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# ANTIDIABETIC ACTIVITY OF *PARKINSONIA ACCULEATA* LINN IN RABBITS, EMPHASIS ON C REACTIVE PROTIENS

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## ABSTRACT

*Parkinsonia acculeata* is used in traditional medicine for the treatment of jaundice and diabetes. Accordingly, the present study was designed to investigate the effects of Pet ether and aqueous extracts of the leaves of *Parkinsonia acculeata* on glucose homeostasis in alloxan induced diabetis in rabbits. After 7 days of study it showed that *Parkinsonia acculeata* reduced glucose levels significantly. The extracts were also able to reduce quantatively C reactive proteins and levels of SGOT and SGPT enzymes. It was concluded that due to its potent antioxidant and antidiabetic properties, the *Parkinsonia acculeata* extract exerts remarkable antidiabetogenic effect.

**INTRODUCTION:** The prevalence of insulin resistance and diabetes has increased in the past decades at an alarming rate in all Western countries and in those countries which are adopting a 'western life style'. This trend suggests the impact of environmental factors such as diet, obesity and physical activity on the pathogenesis of diabetes. However it is known that the prevalence and variation of prevalence, as consequence of environmental changes, is different in various ethnic groups. Studies conducted in multiethnic populations suggest that some ethnic groups, such as Hispanics or Asian Indians, might have a particular predisposition, possibly on genetic basis, to develop insulin resistance and diabetes, when exposed to adverse conditions[1].

The most common and life threatening disorder that besets type 2 diabetic subjects is coronary heart disease (CHD). Irrespective of the ethnic background the risk for CHD among diabetic subjects is greater by a factor of 2 to 4 compared to non-diabetic subject [2]. The diabetic condition contributes for initiation and progression of micro and macro vascular complications in diabetics. Of all, cardiovascular complications are the leading cause of mortality and morbidity in diabetics.

As diabetics are at risk of CVD, therefore there is a need to identify markers which would help in prognosis and diagnosis of the disease. C-Reactive protein is the principle down stream mediator of the acute phase response and is primarily derived via IL-6–dependent hepatic biosynthesis. Interleukin 6, a major proinflammatory cytokine, is produced in a variety of tissues, including activated leukocytes, adipocytes, and endothelial cells [3].

C-reactive protein (CRP) is the prototypical, and most commonly used, acute-phase reactant marker of inflammation in the body. Increases in CRP concentration (even when within the clinically normal range and of other inflammatory markers are independently predictive of future cardiovascular events [1]. The major function of CRP include its ability to bind to various ligands exposed on damaged tissue or bacteria (opsonization) for the enhancement of phagocytosis and activation of the compliment pathway, thereby enabling it to exert both anti- and

pro inflammatory functions.CRP is mainly expressed by hepatocytes and its synthesis is regulated at the posttranscriptional level by cytokines [5]. As atherosclerosis involves inflammation of the vascular endothelium, CRP levels tend to be raised. Basic research studies have revealed that inflammatory markers are high among subjects with insulin resistance and diabetics. Inflammation is considered to be a part of insulin resistance syndrome and this to some extend explains high risk for CAD among diabetic subjects [6].

**MATERIALS METHODS:**

**Plant material and Preparation of extracts:**

The leaves of *Parkinsonia Acculeata* were collected form Sholapur district .and were aunthenticated by Departent of Botony, Maulana Azad College Of Arts ,Science and Commerce Aurangabad . A voucher specimen has been deposited in the herbarium of the Department of Botany, Maulana Azad College Of Arts ,Science and Commerce Aurangabad . Leaves were sun dried and grinded into powder form. The powdered leaves were extracted in Soxhlet extractor using petroleum ether and concentrated with vacuum evaporator . The aqueous extract was prepared by maceration of leaves with water for 48h.

**Phytochemical screening:** The extracts of leaves were subjected to preliminary phytochemical screening to identify the presence of various phytoconstituents present .It showed the presence of Alkaloids, glycosides, saponins, flavanoids etc[6].

**Drugs and chemicals:** *Parkinsonia acculeata* extract, alloxan and standard drug Metformin. All other chemicals were of analytical grade.

**Alloxan induced Diabetes Mellitus:** For induction of diabetes , alloxan monohydrate was dissolved in water for injection and given at dose of 120 mg/kg body weight intra peritonially [4].

