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# EFFECT OF *GYMNEMA SYLVESTRE*, *CITRULLUS COLOCYNTHIS* AND *ARTEMISIA ABSINTHIUM* ON BLOOD GLUCOSE AND LIPID PROFILE IN DIABETIC HUMAN

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**Abstract:** The aim of this study was to manage diabetes with medicinal plants (*Gymnema sylvestre*, *Artemisia absinthium* and *Citrullus colocynthis*) in human patients with type II diabetes. Thirty two patients of type II diabetes from both sexes of 30-60 years age were registered for this study and distributed them into four groups, each having 8 patients. Capsules of each, *Gymnema sylvestre*, *Artemisia absinthium* and *Citrullus colocynthis* were given to patients twice a day for 30 days in 1 g per day dosage and investigated for glucose, triglyceride (TGL) and cholesterol level. *Gymnema sylvestre* reduced 37% glucose, 5% TGL, 13% cholesterol and 19% low desity lipoproteins (LDL) level in diabetic individuals. *Citrullus colocynth* reduced glucose, cholesterol and TGL and HDL-cholesterol level by 35, 6, 6, and 5%, respectively. *Artemisia absinthium* reduced 3% high desity lipoproteins (HDL) and 6% LDL level. From results, it can be concluded that the powdered *Gymnema sylvestre*, *Citrullus colocynthis*, and *Artemisia absinthium* possess good anti-diabetic features, however these herbal products had no significant effect on lipid profiles of the diabetic human.

**Keywords:** *Gymnema sylvestre*, *Artemisia absinthium*, *Citrullus colocynthis*, blood glucose, lipid profile, diabetic individuals

Diabetes mellitus is a clinical syndrome characterized by relative or absolute deficiency of insulin or by resistance to the action of insulin at the cellular level (1). It is a disorder of glucose metabolism occurring from dysfunction of pancreatic β cells and insulin resistance, it is characterized by partial or total lack of functioning insulin and there is alteration in carbohydrate, fat and protein metabolism (2).

To manage diabetes with medicinal plants along with dietary restriction has caught the attention of most researchers (3). Even today, natural sources form the basis for a large number of modern drugs and one or more than one active ingredient from them is to be found in 25 percent of all prescriptions (4). There is a dire need for other strategies to the current modern pharmacotherapy of diabetes mellitus. Herbal drugs comprise a significant amount of conventional medicine and literature, which is an indication of anti-diabetic activity exhibited by more than 400 plant species (5).

*Gymnema sylvestre* (Asclepiadaceae), *Citrullus colocynthis* (Cucurbitaceae) and *Artemisia absinthium* (Asteraceae) have been used for its antidiabetic, antihelmintic, stomachic, antibacterial, antifeedant, antifertility, antipyretic, cytostatic, antitumor, and antimalarial action (6, 7). The literature study has shown the antidiabetic effect of these plants in study subjects with hyperglycemia induced by streptozocin or other compounds. There was no study about antidiabetic effect of these herbal drugs in diabetic patients. Therefore, this study was designed to

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assess the effect of *Gymnema sylvestre*, *Citrullus colocynthis* and *Artemisia absinthium* on blood glucose and lipid profile in type II diabetic individuals of Tehsil Sarai Naurang of District Lakki Marwat, Khyber Pakhtoonkhah (KPK) province, Pakistan.

## METHODOLOGY

### Location of study

This study was designed and directed by Dongzhimen Hospital, Beijing University of Chinese Medicine, and got supports from other research institutions, and conducted in Tehsil Sarai Naurang of District Lakki Marwat, on type II diabetic individuals, who were properly registered for the study.

### Selection criteria, sample size and study design

This study was approved (Approval no. 34-2012/HU/PHM) by the Departmental Review Committee (University of Hazara) and was conducted in accordance with international guidelines for Good Clinical Practice and Hilsinki guidelines for human use in laboratory (8, 9).

The study was advertised through personal contacts, telephone calls to diabetic individuals and by visiting diabetic centers and surrounding villages. The questionnaire contained querries about demography, diabetic type, medication for diabetes and medication for other diseases. Their fasting blood glucose was determined. Those diabetic individuals whose fasting blood sugar level was 125 mg/dL or above, and who were not taking insulin or any other medicines for any other diseases were registered for the study. Thirty-two patients of type II diabetes from both sexes of 30-60 years age (mean age 49.5 years) were registered for the study. These individuals were divided into four groups namely group 1, 2, 3 and 4. Each group was having 8 individuals: Group 1, assigned for *Gymnema sylvestre*, group 2 for *Artemisia absinthium*, group 3 for *Citrullus colocynth* and group 4 for placebo.

