EFFECT OF A COMPOUND RECIPE (MEDICINAL PLANTS) ON SERUM INSULIN LEVELS OF ALLOXAN INDUCED DIABETIC RABBITS

Noreen Wadood, Muhammad Nisar*, Abdul Rashid, Abdul Wadood†, Gul-Nawab‡, Ayub Khan‡**

Department of Biochemistry, Kabir Medical College, Peshawar, *Department of Pharmacy, University of Peshawar, **Department of Pharmacology, Ayub Medical College, Abbottabad, Department of Pharmacology, †Khyber Medical College, Peshawar, ‡IRNUM Hospital, Peshawar.

Background: The present study was planned to observe the hypoglycaemic effect of the '*Compound recipe'* a combination of traditional medicinal plants in normal and alloxan induced diabetes mellitus. This study was performed to study the possible role of indigenous medicinal plants in the regeneration of pancreatic β- cells and in treatment of insulin dependent diabetes mellitus. **Methods:** The '*Compound recipe'* was administered daily in doses of 400-mg/kg body weight to normal and alloxan induced diabetic rabbits for a period of 4 months. The blood glucose and serum insulin levels were estimated before and 1, 2, 3 and 4 months after the administration of the extract. **Results:** The extract exerted a significant ($P<0.05$) hypoglycemic effect in alloxan diabetic rabbits. The hypoglycemic effect was not significant ($P> 0.05$) in normal rabbits. The extract exerted a significant ($P<0.05$) increase in insulin levels in alloxan diabetic rabbits. The effect on the insulin levels was not significant ($P> 0.05$) in normal rabbits. The doses used did not show acute toxicity or result in behavioral changes. **Conclusion:** From this study it may be concluded that the *Compound recipe* causes an increase in serum insulin levels in alloxan induced diabetic rabbits possibly due to regeneration of pancreatic β cells.

Keywords: Compound recipe, hypoglycemic effect, alloxan-induced diabetes, serum insulin.

INTRODUCTION

Since ancient times, plant remedies have been used to help to relieve diabetes. In the 6th century B.C., Sushruta, an Indian physician classifying diabetes as a urinary disorder recommended plant remedies for its treatment and Gymnema sylvestre was advised for its treatment[1]. Subsequently many plants have been used throughout the world for the treatment of diabetes. In fact, more than 50 such plant extracts have been documented [2]. In view of this wide usage, the WHO expert committee on diabetes mellitus (1980) has recently recommended that it is important to investigate the effect of agents of plant origin used in traditional medicine [3].

The use of medicinal plants has a long folk history for the treatment of diabetes mellitus.[4-9] Prior to the development of insulin injection therapy in 1921, diabetes was managed entirely with indigenous medicinal plants. Several such plants show hypoglycemic activity when taken orally, for example, Allium cepa[10], Momordica foetida[11], Coccinia indica[12], Momordica charantia[13] and Cuminum nigrum[14]

The composition of medicinal plants used during the course of current investigation is given the name of Compound recipe. The Compound recipe is a composition of ten different medicinal plants possessing hypoglycaemic activity. The components of compound recipe in variable ratio are Acacia catechu, Gymnema sylvestre, Cinamonum tamala, Aegle marelose, Momordica charantia, Azadirachta indica, Tinospora cordifolia, Trigonella foenum graceum, Ficus racemosa and Syzygium cumini. Acacia catechu is used for the first time in this study for regeneration of pancreatic β cells in alloxan induced diabetic rabbits.

For comparison the effect of Pancreas tonic was also studied on blood glucose and serum insulin levels of alloxan diabetic rabbits. Pancreas tonic was used as a standard in this study. Pancreas tonic is also a composition of hypoglycaemic medicinal plants used in the treatment of diabetes mellitus. It components are same as that of Compound recipe. The only exception is Pterocarpus marsupium, which is replaced with Acacia catechu in Compound recipe.

Acacia Catechu is the most important constituent of Compound recipe, while Pterocarpus marsupium is the most important ingredient of Pancreas tonic. Both these plants contain (-)Epicatechin, a chemical compound that is claimed to be responsible for regeneration of pancreatic β cells.

