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Hypoglycemic activity and ALP lowering role of *Hedera nepalensis* K. Koch Leaves in Alloxane monohydrate induced Diabetic rabbits

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Diabetes mellitus is a multifactorial disease that has a significant impact on the health, quality of life and expectancy of patients, as well as on the health care system. This study aims to evaluate *Hedera nepalensis* K. Koch plant for antidiabetic studies in rabbits. The effect of Methnolic extract of *Hedra nepalensis* on blood glucose and ALP level were studied. Rabbits were made diabetic by injecting Alloxane monohydrate at the dose rate of 100mg/kg per body weight consecutively for three days. Diabetic rabbits were divided into different groups. One group was kept unmedicated, non-diabetic control and other group as unmedicated diabetic control. The crude plant methanolic extract was given to three diabetic groups at the dose rate of 100mg, 200mg and 300mg/kg per body weight. Twenty mg/kg Metformin 2HCl was given to one group. Blood samples were collected from entire group at

regular interval. There was hyperglycemia as well as increased ALP level in all alloxane treated groups. Results showed a significant decrease in glucose 89.15 mg/kg and ALP 327.65 IU/L levels among all the groups. It has been revealed that *Hedra nepalensis* has antidiabetic role. Further work may be done on pure extract to identify the exact compound having such potential..

Keywords: Alloxane, Glucose, ALP, Metformin, diabetes

INTRODUCTION

Diabetes mellitus has tremendously affected human life. Worldwide, the number of people with diabetes is expected to double over the 13 year period from 1997 to 2010, so that it is expected that there will be over 221 million people with diabetes worldwide by 2010 (Amos et al. 1997). A high level serum ALP represents liver disease. If the ALP level is found to be elevated, normal physiologic elevation owing to age or pregnancy should be excluded, along with spurious elevation caused by a recent albumin infusion (Prati, 2002). Although a reasonable attempt can usually be made at estimating the source of elevated ALP, occasionally, it may be necessary to identify the isoenzymes biochemically. Heat inactivation and L-phenylalanine inhibition have been used. Placental and tumor ALP tends to be heat stable, whereas bone is heat labile (Broyles et al., 1998).

Hedra nepalensis K. Koch belongs to family Araliaceae. There are more than 1200 plants species worldwide that are used in the treatment of diabetes mellitus and a substantial number of plants have shown effective hypoglycemic activity after laboratory testing (Eddouks et al. 2005). This work was designed to study the effect of plant extract on diabetes. The benefit of the study alloxane and plant extract was used at different dosage level to check the antidiabetic activity.

MATERIALS AND METHODS

Plant Material:

Hedra nepalensis was collected from Kharkai Dargai, District Malakand.

Preparation of Extract:

Methanolic extract was prepared and were stored for further use.

Selection rabbits:

Rabbits *Oryctolagus cuniculus* were nominated for this study and were reared at the biopark of University of Malakand.

Induction of Diabetes mellitus:

Diabetes mellitus was induced through jugular vein injection of alloxan monohydrate and ALP and blood glucose level were studied.

Extract administration:

No extract was given to group A. Group B was given Metformin 2 HCl at the dose rate of 17 mg/kg/bw. Similarly group C, D and E were given the plant extract at the dose rate of 100mg/kg, 200mg/kg and 300mg/kg respectively (Romman et al., 2015).

RESULTS

The decrease in glucose level was (140.14±1.00mg/dl) in group A when compared to non-diabetic non medicated control (75-155 mg/dl). But glucose level in group A was high when compared to the medicated groups. In group B, there was persistent decrease in glucose level and at the end of experiment, the rabbits were quite normal having glucose level of (76.20±1.19mg/dl). The group C, D and E has also a significant decrease in glucose level that were fed with plant extract at three different dose level. At day 2nd the blood glucose level in group was 80.15±0.92mg/dl, in group D, it was 79.14±0.91mg/dl and in group E blood glucose level tended towards decrease when compared with non-medicated diabetic control. The rate of falling of glucose was high in medicated groups as compared to non-compared diabetic group. The results have been shown in table 01 and figure 01.

