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Screening Of Polyherbal Suspension For Anti-Diabetic Activity

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Abstract: Diabetes mellitus is a metabolic disorder in which a person has high blood sugar level because either the pancreas does not produce enough insulin or cells do not respond to it. Diabetes mellitus is of three types. Type 1 or Insulin Dependent Diabetes Mellitus, Type 2 or Non-Insulin Dependent Diabetes Mellitus and Gestational Diabetes. The Siddha system of medicine is the oldest traditional treatment system generated from Dravidian culture. In Siddha system of medicine, many single and polyherbal formulations and higher medicines like parpam, chendooram and chunnam have been practiced to cure or control Diabetes mellitus from time immemorial. It is caused by the deficiency or ineffective production of insulin by pancreas which results in increase or decrease in concentrations of glucose in the blood. There are lots of chemical agents available to control and to treat diabetic patients, but total recovery from diabetes has not been reported up to this date. In this article antidiabetic activity of Amla, Baheda, Jamun, Karela, Nut Tree, Smilex China are worked on Streptozocin induced Diabetic in mice.

Keywords: Glucose, Diabetes, Herbal, Insulin, Blood. antidiabetic activity of Amla, Baheda, Jamun, Karela, Nut Tree, Smilex China

I. Introduction of Diabetes

Diabetes mellitus is a systemic metabolic disease characterized by hyperglycemia, hyper lipedemia, hyper aminoacidemia, and hypo insulinaemia it leads to decrease in insulin, secretion and insulin action. Currently available therapies for diabetes include insulin and various oral antidiabetic agents such as sulfonylureas, biguanides, α-glucosidase inhibitors and glinides. In developing countries products are expensive and not easily accessible.1 Diabetes is a heterogeneous metabolic disorder characterized by altered carbohydrate, lipid, and protein metabolism which causes hyperglycemia resulting from insufficient insulin

secretion, insulin action or both. It is one of the refractory diseases identified by Indian Council of Medical Research for which an alternative medicine is a need for the treatment. Diabetes mellitus has become a growing problem in the contemporary world. A number of medicinal plants, traditionally used for over 1000 years named Rasayana are present in herbal preparations of Indian traditional health care systems. The current review focuses on herbal drug preparations and plants used in the treatment of diabetes mellitus, a major crippling disease in the world leading to huge economic losses.

II. Introduction of Anti-diabetic herbs

For most herbs, the specific ingredient that causes a therapeutic effect is not known. Whole herbs contain many ingredients, and it is likely that they work together to produce the desired medicinal effect. The type of environment in which a plant grew will affect its components, as will how and when it was harvested and processed. Evaluating the hypoglycemic ability of medicinal plants has therefore become essential. In the current study, antidiabetic activity is being investigated, a polyherbal extract made from an equal mixture of Amla, Baheda, Jamun, Karela, Nut Tree, Smilex China, fruit coat is prepared, polyherbal Formulations are made, evaluated, and their stability is being studied. Unani polyherbal formulations like Amla, Baheda, Jamun, Karela, Nut Tree, Smilex China, and the like are used in treatment of Diabetes mellitus. Among the Unani anti-diabetic formulations, **"**Amla, Baheda, Jamun, Karela, Nut Tree, Smilex China,**"** is a reputed and popular polyherbal formulation scientifically under explored. This formulation suffers from patient's non-compliance because of cumbersome dosage form, instability, difficulty in dose selection and administration. Sophisticated, modern instruments were used as an advanced tool in phyto pharmaceutical evaluation of the selected polyherbal formulations so as to prescribe the quality standards for better therapeutic efficacy. The toxicological evaluation of herbal drug ingredients like determination of pesticide residues, heavy metal contamination and microbial contamination and their formulation Amla, Baheda, Jamun, Karela, Nut Tree, Smilex China, for acute toxicity studies using recent advanced analytical tools have been carried out in keen interest of uplifting the herbal drug to the global markets. The extract of Amla, Baheda, Jamun, Karela, Nut Tree, Smilex China, exhibited significant anti-hyperglycemic activity in Streptozotocin (STZ) induced diabetic rats. This extract showed improvement in parameters like body weight, food consumption, organ weight and biochemical parameters and might be of great valuable in diabetic treatment.

A. Streptozotocin induced diabetic model

The animals were selected, weighed then marked for individual identification. Streptozotocin was first weighed individually for each animal according to the weight and then solubilized with 0.2 ml saline just prior to injection. Diabetes was induced by injecting it at a dose of 150 mg/kg b.w. intra peritoneally. After one hour of Streptozotocin administration the animals were given feed ad libitm and 5% dextrose solution were also given in feeding bottle for a day to overcome the early hypoglycemic Phase[11]. The animals were kept under observation and after 48 h blood glucose was measured by gluco-meter[12]. The diabetic rats (glucose level > 300 mg/dl) were separated and divided into different groups for experimental study, each group contain six animals.

B. Oral glucose tolerance test (OGTT)

Fasted rats were divided into six groups of six rats each. Group I served as normal control and received distilled water with Tween 80. Groups II received standard drug Glimipride as an aqueous suspension at a dose of 600µg/kg body weight. Group III to VI received different extracts at a dose of 500mg/kg body weight as a fine tween 80 suspension. After 30min of extract administration, the rats of all groups were orally treated with 2g/kg of glucose. Blood samples were collected from the rat tail vein just prior to glucose administration and at 30 and 60 and 120 min after glucose loading. Blood glucose levels were measured immediately by using Gluco-meter[13].

C. Preparation of dose for dried extracts

The petroleum ether (60-80 ^{0}C), chloroform, alcohol and aqueous extracts (500 mg/kg b.w) were formulated as suspension in distilled water using Tween-80 as suspending agent since Tween-80 has negligible effect on normal blood glucose level. The strength of the suspension was according to the dose administered and was expressed as weight of dried extract.

D. Preparation of standard drugs

Glimipride was used as the reference standard drug for evaluating the antidiabetic activity which was made into suspension in distilled water using Tween-80 as a suspending agent. The strength of suspension was prepared according to 600µg/kg b.w.