### Preparation of *Gymnema sylvestre*, *Citrullus colocynthis* and *Artemisia absinthium* capsules

The required amount of *Gymnema sylvestre*, *Citrullus colocynthis* and *Artemisia absinthium* leaf were purchased from the local market and ground finely. The ground herbs were packed into the hard gelatin capsules so that each capsule contained 0.5 g. The capsules were stored in a dry, cool place.

### Experimental protocol

The capsules of *Gymnema sylvestre*, *Citrullus colocynthis*, and *Artemisia absinthium* were given 1 g/day dosage (in two divided doses 12 hourly) for 30 days to group 1, group 2 and group 3, respectively. From day 30 to day 40 (10 days) was the wash period and no dose was given in those 10 days; however, blood samples were collected on day 40 to assess the effect of these herbal drugs. One gram placebo doses/day were given for 30 days to group 4.

### Blood collection and analysis

Approximately, 5 mL fasting blood samples were taken from each individual of each group on day 0, 10, 20, 30 and 40. Blood samples were transferred to sterilized centrifuge tubes and allowed for clotting at room temperature. The samples were centrifuged for 5 min in a centrifuge (Hiki, China) at 4000 rpm for serum separation. Separated serums were transferred to Eppendorf tubes and were stored in freezer at 0$^{o}$C for later analysis. Glucose was determined by the method of Barham et al. using Spectrophotometer (S-200D, England) and Randox Kit (CAT No. GL2586/s) (10). Trigliceride was determined by the method of Tietz (11) using Spectrophotometer (S-200D, England) and Randox Kit (REF TR210). Cholesterol was determined by enzymatic colorimetric method as mentioned in the report of the National Cholesterol Education Program (12). Spectrophotometer (S-200D, England) and Randox kit (CAT No. CH 207) were used for this purpose. Low-density lipoproteins (LDL) were precipitated by adding phosphotungstic

Table 1. Information of diabetic individuals on the day of screening.

| Group | Age | BMI | Glucose (mg/dL) | TGL (mg/dL) |
|---|---|---|---|---|
| 1 | 48 ± 7 | 29.1 ± 7.1 | 178 ± 35 | 231 ± 15 |
| 2 | 51 ± 9 | 28.9 ± 4.2 | 170 ± 30 | 219 ± 42 |
| 3 | 49 ± 7 | 26.9 ± 4.1 | 169 ± 25 | 230 ± 20 |
| 4 | 50 ± 9 | 27 ± 6.2 | 162 ± 22 | 210 ± 25 |

acid and magnesium ions to the sample. Centrifugation left only the HDL (high-density lipoproteins) in the supernatant; their cholesterol content was determined (13, 14).

**Statistical analysis**

The data were statistically analyzed by analysis of variance and LSD test with $p < 0.05$ using statistical software Mstat C. (The MSTAT C with MGRAPH by Russell D. Freed MSTAT Director, Crop and Soil Science Department, Michigan State University version).

## RESULTS AND DISCUSSION

This study was conducted on type II diabetic individuals for 40 days. These individuals were on hypoglycemic drugs but were not on insulin therapy. Their serum glucose concentration, as noted from their previous laboratory reports were either 125 mg/dL or above. The information about these 32 diabetic individuals on the day of screening in terms of age, BMI, serum glucose and serum trigliceride are given in Table 1.

