STUDIES ON ANTIDIABETIC ACTIVITY AND RELATED BLOOD BIOCHEMISTRY PROFILE OF SOME INDIGENOUS PLANTS

ABSTRACT

Chapter-1: INTRODUCTION

Diabetes mellitus is a syndrome of disturbed energy homeostasis caused by a deficiency of insulin or of its action resulting in abnormal metabolism of carbohydrate, protein, and fat. Morbidity and mortality stem from metabolic derangements and from long-term complications that can result in retinopathy, nephropathy, neuropathy and so on.s.

Classified into:
Type I Diabetes (*insulin-dependent diabetes mellitus*, IDDM)
Type II Diabetes (*non-insulin-dependent diabetes mellitus*, NIDDM)

Currently available pharmatherapy for the treatment of diabetes mellitus include oral hypoglycemic agents and insulin. However, these current drugs do not restore normal glucose homeostasis and they are not free from side effects. Moreover, due to high cost of allopathic drugs, it is difficult to provide modern medical health care especially in developing countries.

It is therefore become necessary to make use of vast reserves of plant origins for medical purposes which will help to search effective as well as safer drug remedy for diabetes mellitus.

Chapter-2: MATERIALS AND METHODS

Collection of plant materials

*Pterocarpus marsupium* powder was obtained locally from a medicine shop. It was dried in open air and finely ground into powder.
**Confirmation of Diabetes**

After seven days of stabilization period blood samples were obtained from animals fasted overnight. The alloxan injected group which had more than 200 mg% of blood glucose were included in the study.

**Treatment schedule**

The treatment schedule of the various groups is as detailed. On 15\textsuperscript{th} and 30\textsuperscript{th} day of treatment, blood from animals fasted overnight was drawn and the biochemical parameters were assessed.

- NC – Normal Control – Vehicle (propylene glycol)
- IN – Insulin treated – 6 units / kg body weight
- Aqueous extract – 75 mg / kg bodyweight (decoction of heart wood)
- EE – Ethanol extract treated – 75 mg / kg bodyweight
- PE – Petroleum ether extract – 75 mg/kg body weight
- DE – Diethyl ether extract – 75 mg / kg body weight.
- EA – Ethyl acetate extract – 75 mg / kg body weight

The various extracts were dissolved in propylene glycol and the extract was administered orally.

- Recording of body weight -
- Estimation of blood glucose, lipid profile, urea, uric acid & creatinine, Serum Protein Thiols, Antimicrobial screening, liver glycogen, Major active constituents were assayed.

Statistical analysis data was expressed as mean ± SE.

**Chapter-3: RESULTS**

**Preliminary study**

In the present study, an attempt was made to screen the hypoglycemic effect of ethanolic extracts of three different plants namely *Pterocarpus marsupium*, *Tinospora cordifolia* and *Caesalpiniaboundcelfleming*. 
Body weight changes in different groups

Diabetic control group: On day 1, insulin treated and petroleum ether treated groups gained more body weight when compared to diabetic group. There was no significant difference between other groups.
On day 15, insulin treated, alcohol treated and diethyl ether treated groups gained more body weight than diabetic control. However, there was no significant difference between diabetic control and other groups.
On day 30, diabetic control gained more body weight when compared to insulin treated group. However, there was no significant difference between diabetic control and other groups.

Insulin treated group: On day 1, insulin treated group gained more body weight compared to diethyl ether treated, ethyl acetate and aqueous extract treated groups. However, there was no difference between other groups.
On day 15, insulin treated group gained more body weight compared to petroleum ether, ethyl acetate and aqueous extract treated groups. However, no difference was found between other groups.
On day 30, insulin treated group gained more body weight compared to other experimental groups.

Alcohol treated group: On day 1, ethyl acetate treated group gained more body weight compared to alcohol treated group. There was no difference between other groups and alcohol treated groups.
On day 15, there was no difference between any of the groups.
On day 30, alcohol treated group gained more body weight when compared to ethyl acetate treated group. However, there was no significant difference between other groups.

Diethyl ether treated group
On day 1, ethyl acetate treated group gained more body weight compared to alcohol treated group. There was no difference between other groups.
On day 15, there was no difference between any of the groups.
On day 30, alcohol treated group gained more body weight when compared to ethyl acetate treated group. However, there was no difference between other groups.

**Petroleum ether treated group:**
On day 1, ethyl acetate treated group gained more body weight compared to alcohol treated group. There was no difference between other groups. On day 15, there was no difference between any of the groups. On day 30, alcohol treated group gained more body weight when compared to ethyl acetate treated group. However, there was no difference between other groups.

**Ethyl acetate treated group**
On day 1, ethyl acetate treated group gained more body weight compared to alcohol treated group. There was no difference between other groups and alcohol treated groups. On day 15, there was no difference between any of the groups. On day 30, alcohol treated group gained more body weight when compared to ethyl acetate treated group. However, there was no difference between other groups.

**Blood glucose changes in different groups**

**Diabetic Control:** On day 1, EA and aqueous group had a decrease in blood glucose level compared to DC. There was no difference between other treated groups. On day 15, alcohol, EA, DE and PE treated groups had a decrease in blood glucose when compared to DC. There was no difference between DC and insulin and aqueous treated groups. On day 30, DE, PE, alcohol, insulin and EA had decreased blood glucose level when compared to DC. There was no difference between other groups.