Table 1: Blood Glucose (mg/dl) level of Rabbits after treatments

| Groups | Day 1 | Day 03 | Day 05 | Day 07 |
|----------------------------|-------------|-------------|-------------|-------------|
| Group A (alloxane control) | 165.22±1.05 | 158.28±1.07 | 154.40±1.12 | 140.14±1.00 |
| Group B (Glucophage) | 140.14±0.99 | 90.14±1.00 | 84.32±0.88 | 76.20±1.19 |
| Group C (100 mg/dl) | 125.29±0.79 | 101.35±0.65 | 90.30±0.94 | 80.15±0.92 |
| Group D (200 mg/kg) | 120.19±1.15 | 96.25±0.96 | 88.27±0.85 | 79.14±0.91 |
| Group E (300mg/kg) | 100.14±1.00 | 93.10±1.10 | 86.08±1.10 | 77.31±1.05 |

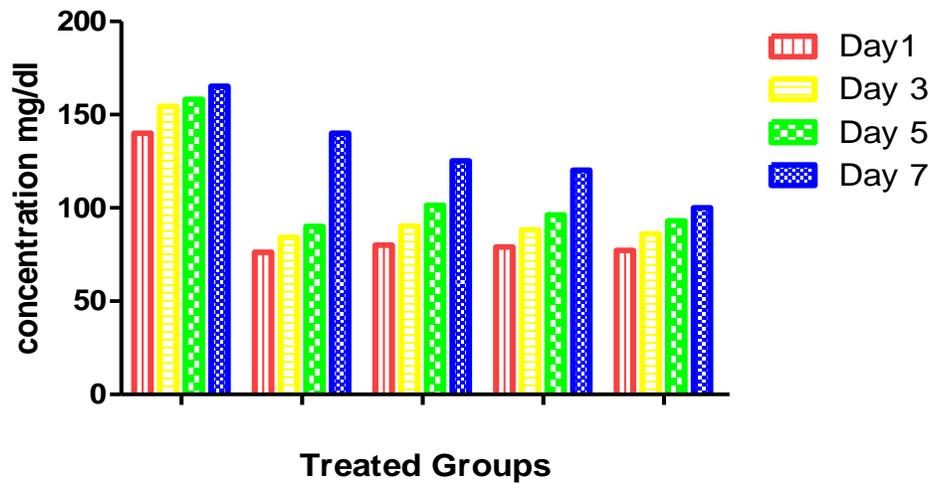


Figure1: Showing Blood Glucose level of Rabbits

Table 2: Blood ALP (IU/L) level of Rabbits after treatments

| Groups | Day 1 | Day 03 | Day 05 | Day 07 |
|----------------------------|-------------|-------------|-------------|-------------|
| Group A (Alloxane Control) | 455.65±1.06 | 442.34±1.10 | 433.29±0.78 | 417.51±1.08 |
| Group B(Glucophage) | 323.46±0.98 | 311.61±1.05 | 301.85±1.12 | 279.23±1.06 |
| Group C (100 mg/dl) | 383.51±0.95 | 371.24±0.92 | 353.62±1.01 | 342.13±0.79 |
| Group D (200 mg/kg) | 372.15±0.74 | 351.52±0.85 | 337.60±0.94 | 324.41±1.20 |
| Group E (300mg/kg) | 381.42±1.17 | 356.47±0.95 | 339.34±1.13 | 327.65±1.35 |

