



Effect of *Gymnema sylvestre* extract on Liver and Kidney functioning: In-vivo study

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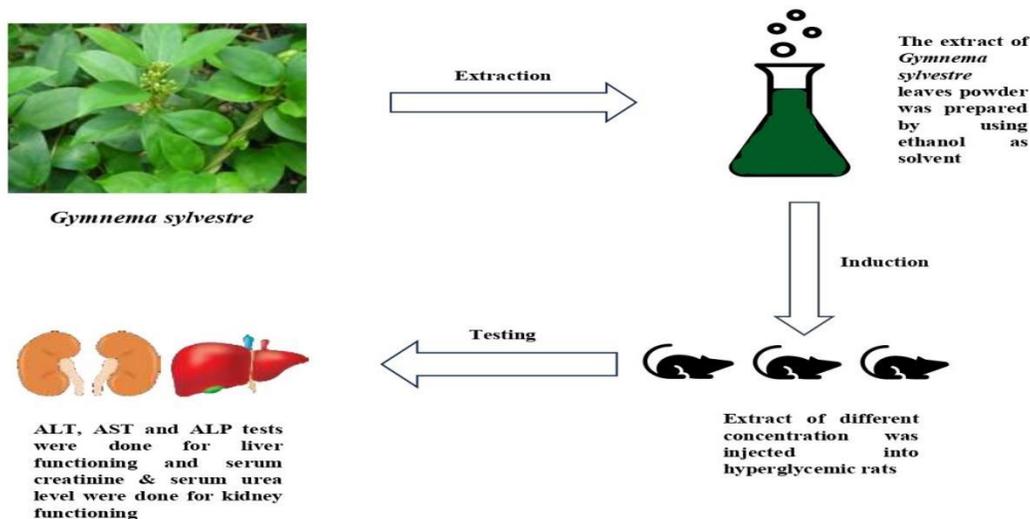
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Abstract: The extract and powder form were used to treat the hyperglycemia because many studies shows that, it have a great impact on the reduction of high level of glucose in blood together with total lipid profile. *Gymnema sylvestre* related to a family Asclepiadaceae. The group of gymnemic acids and gurmamin are the chief bioactive elements which are found in the *Gymnema sylvestre*. It is a familiar curative plant have an ancient history of use in homeopathic customary medication and have been widely studied for its value or efficiency in the diabetes mellitus type 2 treatment. Experimental rats were fed a standard commercial rat diet and ordinary water. The Extract and powder of *Gymnema sylvestre* leaves were given after disease induction. To check its effect on liver and kidney, alanine transaminase (ALT), aspartate aminotransferase (AST), alkaline phosphate (ALP), urea levels and serum creatinine level will be examined. The positive results were obtained in the reduction of hyperglycemia. The results of this trail declared that the extract of *Gymnema sylvestre* leaves have a great effect than the leaves powder on rats with hyperglycemic conditions.

[Raheel Nazim, Ayesha Nadeem Choudhary, Asif Meraj, Fizza Tahir, and Muhammad Talha Sohail. *Effect of Gymnema sylvestre extract on Liver and Kidney functioning: In-vivo study*. *Life Sci J* 2023;20(9)1-11]. ISSN 1097-8135 (print); ISSN 2372-613X (online). <http://www.lifesciencesite.com>. 01.doi:10.7537/marslsj200923.01.

Key words: *Gymnema sylvestre* extract, Liver, Kidney, food nutrition

Graphical Abstract



INTRODUCTION

Gymnema sylvestre is perennial climber related to a family Asclepiadaceae and broadly distributed in south eastern, areas of Asia, Srilanka,

japan, India, Vietnam, Malaysia and china (WWF-India 2005). In many plants the structurally diverse group of compounds present which are based on the carbon skeleton termed as saponins. The *Gymnema*

sylvestre have some type of gymnemasaponins I–V which are antisweat principles. (Vincken *et al.*, 2007). The slow growing, perennial woody climber *Gymnema sylvestre* is spread over the whole Asia, tropical Africa, China and abundantly in the Indian region. Further in the India the main area of the production of this miracle plant is Kota, which is the district of Rajasthan (Preuss *et al.*, 2004).

It is used for number of major health issues primarily used for cardiovascular disorder, obesity, hypercholesteremia, osteoporosis, eye problems, asthma and snake bite in different cultures and traditions. With these all health assistances it is helpful to control hyperglycemia and regarded as a strong moderator beside insulin resistance and diabetes induced hyperglycemia. It scavenges free radicals from the body and provides purifying effect (Tiwari *et al.*, 2014). This plant is very effective against the many health complications. It is the package of beneficial nutrients and phenolic compounds and have a great variety of some important minerals like calcium, phosphorus, zinc, copper, iron, magnesium and chromium, all these micronutrients are valuable for the proper functioning of the body to maintain the healthy structure and mechanisms (Patel *et al.*, 2012). The herbaceous plant, *Gymnema sylvestre* mainly recognized as “sugar destroyer” in the earliest time, it is elucidated by the medical doctors this plant with their small leaves blocks and halts the sugar taste by chewing them. The herbaceous plant, *Gymnema sylvestre* mainly recognized as “sugar destroyer” in the earliest time, it is elucidated by the medical doctors this plant with their small leaves blocks and halts the sugar taste by chewing them. Gymnemic acid, the bioactive ingredient in the leaves of *Gymnema sylvestre* which targeted the high glycemic level of individual’s body. An investigation of previous researchers exposed that this botanical herb have some remarkable activities such as anti-inflammatory activity, provide healthy treatment against arthritis, obesity and also helps in reducing the lipid level in the body. Traditionally, many health related issues like chronic cough, bronchitis, Cardiac issues, piles, stomatitis, jaundice, asthma and urinary complaints are treated effectively by usage of this miracle plant (Al-Romaiyan *et al.*, 2010).

