# EVALUATION OF THE ANTIDIABETIC ACTIVITY OF A POLYHERBAL FORMULATION IN RATS

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**Summary**

Diasansar, (450mg/ kg,p.o) a polyherbal formulation was evaluated for its antidiabetic activity in streptozotocin(STZ) induced Type 1 diabetic rats. Glibenclamide (500 mcg/kg, p.o) and insulin (6 IU / kg, i.p) served as standard controls. Diasansar reduced the elevated serum glucose, triglycerides, cholestrol, creatinine levels and increased the serum HDL cholesterol, body weight and liver glycogen levels in diabetic rats
Diasansar thus exhibited a significant antihyperglycemic, antihyperlipidemic activity in STZ induced diabetic rats.

**Key words**: Antihyperglyemic, antidiabetic, polyherbal, streptozotocin

## Introduction

Diabetes is the worlds largest endocrine disease involving metabolic disorder of carbohydrate , fat and protein . Diabetes mellitus has reached epidemic proportions worldwide as we enter the new millennium. The World Health Organization (WHO) has commented there is ‘an apparent epidemic of diabetes which is strongly related to lifestyle and economic change’. According to W.H.O projections, there are over 150 million diabetics worldwide currently and this number is likely to increase to 300 million by 2025. There are over 31.7 million diabetics in India currently and this number is likely to increase to 79.4 million by 2030.

Type 1diabetes is characterized by autoimmune destruction of insulin-producing β cells in the pancreas by CD4+ and CD8+ T cells and macrophages infiltrating the islets[1].

The drugs available to treat diabetes in modern medicine are effective enough but like all other drugs used in therapy they too have side effects like insulin resistance after chronic insulin treatment. The thrust these days therefore is to look for drugs with minimal side effects to manage the disease.

Thus an attempt been made through this study to evaluate the usefulness of the investigational formulation DIASANSAR powder (a polyherbal formulation) in diabetic condition in rats.

The study was carried out to evaluate claim of DIASANSAR powder in the management of type-1diabetes mellitus.

## Material and Methods

**Animals:**

Adult male Wistar rats 160±15g were maintained under standard environmental conditions with free access to feed and water during the experimental period.

**Chemicals:**

Streptozotocin: Sigma co., St Louis, MO, USA,

Glibenclamide: Nicholas-Piramal Limited, Madhya Pradesh.

Insulin : Torrent Pharmaceuticals Limited, Mehsana, Gujrat.

Glucose,triglycerides,cholesterol,creatinine, HDL-cholesterol kits : Span Diagnostics Ltd, Surat, India

Serum creatinine reagent: Pinnacle Marketing Private Limited, Mumbai.

All other reagents and chemicals used in the study were of analytical grade.

**Dose selection:**

Based on the clinical dose (5-10g twice a day) the polyherbal formulation, diasansar, was tested at two dose levels of 450 and 900 mg/kg, b.wt. The standard, glibenclamide, was tested at 500 µg/kg, b.wt. All the drugs were suspended in 0.5% w/v sodium carboxymethyl cellulose (CMC) and administered at a dose volume of 10 ml/kg body weight.

## Methods

### Oral glucose tolerance test in normal rats:

Twenty four rats were divided into four groups of six each
Group 1: Received 2% w/v acacia suspension at a dose of 10 ml/kg, p.o. and served as control.
Group 2: Received diasansar 450 mg/kg, p.o.
Group 3: Received diasansar 900 mg/kg, p.o.
Group 4: Received glibenclamide, 500 µg/kg, p.o.
All the animals were fasted for 16 h before the test and received assigned treatment 1 h before the glucose load of 10 g/kg. Blood was collected from retro orbital Plexus at 0, 30, 60 and 120 min. Serum was separated for the estimation of glucose.

### Streptozotocin induced Type-1 diabetes

Diabetes was induced in 16 hours fasted male Wistar rats 160±15g, by intraperitoneal injection of 65 mg/kg body weight of streptozotocin[6]. After 72 hours, animals with levels of blood glucose higher than 245 mg/dl were selected and used. They were divided into five groups of six rats each.

