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Blood Glucose and Alanine transaminase lowering effect of *Nepeta cataria* L. In Alloxan monohydrate induced diabetic Rabbits

Muhammad Romman[1*], Rainaz Parvez[2,3], Farzana Tabassum[1], Rizwana Bilqees[1], Mehroon Nisa[4], Muhammad Shuaib[5], Saraj Bahadur[6], Zahoor Ul Haq[7], Faiz ul Haq[8], Atif Ali Khan Khalil[9], Bashir Ahmad[10], Ali Hazrat[11], Nisar uddin[12], Muhammad Adnan[13], Zakir ullah[14], Noor Muhammad[15], Saqibullah[16] and Muhammad Ishaq[17], Saqib ur Rahman[3], Zahir Shah[11]

[1]Pharmacognosy Lab, Department of Botany, University of Chitral, KP, **Pakistan**
[2]Department of Botany, Government Girls Degree College Dargai, District Malakand, KP, **Pakistan**
[3]Department of Botany, Abdul Wali Khan University Mardan, KP, **Pakistan**
[4]Department of Zoology, University of Chitral, KP, **Pakistan**
[5]Department of Weed Science, The University of Agriculture, Peshawar, KP, **Pakistan**.
[6]Institute of Tropical Agriculture and Forestry, Hainan University Haikou, **China**
[7]Department of Botany, Shaheed Benzir Bhutto University, Sheringal, Dir Upper, KP, **Pakistan**
[8]Department of Microbiology, University of Health Sciences Lahore, **Pakistan**
[9]Department of Biological Sciences, National University of Medical Sciences, Rawalpindi, **Pakistan**
[10]Department of Zoology, University of Malakand, KP, **Pakistan**
[11]Department of Botany, University of Malakand, KP, **Pakistan**
[12]Department of Botany, Hazara University, KP, **Pakistan**
[13]Department of Agriculture, University of Swabi, KP, **Pakistan**
[14]Plant Biochemistry and Molecular Lab, Quaid i Azam University Islamabad, **Pakistan**
[15]Department of Pomology, The College of Horticulture Hebei Agricultural University Baoding, Hebei **China**
[16]Department of Botany, Qurtuba University of Science and Information Technology, Peshawar,KP, **Pakistan**
[17]Department of Botany, Bacha Khan University Charsadda, KP, **Pakistan**

***Correspondence:** dr.romman.uom@gmail.com **Received 10-10-2020, Revised: 16-12-2020, Accepted: 18-12-2020 e-Published: 27-12-2020**

Diabetes mellitus is has become world most dangerous disease which needs attention as soon as possible. Hyperglycemia in blood badly affects different organs like eyes, kidneys, nerves and human circulatory system. Anti-diabetic capability of *Nepeta Cateria* has been investigated in rabbit. Group A, worked as normal control, and Group B remain Diabetic control. This group was interacted or treated by Glucophage with a dose rate of 8 mg / kg weight and for comparison with the other groups which were kept on feeding *N. cateria* extract as a treatment. Group C, D and E were given with plant extract at the quantity of 120 mg / kg, 220 mg / kg and 320 mg / kg of its body weight respectively. The blood samples were composed of all the groups by particular schedule i.e. two hours, four hours, six hours and eight hours concurrently. In every of two hours' sample of blood was collected with particular fashion, serum detached and level of glucose and ALT level was examined by the kit method and found that ALT level reduced to 54 IU/L. The result showed that treatment of 320 mg/kg dose is effective lowering blood glucose up to 159.33 mg/Kg and ALT in the experimental animal. The data obtained disclose that *N. cateria* ethanol extract reduced the glucose level. So, it is determined that the *N. cateria* possess major

diabetic compressed activity.

Keywords: Diabetic mellitus, N.cateria, alloxan monohydrate, glucose

INTRODUCTION

Nepeta Cataria (family Lamiaceae) is generally known as catnip, and catmint. The plant includes more than 280 species (Kashif et al., 2020). *N. cataria* is an aromatic plant, which is mostly perennial and herb in nature. *N. cataria* is a perennial herb that is usually used as a food stabilizer. The plant have an essential oils in their stem, the oil is used against for the food born infections. This is taken by a method, known as micro dilution method. Gas chromatography is the method by which the chemical all the component of essential oil has been analyzed in Nepeta cataria. The analysis of the essential oil indicate that (30–31.2%) nepetalactone and (55–58%) nepetalactone, which was the main compounds of essential oils at all in developmental stages. A research study shows the essential oil has a great impact as antimicrobial activity against the food borne pathogens. So it hypothesized that the essential oil of N. cataria can probably be used in food stuff manufacturing as natural preservative agent (Kokil et al., 2015).