**Insulin treated:** On day 1, insulin treated group had an increase blood glucose level compared to PE and EA groups. There was no difference between other groups. On day 15, there was no statistical significant difference in other treated group. On day 30, PE treated had an decrease in blood glucose level compared to insulin. There was no difference between other groups.

**Alcohol treated:** On day 1, alcohol treated group had increase blood glucose level compared to EA and aqueous extract treated groups. There was no difference in DE and PE treated groups. On day 15, alcohol treated group had increase blood glucose level compared to EA.
There was no difference in other treated groups. On day 30, there was no statistical significant difference in other treated groups.

**Diethyl Ether treated group:** On day 1, DE had increase in blood glucose level compared to PE, EA and aqueous extract treated groups. On day 15, there was no statistical significance in PE, EA and aqueous extract treated group. On day 30 also there was no statistical significant difference in other extract treated groups.

**Petroleum ether:** On day 1, PE had increase blood glucose level compared to aqueous extract treated group. On day 15, there was no statistical significant difference in other treated groups. On day 30, PE had decrease in blood glucose level compared to EA.

**Ethyl acetate:** When EA was compared with aqueous extract treated group there was no statistical significant difference on day 1, 15 and 30.

**Serum cholesterol levels in different groups:** When the insulin treated group was compared with the diethyl ether and petroleum ether treated groups, there was statistical difference in which DE and PE had an decrease in cholesterol level when compared to insulin treated group.

**Serum Triglyceride level in different groups**

There was statistical difference when DC was compared other experimental treated group.

**Serum HDL & LDL levels in different groups**

In none of the groups there was any significant difference in HDL level when compared with diabetic group at the end of 30 days.

**Serum urea, uric acid and creatinine level in different groups**

**Urea:** When the diabetic control group was compared with the alcoholic treated group there was significant difference in which alcoholic group had a decrease in blood urea level. When the alcoholic group was compared with EA and aqueous treated group there was significant difference in which alcohol group had a decrease in blood urea level. However, there was no significant difference in other extract treated groups at the end of 30 days.
**Uric acid:** There was no significant difference in other extract treated groups at the end of 30 days.

**Creatinine:** When DC was compared with PE treated group there was significant difference in which DC had a decrease in creatinine level. However, there was no significant difference in other extract treated groups at the end of 30 days.

**Serum protein thiols:** There was statistical significant difference in petroleum ether, ethyl acetate and aqueous extract treated groups when compared with alcohol, DE and PE treated groups in which the former groups had a decrease in protein thiol level. However, there was no significant difference in other groups at the end of 30 days.

**Glycogen:** When insulin group was compared with DE treated group there was significant difference in which insulin group had an decrease in glycogen content. When alcohol treated group was compared with DE group there was significant difference in which alcohol treated group had a decrease in glycogen content. However, there was no significant difference in other extract treated groups at the end of 30 days.

**Chapter-4: DISCUSSION**

**Body weight**
- The breakdown of structural proteins is known to contribute to body weight, thus the decrease can be contributed to loss or degradation of these structural proteins.
- Insulin has potent lipogenic effect and when administered IV, a significant attenuation of fat mass was observed.

**Blood Glucose**
- A significant decrease in the blood glucose level, was observed which may be an indication of the progressive metabolic control of the extract.
Serum Cholesterol

- In the present study, there was an decrease in the cholesterol level for DE and PE treated groups which could have resulted from the antioxidant effect of the DE and PE fraction of the plant indicating that, the hypocholestermic effect may be an indication of progressive metabolic control of the plant extract.

Triglyceride

- In the present study, a reduction in TG levels may be due to decreased lipogenesis and increased lipolytic activation of the hormone sensitive lipase (Al-Shamaony l et al, 1994)
- However, decrease in cholesterol and triglyceride indicates that the plant extract is more useful in the treatment of diabetes as it has hypolipidemic effect.

HDL, LDL

- In our present study there was no significant change in HDL levels which indicates a low risk factor for atherosclerosis.

Urea, uric acid, creatinine

- In the present study, no increase in the levels of urea, uric acid and creatinine in the experimental treated groups indicating that these extracts do not cause impairment in the renal function.

Glycogen

- Administration of alloxan causes decrease in glycogen content due to enhanced glycogenolysis, which is due to insulin deficiency (Dheer R, Bhatnagar P, 2010).
- In the present study, decrease in the glycogen content in the insulin and alcohol treated groups which could be due to disturbances in glycogen synthetase system.

Protein thiols

- In this study, the PE, EA and aqueous treated group had a statistical significant decrease compared to alcohol treated group which could have resulted from the presence of phytochemical component which is known for its anti-oxidant effect.
• Administration of the extract has caused significant reduction in blood glucose and a reduction in protein thiol, which indicates that, there is an improved glycemic control in these rats which accounts for the lowering of protein thiols as an adaptive response.

• Decrease in total thiols would probably represent increased utilization for neutralizing free radicals.

**Phytochemical constituents**

• The presence of saponins, triterpenes, tannins and flavonoids in the heart wood of P.marsupium could also be a probable cause for the antidiabetic effect of our extract.

• The presence of flavonoids, regenerate the damaged β- cells of pancreas

• Saponins found in the plant extracts are suggestive of their antihyperlipidemic properties(Oakenfull D, 1996).

**Antimicrobial action**

• The antimicrobial activity towards both Gram +ve and –ve test organism at 100µg of the alcoholic extract may be due to the presence of saponins with the extract.

• It has been reported to possess a wide range of biological activities which include antifungal, antiviral and antibacterial activities (Lacaille-Dubois and Wagner 1996; Milgate and Roberts, 1995).