The effect of *Gymnema sylvestre* on the serum glucose and lipid profile is portrayed in Table 2. The values on day 0 indicate the fasting values of the studied biochemical parameters of diabetic individuals before the start of treatment and were considered as control values. On the starting day of experiment (day 0), mean fasting serum glucose, TGL, cholesterol, HDL and LDL concentration of the diabetic individuals of group 1, were 219 ± 41, 218 ± 70l, 274 ± 70, 37 ± 6 and 191 ± 63 mg/dL, respectively. When the diabetic individuals of these groups used 1 g of *Gymnema sylvestre* doses/day for 30 days, their mean fasting serum glucose, TGL, cholesterol, HDL and LDL level changed to138 ± 17, 208 ± 72, 238 ± 56, 43 ± 11 and 154 ± 54 mg/dL, respectively. Use of *Gymnema sylvestre* capsules for 30 days significantly ($p < 0.05$) reduced the serum glucose level of diabetic individuals as compared to serum glucose values on day 0 of this group. The data show that 1 g dose of *Gymnema sylvestre* reduced 37% glucose, 5% TGL, 13% cholesterol, 2% HDL, and 19% LDL level in diabetic individuals. The decrease in glucose level was significant ($p < 0.05$), while the decrease in all other parameters was non-significant ($p > 0.05$). The mean fasting serum glucose, TGL, cholesterol, HDL and LDL concentration of the diabetic individuals of group 1, on day 40 (when they did not receive *Gymnema sylvestre* for the last 10 days) returned back to the control values and their difference from control values was non-significantly different ($p > 0.05$).

The effect of *Citrullus colocynthis* on the serum glucose and lipid profile is given in Table 2. The values on day 0 indicate the fasting values of the studied biochemical parameters of diabetic individuals before the start of treatment and were con-

Table 2. Effect of the studied herbs on various biochemical parameters in diabetic individuals (n = 8, the mean ± SD).

| Group | Biochemical parameters (mg/dL) | Values | | | | |
|---|---|---|---|---|---|---|
| | | Day 0 | Day 10 | Day 20 | Day 30 | Day 40 |
| *Gymnema Sylvestre* | Fasting glucose | 219 ± 41 | 159 ± 26 | 157 ± 24 | 138 ± 17 | 181 ± 38 |
| | TGL | 218 ± 70 | 218 ± 75 | 212 ± 74 | 208 ± 72 | 230 ± 87 |
| | Cholesterol | 274 ± 70 | 263 ± 62 | 261 ± 65 | 238 ± 56 | 249 ± 54 |
| | HDL | 37 ± 6 | 39 ± 8 | 41 ± 11 | 43 ± 11 | 37 ± 7 |
| | LDL | 191 ± 63 | 180 ± 57 | 177 ± 61 | 154 ± 54 | 166 ± 51 |
| *Citrullus colocynthis* | Fasting glucose | 215 ± 56 | 188 ± 49 | 156 ± 48 | 140 ± 35 | 213 ± 69 |
| | TGL | 253 ± 76 | 248 ± 74 | 242 ± 72 | 238 ± 69 | 256 ± 74 |
| | Cholesterol | 257 ± 80 | 249 ± 76 | 249 ± 71 | 241 ± 72 | 253 ± 79 |
| | HDL | 38 ± 12 | 39 ± 11 | 41 ± 10 | 40 ± 12 | 38 ± 11 |
| | LDL | 168 ± 83 | 160 ± 79 | 158 ± 75 | 153 ± 77 | 167 ± 77 |
| *Artemisia absinthium* | Fasting glucose | 211 ± 57 | 204 ± 262 | 182 ± 43 | 143 ± 30 | 191 ± 26 |
| | TGL | 187 ± 65 | 185 ± 64 | 181 ± 59 | 169 ± 64 | 190 ± 68 |
| | Cholesterol | 239 ± 35 | 237 ± 36 | 234 ± 34 | 226 ± 32 | 238 ± 31 |
| | HDL | 39 ± 8 | 39 ± 8 | 40 ± 9 | 40 ± 9 | 39 ± 8 |
| | LDL | 163 ± 36 | 161 ± 36 | 157 ± 33 | 153 ± 32 | 162 ± 38 |

sidered as control values. On the starting day of experiment (day 0), mean fasting serum glucose, TGL, cholesterol, HDL and LDL concentration of the diabetic individuals of group 1, were 215 ± 56, 253 ± 76l, 257 ± 80, 38 ± 12 and 168 ± 83 mg/dL, respectively. When the diabetic individuals of these groups used 1 g of *Citrullus colocynth* doses/day for 30 days, their mean fasting mean fasting serum glucose, TGL, cholesterol, HDL and LDL level changed to 140 ± 35, 238 ± 69, 241 ± 72, 40 ± 12 and 153 ± 77 mg/dL, respectively. Use of *Citrullus colocynth* capsules for 30 days significantly ($p < 0.05$) reduced the serum glucose level of diabetic individuals as compared to serum glucose values on day 0 of this group. The data show that 1 g dose of *Citrullus colocynthis* reduced 35% glucose, 6% TGL, 6% cholesterol, 5% HDL, and 9% LDL level in diabetic individuals. The decrease in glucose level was significant ($p < 0.05$), while the decrease in all other parameters was non-significant ($p > 0.05$). The mean fasting serum glucose, TGL, cholesterol, HDL and LDL concentration of the diabetic individuals of group 1, on day 40 (when they did not receive *Citrullus colocynthis* for the last 10 days) returned back to the control values and their difference fron control values was non-significantly different ($p > 0.05$).