Group 1: Received 2% w/v acacia suspension at a dose of 10 ml/kg, p.o. and served as control.
Group 2: Received diasansar, 450 mg/kg, p.o.
Group 3: Received glibenclamide, 500 µg/kg, p.o.
Group 4: Received insulin[7] 6IU/kg, i.p.
Group 5: Received diasansar 450 mg/kg, p.o. and insulin (6 IU/kg, i.p)

The polyherbal formulation was administered twice daily for period of 20 days. Fasting blood was collected from the retro orbital plexus for estimation of serum glucose, cholesterol, triglyceride, creatinine and HDL-cholesterol and liver was dissected out for the estimation of glycogen[8, 9]. Body weights of all animals were recorded prior to the treatment and sacrifice.

All data are means ± SEM. Data were analyzed by ANOVA and, followed by comparisons using Dennett's test. Values considered significant were $P < 0.05$

## Results

"Table 1: Effect of diasansar on oral glucose tolerance in normal rats"

| Group | Treatment | Serum Glucose mg/dl (% change) | | | |
|---|---|---|---|---|---|
| | | 0 min | 30 min | 60 min | 120 min |
| Group 1 | Control,2% w/v,acacia suspension p.o. | 71.71± 0.63 | 97.98± 0.74<br>36.56±2.13% | 123.81± 0.94<br>72.70±1.90% | 100.98±0.74<br>40.85± 2.14% |
| Group 2 | Diasansar (450mg/kg, p.o) | 81.85± 0.49 | 90.08± 0.34<br>10.06± 0.41%* | 78.1± 0.28<br>-4.56± 0.85%* | 88.65± 0.3191<br>8.33± 0.802%* |
| Group 3 | Diasansar (900mg/kg, p.o | 77.81± 0.77 | 86.66±0.33<br>11.43±1.37%* | 76.28± 0.20<br>1.88±0.85%* | 81.38± 0.33<br>4.64± 1.36%* |
| Group 4 | Glibenclamide (500mcg/kg,p.o) | 76.58± 0.63 | 108.2± 0.51<br>41.30± 1.40* | 88.35± 0.47<br>17.96±2.80%* | 100.6± 0.182<br>31.38±1.10%* |

Values are in mean ± SEM, n = 6; Values are in mean ± SEM of serum glucose mg/dl, n = 6; P < 0 .001 when compared to the Control group 1

"Table 2: Effect of Diasansar on serum glucose levels in diabetic rats"

| Group | Treatment | Serum glucose level | | % Change |
|---|---|---|---|---|
| | | Initial | Final | |
| Group 1 | Control,2% w/v,acacia suspension p.o. | 260.33±3.71 | 252±2.06 | -3.12± 1.01 |
| Group 2 | Disansar (450mg/kg, p.o.) | 265.33±2.26 | 122±3.21*$ | -53.96±1.25*@ |
| Group 3 | Glibenclamide (500mcg/kg, p.o.) | 251.16±2.30 | 135.83± 3.08*$ | -45.84± 1.36*@ |
| Group 4 | Diasansar(450 mg/kg,p.o)+ Insulin ( 6IU/kg , i.p) | 272.33±3.22 | 101.16± 3.98*$ | -62.15± 1.19*@ |
| Group 5 | Insulin(6IU/kg,i.p) | 286± 3.30 | 131.66± 3.26*$ | -53.93±0.99*@ |

Values are in mean ± SEM, n = 6; Values are in mean ± SEM of serum glucose mg/dl, n = 6, P < 0.001@when experimental groups compared with control (Gr1)

"Table-3: Effect of Diasansar on serum cholesterol, triglycerides, HDL cholesterol creatinine in diabetic rats"

| Group | Treatment | Cholestrol (mg/dl) | Triglycerides (mg/dl) | HDL Cholestrol (mg/dl) | Creatinine (µmol/l) |
|---|---|---|---|---|---|
| Group – 1 | Control 2% w/v acacia suspension p.o. | 92.51±2.19 | 68.3±2.32 | 41.81±1.92 | 72.65±1.20 |
| Group – 2 | Diasansar (450 mg/kg , p.o) | 53.2± 2.26* | 43.06±1.99* | 66.81±2.05* | 50.9± 0.40* |
| Group – 3 | Glibenclamide (500mcg/kg, p.o) | 62.33±2.13* | 51.48±2.45* | 63.23±1.44* | 53.8±1.13* |
| Group 4 | Diasansar(450mg/kg,p.o+Insulin (6IU/kg,i.p) | 36.9± 2.49* | 32.11± 1.83* | 73.63± 2.41* | 47.66± 0.592* |
| Group - 5 | Insulin(6IU/kg,i.p) | 65.38±2.55* | 50.23±1.89** | 50.56±1.17** | 49.05±0.31* |