The brief description of components of Compound recipe is given as follows: -

Acacia catechu is one of the very important plants of Indian subcontinent. It is a small to medium-sized deciduous tree. It belongs to the family Leguminoseae-mimoseae. The heartwood of Acacia catechu contains (-) Epicatechin. Acacia catechu has

traditionally been used in eastern medicine to treat diabetes mellitus[16,17].

Gymnema sylvestre, also called gurmar, has been used as a traditional treatment for diabetes in India. It is a member of the Aclepiadaceae family. Gymnema is reported to increase glucose uptake and utilization and improve the function of pancreatic beta cells. Gymnema may also decrease glucose absorption in the gastrointestinal tract[18 - 20].

Cinamonum tamala (Tespat) is a tree found in Bangladesh. It belongs to the family Lauraceae. Its leaves are carminative and are used in intestinal colic and diarrhea. The leaves and bark have been claimed to be effective in the management of diabetes. Oral administration of 50% ethanolic extract of Cinamonum tamala leaves significantly lowered the plasma glucose levels in normoglycaemic and streptozotocin hyperglycemic rats[21].

Aegle marmelos belong to the family Rutaceae. Hypoglycaemic activity of fruits has been reported. The extract of leaves is used in diabetes mellitus.

Momordica charantia also referred to as bitter melon, bitter gourd and karela, is a member of the Curcurbitaceae family and is commonly used as a traditional remedy for diabetes in Asia, Africa and South America[24].

Azadirachta indica belongs to the family Meliaceae. The oil from the seeds of Melia azadirachta exhibited significant hypoglycaemic activity in fasting rabbits. It has been reported that the aqueous extract of tender leaves of Azadirachta indica tree reduced blood sugar in dogs. Also, its oil, leaf decoction and nimbidin significantly delayed the peak rise in blood sugar after glucose administration. Further, it was found that glucose tolerance test curves are similar to that of Tolbutamide[25, 26].

Tinospora cordifolia belongs to the family Menispermaceae. It has been proved to be a hypoglycaemic agent. Plant extract caused reduction in fasting blood sugar in rabbits and rats[27]

Trigonella foenum-graecum belongs to the family Leguminosae. Its seeds have been shown to possess hypoglycemic properties in both animal and human subjects. The soluble dietary fiber (SDF) when fed simultaneously with glucose showed significant hypoglycemic effect in rats. However, compounds other then SDF are also involved in the hypoglycemic activity[28].

Ficus racemosa belongs to the family Urticaceae.This is an herbal substance that has been reported to have hypoglycaemic activity[29].

Syzygium cumini, a moderate size tree belonging to family Myrtaceae. Its fruit juice has anti-diabetic activity. The powdered seeds are claimed to be effective in treatment of diabetes mellitus[30].

The composition of Pancreas tonic is same as that of Compound recipe. The only exception is Pterocarpus marsupium, which is used in Pancreas tonic instead of Acacia catechu.

Pterocarpus marsupium belonging to family Leguminosae, is used as a traditional antidiabetic plant in Ayurvedic medicine. The heartwood of Pterocapus marsupium is claimed to be the main hypoglycemic ingredient that is responsible for regeneration of pancreatic beta cells[18,19]. It is not available in Pakistan and is very expensive.

In the present study Pterocarpus marsupium is replaced by Acacia catechu that has got hypoglycaemic activity and is freely available in Pakistan. This plant contains (-) Epicatechin that is also present in Pterocarpus marsupium and is reported to be responsible for regeneration of β islet cells of pancreas. The idea of the present study is to observe that whether the change in the 'patent prescription' has got the same hypoglycemic activity/regeneration of pancreatic β cells or otherwise.

MATERIAL AND METHODS

Animals used

Healthy male rabbits (Oryetolagus cuniculus) of local strain, weighing 1-1.65 kg were used in these experiments. Before using the rabbit for experiment, rabbits were kept under observation for a week in animal house of Khyber Medical College, Peshawar. The animals were offered a balanced rabbits diet consisting of green leaves, fodder, pulses and water ad libitum.