E. Estimation of blood glucose level

The Accu-chek® Active blood glucose strips (stored in refrigerator) taken out from the Container. The gluco-meter was calibrated as according to the specifications mentioned in the strips. The blood removed from the rat-tail vein, is immediately spread on the marked end of the strip. The strip is inserted in the gluco-meter & after few seconds the gluco-meter displayed the blood glucose level.

F. Body weight measurement

Body weight has been measured totally two times during the course of study period (i.e., on before Streptozotocin induction (initial values), 1st day and **7**th day of the treatment period), using a weighing scale. The above treatments were given for a period of 7 days both in diabetic and non-diabetic animals. In OGTT animals treatments were given for a single day with a single dose administration of extracts.

III. Development and Evaluation of Anti Diabetic Polyherbal Formulation

Table No. 1 General formula for development of herbal formulation

Sr. No.	Ingredient	Quantity in % w/w
1	Bio-active extract	10
2	Tween 80	0.1 %
3	Sodium CMC	2 gm
4	Methyl paraben	0.20 %
5	Lemon oil	0.01 %
6	Purified water	100 ml

Suspension was prepared using various bioactive extracts of selected drugs by following trituration method in mortar and pestle by using suitable suspending agent of Tween 80 and sodium CMC (Sodium

carboxy methyl cellulose) along with other excipients given in general formula.

Polyherbal Suspension (PHS 100)

The polyherbal formulation of polar bioactive extracts was prepared by following above mentioned procedure and by using the formula given in Table 26. The polar extracts used in the formulation are given. The polar extracts were combined in equal proportion and formulated.

Table No. 2 Antidiabetic Bioactive Polar Extracts Used For Polyherbal Suspension 100

Sr. No.	Crude drugs	Bio-active extracts
1	Amla	Aqueous
2	Baheda	Ethanolic
3	Jamun	Ethanolic
4	Karela	Aqueous
5	Nut Tree	Ethanolic
6	Smilex China	Ethanolic

Polyherbal Suspension (PHS 200)

The polyherbal formulation of non-polar bioactive extracts was prepared by following above mentioned procedure and by using the formula given in Table 26. The non polar extracts used in the formulation are given. The non-polar extracts were combined in equal proportion and formulated.

Table No 3 Antidiabetic Bioactive Non-Polar Extracts Used For Polyherbal Suspension 200

Sr. No.	Crude drugs	Bioactive extracts
1	Amla	Pet-ether
2	Baheda	Chloroform
3	Jamun	Pet-ether
4	Karela	Chloroform

Polyherbal Suspension (PHS 200). The polyherbal formulation of combined bioactive extracts was prepared by following above mentioned procedure and by using the formula given**.** The polar extracts used in the formulation are given. The combined extracts were combined in equal proportion and formulated.

Table No. 4 Anti-Diabetic Bioactive Polar and Non-Polar (Combined) Extracts Used For Polyherbal Suspension 400

Sr. No.	Crude drugs	Bioactive extracts
1	Karela	Aqueous
2	Karela	Ethanolic
3	Baheda	Ethanolic
4	Simlex China	Ethanolic
5	Amla	Aqueous

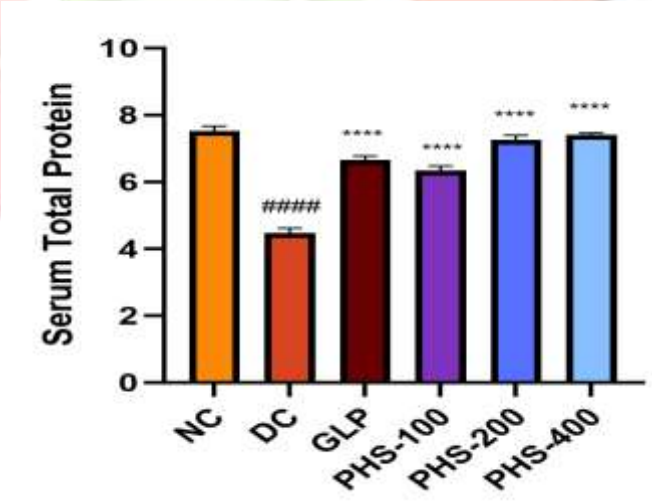
6	Karela	Ethanolic
7	Jamun	Pet-ether
8	Karela	Chloroform
9	Baheda	Chloroform
10	Amla	Pet-ether

Table No. 5 Effect of Glimepiride and Polyherbal suspension on serum Total Protein (TP) level in STZ induced diabetes in rats.

Group	Serum TP (mg/dl)
NC	7.527 ± 0.1408
DC	4.468 ± 0.1566####
GLP	6.653 ± 0.1273****
PHS-100	6.348 ± 0.1326****
PHS-200	7.265 ± 0.1281****
PHS-400	7.403 ± 0.0616****

NC- Normal Control, DC- Diabetic Control, GLP-Glimepiride, PHS-100- Polyherbal Suspension 100mg/kg, PHS-200- Polyherbal Suspension 200mg/kg, PHS-400- Polyherbal Suspension 400mg/kg. Result are presented as means ± SEM (n=6) one way ANOVA followed by Bonferroni Test for multiple comparison. ####P<0.0001 when compared to normal control (NC), ****P<0.0001 when compared to Diabetic control (DC)

Figure 1:- Effect of Glimepiride and Polyherbal suspension on serum TP level in STZ induced diabetes in rats.



NC- Normal Control, DC-Diabetic Control, GLP-Glimepiride, PHS-100-Polyherbal Suspension 100mg/kg, PHS-200-Polyherbal Suspension 200mg/kg, PHS-400-Polyherbal Suspension 400mg/kg. Result are presented as means ± SEM (n=6) one way ANOVA followed by Bonferroni Test for multiple comparison. ####P<0.0001 when compared to normal control (NC), ****P<0.0001 when compared to Diabetic control (DC)

Effect of Glimepiride and Polyherbal suspension on serum TP level in STZ induced diabetes in rats.