It is a familiar curative plant have an ancient history of use in homeopathic customary medication and have been widely studied for its value or efficiency in the diabetes mellitus type 2 treatment (Pham *et al.*, 2018). *Gymnema sylvestre* reduce the high blood glucose level through proper mechanism. It promotes the renewal of islet cells. By stimulation it increases insulin secretion from pancreas. It inhibits the absorption of glucose from the intestinal tract. By increasing the activity of the enzymes responsible for

the use of glucose by the insulin-dependent pathways, the use of glucose increases, an increase in the activity of phosphorylase, a decrease of the gluconeogenic enzymes and sorbitol dehydrogenase. Which leads to a decrease in the high glucose concentration in the blood (Kanetkar *et al.*, 2007). Gymnemic acid prevents the activation of taste buds by glucose molecule present in nutriment, because its atomic arrangements to taste buds are alike to glucose molecules which fill the receptors in the taste buds. In the same way prevents the absorption of glucose molecule by intestine, it attaches to the receptor present in peripheral layer of small intestine. It shows, role of *Gymnema sylvestre* in curing hyperglycemia in diabetes is chief. This plant with its macronutrients and micronutrients profile also rich in the poly phenolic compounds which all are have an amazing properties against different ailments (Tiwari *et al.*, 2014). Liver tissue, adipose tissue and muscle cells are chief metabolic tissues that manage glucose and lipid homeostasis. Diabetes is an endocrine disorder which happens due to hyperglycemia and the key reason of hyperglycemia is insufficient supply of endogenous insulin. The hormonal balance of the body is disturbs chronically when the patient have a complaint of diabetes and when the state of hormonal imbalance occurs in the body then all the mechanisms of body disturbed at different levels with the passage of time which further leads to many complication from which some are non-reversible and problematic such as cancer, heart failure, brain hemorrhage and etc. so, it is necessary to achieve and maintains a healthy life to prevent from biggest losses (de M Bandeira *et al.*, 2013). Ketoacidosis, diabetic non ketosis coma and diabetic coma are the some complications which caused by small problems. The circulatory system and blood vessels of body may suffer from large damage and vessels get ruptured due to severe and prolonged complications. Many severities in diabetes are congregated like micro vascular disease which is due to loss of small blood vessels and macro vascular diseases which is due to damage to the blood arteries (Thomas *et al.*, 2005). These micro and macro vascular diseases are further classified according to their effect like damage to the basic functional unit of brain that is neuron which is termed as neuropathy, damage to the retina of eye which is named as retinopathy and damage to basic purposeful unit of renal that is nephron which is stated as nephropathy while anemia may be caused in case of nephropathy, all these damages fall under the micro vascular disease (Halder *et al.*, 2003). The macro vascular diseases which leads to the many cardiac problems as like cardiovascular system that is additional leads to the atherosclerosis (Ali *et al.*, 2010).

Disease causes the renal weight increase due to the subsequent enhancement in glycogen synthesis and glucose overutilization, synthesis of protein and fat synthesis although the weight of liver reduce due to the raised catabolic processes like breakdown of protein to amino acids, lipids to fatty acids and glycogen to glucose which termed as proteolysis, lipolysis and glycogenolysis respectively, that is result of lack of insulin in the cells of liver. DM causes several complications include : (I) Myocardial infarction, Angina, stroke, CVD (II) Ischemia (III) foot intermediate problems like diabetic foot is caused in which involves the pain and swelling of foot, in this type gangrene may also be appears on foot. There is a dire need to treat the diabetes, because it causes severe complications leading towards premature death if diabetes is not treated timely. The utilization of insulin production agents and lowering serum glucose medications are involved in the treatment of diabetes (Daisy *et al.*, 2009). The researches also revealed that, production of endogenous insulin enhanced by the oral administration of *Gymnema sylvestre* leaves extract (Pandey *et al.*, 2011).

Many surveys showed that the usage of *Gymnema sylvestre* in the form of extract gives a wide variety benefits to the disturbed physiological patterns like abnormal β -cells and insulin production, chronic inflammation, errors in the functioning of enzymes, overweight which are some clear factors interrelated to the diabetes mellitus (Leach, 2007). The plant *Gymnema sylvestre* have many health benefits and is used mainly for the treatment of diabetes type I and type II in folk and Ayurvedic system. Other than the diabetic consequences, this plant shows its miracle effects to get the relief from urinary complaints, asthma, breathing troubles, cardiopathy, chronic cough, piles, and constipation, bronchitis, stomatitis and eye problems. It also used to neutralize the toxic effect of snake bite (Leach, 2007). The *Gymnema sylvestre* is analgesic, astringent, anthelmintic, emetic, uterine tonic, cardiogenic, alexipharmic, bitter, stomachic, pungent, expectorant, antipyretic, laxative, digestive, stimulant, diuretic; valuable in dyspepsia, jaundice, constipation, leukoderma, conjunctivitis, amenorrhoea, cardiopathy, intermittent fever hemorrhoids, bronchitis, inflammations, cough, hepatosplenomegaly and asthma (Pragada *et al.*, 2012).

Approximately 228 million people are affected by the disease of diabetes as stated by the WHO. In top 10 countries the Pakistan has 7th rank with the utmost number of diabetic patients. In 2025, 14.5 million people will be suffering from diabetes in Pakistan. More or less 422 million natives have been

found out to be diabetic. The rate of frequency has been expanded from 4.7% to 8.5% in past 2 years. In Pakistan, current situation of diabetic women is 6.8% and diabetic men is 5.1% in municipal areas. In rural regions the recognition of diabetes is 4.8% in females and 5.0% in males. In urban regions hyperglycemic patients related to rural areas 14.2% in females and 6.3% in males against 10.9% in females and 6.9% in males (Zafar *et al.*, 2016).