**Experimental design:**

**Selection of animals**: Adult rabbits of either sex weighing between 1-2 kg were taken. They were fed on natural plant diet and were maintained under standard conditions for 1 week for acclimatization. Water was provided ad libitum and all rabbits were kept in cages.[5] (the evalution of soyaen ref 10) After one week of acclimatization the rabbits were divided in to seven groups of six rabbits each of either sex. Experimental protocols were reviewed and approved by institutional IAEC.

**TABLE 1: EXPERIMENTAL GROUPS AND TREATMENT GIVEN**

| Groups | Treatment (dose/kg, p.o.) |
|---|---|
| Group I : | Normal control. |
| Group II : | (Diabetic control group) Alloxan Monohydrate 120 mg/kg body weight. |
| Group III : | Metformin 500mg (Standard drug) |
| Group IV : | *Parkinsonia acculeata* Pet ether extract 500 mg/kg |
| Group V : | *Parkinsonia acculeata* Chloroform extract 500 mg/kg |
| Group VI: | *Parkinsonia aculeata* Methanol extract 500 mg/kg |
| Group VII: | *Parkinsonia acculeata* Aqueous extract 500 mg/kg |

Alloxan Mono hydrate was given intraperitonially in the dose of 120 mg/kg and after 03 days rabbits showing blood glucose above 250 mg/dl were selected for study. Pet ether and Chloroform *Parkinsonia acculeata* extracts,were suspended in Tween 40 and aqueous and methanol are water soluble, were administered at the doses of 500 mg/kg orally for 7 days to the animals of groups IV, V, VI, and VII, and metformin to standard group in a dose of 500 mg/kg[7] respectively.

Blood samples were collected from the marginal ear vein with the help of sterilized needle and syringe on 1st, 3rd, 5th and 7th day after drug administration [8]. Blood glucose concentration was determined in serum by commercially available glucose kit (Accu-check). The glucose levels were expressed as mg/dl as shown in **fig. 1**.

On day 7 the animals were sacrificed under ether anesthesia, blood sample was collected by carotid bleeding and samples were immediately centrifuged for serum. Liver, pancreas were isolated and preserved in 10% solution of formaldehyde.

**Biochemical Analysis:** The blood samples collected were immediately centrifuged and subjected to estimation of SGOT, SGPT [10], Triglycerides, LDL [11], Urea, Creatinine [9] and C reactive proteins. Tulip and Crest kits were used to estimate the enzymes. The enzyme estimation was carried out on Robnic Preitest touch Autoanalyser. The instrument was calibrated as per the instruction manual. Liver glycogen was estimated as per method described by J. Van Der Vies [12].

**RESULTS:**

1. **Estimation of blood glucose concentration:** Treatment with aqueous, Pet ether extracts of *P. acculeata* significantly decreased the blood glucose levels of diabetic groups The blood glucose concentration of diabetic rabbits was increased significantly as compared to the normal control group. The blood levels of glucose of control, diabetic & treated groups is shown in **table 1**.

**TABLE 1: TABLE SHOWING MEAN BLOOD GLUCOSE CONCENTRATION (mg/dl)**

| Groups | Dose mg/kg | Mean Blood Glucose Concentration | | | |
|---|---|---|---|---|---|
| | | Day 1 | Day 3 | Day 5 | Day 7 |
| Normal | - | 107.5±1.4 | 111.8±1.3 | 107.1±1.4 | 105.3±1.7 |
| Diabetic Control | 120 | 285.3±4.9 | 302.1±3.6 | 308.6±5.1 | 321.5±3.1 |
| Std. Metformin | 500 | 269.1±5.5 | 162.8±1.2 | 167.6±1.4 | 151.5±1.8 |
| Pet ether | 500 | 268.5±4.8 | 209.6±1.2 | 149.5±1.1 | 121.1±1.9 |
| Chloroform | 500 | 301.5±3.3 | 309.6±4.7 | 298.6±6.1 | 291±5.8 |
| Methanol | 500 | 292.3±5.3 | 309.5±3.9 | 317.8±4.8 | 302.1±6.7 |
| Aqueous | 500 | 278.5±3.9 | 213.8±1.7 | 150.3±1.1 | 130.1±1.5 |