- **(PHS-200):** Polyherbal Suspension 200mg/kg shows significantly increased (****P<0.0001) in serum SGPT level when compared to DC at the end of study.
- **Polyherbal Diabetic control (DC):** Serum TP level was significantly decreased (####P<0.0001) when compared to NC at the end of study.
- **Glimepiride (GLP):** Treatment with Glimepiride shows significantly increased effect (****P<0.0001) in a serum TP level when compared to DC at the end of study.
- **Polyherbal Suspension (PHS-100):** Polyherbal Suspension 100mg/kg shows significantly increased (****P<0.0001) in serum TP level when compared to DC at the end of study.
- **Polyherbal Suspension (PHS-400):** Polyherbal Suspension 400mg/kg shows significantly increased (P<0.0001) in serum TP level when compared to DC at the end of study.

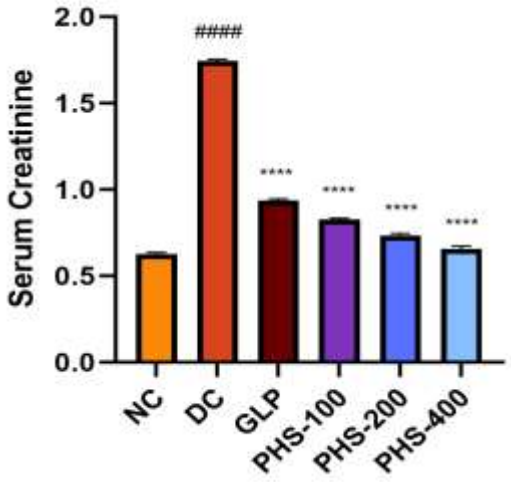
In Summary, Glimepiride and all Polyherbal suspension viz PHS-100, PHS-200 and PHS-400 shows significant increase in serum TP level when compared to DC.

Table No. 6 Effect of Glimepiride and Polyherbal suspension on Serum Creatinine level in STZ

Group	Serum Creatinine (mg/dl)
NC	0.6267 ± 0.0098
DC	1.743 ± 0.0105####
GLP	0.935 ± 0.0114****
PHS-100	0.8267 ± 0.0080****
PHS-200	0.735 ± 0.0111****
PHS-400	0.6583 ± 0.0147****

NC- Normal Control, DC- Diabetic Control, GLP-Glimepiride, PHS-100- Polyherbal Suspension 100mg/kg, PHS-200- Polyherbal Suspension 200mg/kg, PHS-400- Polyherbal Suspension 400mg/kg. Result are presented as means ± SEM (n=6) one way ANOVA followed by Bonferroni Test for multiple comparison. ####P<0.0001 when compared to normal control (NC), ****P<0.0001 when compared to Diabetic control (DC)

Figure 2:- Effect of Glimepiride and Polyherbal suspension on Serum Creatinine level in STZ induced diabetes in rats.



NC- Normal Control, DC-Diabetic Control, GLP-Glimepiride, PHS-100-Polyherbal Suspension 100mg/kg, PHS-200-Polyherbal Suspension 200mg/kg, PHS-400-Polyherbal Suspension 400mg/kg

Result are presented as means ± SEM (n=6) one way ANOVA followed by Bonferroni Test for multiple comparison.

####P<0.0001 when compared to normal control (NC), ****P<0.0001 when compared to Diabetic control (DC)

Effect of Glimepiride and Polyherbal suspension on Serum Creatinine level in STZ induced diabetes in rats.

- **Diabetic control (DC):** Serum Creatine level was significantly increased (####P<0.0001) when compared to NC at the end of study.
- **Glimepiride (GLP):** Treatment with Glimepiride shows significantly decreased effect (****P<0.0001) in a serum creatinine level when compared to DC at the end of study.
- **Polyherbal Suspension (PHS-100):** Polyherbal Suspension 100mg/kg shows significantly decreased (****P<0.0001) in serum creatinine level when compared to DC at the end of study.
- **Polyherbal Suspension (PHS-200):** Polyherbal Suspension 200mg/kg shows significantly decreased (****P<0.0001) in serum creatinine level when compared to DC at the end of study.
- **Polyherbal Suspension (PHS-400):** Polyherbal Suspension 400mg/kg shows significantly decreased (P<0.0001) in serum creatinine level when compared to DC at the end of study.

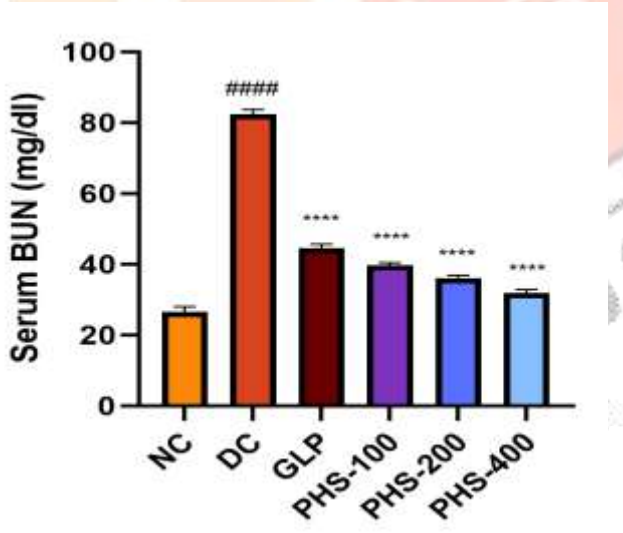
In Summary, Glimepiride and all Polyherbal suspension viz PHS-100,PHS-200 and PHS-400 shows significant reduction in serum creatinine level when compared to DC.

Table No. 7 Effect of Glimepiride and Polyherbal suspension on serum BUN level in STZ induced diabetes in rats.

