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EFFECT OF VITIS VINIFERA LEAF EXTRACT ON BLOOD GLUCOSE LEVELS IN ALLOXAN-INDUCED DIABETIC RABBITS.

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ABSTRACT

Background

Diabetes mellitus is a metabolic disturbance due to deficiency of insulin secretion, its action or combination of both. The deficiency of insulin causes persistent hyperglycemia leading to disturbance of carbohydrate, protein and lipid metabolism. It is the most common endocrine disease and about 422 million people have this order throughout the world by the year 2021. The diabetes mellitus is responsible for 1.5 million deaths each year. The number of cases has been increasing over the past few decades. The oral hypoglycemic drugs consist of sulphonylureas, biguanides, meglitinides, thiazolidinediones, α-glucosidase inhibitors, DPP-IV inhibitors, GLP-1–

receptor agonist, amylin analogues, D2 dopamine receptor agonist and SGLT2 inhibitors. Most of the plants show hypoglycemic activity when taken orally and clinical trials are recommended to establish real dosage schedule for these less expensive and relative toxic effects free of drugs from medicinal plants.

Objective

To investigate the effect of alcoholic extracts from Vitis vinifera leaves on the blood sugar levels of both healthy and alloxan-induced diabetic rabbits.

Material and Methods

The alcoholic extracts of the leaves of Vitis vinifera were given in doses of 50 mg/Kg, 100 mg/Kg, 150 mg/Kg and 200 mg/Kg were given to alloxan treated diabetic rabbits. The blood glucose levels were estimated before and 2, 4, 6 and 8 hours after administration of the extract.

Results

The alcoholic extract of the leaves of Vitis vinifera did not show any significant ($P > 0.05$) effect on blood glucose levels of alloxan induced diabetic rabbits. From this study, it may be concluded that leaves of Vitis vinifera have no value in the treatment of diabetic patients having no functioning β-pancreatic cells.

Conclusion

The leaf extract of Vitis vinifera induces hypoglycemia in normoglycemic individuals, but it does not have the same effect in alloxan-induced diabetic experimental subjects. The mechanism of action of Vitis vinifera appears to be similar to that of sulphonylureas, which also trigger hypoglycemia in normoglycemic animals.

Key words: Vitis vinifera, Alloxan, Diabetes mellitus, Plant extract.

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterized by high blood glucose levels due to relative deficiency of insulin, resistance to insulin or both.[1] It is associated with disturbance of carbohydrate, lipid and protein metabolisms due to lack of insulin in the body. The symptoms of diabetes include frequent urination, increased thirst and increased hunger.[2]

Type 1 diabetes mellitus used to be known as insulin dependent diabetes mellitus (IDDM) that occurs due to cellular-mediated autoimmune destruction of the pancreatic β- cells. This destruction of the β-cells causes absolute insulin deficiency.[3,4]

Type 2 is the most common form of diabetes, which is non-insulin dependent diabetes mellitus (NIDDM) and its incidence is about 90%. Its occurrence is rapidly growing due to increase in population and life span of people. The other factors are its onset at an early stage, better methods to diagnose it, increased incidence of obesity in the society, decreased physical activity and low quality diet. Hypertension is also a risk factor for development of type 2 DM.[5] The research workers have reported that incidence of diabetes has been reduced about 13% after a period of five years in those hypertensive patients with glucose intolerance receiving angiotensin receptor blocking drugs.[6]

Type 2 DM is more prevalent in Middle East and Pacific Islands. The majority of type 2 diabetes

patients reside in middle and low income countries and its rapid increase in incidence can be seen in countries having rapid growing economics like India and China. The incidence of type 2 diabetes is more in urban than rural areas.[7,8] The incidence of cardiovascular disease is very high in patients having type 2 diabetes and about 65% deaths occur due to cardiovascular complications. The patients of type 2 diabetes have high incidence of stroke and ischemic heart disease.[9] There is increased incidence of visual impairment (1.9%) and retinopathy (2.6%) in patients of diabetes, these complications lead to blindness.[10, 11] A research study reveals that about 80% cases of End Stage Renal Disease (ESRD) are due to hypertension, diabetes or both the diseases are present simultaneously.[12] The infected foot ulcers are another complication of diabetes mellitus that leads to amputation of lower extremity.[13]

A large number of plants have also been used in the treatment of diabetes mellitus.[14] A large number of conventional drugs have been introduced in the market derived active substances present in the medicinal plants. The example can be quoted that of metformin which is an oral antidiabetic drug. It was discovered while studying the hypoglycemic effects of guanidine derived from the plant Galega officinalis. Thus study on guanidine led to the development of biguanides and metformin.[15]