Diabetes mellitus is among the major metabolic disease caused by the high sugar (glucose) level in blood, (Shiheng et al., 2017). It seems a global health challenge across the world. The main cause of these diseases is, due abnormal secretion of insulin or either insufficient insulin action. Treatment requires to maintain normal range of blood glucose and also preventing its metabolic complications Romman et al., 2020).

Mostly herbs are used for the treatment of several diseases for their convenience access and less side effects, such as *N. cateria* used against diabetes mellitus in ancient medicine (Hazrat et al., 2020). Another plant species i.e. the root of *Capparis spinosa* have many important biochemical compounds, such as flavonoids, saponins, tannins, pectin, essential oils, and particularly glycosinolate and glycosides which are helpful against the disease, It is an enzyme generally known as transaminase. Alanine transaminase (ALT) was first discovered in the 1950s by a scientist Arthur Karmen and his colleagues (Karmen et al., 1955). ALT is naturally found in plasma of the cell, and in different tissues in the body and abundantly found in liver. Being catalytic enzyme they breakdown parts of alanine cycle. The level of Serum ALT, serum AST, and their relative ratio (AST/ALT ratio) are mainly considered good source for the health of liver (Romman et al., 2015). This study aims to evaluate N. cataria for hypoglycemic and ALT lowering role in alloxane induced diabetic rabbits.

MATERIALS AND METHODS

Collection of Plant:

The plant *N. cataria* were collected from Mastuj Valley Tehsil Mastuj, District Upper Chitral from where they are collected.

Drying of Plant:

With fresh water the collected plant was washed. Then for 21 days for drying of the wash plants were preserved on the side in shad. And the materials of the plant was out in the open to sun light to keep away from fungal attack time to time.

Grinding of Plant:

To get powder the shadow-dehydrated complete plants be located exposed to humiliation. The dried parts of plants were grinded with grinder.

Extraction from Plant:

From the dried shrub precipitate or powder of 2250 gram remained assorted by means of 1650 ml ethanol. The ethanol is decidedly combustible. And it is poisonous by way of breathing and for eyes. The extract was filtered by filter paper after a week. The extract remained at that pointed wide-open to rotate evaporator, and then the ethanol stood removed then collected the filtrate in hipflask after passing it through the rotary evaporator. Remainder was yet again diversified by ethanol on behalf of 5 days. From plant residue the extraction was separated and exposed to rotational evaporator after 5 days. The ethanol was another time detaches additionally the dehydrated filtration practiced in a flask assembled. The ethanol is mixed in another time, for the correct result is about for five days. From the statement of plant, the surpluses were incoherent and amazing to rotating, evaporator in equal way. In flask again the excesses samples were collected. For making to used, it make dry for more time, and the extract were further reserved in room temperature, for proper dryness.

Animals Selection:

Rabbits were selected as an experimental animal. The all of rabbits were transferred for adaptation for duration of few days underneath ordinary environmentally friendly situation of high temperature, comparative moisture, in addition to light and dark cycle to Bio Park of University of Chitral. Animals are pronounced by means of abstaining be situated depressed of water then fodder were obtainable ad libitum.

Grouping of animals:

The duration of the many days of rearing the rabbits in a Bio Park, were randomly selected 6 numbers of rabbits. Depending upon their weight, they rabbits were divided into 2 groups. The same massed rabbits were being reserved in similar group and each has 3 rabbits in the group.