Group	Serum BUN (mg/dl)
NC	26.66 ± 1.379
DC	82.48 ± 1.266####
GLP	44.56 ± 1.154****
PHS-100	39.68 ± 0.7432 ****
PHS-200	36.15 ± 0.7234****
PHS-400	32 ± 0.8541****

NC- Normal Control, DC- Diabetic Control, GLP-Glimepiride, PHS-100- Polyherbal Suspension 100mg/kg, PHS-200- Polyherbal Suspension 200mg/kg, PHS-400- Polyherbal Suspension 400mg/kg. Result are presented as means ± SEM (n=6) one way ANOVA followed by Bonferroni Test for multiple comparison. ####P<0.0001 when compared to normal control (NC), ****P<0.0001 when compared to Diabetic control (DC)

Figure 3:- Effect of Glimepiride and Polyherbal suspension on serum BUN level in STZ induced diabetes in rats.



NC- Normal Control, DC-Diabetic Control, GLP-Glimepiride, PHS-100-Polyherbal Suspension 100mg/kg, PHS-200-Polyherbal Suspension 200mg/kg, PHS-400-Polyherbal Suspension 400mg/kg. Result are presented as means ± SEM (n=6) one way ANOVA followed by Bonferroni Test for multiple comparison. ####P<0.0001 when compared to normal control (NC), ****P<0.0001 when compared to Diabetic control (DC)

Effect of Glimepiride and Polyherbal suspension on serum BUN level in STZ induced diabetes in rats.

- **Diabetic control (DC):** Serum BUN level was significantly increased ($^{####}$P<0.0001) when compared to NC at the end of study.
- **Glimepiride (GLP):** Treatment with Glimepiride shows significantly decreased effect (****P<0.0001) in a serum BUN level.
- **Polyherbal Suspension (PHS-100):** Polyherbal Suspension 100mg/kg shows significantly decreased (****P<0.0001) in serum BUN level when compared to DC at the end of study.
- **Polyherbal Suspension (PHS-200):** Polyherbal Suspension 200mg/kg shows significantly decreased (****P<0.0001) in serum BUN level when compared to DC at the end of study.
- **Polyherbal Suspension (PHS-400):** Polyherbal Suspension 400mg/kg shows significantly decreased (P<0.0001) in serum BUN level when compared to DC at the end of study.

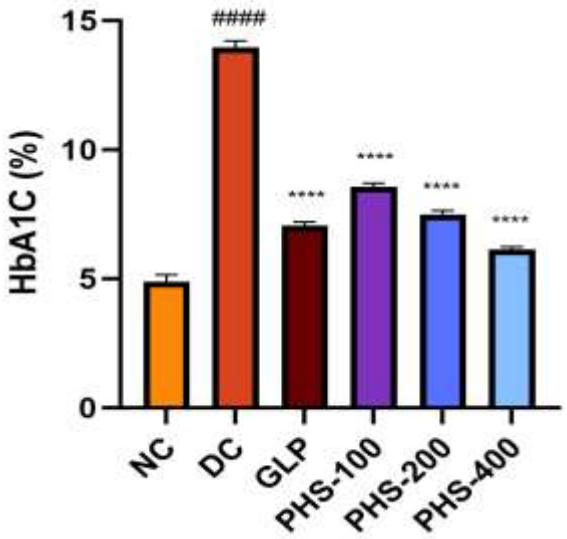
In Summary, all polyherbal suspension viz PHS-100, PHS-200 and PHS-400 and Glimepiride shows significant reduction in serum BUN level.

Table No. 8 Effect of Glimepiride and Polyherbal suspension on serum HbA1C level in STZ induced diabetes in rats.

Group	Serum HbA1C (%)
NC	4.9 ± 0.2583
DC	13.96 ± 0.2576$^{####}$
GLP	7.05 ± 0.159****
PHS-100	8.553 ± 0.1527 ****
PHS-200	7.492 ± 0.1461****
PHS-400	6.148 ± 0.0985****

NC- Normal Control, DC- Diabetic Control, GLP-Glimepiride, PHS-100- Polyherbal Suspension 100mg/kg, PHS-200- Polyherbal Suspension 200mg/kg, PHS-400- Polyherbal Suspension 400mg/kg. Result are presented as means ± SEM (n=6) one way ANOVA followed by Bonferroni Test for multiple comparison. $^{####}$P<0.0001 when compared to normal control (NC), ****P<0.0001 when compared to Diabetic control (DC)

Figure 4:- Effect of Glimepiride and Polyherbal suspension on serum HbA1C level in STZ induced diabetes in rats.



NC- Normal Control, DC-Diabetic Control, GLP-Glimepiride, PHS-100-Polyherbal Suspension 100mg/kg, PHS-200-Polyherbal Suspension 200mg/kg, PHS-400-Polyherbal Suspension 400mg/kg. Result are presented as means ± SEM (n=6) one way ANOVA followed by Bonferroni Test for multiple comparison. ####P<0.0001 when compared to normal control (NC), ****P<0.0001 when compared to Diabetic control (DC)

Effect of Glimepiride and Polyherbal suspension on serum HbA1C level in STZ induced diabetes in rats.

- **Diabetic control (DC):** Serum HbA1C level was significantly increased (####P<0.0001) when compared to NC at the end of study.
- **Glimepiride (GLP):** Treatment with Glimepiride shows significantly decreased effect (****P<0.0001) in a serum HbA1C level.
- **Polyherbal Suspension (PHS-100):** Polyherbal Suspension 100mg/kg shows significantly decreased (****P<0.0001) in serum HbA1C level when compared to DC at the end of study.
- **Polyherbal Suspension (PHS-200):** Polyherbal Suspension 200mg/kg shows significantly decreased (****P<0.0001) in serum HbA1C level when compared to DC at the end of study.
- **Polyherbal Suspension (PHS-400):** Polyherbal Suspension 400mg/kg shows significantly decreased (P<0.0001) in serum HbA1C level when compared to DC at the end of study.

