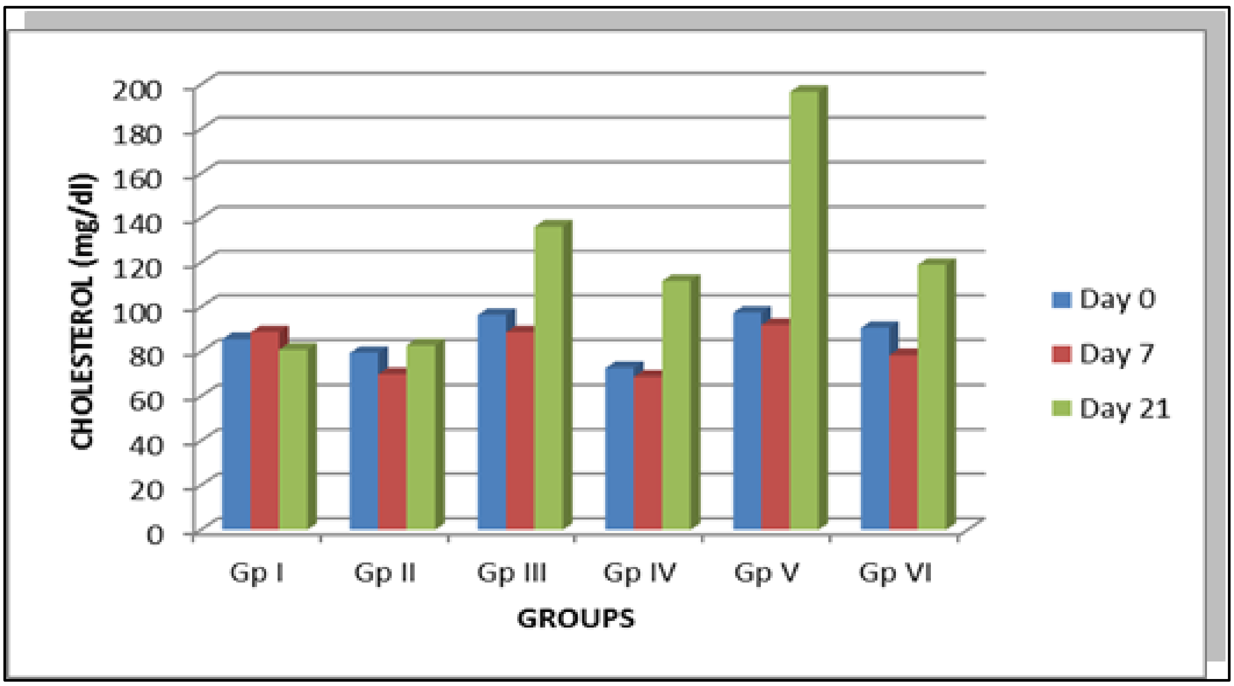

Figure 4: Effects of polyherbal extract on the lipid profile (serum levels of the cholesterol) of common and standardized triggered diabetes albino rats