Induction of Diabetes mellitus:

In rabbits Alloxan was used intended for the Diabetes mellitus induction. This one remained understandable that the Alloxane consumes the propensities to source of diabetes from the preceding research work conducted. On demand from local supplier Alloxane monohydrate, which cause permanent diabetes was purchased. By a particular intraperitoneal instillation or injection of Alloxan monohydrate the rabbits remained made or prepared diabetic. Alloxan was primary weighted separately affording to the weight of body for every animal. To frustrate preliminary hypo-glycemic, glucose of four (4) mg per kg weight of body be situated given dermatologically 5 to 6 hr subsequently the Alloxane inoculation. In addition was provided 5 % of glucose in the drinking containers ad libitum for 24 hours. The collections of blood sample were made randomly in entire groups before the incorporation of drug. Blood samples were weakening ear of rabbits. For the isoloation of blood serum the samples of blood repeated in a colder locality. Blood chemistry analyzer oozed out and therefore it has been analyzed along with glucose concentration.

Drug administration:

Group-1 marked as unprocessed group i.e. the control group.

Group-2 marked as Gluco-phage (Metformin HCl) on the dosage amount of 8 mg/kg as per body weight.

Group-3 marked as plant extract at the dosage amount of 120mg / kg as per body weight.

Group-4 was medicated through plant extract at the amount of 220 mg/ kg as per body weight.

Group-5 was medicated with plant extract, at the level of 320 mg/ kg doses, in a weight of the body.

Blood samples collection:

The blood samples remained drawn as of the ear of rabbits. From the following schedule samples of the blood from each groups remained collected,

The 2 hours samples were collected before the administration of drug.

Serum Isolation:

By separating the samples of blood remain collected since each sets then being analyzed. In falcon tubes serum was collected and then centrifugated by 4000 rpm on behalf of 8 minutes then remained investigated by investigation of blood chemistry analyzer, and scheedzu Double Beam UV Spectro Photometer in different biochemical parameter.

Statistical Analysis:

Data remained obtained statistically scrutinized. Various assemblies remained associated by means of online software Prism Demo version, 2017, downloaded (www.gaphpad.com).