Chemicals used

- Alloxan monohydrate
- Glucose estimation kit
- Insulin estimation kit

Preparation of the solutions and reagents:

Alloxan

Alloxan monohydrate ($C_4H_2N_2O_4.H_2O$) was available in colored bottles containing 25 gm powder. The solution was prepared by dissolving 10 gm in 100 ml of distilled water (10 %).

Preparation of Diabetic rabbits

The rabbits were made diabetic by injecting alloxan monohydrate 150-mg/Kg-body weight intravenously[13]. This dose permanently destroys the β cells of pancreas and produces diabetes mellitus. Eight days after injection of the alloxan monohydrate, blood glucose of all the surviving rabbits was determined by the Diagnostics Elitech method.

Rabbits with blood glucose levels above 200-mg/100 ml were considered as diabetic and employed for further study.

Estimation of Serum Insulin

Insulin estimation was done by radio immunoassay using Insulin Erma Kit. The estimation was performed in the laboratories of IRNUM (Institute of Radiotherapy and Nuclear Medicine), Peshawar.

Principle of the assay

The immunoassay of insulin is a sandwich assay. The same kit may be employed for the measurement of:

- immunoreactive insulin (free insulin + insulin bound to anti-insulin antibodies) directly in serum or plasma,
- free insulin after pre-treatment of samples with PEG

The samples (pre-treated or not with PEG) and standards are incubated in tubes coated with the first monoclonal antibody in the presence of the second monoclonal antibody, which is labelled with ^{125}I. After the incubation, the contents of the tubes are aspirated and the tubes are rinsed so as to remove unbound ^{125}I-labelled antibody. The bound radioactivity is then determined in a gamma-counter. The insulin concentrations of the samples are directly proportional to the radioactivity. Standard curve is constructed as the dependence of determined radioactivity versus the concentration of standards. The insulin concentration is read off this curve.

Plant material

The constituents of Compound recipe, which is used as test, and that of Pancreas tonic that is used as standard were purchased from the local market of Peshawar City with the exception of Acacia catechu which was obtained from Pakistan Forest Institute, Peshawar. These constituents are shown in Table 1.

The components were soaked separately for twenty-four hours in water at the ratio of one to eight, weight to volume. The soaked material with water was then boiled until it was reduced to one-quarter of its initial volume. The extracts were then made into a semisolid by the application of low heat. The extracts thus obtained were air dried at room temperature and made into a powder, which were then mixed.

Grouping of Rabbits

Animals in this experiment were comprised of four groups each group consisting of 15 rabbits.

- First group acts as control, did not receive any treatment and was placed on normal rabbit diet.
- The second group was made diabetic by injecting 150 mg/Kg body weight alloxan monohydrate intravenously. This group was also placed on normal rabbit diet.
- The third group was also made diabetic by giving alloxan monohydrate in a dose of 150-mg/Kg body weights intravenously. This group was placed on normal diet for seven days to have alloxan-induced damage on pancreas. This group was then shifted to Compound recipe. This group received Compound recipe in a dose of 400 mg/Kg daily for a period of 4 months.
- Fourth group was also made diabetic by giving alloxan monohydrate in a dose of 150-mg/Kg body weights intravenously. This group was placed on normal diet for seven days to have alloxan-induced damage on pancreas. This group was then shifted to Pancreas Tonic. This group received Pancreas Tonic in a dose of 400 mg/Kg daily for a period of 4 months.

Body weights and feed consumption were recorded weekly. All animals were observed daily for general health and normal movements in the cages.

Table 1.