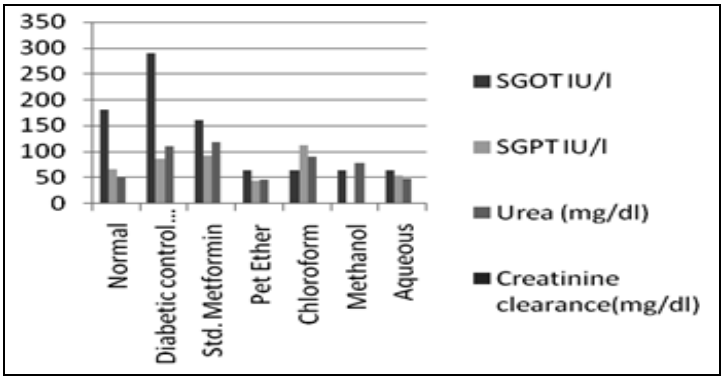
N= 6, Mean ± SEM (Standard error mean),*p<0.01 significant as compared to control

2. **Estimation of Serum Enzymes and Markers:** SGOT & SGPT values increase significantly in diabetic rabbits. *P. acculeata* treatment decreased the SGOT & SGPT values in diabetic rabbits. Urea & Creatinine values were changed significantly in diabetic rabbits and are illustrated in **table 2** showing comparison with normal, *P. acculeata* treated diabetic rabbits.

**TABLE 2: TABLE SHOWING LEVELS OF SGOT, SGPT, UREA & CREATININE**

| Groups | SGOT | SGPT | Urea | Creatinine |
|---|---|---|---|---|
| Normal | 180.6±3.3 | 64.3±1.8 | 49.3± 1.4 | 0.9±0.02 |
| Diabetic Control | 289.8±2.9 | 84.3±1.4 | 108.6±2.3 | 1.3±0.03 |
| Std. Metformin | 159.5±6.4 | 90.8±3.6 | 117.3±2.4 | 1.45±0.01 |
| Pet ether | 62.06±2.2 | 41.8±1.8 | 43.5±1.5 | 1.2±0.06 |
| Chloroform | 62.7±2.5 | 111.6±2.4 | 88.7±1.4 | 1.2±0.02 |
| Methanol | 47.0±2.8 | 29.2±1.0 | 77.4±1.4 | 1.2±0.1 |
| Aqueous | 77.4±1.9 | 52.2±1.3 | 45.7±1.7 | 1.0±0.03 |

N= 6, Mean ± SEM (Standard error mean),*p<0.01 significant as compared to control



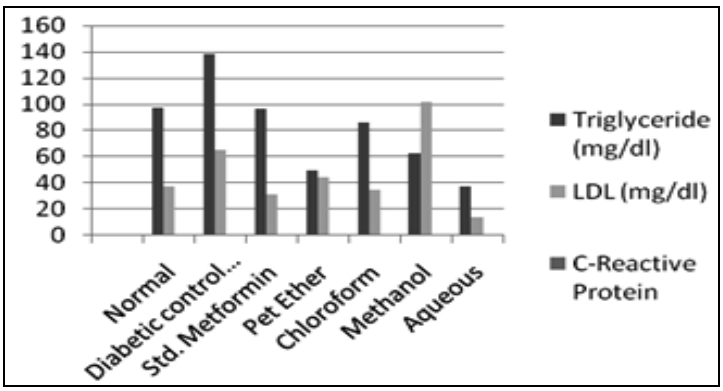

**GRAPH SHOWING LEVELS OF SGOT, SGPT, UREA & CREATININE**

3. **Hypolipidemic effect:** Triglycerides and LDL values increased significantly in diabetic rabbits, where as *P. acculeata* extracts decreased the Triglycerides & LDL values. The lipid profile and the inflammatory marker C-Reactive protein of normal, diabetic & *P. acculeata* extract treated diabetic rabbits is shown in **table 3**.