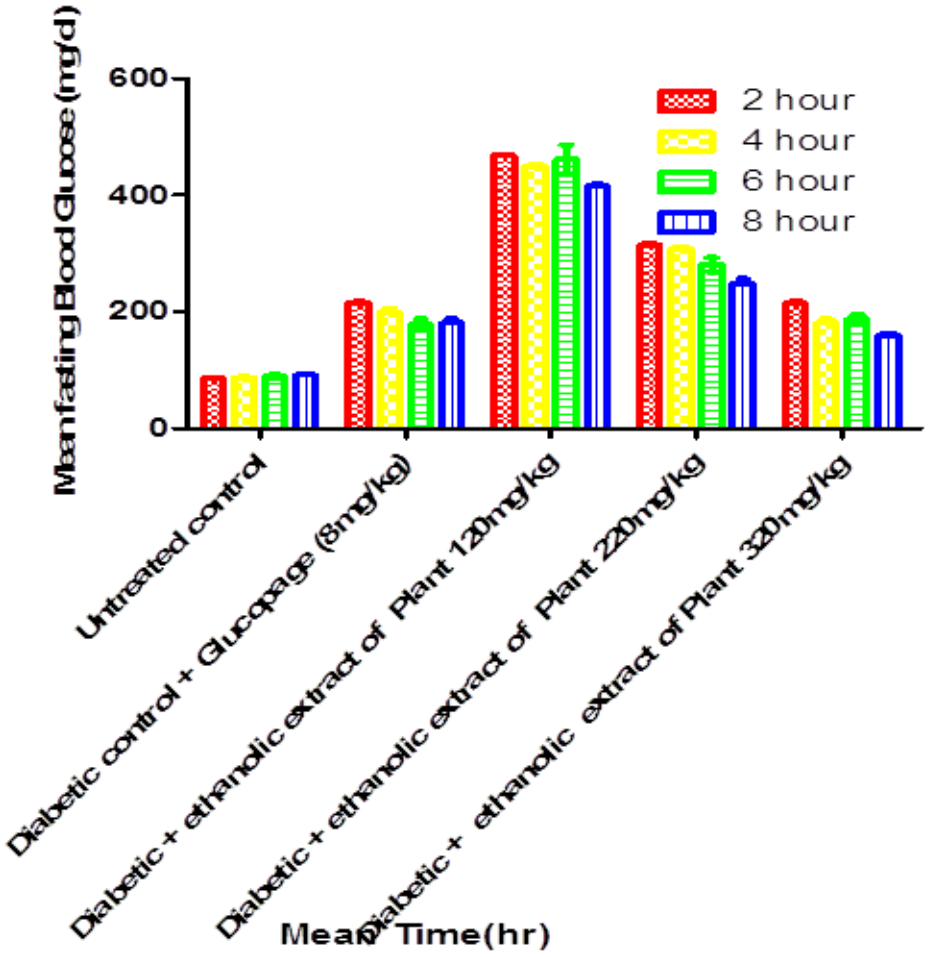
RESULTS

Diabetes mellitus among the different groups of biochemical disease which characteristically having high sugar level in blood, it is because of abnormal insulin formation. As a result, 85-91mg/kg is concerned for the standard value of glucose level in the blood. All the four groups are gives alloxan, except replication A, which is untreated or control group. 85mg/kg was noted as, the level of glucose in untreated replication of blood, which is treated as the normal value of glucose level. After that hypoglycemia was prevent by the, mixture of normal saline throughout I/V and combination of glucose in water. Group A noted as the glucose level in 5 hours i.e. ($p< 0.0001$) was recorded.

Table 1: Showing Blood Glucose Level (mg/dl)

	2 hour			4 hour		
Untreated control	86.0	85.0	86.0	88.0	86.0	89.0
Diabetic control + Glucopage (8mg/kg)	220.0	211.0	213.0	209.0	200.0	189.0
Diabetic + ethanolic extract of Plant 120mg/kg	472.0	467.0	465.0	455.0	447.0	448.0
Diabetic + ethanolic extract of Plant 220mg/kg	322.0	310.0	311.0	312.0	311.0	301.0
Diabetic + ethanolic extract of Plant 320mg/kg	221.0	211.0	211.0	187.0	167.0	188.0

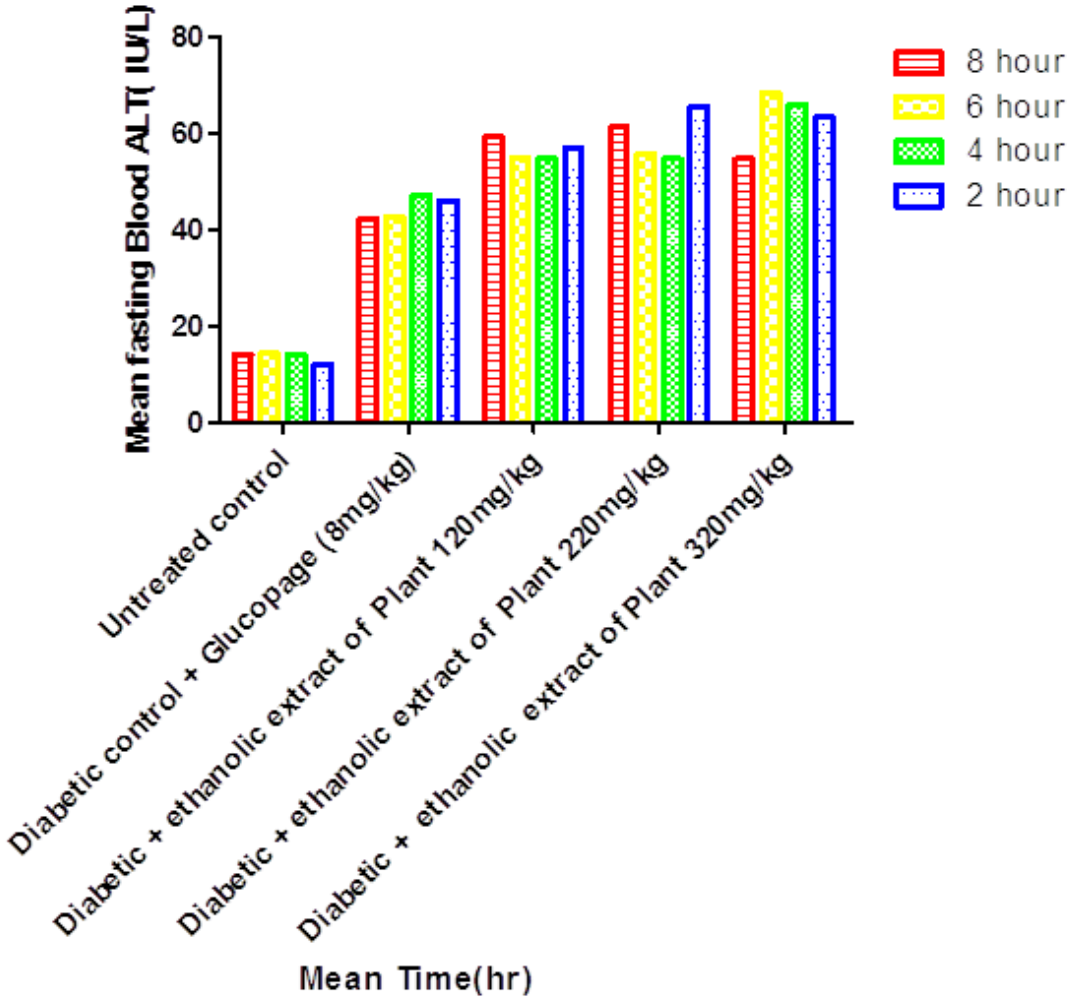
6 hour			8 hour		
90.0	91.0	85.0	91.0	92.0	90.0
180.0	187.0	167.0	167.0	187.0	188.0
467.0	483.0	434.0	422.0	412.0	413.0
288.0	287.0	267.0	256.0	256.0	234.0
178.0	192.0	192.0	155.0	156.0	167.0