Compound recipe		***Pancreas tonic***	
Plant	**Part used**	**Plant**	**Part used**
Acacia catechu.	**Heartwood**	***Pterocarpus marsupium***	**Heartwood**
Gymnema sylvestre.	Leaves	Gymnema sylvestre.	Leaves
Cinamonum tamala .	Leaves	Cinamonum tamala .	Leaves
Aegle marelose.	Leaves	Aegle marelose.	Leaves
Momordica charantia.	Seeds	Momordica charantia.	Seeds
Azadirachta indica.	Leaves	Azadirachta indica.	Leaves
Tinospora cordifolia	Stem	Tinospora cordifolia	Stem
Trigonella foenum graceum	Seeds	Trigonella foenum graceum	Seeds
Ficus racemosa.	Leaves	Ficus racemosa.	Leaves
Syzygium cumini.	Fruit	Syzygium cumini.	Fruit

Preparation and administration of extract solution

The amount of plant extract required for each rabbit was calculated on body weight basis and it was dissolved in 10 ml of water to make a colloidal solution and final solution was then made up to 15 ml. The extract was administered to each rabbit using a stomach tube attached to a standard syringe containing 15 ml of the extract solution. The tube was inserted into the stomach through the esophagus and the plunger was pressed slowly and steadily. Immediate sneezing and coughing indicated injection into the lungs and, in such cases, the tube was at once withdrawn and another animal was taken instead.

Collection of blood

The procedure for collection of blood was adopted as described by Akhtar et al[13]. The rabbit was held in a wooden rabbit holder, and immediately before administration of drug, 0.2 ml of blood for glucose estimation was collected from an ear vein. Similar blood samples were also collected after 1, 2, 3 and 4 months after the drug administration. After collection of blood, the pricked site of the ear was rubbed with cotton wool soaked with 70% alcohol to protect the rabbit against infection.

Blood glucose estimation

Blood glucose estimation was done by the method of Diagnostics Elitech.

Statistical analysis

Mean percent blood glucose were expressed as mg/100 ml ± standard error in all experiments and Student's't' test was used to check their significance.

RESULTS

Blood Glucose estimation

Group-1

Effect of water in a dose of 15 ml on blood glucose levels of normoglycaemic rabbits

The effect on blood glucose levels of 15 normoglycaemic rabbits after oral administration of 15 ml of water used as vehicle for suspending the drugs for administration are shown in Table 2. The percent decreases in blood glucose levels are shown in Table 3. The mean percent decreases in blood glucose levels at 1, 2, 3 and 4 months were 2.18 ± 0.26, 3.46 ± 0.28, 5.07 ± 0.31 and 4.95 ± 0.29 respectively (Table 2). The mean percent decreases in blood glucose levels produced by 15 ml of water at 1, 2, 3 and 4 months are insignificant ($P > 0.05$).

Group-2

Effect of water in a dose of 15 ml on blood glucose levels of alloxan induced diabe tic rabbits

The effect on blood glucose levels of 15 alloxan induced diabetic rabbits after oral administration of 15 ml of water used as vehicle for suspending the drugs for administration are shown in Table 2. The percent decreases in blood glucose levels are shown in Table 3. The mean percent decreases in blood glucose levels at 1, 2, 3 and 4 months were 1.41± 0.23, 2.32 ± 0.24, 2.49 ± 0.22 and 1.68± 0.21 respectively. The mean percent decreases in blood glucose levels produced by 15 ml of water at 1, 2, 3 and 4 months are insignificant ($P > 0.05$).

Group-3

Effect of Compound recipe in a dose of 400mg/Kg on blood glucose levels of alloxan induced diabetic rabbits

The effect on blood glucose levels of 15 alloxan induced diabetic rabbits after oral administration of Compound recipe in a dose of 400 mg/Kg dissolved in 15 ml of water used as vehicle for suspending the Compound recipe for administration are shown in Table 2. The mean percent decreases in blood glucose levels are shown in Table 3. The mean percent decreases in blood glucose levels at 1, 2, 3 and 4 months were 6.71 ± 0.53, 19.48 ± 0.58, 32.14 ±0.82 and 54.5 ± 0.92 respectively The mean percent decreases in blood glucose levels produced by Compound Recipe are significant ($P < 0.05$) after one and two months and highly significant ($P < 0.001$) after 3rd and 4 months.