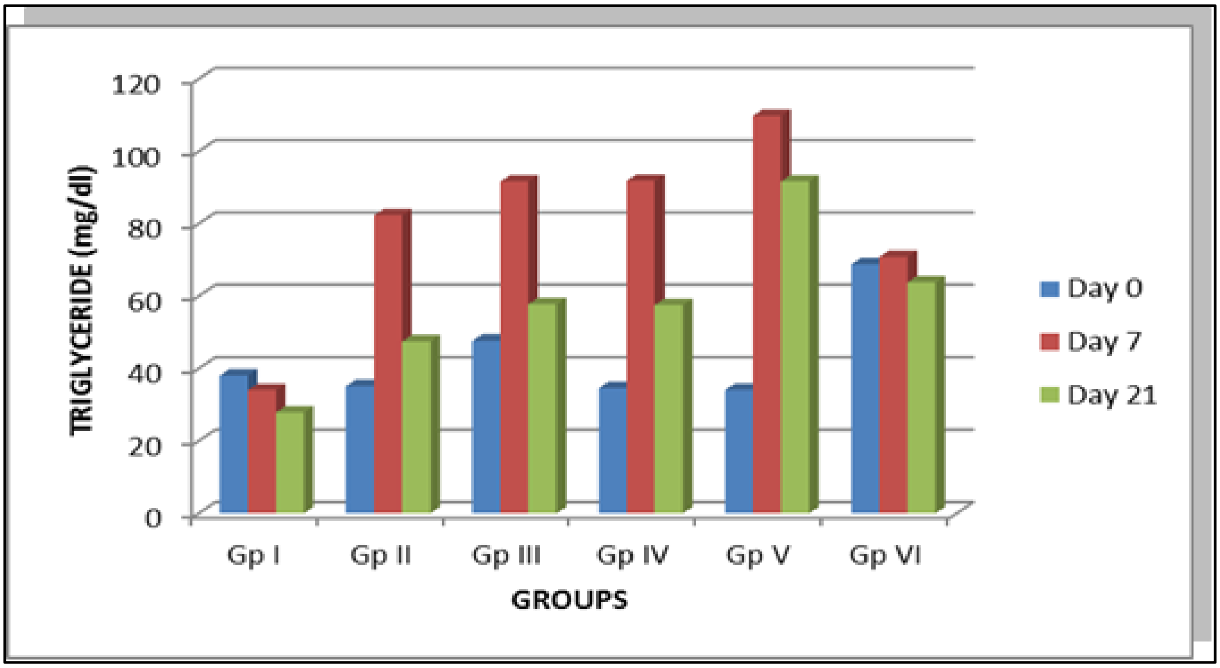

Figure 5: Effects of polyherbal extract on lipid profile (triglyceride level on blood level) on common and standardized triggered diabetes albino rats

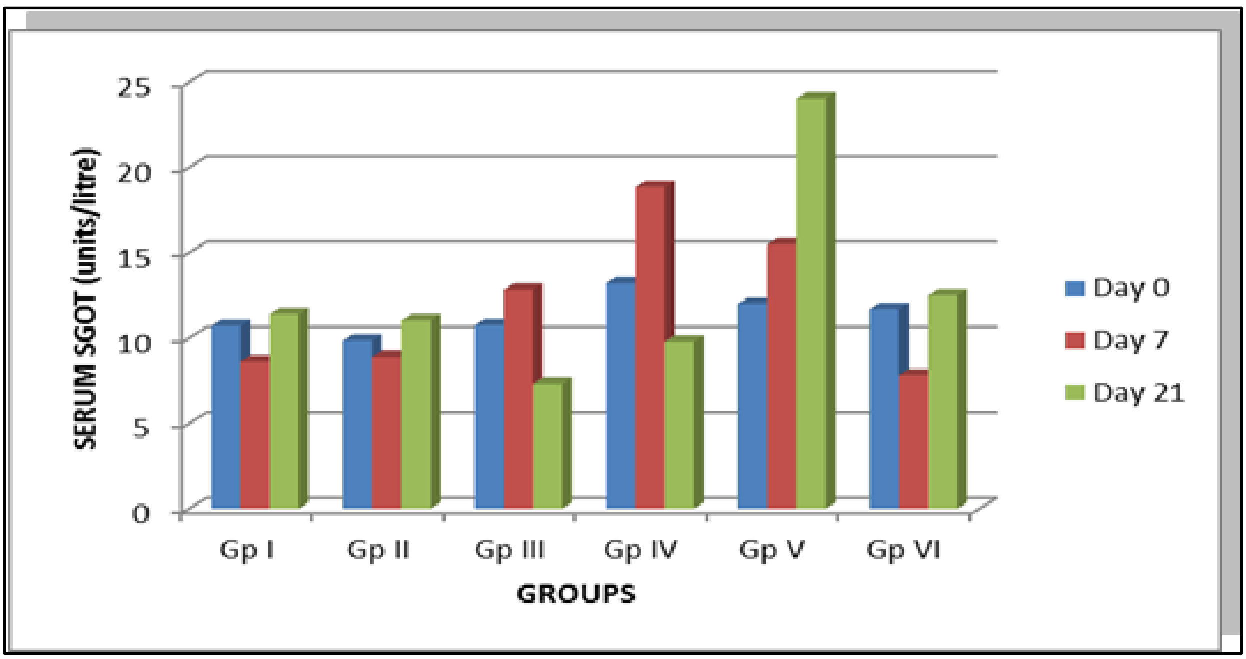

Figure 6: Effects of polyherbal extract on liver function test levels of serum (SGOT) on common and standardized triggered diabetes albino rats