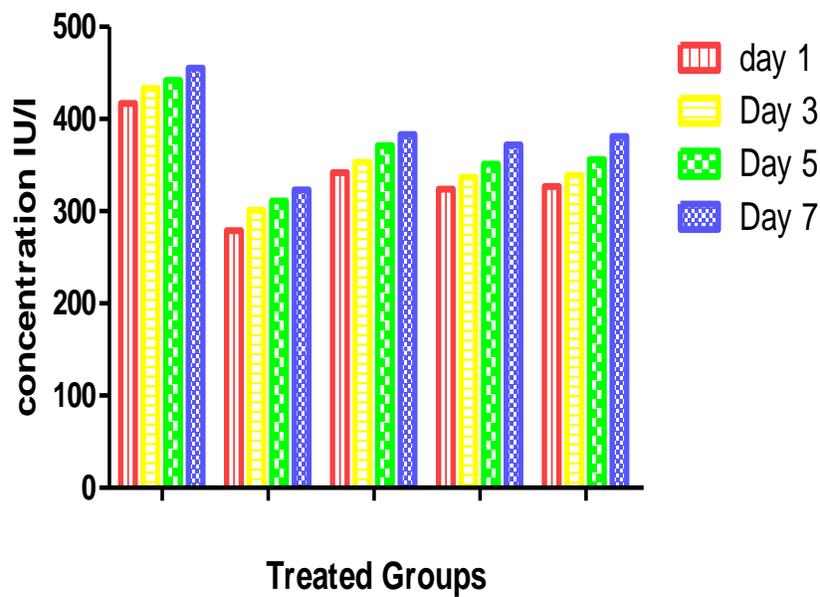


Figure 2: Showing Blood ALP level of Rabbits

The decrease in ALP level was $(417.51 \pm 1.08$ IU/L) in group A when compared to non-diabetic non medicated control ($10-70$ IU/L). But ALP level in group A was high when compared to the medicated groups. In group B, there was persistent decrease in ALP level and at the end of experiment, the rabbits were quite normal having ALP level of $(279.23 \pm 1.06$ IU/L). The group C, D and E has also a significant decrease in ALP level that were fed with plant extract at three different dose level. At day 2nd the blood ALP level in group was 342.13 ± 0.79 IU/L, in group D, it was 324.41 ± 1.20 IU/L and in group E blood ALP level tended towards decrease when compared with non-medicated diabetic control. The rate of falling of ALP level was high in medicated groups as compared to non-compared diabetic group. The results have been shown in table 02 and figure 02.

DISCUSSION

This study was designed to study the hypoglycaemic activity of the methanolic extract of *Hedera nepalensis* and to evaluate the possible beneficial effect of *Hedera nepalensis* infusion on endogenous basal glucose production and whole body insulin sensitivity in multi-low dose alloxane monohydrate-induced diabetic rabbits. Blood glucose level of rabbits was 75-155 mg/dl which was taken as the standard value with which other value can be compared (Bilqees, 2020). The mean value of control group was 76.20 ± 1.19 mg/dl after medicating Metformin HCl. Plant extract at the dose rate of 100 mg/kg was 80.15 ± 0.92 , plant extract at the dose rate of 200 mg/kg was 79.14 ± 0.91 and plant extract at the dose rate of 300 mg/kg was 77.31 ± 1.05 mg/dl. After studying, it showed that the plant extract at the dose rate of 300 mg/kg had the significant effect on blood glucose level of rabbits. The extract of *Dorstenia picta* showed high blood glucose level declined in rats as exposed by Florence et al., (2007). Mallick et al., (2007) studied *Musa paradisiaca* for antidiabetic activities and he found substantial result. Blood glucose level of rabbits was 112-350 IU/L which was taken as the standard value with which other value can be compared and mean value of control group was 406.70 IU/L after medicating Metformin HCl. Plant extract at dose rate of 100mg/kg was 457.18 IU/L, plant extract at dose rate of 200mg/kg was 445.07 IU/L, plant extract at dose rate of 300mg/kg was 456.37 IU/L. This study correlates with the investigation conducted by Lemhadri et al., (2007) while reporting the hypoglycaemic and hypolipidemic

activities of the aqueous extract of CS fruits in streptozotocin-induced diabetic rats, an animal model of human type 1 diabetes mellitus.

CONCLUSION

Hedera nepalensis leaves extract has the ability to reduce the blood glucose and ALP level in rabbits. So the plant may be considered as a good antidiabetic plant.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

MR designed and performed the experiments and also wrote the manuscript. MR performed animal treatments and data analysis. SU designed experiments and RP, WK, MS, SZ, FH, AAKK, NM, ZH, SJ, SW, MI, ZU, RB, HU, IH, AH, MI, MA, SI, MI, IH, RA, ND, SU, MA reviewed the manuscript. All authors read and approved the final version.

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