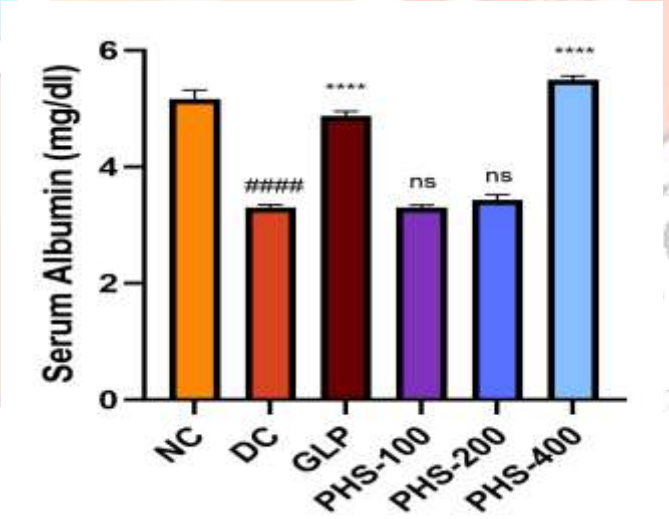
In Summary, all polyherbal suspension viz PHS-100, PHS-200 and PHS-400 and Glimepiride shows significant reduction in serum HbA1C level.

Table No. 9 Effect of Glimepiride and Polyherbal suspension on serum Albumin level in STZ induced diabetes in rats.

Group	Serum Albumin (%)
NC	5.16 ± 0.1564
DC	3.298 ± 0.0478####
GLP	4.875 ± 0.0777****
PHS-100	3.295 ± 0.048 ns
PHS-200	3.432 ± 0.0921 ns
PHS-400	5.493 ± 0.0702****

NC- Normal Control, DC- Diabetic Control, GLP-Glimepiride, PHS-100- Polyherbal Suspension 100mg/kg, PHS-200- Polyherbal Suspension 200mg/kg, PHS-400- Polyherbal Suspension 400mg/kg. Result are presented as means ± SEM (n=6) one way ANOVA followed by Bonferroni Test for multiple comparison. ####P<0.0001 when compared to normal control (NC), ****P<0.0001 when compared to Diabetic control (DC)

Figure 5: - Effect of Glimepiride and Polyherbal suspension on serum Albumin level in STZ induced diabetes in rats.



NC- Normal Control, DC-Diabetic Control, GLP-Glimepiride, PHS-100-Polyherbal Suspension 100mg/kg, PHS-200-Polyherbal Suspension 200mg/kg, PHS-400-Polyherbal Suspension 400mg/kg. Result are presented as means ± SEM (n=6) one way ANOVA followed by Bonferroni Test for multiple comparison. ####P<0.0001 when compared to normal control (NC), ****P<0.0001 when compared to Diabetic control (DC)

Effect of Glimepiride and Polyherbal suspension on serum Albumin level in STZ induced diabetes in rats.

- **Diabetic control (DC):** Serum albumin level was significantly decreased ($^{\#\#\#\#}P<0.0001$) when compared to NC at the end of study.
- **Glimepiride (GLP):** Treatment with Glimepiride shows significantly increased effect ($^{****}P<0.0001$) in a serum albumin level.
- **Polyherbal Suspension (PHS-100):** Polyherbal Suspension 100mg/kg shows non-significant effect ($^{ns}P>0.9999$) in serum Albumin level when compared to DC at the end of study.
- **Polyherbal Suspension (PHS-200):** Polyherbal Suspension 200mg/kg shows non-significant effect ($^{ns}P>0.9999$) in serum Albumin level when compared to DC at the end of study.
- **Polyherbal Suspension (PHS-400):** Polyherbal Suspension 400mg/kg shows significantly increased ($P<0.0001$) in serum albumin level when compared to DC at the end of study.

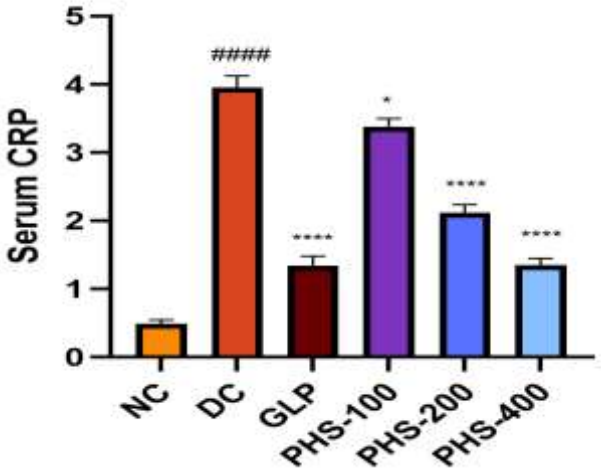
In Summary, all Glimepiride and Polyherbal Suspension PHS-400 shows significant increase in serum albumin level. Whereas PHS-100 and PHS-200 shows non-significant effect.

Table No. 10 Effect of Glimepiride and Polyherbal suspension on serum CRP level in STZ induced diabetes in rats.

Group	Serum CRP (mg/dl)
NC	0.49 ± 0.0558
DC	3.952 ± 0.1695$^{\#\#\#\#}$
GLP	1.343 ± 0.1371****
PHS-100	3.382 ± 0.1157*
PHS-200	2.118 ± 0.1175****
PHS-400	1.35 ± 0.09767****

NC- Normal Control, DC- Diabetic Control, GLP-Glimepiride, PHS-100- Polyherbal Suspension 100mg/kg, PHS-200- Polyherbal Suspension 200mg/kg, PHS-400- Polyherbal Suspension 400mg/kg. Result are presented as means ± SEM (n=6) one way ANOVA followed by Bonferroni Test for multiple comparison. $^{\#\#\#\#}P<0.0001$ when compared to normal control (NC), ****$P<0.0001$ when compared to Diabetic control (DC)

Figure 6:- Effect of Glimepiride and Polyherbal suspension on serum CRP level in STZ induced diabetes in rats.



NC- Normal Control, DC-Diabetic Control, GLP-Glimepiride, PHS-100-Polyherbal Suspension 100mg/kg, PHS-200-Polyherbal Suspension 200mg/kg, PHS-400-Polyherbal Suspension 400mg/kg. Result are presented as means ± SEM (n=6) one way ANOVA followed by Bonferroni Test for multiple comparison. $^{\#\#\#\#}$P<0.0001 when compared to normal control (NC), ****P<0.0001 when compared to Diabetic control (DC)

Effect of Glimepiride and Polyherbal suspension on serum CRP level in STZ induced diabetes in rats.