Group-4

Effect of Pancreas Tonic in a dose of on blood glucose levels of alloxan induced diabetic rabbits

The effect on blood glucose levels of 15 alloxan induced diabetic rabbits after oral administration of ***Pancreas Tonic*** in a dose of 400mg/Kg dissolved in 15 ml of water used as vehicle for suspending the drugs for administration are shown in Table 2. The mean percent decreases in blood glucose levels are shown in Table 3. The mean percent decreases in blood glucose levels at 1, 2, 3 and 4 months were 9.46 ± 0.54, 18.66 ± 0.94, 34.23 ± 0.83 and 55.32 ± 0.96 respectively . The mean percent decreases in blood glucose levels produced by Pancreas Tonic are significant ($P < 0.05$) after one and two months and highly significant ($P < 0.001$) after three and four months.

Serum Insulin estimation

Group-1

Insulin estimation in normoglycaemic rabbits

The effect on serum insulin levels of normoglycaemic rabbits after oral administration of 15 ml of water used as vehicle for suspending the drugs for administration are shown in Table 4. The mean percent changes on serum insulin levels are shown in Table 5. The mean percent increases in serum insulin levels at 1, 2, 3 and 4 months were 4.67 ± 2.01, 6.16 ± 1.97, 7.96 ± 1.60 and 9.45 ± 1.95 respectively. The mean percent decreases in serum insulin levels in normoglycaemic rabbits at 1, 2, 3 and 4 months are insignificant ($P > 0.05$).

Group-2

Insulin estimation in Alloxan induced diabetic rabbits

The effect on serum insulin levels of Alloxan induced diabetic rabbits after oral administration of water used as vehicle for suspending the drugs for administration are shown in Table 4. The mean percent changes on serum insulin levels are shown in Table 5. The mean percent decreases in serum insulin levels at 1, 2, 3 and 4 months were 7.95 ± 1.32, 5.13 ± 2.02, 4.58± 1.24 and 4.05 ± 2.53 respectively. The mean percent decreases in serum insulin levels in alloxan diabetic rabbits at 1, 2, 3 and 4 months are significant ($P < 0.05$).

Group-3

Insulin estimation in alloxan induced diabetic rabbits receiving Compound recipe

The effect on serum insulin levels of Alloxan induced diabetic rabbits after oral administration of Compound recipe is shown in Table 4. The mean percent changes on serum insulin levels are shown in Table 5. The mean percent increases in serum insulin levels at 1, 2, 3 and 4 months were 12.51 ± 1.65, 22.84 ± 1.30, 33.13 ± 3.03 and 43.25± 1.95 respectively. The mean percent increases in serum insulin levels in alloxan induced diabetic rabbits at 1, 2, 3 and 4 months are highly significant ($P < 0.01$).

Group-4

Insulin estimation in Alloxan induced diabetic rabbits receiving Pancreas tonic

The effect on serum insulin levels of Alloxan induced diabetic rabbits after oral administration of ***Pancreas tonic*** is shown in Table 4. The mean percent changes on serum insulin levels are shown in Table 5. The mean percent increases in serum insulin levels at 1, 2, 3 and 4 months were 17.61 ± 2.11, 32.29 ± 3.12, 39.11 ± 2.57 and 49.80 ± 2.7 respectively. The mean percent increases in serum insulin levels in alloxan induced diabetic rabbits at 1, 2, 3 and 4 months are highly significant ($P < 0.01$).

Table 2. Effect of Compound Recipe and Pancreas Tonic on Blood glucose levels of Normal and Alloxan induced diabetic rabbits at different time intervals

Time interval (Months)	Blood glucose level in mg/ dl			
	Control (Normal)	Control (Diabetic)	Compound Recipe (400 mg/Kg)	Pancreas Tonic (400 mg/Kg)
0	93.54 ± 2.60 (15)	219.25 ± 3.76 (15)	225.31 ± 4.31 (15)	218.1 ± 3.78 (15)
1	91.46 ± 3.07 (15)	215.50 ± 2.36 (15)	210.21 ± 3.70 (15)	195.23 ± 4.21 (15)
2	90.28 ±2.81 (15)	213.46 ±3.21 (15)	180.89 ± 3.66 (15)	178.15 ± 2.89 (15)
3	88.75 ±3.27 (15)	213.10 ± 3.74 (15)	152.80 ± 2.98 (15)	143.41 ± 3.76 (15)
4	88.80 ± 2.51 (15)	215.14 ± 2.86 (15)	102.43 ± 3.58 (15)	97.35 ± 2.88 (15)

Figures in Parenthesis indicate number of animals. Each value represents the mean ± standard error

Table 3. Mean percent decrease in blood glucose by Compound Recipe and Pancreas tonic at different time intervals.