Some essential enzymes like glycogen synthetase, glucose 6-phosphate dehydrogenase, and hexokinase and glyceraldehyde 3-phosphate dehydrogenase are those enzymes which are dependent on the insulin and the activity of these particular enzymes was lowered in the tissue of diabetic rabbits. Although on the other hand, the activity of fructose 1,6-diphosphatase, glycogen phosphorylase, glucose 6-phosphatase, sorbitol dehydrogenase of polyol pathway and gluconeogenic enzymes in the tissues of diabetic rabbits was increased totally but on the *Gymnema sylvestre* administration it reversed. The treatment of beryllium nitrate-treated rats with leaves of *Gymnema sylvestre* helped to maintain the glucose level of blood, which disturbed with metabolism of carbohydrate leading to damage of liver and in liver inhibited activity of hexokinase. Similarly, in the alloxan induced diabetic rats, dogs and rabbits the particular treatment also brought to a close serum insulin and serum glucose homeostasis. It could be possible due to the repairment and regeneration of beta cells in islets of Langerhans of pancreas. In the normal rats with normal glycaemic conditions the release of insulin from pancreas did not increase upon administration of water-soluble extract of *Gymnema sylvestre* but the release of this particular hormone enhanced in diabetic islets (Kar *et al.*, 2003).

MATERIAL AND METHODS

Study area:

The experimental analysis was conducted in the Food Microbiology and Biotechnology Laboratory of National Institute of Food Science and Technology, Department of UAF. To evaluate the therapeutic effect of *Gymnema sylvestre* leaves against the complication of hyperglycemia. The leaves of *Gymnema sylvestre* (gurmar) were acquired from the local market of Faisalabad and afterward these leaves were subjected for further procedures

Sample preparation:

The raw material was cleaned in order to eliminate stones, dust and straw pieces. These leaves were dried completely in Lab Scale Dehydrator for 24 hours at 50°C and then these dried leaves were ground into fine powder by using of electric grinder machine in canning hall. Finally, the resultant powder was

examined for preparation of extract and their biochemical attributes. The extract of *Gymnema sylvestre* leaves powder was prepared by using ethanol as solvent according to the protocols as specified by Sheoran *et al.* (2015) with little modification. The powder was soaked in the 200 mL of 85% ethanol solution for 4 hours after processing with ethanol the extract of sample was filtered by using the filter paper (Whatman no. 1) and then the sample placed in rotary evaporator to get concentrated extract under reduced pressure below 40°C. The semi-solid extract of blackish-green color was obtained.

In vivo studies:

Gymnema sylvestre leaves were used in the study on male albino rats to assess their potential as a treatment for hyperglycemia. The duration of this particular research was one month.

In the Animal Room of NIFSAT, University of Agriculture, Faisalabad, twelve adult male albino rats weighing 160-180 g and between 2-3 months old were acquired and kept in good health. Individually caged rats were kept under ideal environmental circumstances, which included humidity, light, and temperature, throughout the duration of the study. Every experiment was carried out in accordance with the accepted standards for the use of animals and the international association's ethical guidelines.

Induction of hyperglycemia in normal healthy rats:

To induce the hyperglycemia in rats the streptozotocin (STZ) injection of 60 mg/kg was

administered to rats. Total of 7.2 mg of streptozotocin with 12 ml of distilled water was directed to 12 rats. Each rat received 0.6 mg of streptozotocin with 1 ml of distilled water. And after the 1 week of administration the diabetes was induced because the blood sugar levels were elevated when checked by the glucometer. The rats were also changed their behavior when they have high blood glucose level. Then the rats were given extract and powder of *Gymnema sylvestre* leaves to observe the effect on the serum glucose and insulin level. These particular doses were administered to rats for 1 month to evaluate their effects on the hyperglycemic rats.

Efficacy study plan :

Distributed twelve rats into 4 groups, in this way each group containing 3 rats. The 1st group having hyperglycemic rats which is a diabetic control group and normal diet fed to these hyperglycemic rats. The 2nd group containing hyperglycemic rats and they were fed with 350 mg/kg of *Gymnema sylvestre* leaves extract in normal diet. Similarly, the 3rd group also containing a hyperglycemic rats and fed them with *Gymnema sylvestre* leaves extract in normal diet but with a quantity of 450 mg/kg. The 4th group of rats also having a hyperglycemic rats but they fed with *Gymnema sylvestre* leaves powder of 25 mg/day. These hyperglycemic rats were fed for one month of time period. In this period the blood tests were done on weekly basis to observe the effect of doses on the blood glucose and insulin level of these rats.

Table 1: Treatment plan for *Gymnema sylvestre* leaves dosage to rats

Groups	Treatments
G1	Hyperglycemic rats + normal diet (diabetic control group)
G2	Hyperglycemic rats + 350 mg/kg <i>G.Sylvestre</i> leaf extract
G3	Hyperglycemic rats + 450 mg/kg <i>G.Sylvestre</i> leaf extract
G4	Hyperglycemic rats + 25mg/day <i>G.Sylvestre</i> leaf powder

Liver and kidney functioning test:

The liver responsibility in sugar stability management desired for numerous physical, biochemical and biological modifications. By the following protocol of Monterio *et al.* (2017) the liver function tests were assessed that are alanine transaminase (ALT) and aspartate aminotransferase (AST). However, the alkaline phosphate (ALP) was measured according to the method defined by

Nakyinsige *et al.* (2013). On the other hand the renal functioning tests which are urea levels and serum creatinine were also measured by using the method of Malik *et al.* (2018).

Statistical analysis:

Obtained data for each parameter was analyzed statistically to determine the level of significance and means comparison by using the method of Mason *et al.* (2003)

Aspartate transaminase (AST):

The results which were obtained from this study indicated a significant effect ($P < 0.001$) on the aspartate transaminase (AST) concentrations of treatments and time intervals. The interactive impact on aspartate transaminase (AST) concentrations and the intervals of treatment also showed a very significant impact.