**TABLE 3: LEVELS OF TRIGLYCERIDE, LDL & C-REACTIVE PROTEIN**

| Groups | Triglyceride mg/dl | LDL mg/dl | C-Reactive Protein |
|---|---|---|---|
| Normal | 97.3±3.3 | 37.5±1.6 | 0.037 |
| Diabetic Control | 138.16±2.9 | 65.1±2.1 | 0.07 |
| Std. Metformin | 96.56±4.1 | 30.93±1.4 | 0.03 |
| Pet ether | 49.98±1.5 | 44.6±1.9 | 0.04 |
| Chloroform | 85.8±3.5 | 34.8±2.1 | 0.05 |
| Methanol | 62.4±2.3 | 101.5±2.8 | 0.07 |
| Aqueous | 37.75±1.5 | 13.8±1.7 | 0.04 |

N= 6, Mean ± SEM (Standard error mean),*p<0.01 significant as compared to control

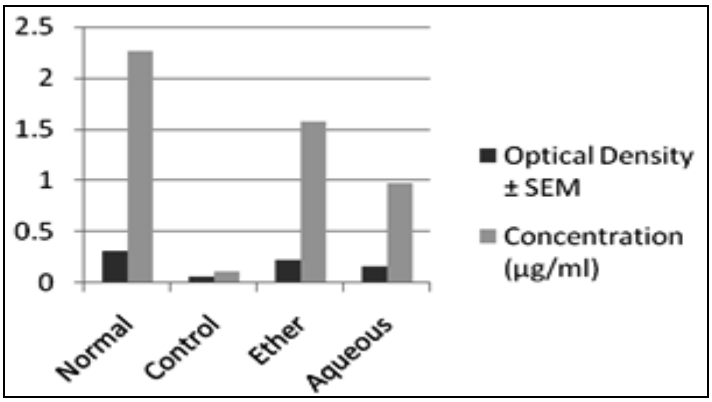



**GRAPH SHOWING LEVELS OF TRIGLYCERIDE, LDL & C-REACTIVE PROTEIN**

**TABLE 4: LEVELS OF LIVER GLYCOGEN**

| Group | Optical Density ± SEM | Concentration (µg/ml) |
|---|---|---|
| Normal | 0.31±0.008819 | 2.26 |
| Control | 0.06 ±0.08954 | 0.11 |
| Ether | 0.23±0.004282 | 1.57 |
| Aqueous | 0.16 ± .001078 | 0.97 |

N= 6, Mean ± SEM (Standard error mean),*p<0.01 significant as compared to control




**GRAPH SHOWING LEVELS OF LIVER GLYCOGEN**

**DISCUSSION:** Alloxan and streptozotocin are widely used to induce experimental diabetes in animals because of their ability to produce β cell necrosis [13, 14]. It is commonly accepted that both of these diabetogenic compounds are involved in free radical generation causing pancreatic cell damage [15, 16].

The present study was under taken to evaluate the antidiabetic activity of *Parkinsonia acculeata*. The studies revealed that Pet ether and aqueous extracts of *Parkinsonia acculeata* significantly reduced the levels of blood glucose. It was observed during the study that the levels of various enzymes were elevated reflecting the damage caused to pancreas and liver. SGOT/SGPT ratio is a sensitive index of liver cell destruction. The levels of SGOT and SGPT were significantly decreased as compared to diabetic control.

Elevated levels of Triglycerides are indicators of hyperglycemia which is an important contributor to Diabetic complication like hypertension and athero-sclerosis. LDL are reported to have atherogenic activity in diabetis. From the present study, it is revealed that the extracts of *Parkinsonia acculeata* have reduced the levels of triglycerides and LDL which may be helpful in reducing the diabetic complications. C-Reactive protein is the principle down stream mediator of the acute phase response and is primarily derived via IL-6–dependent hepatic biosynthesis. The present study has revealed that the C-reactive protein were considerably reduced in the pet ether, aqeous extracts of Parkinsonia acculeata as compared to control group. This highlights the facts that in order to characterize the risk of cardiovascular events, CRP should be considered in the list of screening tests of diabetic studies.

Glycogen is the primary intracellular storable form of glucose and its levels in various tissues especially skeletal muscles are direct reflection of insulin activity. In diabetis the stores of glycogen are depleted as an alternative source of energy. In the present study it is observed that extracts of Parkinsonia acculeata treated groups showed higher levels of glycogen as compared to control. Experimental and bio analytical result shows that Parkinsonia acculeata has significant antidiabetic activity.

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