Time interval (Months)	Blood glucose level in mg/dl			
	Control (Normal)	Control (Diabetic)	Compound Recipe (400 mg/Kg)	Pancreas Tonic (400 mg/Kg)
1	2.18 ± 0.26 (15)	1.41± 0.23 (15)	6.71 ± 0.53 (15)	9.46 ± 0.54 (15)
2	3.46 ± 0.28 (15)	2.32 ± 0.24 (15)	19.48 ± 0.0.58 (15)	18.66 ± 0.94 (15)
3	5.07 ± 0.31 (15)	2.49 ± 0.22 (15)	32.14 ±0.82 (15)	34.23 ± 0.83 (15)
4	4.95 ± 0.29 (15)	1.68± 0.21 (15)	54.5 ± 0.92 (15)	55.32 ± 0.96 (15)

Figures in Parenthesis indicate number of animals. Each value represents the mean ± standard error

Table 4. Effect of Compound Recipe and Pancreas Tonic on Serum Insulin levels of Normal and Alloxan induced diabetic rabbits at different time intervals

Time Interval (Months)	Serum Insulin Level m IU/ml			
	Control (Normal)	Control (Diabetic)	Compound Recipe (400mg/Kg)	Pancreas Tonic (400mg/Kg)
0	10. 05 ± 1.30 (15)	6.24 ± 0.86 (15)	6.62 ± 1.52 (15)	6.10 ± 2.40 (15)
1	10.52 ± 2.01 (15)	6.05 ± 1.32 (15)	7.87 ± 1.65 (15)	7.96 ± 2.11 (15)
2	10.67 ± 1.97 (15)	5.73 ± 2.02 (15)	8.90± .1.30 (15)	9.42 ± .3.12 (15)
3	10.85 ± 1.60 (15)	5.84 ± 1.24 (15)	9.93 ± 3.03 (15)	10.62 ± 2.57 (15)
4	11.00 ± 1.95 (15)	4.45 ± 2.53 (15)	10.90 ± 1.95 (15)	11.00 ± 2.7 (15)

Figures in Parenthesis indicate number of animals. Each value represents the mean ± standard error

Table 5. Mean percent increases in Serum Insulin Levels produced by Compound Recipe and Pancreas tonic at different time intervals.

Time interval (Months)	Serum Insulin Level mUI/ml			
	Control (Normal)	Control (Diabetic)	Compound Recipe (400mg/Kg)	Pancreas Tonic (400mg/Kg)
1	4.67 ± 2.01 (15)	7.95 ± 1.32 (15)	12.51 ± 1.65 (15)	17.61 ± 2.11 (15)
2	6.16 ± 1.97 (15)	5.13 ± 2.02 (15)	22.84 ± .1.30 (15)	32.29 ± .3.12 (15)
3	7.96 ± 1.60 (15)	4.58± 1.24 (15)	33.13 ± 3.03 (15)	39.11 ± 2.57 (15)
4	9.45 ± 1.95 (15)	7.91 ± 2.53 (15)	43.25± 1.95 (15)	49.80 ± 2.7 (15)

(Figures in Parenthesis indicate number of animals. Each value represents the mean ± standard error)

DISCUSSION

In Alloxan diabetic rabbits, the blood glucose levels are raised due to permanent destruction of pancreatic β cells[33]. Moreover, the serum insulin levels are decreased in Alloxan diabetic rabbits due to destruction of pancreatic β cells. The increase in serum insulin levels of diabetic rabbits as observed in the present work shows that some regeneration of pancreatic β cells has occurred with the use of Compound recipe. This regeneration of pancreatic β cells has occurred slowly and was maximum after a period of 4 months. This finding is in accordance with the observations of Dhaliwal.