Values are in mean ± SEM, n = 6; Values are in mean ± SEM of serum lipid profile mg/dl, Creatinine, experimental groups compared with control (Gr1) *P< 0.001 □□ **P<0.01

## Discussion

Diasansar, a polyherbal formulation manufactured by Pradhan herbalcompany,Bangalore, contains gymnema sylvestris, withania somnifera, emblica officinalis,curcuma longa, azadirachta indica, eugenia jambolana, trigonella foenum graceum and momordica charantia. These plants have been individually shown to possessantihyperglycemic activity through varied mechanisms of action[10]. Gymnema containsgymnemic acid and gymnemosides, which have been reported to show antihyperglycemic activity in different models of diabetes [10]. Azadirachta indica hasbeen reported to inhibit the action of epinephrine on glucose metabolism, eugeniajambolana and trigonella foenum graceum have been reported to stimulate insulinsecretion[11, 12] the soluble and insoluble fibers present in curcuma longa has been reported to retard the absorption of carbohydrates from the gastrointestinal tract [12]Momordica charantia has been shown to increase peripheral utilization of glucose and also reported to posses insulin like molecules [13, 14, 15]

"Table 4. Effect of Diasansar on body weight and liver glycogen in diabetic rats".

| Group | Treatment | Body weight | | % change | Liver Glycogen (mg/100g tissue) |
|---|---|---|---|---|---|
| | | Initial | Final | | |
| Group 1 | Control,2% w/v,acacia suspension p.o. | 171±1.06 | 158.33±1.14$^{*\$}$ | -7.35± .73 | 654.06±3.17 |
| Group 2 | Disaansar 450mg/kg, p.o. | 168.83±1.04 | 178.5±0.84$^{*\$}$ | 5.68±0.61$^{*@}$ | 1124.5±3.22$^{*}$ |
| Group 3 | Glibenclamide (500mcg/kg, p.o.) | 180.33±1.68 | 189.16±2.83$^{***\$}$ | 505± 1.70$^{*@}$ | 917.96±3.09$^{*}$ |
| Group 4 | Diasansar (450 mg/kg, p.o ) + Insulin ( 6IU/kg , i.p) | 179.83±1.47 | 193.5± 1.54$^{*\$}$ | 7.58± 1.00$^{*@}$ | 1325.96±2.81$^{*}$ |
| Group 5 | Insulin(6IU/kg , i.p) | 169.66±1.30 | 175.83± 1.13$^{**\$}$ | 3.63±068$^{*@}$ | 833±2.42$^{**}$ |

Values are expressed in mean ± SEM, n = 6, $^{*}P < 0.001$, $^{**}P < 0.01$, $^{***}P < 0.05$ . when $^{@}$ experimental groups compared with control (Gr1)

Streptozotocin induces diabetes in rats by β cell destruction, through the generation offree radicals, causing alkylation of DNA and ultimately inducing hyperglycemia. Rats fed with high fructose diet develop hyperlipidemia, insulin resistance, hyperinsulinemia and mild hypertension, which are features associated with the obesity-related hypertension[16, 17, 18]. Diasansar prevented the alterations in the levels of serum glucose, cholesterol, triglycerides, HDL cholesterol., creatinine and body weight, diasansar exhibited better antihyperglycemic, antihyperlipidemic activity compare to glibenclamide and insulin. Diasansar showed synergistic antihyperglycemic effect with insulin compared to diasansar, insulin and glibenclamide treated groups. Ddiabetic nephropathy is associated with increase in the serum creatinine value[19]iasansar reduced the elevated serum creatinine levels in diabetic rats. In addition to its antihyperglycemic activity; it also prevented the secondary cardiovascular, renal complications of diabetes.

## Conclusion

- Diasansar (450 mg/kg, p.o) exhibited antihyperglycemic activity in streptozotocin induced diabetic rats.
- Diasansar also significantly reduced the hyperglycemia in glucose fed normal rats.
- Diasansar showed antihyperlipidemic activity
- Diasnasar improved the elevated serum creatinine levels in diabetic rats
- Thus Diasansar could be of benefit in overcoming accompanying cardiovascular and renal complications of diabetes
- Diasansar was found to be a very promising formulation in managing diabetes mellitus in laboratory rats.
- Further studies will be necessary to establish the probable mechanisms of action of Diasansar powder. These could include measurement of serum insulin levels and liver enzyme levels involved in glucose metabolism.

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