On the other hand, the results concerning aspartate transaminase (IU/L) of diabetic rats for different doses of *Gymnema sylvestri* leaves treatments are set in (Table 2). The results were showed the significant effect in the hyperglycemic rats on aspartate transaminase (AST) level. In the diabetic conditions the aspartate transaminase (AST) level becomes high. At the initial stage the lowest value of AST level was noted in G₁ (diabetic control group) that was 47.733±0.47 IU/L. Whereas the highest AST level was noted in the G₂ that was 49.800±1.99 IU/L

followed by G₃ and G₄ that was 48.867±1.92 IU/L and 48.133±1.72 IU/L respectively. When the rats were fed with the extract and powder of the *Gymnema sylvestri* leaves then the results showed that the AST level of rats was decreased with the passage of time. At the final stage of study the lowest value of AST level was noted in G₃ (450 mg/kg leaves extract) that was 24.433±1.96 IU/L followed by G₂ (350 mg/kg leaves extract) and G₄ (25 mg/day leaves powder) that was 30.067±1.47 IU/L and 33.733±1.06 IU/L respectively. While the maximum AST level was noted in the G₁ (diabetic control group) that was 62.533±2.10 IU/L. Shiyovich *et al.* (2010) demonstrated that the leaves of *Gymnema sylvestri* have a momentous decrease in the aspartate transaminase (AST) level 22% in the diabetic rats, Because this plant have many amazing properties for maintaining the healthy life.

Table 2: Treatment means of serum AST (IU/L)

Treatment	Days		Mean
	7	28	
G ₁	47.733±0.47	62.533±2.10	55.133 ^a
G ₂	49.800±1.99	30.067±1.47	39.933 ^b
G ₃	48.867±1.92	24.433±1.96	36.650 ^c
G ₄	48.133±1.72	33.733±1.06	40.933 ^b
Mean	48.633 ^a	37.692 ^b	

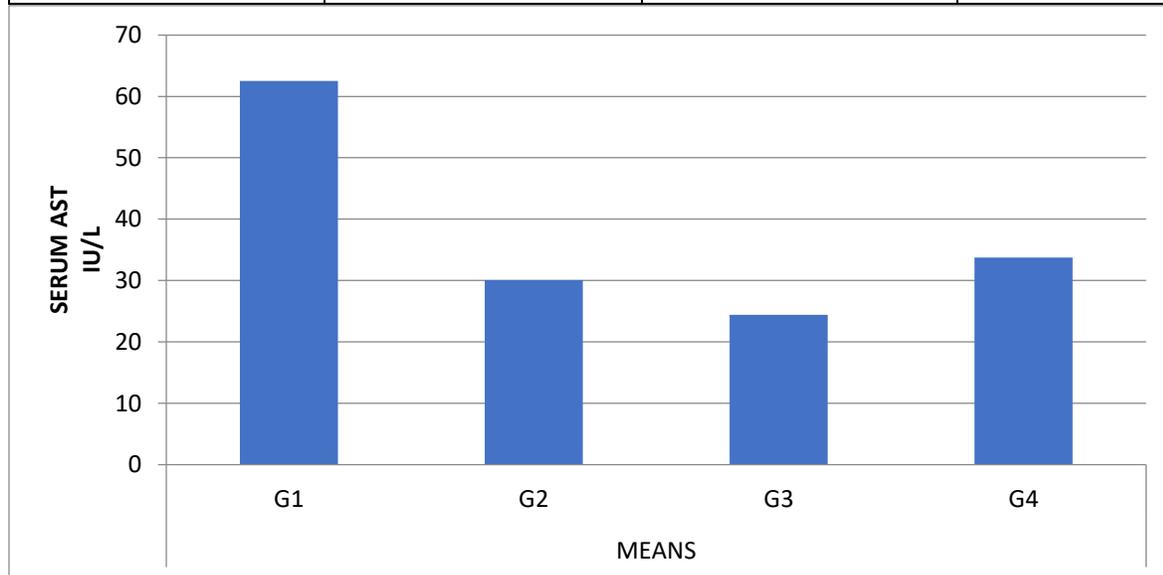


Fig 1: Comparative effect of treatments on Serum AST level of rats

Alanine transaminase (ALT):

On the other hand, the results concerning alanine transaminase (IU/L) of diabetic rats for different treatments means different doses of *Gymnema sylvestre* leaves are set in (Table 3). The results were showed the significant effect in the hyperglycemic rats on alanine transaminase (ALT) level. In the diabetic conditions the alanine transaminase (ALT) level becomes high. At the initial stage the lowest value of ALT level was noted in G₁ (diabetic control group) that was 50.467±1.22 IU/L. Whereas the highest ALT level was noted in the G₃ that was 48.967±1.17 IU/L followed by G₂ and G₃ that was 48.400±2.17 IU/L and 48.367±1.70 IU/L respectively. When the rats were fed with the extract and powder of the *Gymnema sylvestre* leaves then the results showed that the ALT level of rats was declined as compared to initial values with the passage of time.

At the final stage of study the lowest value of ALT level was noted in G₃ (450 mg/kg leaves extract) that was 22.500±0.7 IU/L followed by G₂ (350 mg/kg leaves extract) and G₄ (25 mg/day leaves powder) that was 26.433±1.05 IU/L and 31.433±1.15 IU/L respectively. While the maximum ALT level was noted in the G₁ (diabetic control group) that was 54.867±2.76 IU/L. Chiabchalar *et al.* (2010) demonstrated that the leaves of *Gymnema sylvestre* have a momentous decrease in the alanine transaminase (ALT) level by 26% in the diabetic rats. The findings of this study revealed that the treatments' and time periods' alanine transaminase (ALT) concentrations had a significant impact (P 0.001). An extremely significant connection was also seen between the treatment intervals and the effects on alanine transaminase (ALT) concentrations.