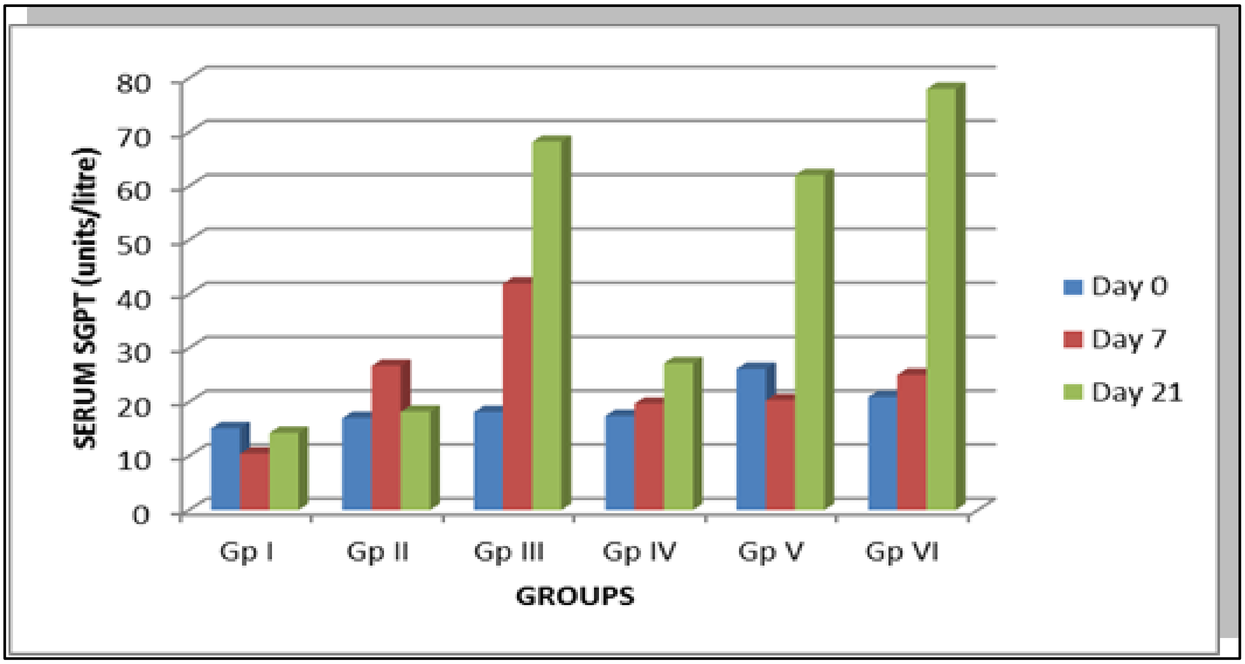

Figure 7: Effects of polyherbal extract on liver function test levels of serum (SGPT) on common and standardized triggered diabetes albino rats

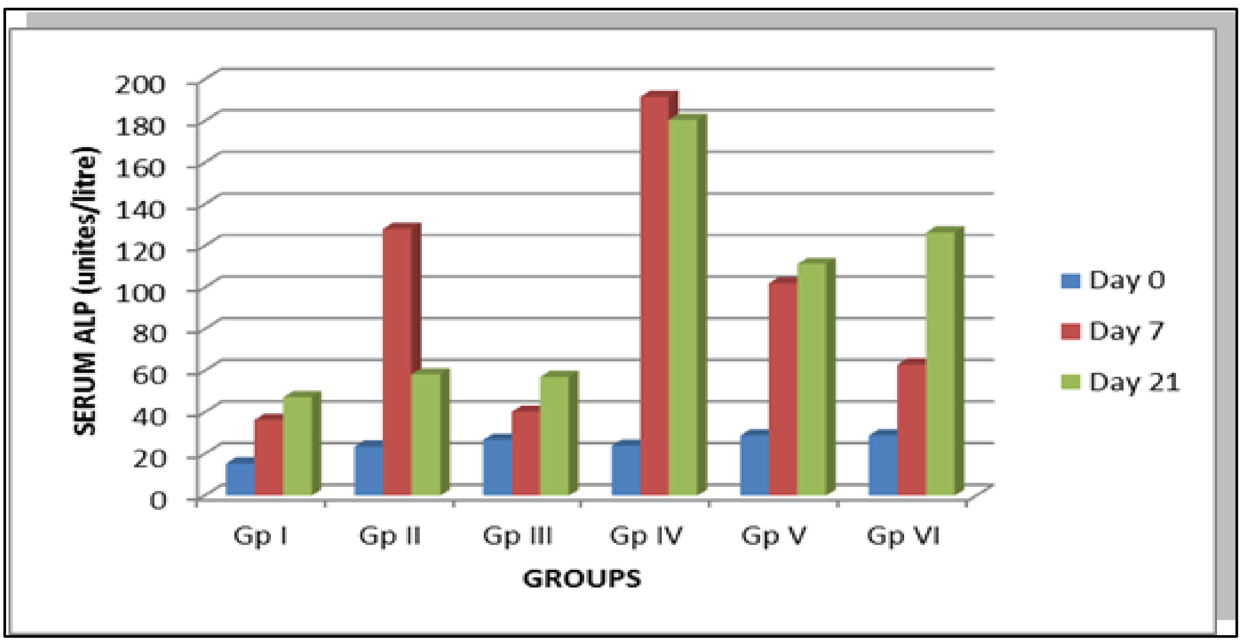

Figure 8: Effects of polyherbal extract on alp in common and standardized triggered used diabetic albino rats

CONCLUSION

The anti-hyperglycemic effect of various dosages of polyherbal formulation was tested in Streptozotocin (STZ)- produced diabetes on rats in this study. Orally administered polyherbal formulation at the dose of 300 & 500 milligram/kilogram of body weight shows major anti-hyperglycemic activity at the end of 21th day. Anti-diabetic effect of it at both the dose is comparable to that of herbal control as well as Glibenclamide at 10mg/Kg dose. The anti-diabetic effect of polyherbal formulation can be due to presence of more than one anti-hyperglycemic principle and their synergistic properties as each individual drug in this polyherbal mixture extract has been reported to exhibit anti-diabetic property.

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