- **Diabetic control (DC):** Serum CRP level was significantly increased ($^{\#\#\#\#}$P<0.0001) when compared to NC at the end of study.
- **Glimepiride (GLP):** Treatment with Glimepiride shows significantly decreased effect (****P<0.0001) in a serum CRP level.
- **Polyherbal Suspension (PHS-100):** Polyherbal Suspension 100mg/kg shows slightly significant effect (*P=0.0338) in serum CRP level when compared to DC at the end of study.
- **Polyherbal Suspension (PHS-200):** Polyherbal Suspension 200mg/kg shows significantly decreased effect (****P<0.0001) in serum CRP level when compared to DC at the end of study.
- **Polyherbal Suspension (PHS-400):** Polyherbal Suspension 400mg/kg shows significantly decreased effect (****P<0.0001) in serum CRP level when compared to DC at the end of study.

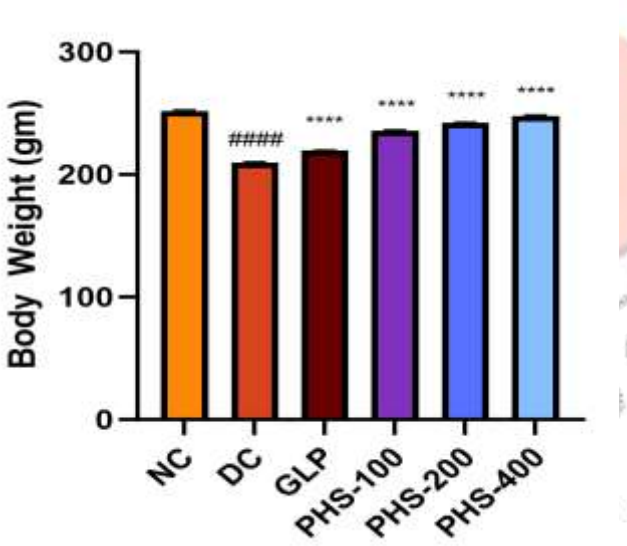
In Summary, all Glimepiride and Polyherbal Suspension PHS-200 and PHS-400 shows significant reduction in serum CRP level. Whereas PHS-100 shows less significant effect when compared to DC group.

Table No. 11 Effect of Glimepiride and Polyherbal suspension on Body weight in STZ induced diabetes in rats.

Group	Body Weight (Initial) (gm)	Body Weight (Final) (gm)
NC	231.8 ± 0.9252	251.9 ± 0.6508
DC	237 ± 0.9281####	209.8 ± 0.5455####
GLP	234.5 ± 0.6402****	219.7 ± 0.3057****
PHS-100	232.5 ± 0.6384*	235.5 ± 0.7473*
PHS-200	232.6 ± 0.6570****	242.1 ± 05615****
PHS-400	232.5 ± 1.127****	247.9 ± 0.8022****

NC- Normal Control, DC- Diabetic Control, GLP-Glimepiride, PHS-100- Polyherbal Suspension 100mg/kg, PHS-200- Polyherbal Suspension 200mg/kg, PHS-400- Polyherbal Suspension 400mg/kg. Result are presented as means ± SEM (n=6) one way ANOVA followed by Bonferroni Test for multiple comparison. ####P<0.0001 when compared to normal control (NC), ****P<0.0001 when compared to Diabetic control (DC)

Figure 6:- Effect of Glimepiride and Polyherbal suspension on Body weight in STZ induced diabetes in rats.



NC- Normal Control, DC-Diabetic Control, GLP-Glimepiride, PHS-100-Polyherbal Suspension 100mg/kg, PHS-200-Polyherbal Suspension 200mg/kg, PHS-400-Polyherbal Suspension 400mg/kg. Result are presented as means ± SEM (n=6) one way ANOVA followed by Bonferroni Test for multiple comparison. ####P<0.0001 when compared to normal control (NC), ****P<0.0001 when compared to Diabetic control (DC)

Effect of Glimepiride and Polyherbal suspension on Body weight in STZ induced diabetes in rats.

- **Diabetic control (DC):** The body weight was significantly decreased ($^{####}P<0.0001$) when compared to NC at the end of study.
- **Glimepiride (GLP):** Treatment with Glimepiride shows significantly increased ($^{****}P<0.0001$) in a body weight when compared to DC at the end of study.
- **Polyherbal Suspension (PHS-100):** Polyherbal Suspension 100mg/kg shows significantly increased ($^{****}P<0.0001$) in a body weight when compared to DC at the end of study.
- **Polyherbal Suspension (PHS-200):** Polyherbal Suspension 200mg/kg shows significantly increased ($^{****}P<0.0001$) in body weight when compared to DC at the end of study.
- **Polyherbal Suspension (PHS-400):** Polyherbal Suspension 400mg/kg shows significantly increased ($^{****}P<0.0001$) in body weight when compared to DC at the end of study.

In Summary, all Polyherbal Suspension PHS-100, PHJS-200 and PHS-400 and Glimepiride shows significant increase in body weight when compared to DC.

These results indicate changes in body weight from initial to final measurement. Notably the disease control group (DC) showed a decreased in body weight, while treatment with glimepiride (GLP) and All Polyherbal Suspension PHS-100, PHS-200 and PHS-400 led to significant increase in body weight as compared to DC.

IV. Statistical Analysis

Amla Streptozotocin induced model, the aqueous and petroleum ether extracts were found to possess blood glucose lowering potential but the action was delayed. It could only produce the significant reduction in glucose effects only after 5 hours as compare to diabetic control. This delayed action may be due to poor absorption of the drug extracts.

In OGTT, Maximum glucose tolerance was observed in aqueous extract (108.33±6.687) and minimum glucose tolerance was observed in chloroform extract (125.0±2.708) in 90 minutes compared with the normal control.