Table 3: Treatment means of Serum ALT (IU/L)

Treatment	Days		Mean
	7	28	
G ₁	50.467±1.22	54.867±2.76	52.667 ^a
G ₂	48.400±2.17	26.433±1.05	37.417 ^c
G ₃	48.367±1.70	22.500±0.7	35.433 ^c
G ₄	48.967±1.17	31.433±1.15	40.200 ^b
Mean	49.050 ^a	33.808 ^b	

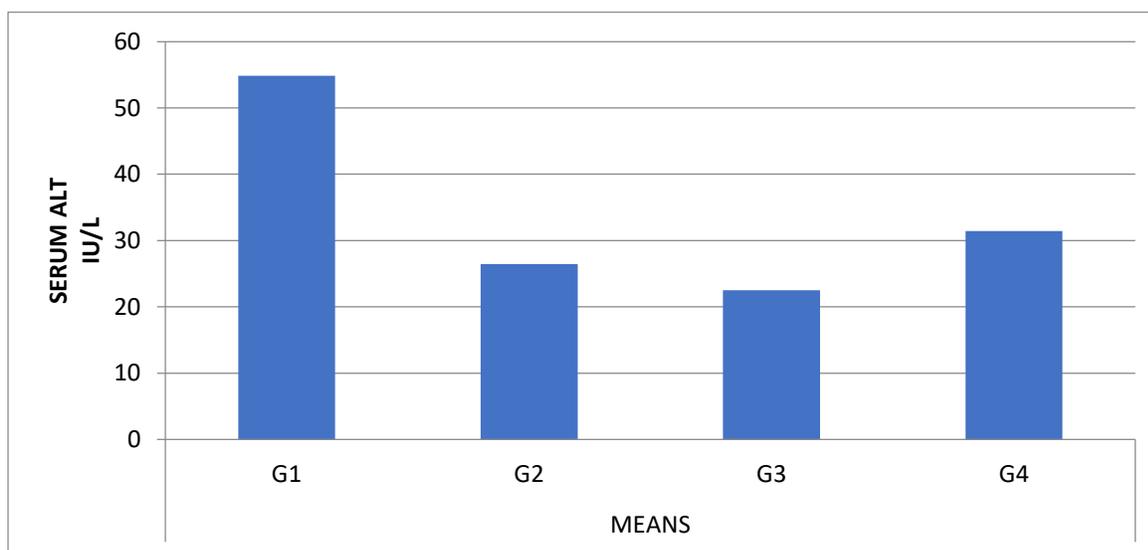


Fig 2: Comparative effect of treatments on Serum ALT level of rats

Alkaline phosphatase (ALP):

The findings of this investigation showed a strong relationship between the alkaline phosphatase (ALP) concentrations of treatments and time intervals (P 0.001). A highly substantial interaction between the treatment intervals and alkaline phosphatase (ALP) values was also observed. Results for alkaline phosphatase (IU/L) of diabetic rats treated with various dosages of *Gymnema sylvestre* leaves are presented in relation to the current experimental investigation (Table 4). The findings demonstrated a considerable impact on alkaline phosphatase (ALP) levels in hyperglycemic rats. Alkaline phosphatase (ALP) levels rise in diabetes circumstances. The G1 (diabetes control group) had the greatest ALP level in the beginning, which was 130.53 1.91 IU/L, while the G3 had the lowest ALP level, which was 126.00 4.15 IU/L. However, the ALP levels for G2 and G3 were found to be greater than those for G4 and were

126.070.65 and 127.133.78 IU/L, respectively. The results demonstrated that over time, the rats' ALP levels decreased in comparison to their baseline values when they were fed with the extract and powder of *Gymnema sylvestre* leaves. At the end of the trial, G3 (450 mg/kg leaves extract) had the lowest ALP level with a reading of 70.50 1.17 IU/L, followed by G2 (350 mg/kg leaves extract) and G4 (25 mg/day leaves powder), with readings of 87.00 1.51 IU/L and 93.60 1.11 IU/L, respectively. While a maximal ALP level of 151.50 3.81 IU/L was recorded in the G1 (diabetic control group). Alkaline phosphatase (ALP) levels in diabetic rats were significantly reduced by 42% when *Gymnema sylvestre* leaf extract was used, according to El Shafey *et al.* (2013). Furthermore, When rats were fed powdered *Gymnema sylvestre* leaves, Bilal *et al.* (2011) noticed a substantial decrease in ALP levels in diabetic male albino rats. The animals were STZ-induced diabetic rats.

Table 4 : Treatment means of ALP (IU/L)

Treatment	Days		Mean
	7	28	
G ₁	130.53±1.91	151.50±3.81	141.02 ^a
G ₂	126.07±0.65	87.00±1.51	106.53 ^b
G ₃	126.00±4.15	70.50±1.17	98.25 ^c
G ₄	127.13±3.78	93.60±1.11	110.37 ^b
Mean	127.43 ^a	100.65 ^b	