Graph 1: showing blood glucose level (mg/dl) level of rabbits.

Table 2: Showing alanine aminotransferase (ALT)

	2 hour			4 hour			6 hour			8 hour		
Untreated control	13.0	12.0	11.0	13.0	14.0	15.0	16.0	13.0	14.0	15.0	14.0	13.0
Diabetic control + Glucopage (8mg/kg)	45.0	46.0	47.0	48.0	49.0	45.0	44.0	43.0	41.0	42.0	43.0	42.0
Diabetic + ethanolic extract of Plant 120mg/kg	56.0	57.0	58.0	59.0	52.0	53.0	52.0	56.0	57.0	58.0	59.0	61.0
Diabetic + ethanolic extract of Plant 220mg/kg	67.0	63.0	67.0	56.0	54.0	54.0	53.0	56.0	58.0	59.0	63.0	62.0
Diabetic + ethanolic extract of Plant 320mg/kg	62.0	63.0	65.0	63.0	67.0	68.0	69.0	71.0	65.0	63.0	45.0	56.0



Graph 2: showing Blood ALT (U/L) level of rabbits

Group-2 was prearranged, the nearby accessible model drug, the Glucophage (Glibenclamide) for normal eight hours, at the principal of two hrs, four hrs, six hrs and eight hrs. On the remain leaving, of the means of care a major cut of 188 mg/kg was showing, it is going to decrease from 220 mg/kg to 188mg/kg. Group-3 was held in reserve, going on *N. cataria* plant's drugs at the dosage of 120mg/kg on behalf of constant eight hrs, at the short-term of two hrs, four hrs, six hrs and eight hrs. At the ultimate momentous considerable decrease of 413 mg/dl was record, in the amount of glucose, presentation that 120 mg/kg drug has opposed blow on the glucose level in blood. The 4 number of group was considered, by the extraction of *N. cataria* on the amount of, 220 mg/kg for permanent eight hrs, at the short-term of two hrs, four hrs, six hrs and eight hrs. At the carry on, of the procedure of healing a considerable decrease of 234mg/dl was recorded in glucose concentration, screening that 220 mg/kg drug has not bright make happen on glucose. The glucose level of group 4 is going to decrease from 322mg/kg to 234mg/kg (Table 1).

Put together Group 5 was treated, with the extract of plant; on the dose grade of 320mg/dl for ordinary eight hrs. It was certain the gap of two hrs between the duration of 2two hrs, four hrs, six hrs and eight hrs. As a consequence, the major decrease of 167mg/dl was experiential, so as this is recorded in glucose rank at the end of the treatment (Graph 1).