It is claimed that Pancreas tonic, which is composed of several medicinal plants, causes a significant reduction in blood glucose levels due to the regeneration of pancreatic β islet cells. The regeneration is mainly due to presence of Pterocarpus marsupium that contains significant quantity of (-) Epicatechin. It has been reported that aqueous extracts of the plant produced a significant reduction in the blood glucose levels in rabbits[34]. Epicatechin obtained from Pterocarpus marsupium was tested for antidiabetic activity in albino rats and was found to be effective against alloxan-induced diabetes. The other constituents of ***Pancreas tonic*** potentiate the actions of Pterocarpus marsupium. These constituents also have the ability to reduce the blood glucose levels of normal rabbits but they have no effect on blood glucose levels of alloxan diabetic rabbits. This is due to the fact these plants have the ability to reduce blood glucose levels of normal rabbits by stimulating the pancreatic β islet cells and thus increasing the quantity of insulin. As alloxan destroys pancreatic β islet cells, these constituents have no effect on diabetic animals.

The data revealed that Pancreas tonic and Compound recipe had no significant hypoglycaemic effect in normal rabbits but they had caused significant blood reduction in blood glucose levels of alloxan diabetic rabbits. These observations reveal that these compounds have action different to that of insulin as insulin causes reduction in blood glucose levels of normal as well as Alloxan diabetic rabbits. These observations suggest that these compounds possibly regenerate the pancreatic beta cells that secrete insulin that is responsible for reduction in blood glucose levels.

It was further noticed that the compound containing Acacia catechu is as potent as the compound containing Ptrecarpus marsupium.

As Pterocarpus marsupium and Acacia catechu both contain (-) Epicatechin, it might be suggested that the hypoglycemic activity may be due to presence of (-) Epicatechin.

CONCLUSION

Histological studies of pancreas can further help in arriving at a clear-cut conclusion. At this stage, the only conclusion is that the possible use of this cheap and relatively non-hazardous natural remedies of plant origin for the treatment of diabetes mellitus may further be explored.

REFERENCES

1. Shanmugasundaram ER, Rajeswari G, Baskaran K. Use of Gymnema sylvestre leaf extract in the control of blood glucose in insulin-dependent diabetes mellitus. J Ethnopharmacol. 1990;30(3):281-94
2. Bever OB, Zahnd GR. Plants with oral hypoglycemic action (review). Quart J Crude Drug Res. 1979; 17: 139-96.
3. Perrot E and Paris RV. Les plantes medicinales, 2 vols. Presses Universitaries de France: Vendome, 1971.
4. Shoaib MA. Hypoglycemic activities of some indigenous medicinal plants traditionally used as anti-diabetic drugs. J Pak Med Assoc: 1992; 42: 271-77.
5. Marles RJ, Farnsworth N. Antidiabetic Plants and their Active Constituents: An update Prot.J Bot Med 1996; 1(3):85-135.
6. Twaij HA, Al-Badr AA. Hypoglycemic activity of Artemisia herba alba.: J Ethnopharmacol 1988; 24(2-3):123-6
7. Ahmad N, Hassan MR, Bennoor KS. Effect of Mormordica charantia (Karolla) extracts on fasting and postprandial serum glucose levels in NIDDM patients. Bangladesh Med Res Counc Bull. 1999; 25(1):11-3.
8. Sharma RD, Sarkar A, Hazra DK, Mishra B, Singh JB, Sharma SK et al.. Use of Fenugreek seed powder in the