A. Baheda

Ethanolic and chloroforn extract had led to a significant fall in the blood glucose level. Pet ether extract was non-significant for acute study but it gradually restored glucose level nearer to normal level in subsequent days. The effect of aqueous extract did not showed significant activity on prolonged treatment but showed significant ($P<0.01$) activity at 1 hr in acute study compared to diabetic control. Ethanolic extract had significantly reduced glucose level at 3 hr and significant reduction was maintained for another 4 hour in a day. In prolonged treatment, the effects of alcoholic extract were nearly equal to that reference drug Glimipride.

In OGTT, maximum glucose tolerance was observed in ethanolic extract (115.50 ±3.394) and minimum glucose tolerance was observed in pet ether extract (148.16 ±6.183) in 90 minutes compared with the normal control.

B. Jamun

Jamun petroleum ether extract showed significant blood glucose lowering effects in Streptozotocin induced rats on prolonged treatment whereas chloroform extract brought down glucose level till (293.33± 6.591 at 3 hrs from 342.50±11.673 mg/dl) in 3 hours after the single dose of 500mg/kg. b.w. as compare to diabetic control.

In OGTT, maximum glucose tolerance was observed in petroleum ether extract (128.66±3.756) and minimum glucose tolerance was observed in aqueous extract (167.33±2.951) in 90 minutes compared with the normal control.

C. Karela

The single dose of ethanolic extract (300 mg/kg b.w.) has more significantly (P<0.01) reduced the blood glucose level as compare to diabetic control at 7th day of the study. Chloroform extract (500 mg/kg b.w.) shown significant reduction of blood glucose after 1 hour whereas ethanolic extract shown the significant reduction at 3 hrs. Aqueous extract of the same plant could not reduce glucose level at subacute level though it showed reduction of glucose level at 7 hr. as compare to diabetic control.

In OGTT, maximum glucose tolerance was observed in chloroform extract (121.00 ±2.966) and minimum glucose tolerance was observed in aqueous extract (155.33 ±3.018 in 90 minutes compared with the normal.

D. Nut Tree

Ethanolic and aqueous extracts demonstrated significant blood glucose lowering effects (P<0.01) after single dose of 500 mg/ kg.b.w. and multiple doses for prolonged treatment. In acute & prolonged treatment, the effects of alcoholic extract were nearly equal to that reference drug Glimipride whereas aqueous extract shown significant reduction only in prolonged treatment.

In OGTT, maximum glucose tolerance was observed in ethanolic extract (149.16±4.159) and minimum glucose tolerance was observed in petroleum ether extract (163.33±5.542) in 90 minutes compared with the normal control.

E. Smilex China

The ethanolic and aqueous extracts were able to reduce blood glucose level significantly(P<0.01) as compare to diabetic control but Pet. Ether extract in prolonged treatment significantly reduced glucose level as compare to diabetic control.

In OGTT, Maximum glucose tolerance was observed in aqueous extract (113.16 ±3.620) and minimum glucose tolerance was observed in Chloroform extract (130.66 ±4.971) in 90 minutes compared with the normal control.

Oral treatment with standard hypoglycemic agent Glimipride 600µg /kg body weight also able to reduce the elevated blood glucose level towards the normal (105.66 ±5.097) at 7th day of treatment.

Glimipride treated group (600µg/kg) also prevented significantly glucose induced hyperglycemia at 30 min and 90 min (171.83 - 4.214 and 106.16 - 4.316) as compare to Normal control (167.83±2.301 & 146.83±2.960).

Plant extracts fed groups prevented significantly glucose-induced hyperglycemia at 30min and 90 min. as compare to that of normal control at 30 min and 90 min (167.83±2.301 and 146.83±2.960).

Conclusion

Herbal therapy for diabetes has been followed all over the World successfully. Herbs are used to manage Type 1 and Type II diabetes and their complications. For this, therapies developed along the principles of western medicine (allopathic) are often limited in efficacy, carry the risk of adverse effects, and are often too costly, especially for the developing world. The plants viz. Amla, Baheda, Jamun, Karela, Nut Tree, Smilex China, have been considered for their possible hypoglycemic actions and the researchers have carried out some preliminary investigations. Scientific validation of several Indian plant species has proved the efficacy of the botanicals in reducing the sugar level could be considered as of possible therapeutic value. Thus many different plants have been used individually or in formulations for treatment of diabetes.

References:

1. Gobinath R, Parasuraman S, Sreeramanan S, Enugutti B, Chinni SV. Antidiabetic and Antihyperlipidemic Effects of Methanolic Extract of Leaves of Spondias mombin in Streptozotocin-Induced Diabetic Rats. Front Physiol. 2022;13:870399.
2. Akinyede KA, Oyewusi HA, Hughes GD, Ekpo OE, Oguntibeju OO. In Vitro Evaluation of the Anti-Diabetic Potential of Aqueous Acetone Helichrysum petiolare Extract (AAHPE) with Molecular Docking Relevance in Diabetes Mellitus. Molecules. 2021;27(1):155.
3. Andargie Y, Sisay W, Molla M, Tessema G. Evaluation of Anti-diabetic and Antihyperlipidemic Activity of 80% Methanolic Extract of the Root of Solanum incanum Linnaeus (Solanaceae) in Mice. Evid Based Complement Alternat Med. 2022;2022:4454881.
4. Tegegne BA, Mekuria AB, Birru EM. Evaluation of Anti-Diabetic and Anti-Hyperlipidemic Activities of Hydro-Alcoholic Crude Extract of the Shoot Tips of Crinum abyssinicum Hochst. ex A. Rich (Amaryllidaceae) in Mice. J Exp Pharmacol. 2022;14:27-41.
5. Kasznicki J, Sliwinska A, Drzewoski J. Metformin in cancer prevention and therapy. Ann Transl Med. 2014;2(6):57.
6. Tafesse TB, Hymete A, Mekonnen Y, Tadesse M. Antidiabetic activity and phytochemical screening of extracts of the leaves of Ajuga remota Benth on alloxan-induced diabetic mice. BMC Complement Altern Med. 2017;17(1):243.
7. Mahapatra SK, Verma S. Preparation and Evaluation of Novel Antidiabetic Polyherbal Formulation. Research Journal of Phar-macy and Technology. 2022; 15(7):3015-9.
8. Grigore A, Vulturescu V, Neagu G, Ungureanu P, Panteli M, Rasit I. Antioxidant-Anti-Inflammatory Evaluation of a Polyherbal Formula. Pharmaceuticals (Basel). 2022 Jan 18;15(2):114.
9. Singh J, Sahu RK, Prasad DN, Jangde R, Gupta R. Evaluation of anti-diabetic potential of Ougeinia oojeinensis leaves in streptozotocin-induced-diabetic rats. Pharmacology online, 2011; 2(2): 1046-1052.
10. Osmani OH, Sekar DS, Senthil Kumar KL, Sahu RK, Roy A. In- vivo anti-diabetic potential of Artocarpus heterophyllus plant seeds in streptozotocin-induced-diabetic rats. Biomedical and Pharmacological Journal, 2009; 2(2): 339-343.
11. Mohammed SM, Abd-Almonuim AE, Majeed A, Khlaf H. The Anti-Diabetic and Anti-Hyperlipidemia