Subsequently extreme, as the standard charge of ALT point, in the blood, is nervous that is 12-16mg/dl. Altogether the groups were gives alloxan, excluding group A. which is shown untreated or control group. The concentration of glucose with untreated groups; blood was well-known as 12-16mg/dl which is the average value of the group. Group 2 was agreed, that the nearby available usual medicine; the Glucophage (Glibenclamide) for consistent of eight hours at the provisional of two hrs, four hrs, six hrs and eight hrs. At the keep on the course of action of medication a significant decrease of 42mg/dl was observed and noted. The glucose level in the blood serum is decrease from 45mg to 42mg. Group 3 reserved on *N. cataria* extract, at the measure distance of 120mg/dl for continuous eight hrs at the short-term of two hrs, four hrs, six hrs and eight hrs. At the take momentous rise of increase of 61mg/dl was recorded; in glucose smooth performances to 120 mg/kg drug has defy result on the next of glucose level in blood. Group 4 was treated, with the extract of *N. cataria* at measured quantity of 220 mg/kg for permanent eight hrs, at the provisional of two hrs, four hrs, six hrs and eight hrs respectively (Table 2). At the deal with the healing a significant decrease of 62mg/dl was recorded, in glucose point performance that 220 mg/kg drug has no roll realize tablet on glucose. The level of glucose is decrease at the point of 67mg to 62mg. Group 5 was treated with the extract of plant, with the amount of 320mg/dl dose rate for even eight hrs. It was put with the space of two hrs, four hrs, six hrs and eight hrs. As a consequence reduce of 56 mg/dl was experiential that was recorded in glucose parallel with the ground at the most recent of healing. In the last group, the level of glucose is decrease from 62mg to 56mg was recorded (Graph 2).

DISCUSSION

Diabetes mellitus is a most important cluster of metabolic diseases, which is caused by the high blood level in glucose. The diseases are connected to durable complications, while the disease is commonly affecting on different body parts, especially eyes, kidneys, nerves, heart and blood vessels (Fontbonne et al., 2004). In a worldwide level the main reason of its occurrence, is because of continues increase due to ageing and socio-economic changes, (Kokil et al., 2015). *N. cataria* were showing a significant decrease with ethanolic extract at present of experimental animal rabbits, glucose level was decrease by increasing dose level. When the diabetic rabbits are treated with ethanolic plant extract at the amount of 120kg, the level is increase up to 413.0, this is noted as a significant change, but if the diabetic rabbits are treated with *N. cataria* extract with the amount of 320kg, it will show a significant decrease, which is 167.0. Therefore is known as most effective dose, it is purposed that the plant play an important role in the decreasing of glucose level. The oral management of different doses of the indigenous drug has caused a decrease in the blood glucose of normal rabbits. The crude drug produced a significant and consistent hypoglycaemic response in rabbits. Similar, hypoglycaemic activity has already been reported in several plants (Marquis et al., 1977). On the other hand if the plant extract is treated with ALT level at the amount of 120kg, it can show significant changes that are 42.0, but if the *N. catria* plant extract is treated at the amount of 320kg, than it is increase from 42 to 56. ALT level

shows very small changes, it can be change but this is not a significant change. Therefore this is show that the plant extract show a small changes on ALT level. Our study correlates with the study conducted by Rajasekhar et al. (2019) on Asparagus gonoclados and establish that the ethanol plant extract at a dose of 500 mg/kg b.wt has made maximum (67%) drop in fasting blood glucose levels (FBG) in diabetic treated rats after 6 h of oral administration when related to the standard drug glibenclamide (40%).

CONCLUSION

The present research was conducted during 2019 to provide the avowedness about *N. cataria*. This study shows that the *N. cataria* extracts is important anti-diabetic activity. It has antioxidant latent for oxidative stress shaped by diabetes, primarily second hand for antispasmodic, cold, and fever. The drugs capably showed exceptional and cleaned style.

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, RP, FT designed and performleed the experiments and also wrote the manuscript. FT performed animal treatments, flow cytometry experiments, tissue collection, and data analysis. SJ, AAKK, WK, BA, MA, RB, MS, SB, KS, FH, AH, NU, MA, SF, ZU, NM, RA, HAJ, IUH, AR, SU, MI designed experiments and reviewed the manuscript. All authors read and approved the final version..

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