management of non-insulin dependent diabetes mellitus. Nutr Res. 1996;16:1331-39.
9. Ernst E. Plants with hypoglycemic activity in humans. Phytomed. 1997; 4:73-8.
10. Augusti KT, Benaim ME. Effect of essential oil of onion (APDS) on blood glucose, free fatty acids and insulin levels of normal subjets. Clin Chim Act 1975; 60:121.
11. Marquis VO, Adanlwo TA, Olaniyi AA. The effect of foetidin from Momordica foetida on blood glucose of albino rats. Planta Med. 1977; 31: 367-74.
12. Khan AKA, Akhtar MS, Mehtab H. The treatment of diabetes mellitus with Coccinia indica. BMJ 1980; 280: 1044.
13. Akhtar MS, Athar MA and Yaqub M. Effect of Momordica charantia on blood glucose levels of normal and alloxan diabetic rabbits, Planta Med. 1981; 42: 205-12.
14. Akhtar MS, Ali MR. Study of hypoglycemic activity of Cuminum nigrum seeds in normal and alloxan diabetic rabbits. Planta Med 1985; 2: 81-5.
15. Singh KN., Chandra V. and Barthwal KC. Hypoglycaemic activity of Acacia arabica, Acacia benthami and Acacia modesta leguminous seed diets in normal young albino rats. Indian J Physiol Pharmacol. 1975; 19(3): 167-8.
16. Chakravarthy, B.K. Saroj gupta and Gode, K.B. Preliminary report on harmalogical and toxiocolsgical studies of Acacia catechu wild. Indian Drugs,1983,20: 399.
17. The Review of Natural Products by Facts and Comparisons. St Louis, MO: Wolters Kluwer Co., 1999.
18. Shanmugasundaram ER, Paneerselvam C, Samudram P, Shanmugasundaram KR. Enzyme changes and glucose utilisation in diabetic rabbits: the effect of Gymnema sylvestre. R Br J Ethnopharm 1983;7(2):205-234.
19. Shanmugasundaram ER, Gopinath KL, Shanmugasundaram KR, Rojendran VM. Possible regeneration of the islets of Langerhans in streptozocin-diabetic rats given Gymnema sylvestre leaf extracts. J Ethnopharm 1990;30:265-279.
20. Sharma SR, Dwivedi SK, Swarup D. Hypoglycaemic and hypolipidemic effects of Cinnamom tamala Nees leaves. Indian J. Exp. Biol. 1996,34: 372.
21. Ahmad N, Hassan MR, Bennoor KS. Effect of Mormordica charantia (Karella) extracts on fasting and postprandial serum glucose levels in NIDDM patients. Bangladesh Med Res Counc Bull 1999;25:11-13.
22. Murthy, KS, Rao Dn, Rao DK, Murty LBG. A preliminary study on hypoglycemic activity and antihyperglycemic effects of Aazadiracta indica. Indian J. Pharmacol 1978; 10: 247.
23. Pillai, N R, Santhakumar, G. Hypoglycemic activity of melia Azadiracta linn (neem). Indian J Med Res 1981;74: 937.
24. Noreen W., Wadood A., and Shah SAW: Effect of Tinospora cordiofolia on blood glucose and total lipid levels of normal and alloxan diabetic rabbits. Plant Med 1992;58(2):131-36.
25. Ali L, Azad Khan AK, Hassan Z, Mosihuzzaman M, Nahar N, Nasreen T, et.al. Characterization of the hypoglycemic effects of Trigonellia foenum graecum seed, Planta Med 1995; 61: 358.
26. Kar A, Choudhary BK, Bandyopadhyay NG. Comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in alloxan diabetic rats; J Ethnopharmacol, 2003; 84(1):105-8.
27. Nadeem, MS. and Suraiya,O. Studies of the hypoglycemic properties of Eugenia jambolana. Pak J Med Resch 1969; 2:148-155
28. Akhtar MS. Hypoglycaemic activities of some indigenous medicinal plants traditionally used as antidiabetic drugs. J Pak Med Assoc, 1992,Vol.2, No.11, 271-277.
29. Chakraharty BK, Gupta S, Gambhir SS, Gode KD. The prophylactic action of (-) epicatechin against alloxan induced diabetes in rates. Life Sci `1981; 29: 2043.

Address for Correspondence: Dr. Noreen Wadood, Associate Professor, Department of Biochemistry, Kabir Medical College, Peshawar.