effect of Citrus maxima Fruit Peel extract in Streptozotocin - Induced Diabetic Rats. Research Journal of Pharmacy and Technology, 2021; 14(10):5355-8.

12. Mawlieh BS, Shastry CS, Chand S. Evaluation of Anti-diabetic Activity of two marketed Herbal Formulations. Research J. Pharm. and Tech, 2020; 13(2):664-668.
13. Deore ND, Gupta S, Shrivastav B, Upasni CD, Apte KG, Shaikh AM. Evidence based Evaluation of Anti-diabetic Potential of Yesaka on Streptozotocin Diabetic Rats. Research J. Pharm. and Tech, 2018; 11(11): 4965-4970.
14. Maurya AK, Tripathi S, Kahrana M, Ahmed Z, Sahu RK. Evaluation of anti-diabetic effects of Ficus racemosa extracts in diabetic induced rats. Pharmacologyonline, 2011; 3: 907-914.
15. Roy A, Gupta PP, Bharadwaj S, Chandrakar S. Anti-diabetic activity of Polyherbal formulations from Chhattisgarh State. Research J. Pharm. and Tech. 2021; 14(3):1375-1379.
16. Jagtap P, Nimbalkar Y, Patil V, Patil RY. In Vivo Antidiabetic Activities of Polyherbal Extracts against Streptozotocin Nicotinamide Induced Type 2 Diabetic Mice Model. Tanzania Journal of Science. 2021; 47(3): 877-891.
17. Jayaraju KJ, Ishaq BM. Evaluation of Anti-diabetic Activity of a Novel Polyherbal Preparationagainst Streptozotocin Induced Diabetes Rat Model. Journal of Pharmaceutical Research International. 2021; 33(26A): 42-54.
18. Nagja T, Kumar V, Sanjeev A. Anti-Diabetic Activity of a Polyherbal Formulation in Streptozotocin Induced Type 2 Diabetic Rats. Journal of Natural Remedies. 2016; 16(4): 148-152.
19. Chaudhuri A, Sharma S. Evaluation of Anti-diabetic Activity of Polyherbal Formulation in Streptozotocin-Induced Diabetic Rats. Pharmaceutical and Biosciences Journal. 2016; 4(5): 01-06.
20. Subhasree N, Kamella A, Kaliappan I, agrawal A, Dubey GP. Anti-diabetic and antihyperlipidemic activities of a novel polyherbal formulation in high fat diet/streptozotocin induced diabetic rat model. Indian J Pharmacol 2015;47:509-13
21. Ansel HC, Allen LV. Pharmaceutical dosage forms and drug delivery systems, 7th edition, Lippincott, 2000; 347-56.
22. Aulton ME, Pharmaceutics: The Science of Dosage form. Churchill Livingstone, 1996, 304.
23. Subramani P, Gan ST, Sokkalingam A, Dhanaraj. Polyherbal Formulation: Concept of Ayurveda. Pharmac Rev. 2014; 8(16): 73–80.
24. Shinde JS, Khurde SS, Suchita LS, Chavan SS. Hulmajge SB. Need of polyherbal formulations and its standardization: A Review. World J Pharm Pharmac Scien.2016; 5(11):526-533.
25. Mukherjee PK. Quality Control of Herbal Drugs. New Delhi: Syndicate Binders; 2002.
26. Dandagi PM, Patil MB, Mastiholimath VS, Gadad AP. Development and evaluation of a hepatoprotective polyherbal formulation containing some indigenous medicinal plants. Ind J Pharm Sci Mar-Apr 2008;70(2):265-8.
27. Pandey VN, Rajagopalan. An effective ayurvedic hypoglycemic formulation. J Res Ayur Siddha. 1995; 16:1-14.
28. Khandelwal KR. Practical Pharmacognosy Technique and Experiments. Nirali Prakashan, 15th edition, 2006; 25.1-26.6.

29. Jain NK, Sharma SN. Textbook of Professional Pharmacy, Vallabh Prakashan, New Delhi, 3rd ed, 1994, 228.
30. Stability studies an overview of ICH guidelines for drug products: Natalie McClure, Matrix Pharmaceutical Inc. 1997.
31. Mahato RI. Pharmaceutical dosage forms and drug delivery. Boca Raton: CRC Press, Taylor & Francis group. 2007.123-133.
32. Microbial contamination in non-sterile products, (2.2.9), Volume I, Indian Pharmacopoeia, 2014; 38-50.
33. Stahl E. Thin Layer Chromatography – A Laboratory Hand Book. Second Edition. New York: Springer International Student Edition; 1969:311-471
34. Wagner H, Baldt S, Zagainski EM. Plant Drug Analysis. Germany: Springer-Verlag Berlin Heidelberg; 1994:149-355.
35. Shanthi A, Radha R. pre-formulation Assessment: the fruit of *Cuminum cyminum*, Linn. Int J Curr Res Rev.2011;3(6):49-57.