The effect of *Artemisia absinthium* on the serum glucose and lipid profile is presented in Table 2. The values on day 0 indicate the fasting values of the studied biochemical parameters of diabetic individuals before the start of treatment and were considered as control values. On the starting day of experiment (day 0), mean fasting serum glucose, TGL, cholesterol, HDL and LDL concentration of the diabetic individuals of group 1, were 211 ± 57, 187 ± 65, 239 ± 35, 39 ± 8 and 163 ± 36 mg/dL, respectively. When the diabetic individuals of these groups used 1 g of *Artemisia absinthium* doses/day for 30 days, their mean fasting mean fasting serum glucose, TGL, cholesterol, HDL and LDL level changed to 143 ± 30, 169 ± 64, 226 ± 32, 39 ± 8 and 162 ± 38 mg/dL, respectively. Use of *Artemisia absinthium* capsules for 30 days significantly ($p < 0.05$) reduced the serum glucose level of diabetic individuals as compared to serum glucose values on day 0 of this group. The data show that 1 g dose of *Artemisia absinthium* reduced 32% glucose, 10% TGL, 5% cholesterol, 3% HDL and 6% LDL level in diabetic individuals. The decrease in glucose level was significant ($p < 0.05$), while the decrease in all other parameters was non-significant ($p > 0.05$). The mean fasting serum glucose, TGL, cholesterol, HDL and LDL concentration of the diabetic individuals of group 1, on day 40 (when they did not receive *Artemisia absinthium* for the last 10 days) returned back to the control values and their difference from control values was non-significantly different ($p > 0.05$).

*Gymnema sylvestre*, *Citrullus colocynthis*, and *Artemisia absinthium* were observed to produce hypoglycemic effect in diabetic human. The hypoglycemic action of these three herbs is already reported in the literature. In those studies, the investigators employed extracts of these herbs in hyperglycemic animal models under the effect of glucose lowering compounds e.g., streptozocin and alloxan (15).

In a study, the authors claimed hypoglycemic effect of alcoholic extract of *Gymnema sylvestre*. Another study also proposed the antihyperglycemic effect in diabetic subjects after oral administration (400 mg per day) of leaf extract. Moreover, other investigators observed the stimulation of insulin secretion from isolated human β-cell and mouse cells *in vitro*, without compromising cell viability after treating with the aqueous extract of *Gymnema sylvestre* leaves (16). Moreover, the ethanolic extract of *Citrullus colocynthis* pulp in an oral dose of 300 mg/kg was observed to significantly diminish plasma glucose concentrations in alloxan-induced diabetic rats. In another study, the aqueous, crude, and purified extracts of *Citrullus colocynthis* pulp also illustrated a dose-dependent hypoglycemic effect through the enhancement of insulin release from isolated islets (16). Various parts of *Citrullus colocynthis* such as roots, fruits, seeds, rinds and leaves, have been used in extract preparation. The doses of these extracts range between 10-500 mg per kg body weight of animals per day (17). In a study, hypoglycemic effect was observed in streptozocin-induced hyperglycemic rats after oral administration of different doses (100, 250 and 500 mg/kg of rat body weight) of *Artemisia absinthium* for six weeks (16).

In addition, all these three herbs, *Gymnema sylvestre*, *Citrullus colocynthis*, and *Artemisia absinthium* produce hypoglycemic effect in a dose dependent manner. Mechanistically, it has been proposed that all the three herbs exert antidiabetic effect through insulinomimetic (to increase insulin secretion) and insulinotropic action. Actually, these herbs are believed to be involved in the regeneration and repairmen of pancreatic β-cells (16).

## CONCLUSION

From the results, it can be concluded that the powdered *Gymnema sylvestre*, *Citrullus colocynthis*,

and *Artemisia absinthium* possess good anti-diabetic features, however these herbal products had no significant effect on lipid profiles of the diabetic human.

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