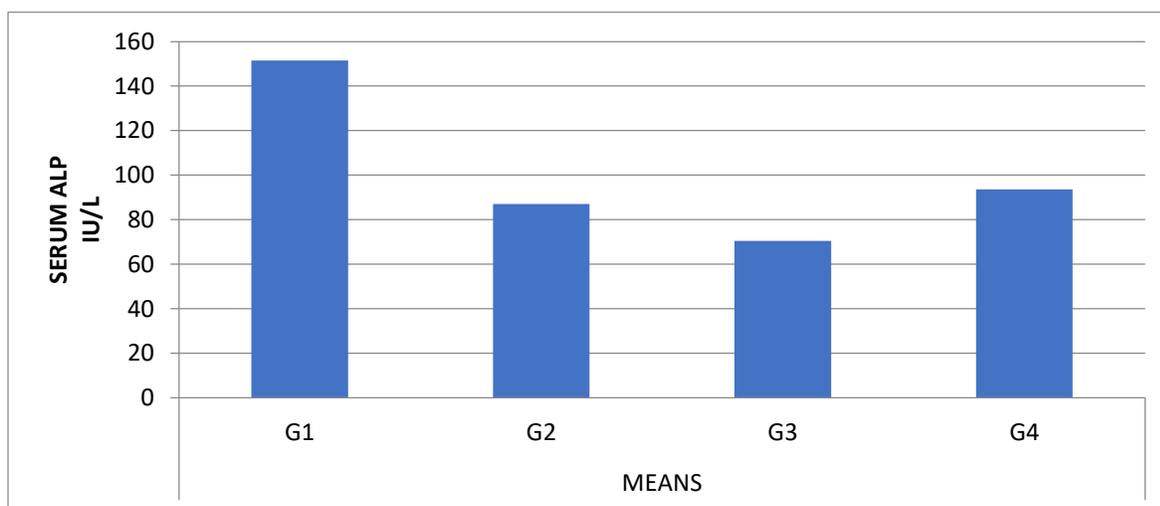


Fig 3: Comparative effect of treatments on Serum ALP level of rats

Serum Urea:

The results which were obtained from this study indicated a significant effect ($P < 0.001$) on the serum urea concentrations of treatments and time intervals. The interactive impact on serum urea concentrations and the intervals of treatment also showed a very significant impact.

The findings of the current research study are shown in Table 5 about the serum urea (mg/dL) of diabetic rats treated with various dosages of *Gymnema sylvestre* leaves. The findings demonstrated a considerable impact on serum urea levels in hyperglycemic rats. The level of serum urea rises in diabetes circumstances. At the beginning of the study, G1 (the diabetes control group) had the lowest value of blood urea, which was 53.5001.17 mg/dL. While the G3 group's serum urea concentration was found to be 57.1334.11 mg/dL. However, the blood urea levels for G2 and G3 were found to be greater than those for G4 and were 58.2670.60 and 58.6671.45 mg/dL,

respectively. When the rats were fed with the extract and powder of the *Gymnema sylvestre* leaves then the results showed that the serum urea level of rats was declined as compared to initial values with the passage of time. At the final stage of study the lowest value of serum urea level was noted in G₃ (450 mg/kg leaves extract) that was 32.300±1.37 mg/dL followed by G₂ (350 mg/kg leaves extract) and G₄ (25 mg/day leaves powder) that was 37.467±1.12 mg/dL and 40.567±1.15 40.567±1.15 mg/dL respectively. While the maximum serum urea level was noted in the G₁ (diabetic control group) that was 82.567±2.35 mg/dL. Kumar *et al.* (2010) confirmed that the leaves extract of *Gymnema sylvestre* have a momentous decrease in the serum urea level by 17% reduction in the diabetic rats. Furthermore, When rats were fed powdered *Gymnema sylvestre* leaves, Bilal *et al.* (2011) reported that the blood urea level of diabetic male albino rats was much lower. The rats were STZ-induced diabetic.

Table 5: Treatment means of Serum Urea (mg/dL)

Treatment	Days		Mean
	7	28	
G ₁	53.500±1.17	82.567±2.35	68.033 ^a
G ₂	58.267±0.60	37.467±1.12	47.867 ^{bc}
G ₃	57.133±4.11	32.300±1.37	44.717 ^c
G ₄	58.667±1.45	40.567±1.15	49.617 ^b
Mean	56.892 ^a	48.225 ^b	

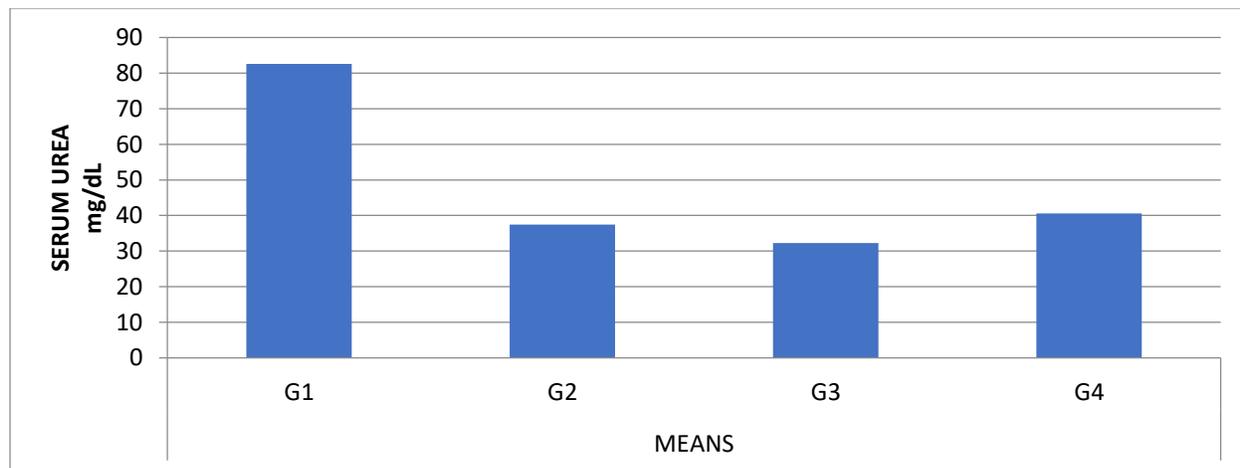


Fig 4: Comparative effect of treatments on Serum Urea level of rats

Serum Creatinine:

The results which were obtained from this study indicated a significant effect ($P < 0.001$) on the serum creatinine concentrations of treatments and time intervals. The interactive impact on serum urea concentrations and the intervals of treatment also showed a very significant impact. Regarding to the current experimental study the results about serum creatinine (mg/dL) of diabetic rats for different doses of *Gymnema sylvestre* leaves treatments are set in (Table 6). The results were showed the significant effect in the hyperglycemic rats on serum creatinine level. In the diabetic conditions the serum creatinine level becomes high. At the initial stage the lowest value of serum creatinine was noted in G₁ (diabetic control group) that was 1.5267±0.06 mg/dL. Whereas the serum creatinine level in the G₃ was noted 1.4767±0.03 mg/dL. On the other hand, the values of

serum creatinine level were found for G₂ and G₃ higher than the G₄ that were 1.6767±0.04 and 1.6833±0.06 mg/dL respectively. When the rats were fed with the extract and powder of the *Gymnema sylvestre* leaves then the results showed that the serum creatinine level of rats was declined as compared to initial values with the passage of time. At the end of the trial, G₃ (450 mg/kg leaves extract) had the lowest blood creatinine level at 0.5100±0.01 mg/dL, followed by G₂ (350 mg/kg leaves extract) and G₄ (25 mg/day leaves powder), with values of 0.6800±0.06 mg/dL and 0.9300±0.05 mg/dL, respectively. The G₁ (diabetic control group) was found to have the highest blood creatinine level, which was 2.3200±0.12 mg/dL. Ramkumar *et al.* (2009) verified that the *Gymnema sylvestre* leaf extract significantly reduced the blood creatinine level in diabetic rats by 12%.

Table 6: Treatment means of Serum Creatinine (mg/dL)

Treatment	Days		Mean
	7	28	
G ₁	1.5267±0.06	2.3200±0.12	1.9233 ^a
G ₂	1.6767±0.04	0.6800±0.06	1.1783 ^c
G ₃	1.4767±0.03	0.5100±0.01	0.9933 ^d
G ₄	1.6833±0.06	0.9300±0.05	1.3067 ^b
Mean	1.5908 ^a	1.1100 ^b	

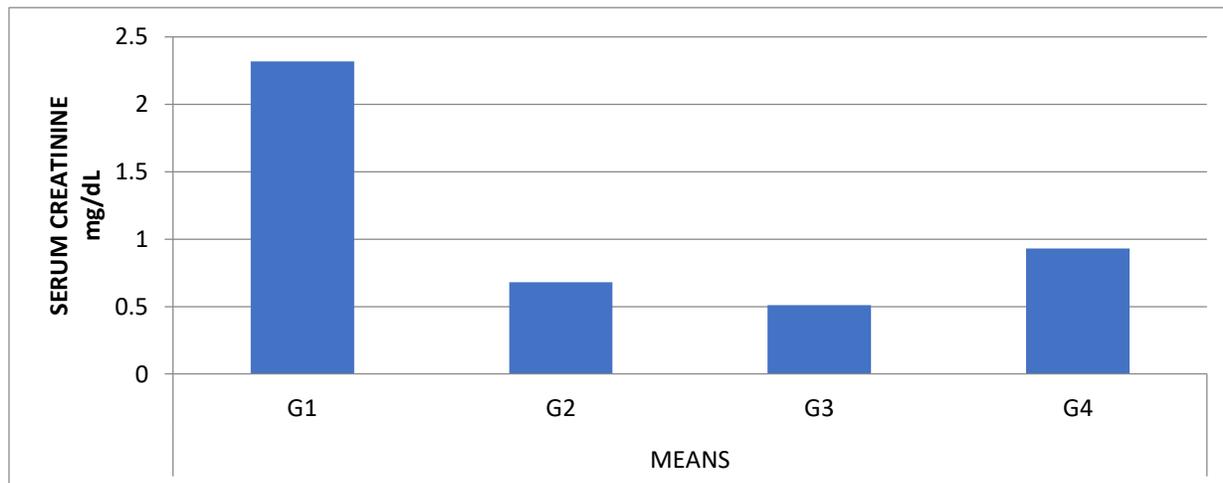


Fig 5: Comparative effect of treatments on Serum Creatinine level of rats

Conclusion

A woody, climbing plant *Gymnema sylvestre* with a nature of sugar killing is found to be very effective against various kind of etiological factors related with DM like inflammation by its oral administration. Insulin is the main hormone, therefore, because of its deficit, insulin is not manufactured or generated sufficiently by pancreas due to cells generating insulin breaking down or malfunctioning. Resistance to insulin may also occur in some instances, leading to insulin manufacturing at an

appropriate rate that most cells resist their function and result in a high blood glucose level. A woody, climbing plant *Gymnema sylvestre* with a nature of sugar killing is found to be very effective against various kind of etiological factors related with DM like inflammation by its oral administration. When the rats were fed with the extract and powder of the *Gymnema sylvestre* leaves then the results showed that the serum creatinine level of rats was declined as compared to initial values with the passage of time.

References:

- [1]. Ali, M. K., K. M. V. Narayan, and N. Tandon. 2010. Dinbctes and coronary heart disease current perspectives. Indian Journal of Medical Research.132: 584-597.
- [2]. Al-Romniyan , A., B. Liu, H. Asare-Anane, C. R. Maity, S. K. Chatarjee and N. Koley. 2010. A Novel *Gymnema sylvestre* extract stimulants Insulin secretion from human Islets in vivo and in-vitro. Phytotherapy Research .24:1370-1376.
- [3]. Bilal, R., M. Zakaria, A. Usman and A. Zia. 2011. Comparison of simvastatin with *Gymnema sylvestre* extract in their effects on alanine transferase, aspartate aminotransferase and creatinine phosphokinase levels of hyperlipidemic rats. Journal of Pakistan Medical Association . 61:190-1194.
- [4]. Chiabchalard, A., T. Tencomnao and R. Santianont. 2010. Effect of *Gymnema inodorum* on postprandial peak plasma glucose levels in healthy human. African Journal of Biotechnology. 9:1079-1085.
- [5]. Daisy, P., J. Eliza and K. A. M. M. Farook. 2009. A novel dihydroxy gymnemic triacetate isolated from *Gymnema sylvestre* possessing normoglycemic and hypolipidemic activity on STZ-induced diabetic rats. Journal of Ethnopharmacology. 126: 339-344.
- [6]. de M Bandeira, S., L. da Fonseca, G. da S Guedes, L. Rabelo, M. Goulart and S. Vasconcelos. 2013. Oxidative stress as an underlying contributor in the development of chronic complications in diabetes mellitus. International Journal of Molecular Science. 14:3265-3284.
- [7]. El Shafey, A. A., M. M. El-Ezabi, M. M. Seliem,, H. H. Ouda and D. S. Ibrahim. 2013. Effect of *Gymnema sylvestre* R. Br. leaves extract on certain physiological parameters of diabetic rats. Journal of King Saud University-Science. 25:135-141.
- [8]. Halder, N., S. Joshi and S.Gupta. 2003. Lens aldose reductase inhibiting potential of some indigenous plants. Journal of Ethnopharmacol .86:113-116.
- [9]. Kanetkar, P., R. Singhal and M. Kamat. 2007. Recent Advances in Indian Herbal Drug Research Guest Editor: Thomas Paul Asir Devasagayam *Gymnema sylvestre*: A Memoir. Journal of Clinical Biochemistry and Nutrition.41:77-81.
- [10]. Kar, A., B. K. Choudhary and N.G. Bandyopadhyay. 2003. Comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in alloxan diabetic rats. Journal of Ethnopharmacology. 84:105-108.
- [11]. Kumar, S. N., U. V. Mani and I. Mani. 2010. An open label study on the supplementation of *Gymnema sylvestre* in type 2 diabetics. Journal of Dietary Supplements. 7:273-282.
- [12]. Leach, M. J. 2007. *Gymnema sylvestre* for diabetes mellitus: a systematic review. The journal of Alternative and Complementary Medicine.13:977-983.
- [13]. Malik, M.Y., H. Tariq, A. Yasmeen, R. Ahmed and A. Naz. 2018. Impaired Colour Vision and Contrast Sensitivity in Patients with Diabetes Mellitus. Pakistan Journal of Ophthalmology. 34:30-35.
- [14]. Mason, R. L., R. F. Gunst and J. L. Hess. 2003. Statistical design and analysis of experiments: with applications to engineering and science. John Wiley and Sons, Inc., Hoboken, NJ, USA.
- [15]. Monteiro, L., M. C. Foss-Freitas, J. Crescêncio, L. G. Júnior, F. Coelis, F. Pereira, E. Carneseca, R. M. Júnior and M. Foss. 2017. Health-Related Physical Fitness in Women with Dunnigan Lipodystrophy with Mutation in LMNA Gene. Endocrinology, Diabetes and Metabolism.12:22-28.
- [16]. Pandey, A., P. Tripathi, R. Pandey, R. Srivatava and S. Goswami. 2011. Alternative therapies useful in the management of diabetes: A systematic review. Journal of pharmacy & bio allied sciences. 3:504-509.
- [17]. Patel, D. K., K. Patel and S. P. Dhanabal. 2012. Development of quality control parameters

- for the standardization of *Gymnema sylvestre*. Journal of Acute Disease. 2:141-143.
- [18]. Pham, H. T. T., M. C. Hoang, T. K. Q. Ha, L. H. Dang, V. O. Tran, T. B. T. Nguyen, C. H. Lee and W. K. Oh. 2018. Discrimination of different geographic varieties of *Gymnema sylvestre*, an anti-sweet plant used for the treatment of type 2 diabetes. Journal of Photochemistry.150:12-22.
- [19]. Pragada, P. M., D. S. Rao and M. Venkaiah. 2012. Study of some ethnomedicinal plants for treatment of dysentery of North Coastal Andhra Pradesh, India. International Journal of Bioscience.2:18-24.
- [20]. Preuss, H. D. , M. Bagchi, C. S. Rao, D. Day and S. Satyanarayana. 2004. Effects of a natural extract of(-)-hydroxyctic acid (HCA_SX) and a combination of HCA-SX plus niacin-bound chromium and *Gymnema Sylvestre* extract on weight loss. Diabetes, Obesity and Metabolism. 6:171-180.
- [21]. Ramkumar, K. M., P. Ponmanickam, S. Ponmanickam, G. Archunan and P. Rajaguru. 2009. Protective effect of *Gymnema montanum* against renal damage in experimental diabetic rats. Food and Chemical Toxicology. 47:2516-2521.
- [22]. Sheoran, S., B. P. Panda, P. S. Admane, A. K. Panda and S. Wajid. 2015. Ultrasound-assisted Extraction of Gymnemic Acids from *Gymnema sylvestre* Leaves and its Effect on Insulin-producing RINm-5 F β Cell Lines. Phytochemical Analysis. 26:97-104.
- [23]. Shiyovich, A., L. Neshet and I. Sztarkier. 2010. Toxic hepatitis induced by *Gymnema sylvestre*, a natural remedy for type 2 diabetes mellitus. The American Journal of The Medical Sciences. 340:514-517.
- [24]. Thomas, M., C. Tsalamandris, R. Macisaac and G. Jerums. 2005. Anaemia in diabetes: an emerging complication of micro vascular disease. Current Diabetes Reviews. 1:107-126.
- [25]. Tiwari, P., B. N. Mishra and N. S. Sangwan. 2014. Phytochemical and pharmacological properties of *Gymnema sylvestre* an important medicinal plant. Biomed Research International.40:20-22.
- [26]. Vincken, J. P., L. Heng, A. de Groot and H. Gruppen. 2007. Saponins, classification and occurrence in the plant kingdom. Phytochemistry. 68:275-297.
- [27]. Zafar, J., D. Nadeem, S. A. Khan, M. M. Jawad Abbasi, F. Aziz and S. Saeed. 2016. Prevalence of diabetes and its correlates in urban population of Pakistan: A Cross-sectional survey. Journal of Pakistan Medical Association.66: 922-927.

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