Most of the plants show hypoglycemic activity when taken orally such as Aloe vera, Allium sativum, Abelmoschus moschatus, Artemisia dracunculus, Artemisia herba-alba, Artemisia herba-alba, Artemisia dracunculus, Achyranthes, Andrographis paniculata L, Asphodelaceae, Azadirachta indica, Bauhinia, Carthamus tinctorius, Caesalpinia bonduc, Combretum, Coccinia grandis, Cactaceae, Caesalpinioideae, Cinnamomum verum, Chrysanthemum morifolium, Ferula assa-foetida, Fabaceae, Gymnema sylvestre, Gongronema latifolium, Liriope, Mangifera indica, Momordica charantia, Mentha, Nigella Sativa, Ocimum tenuiflorum, Ocimum tenuiflorum, Ocimum tenuiflorum, Pachira Panax, Salvia officinalis, Perilla frutescens, Symphytum, Symplocos, Tinospora cordifolia (guduchi), Terminalia chebula, Vachellia nilotica and Zingiber zerumbet. It is claimed that these plants are effective to control and treat diabetes mellitus.[16]

MATERIALS AND METHODS

Objectives

To check the effect of alcoholic extract of leaves of Vitis vinifera on blood glucose levels of alloxan induced diabetic rabbits.

Study Design

It was an experimental study in which rabbits of local strain were made diabetic by an intravenous injection of alloxan monohydrate.

Study Settings and sample size

The study was conducted at Kabir Medical College, Gandhara University Peshawar, Pakistan. The laboratories of Biochemistry Department, Kabir Medical College and Naseer Teaching Hospital, Peshawar, Pakistan were utilized for estimation of blood glucose levels. A total number of 40 rabbits were used in these experiments.

Plant material

The fresh leaves of Vitis vinifera (Grapes; Angoor) were collected from nursery of Agriculture University, Peshawar. These plant materials were identified from Botany section, Pakistan Forest Institute Peshawar, Pakistan. The leaves were washed carefully with water to remove dirt and kept under shade at room temperature for 21 days to be dried. The leaves were finally powdered with electric grinder.

Preparation of Extract

The extract of the leaves of Vitis vinifera was prepared by the method described by Mândru et. al. The powdered plant material was soaked in 70% mg ethanol for a week and then filtered. The residue was re-extracted with fresh ethanol (70%) in the Soxhlet apparatus for 6 hours and then filtered again. The maintained temperature was 60 °C. Both the filters were mixed and the process of evaporation process continued till complete evaporation occurred. A dark brown semi solid extract was obtained and then used in the subsequent experiments.[17]

Administration of Extract Solutions

The amount of Vitis vinifera extract required for each rabbit was calculated on the basis of body weight and dissolved in 15 ml of H_2O. The extract solution was administered orally to each animal by using a standard disposable syringe and stomach tube. The stomach tube was inserted through esophagus in to the stomach and the plunger of syringe was pressed slowly to release the extract.

Preparation of Alloxan solution

Alloxan monohydrate ($C_4H_2N_2O_4.H_2O$) was available in colored bottles containing 25 gm powder. The solution was prepared by dissolving 15 gm in 100 ml of distilled water.

Preparation of Diabetic rabbits

The local strain healthy male adult rabbits weighing about 1100-1600 g were used in these experiments. The method described by Nadeem et al. to induce diabetes mellitus in the rabbits was adopted. A group of rabbits were made diabetic by giving a fresh solution of alloxan monohydrate intravenously in a dose of 150 mg/Kg body weight. The blood glucose levels of the rabbits were estimated after a period of three days of alloxan injection. The blood glucose levels were estimated by using Accu Check advantage[18] Roch Chemicals, Switzerland. The rabbits with blood glucose levels 250-300 mg/100ml were considered diabetic and used in these experiments.[19]

Selection of Doses

Vitis vinifera extract was used in doses of 50 mg/Kg, 100 mg/Kg, 150 mg/Kg and 200 mg/Kg body weight. These doses were selected after performing some pilot experiments. These doses were also used by Nilufar et al.[20]

Grouping of Rabbits

Forty alloxan diabetic rabbits were divided into five groups, each group containing eight animals. The extract of leaves of Vitis vinifera was given to each group in doses of 50 mg/Kg, 100 mg/Kg, 150 mg/Kg and 200 mg/Kg body weight.

Group 1: Received 15 ml of distilled water and act as control.

Group 2: The animals of this group received extract of leaves of Vitis vinifera dissolved in 15 ml of water in a dose of 50 mg/Kg body weight.

Group 3: The animals of this group received extract of leaves of Vitis vinifera dissolved in 15 ml of water in a dose of 100 mg/Kg body weight.
Group 4: The animals of this group received extract of leaves of Vitis vinifera dissolved in 15 ml of water in a dose of 150 mg/Kg body weight.
Group 5: The animals of this group received extract of leaves of Vitis vinifera dissolved in 15 ml of water in a dose of 200 mg/Kg body weight.

RESULTS

Group-1

The effects on blood glucose levels of eight alloxan-diabetic rabbits after oral administration of water used as vehicle for dissolving the extracts for administration are shown in Table 1. The mean decreases in blood glucose levels are also shown in Table 1. The percent decreases in blood glucose levels are shown in Table 2. The mean percent decreases in blood glucose levels at 2, 4, 6 and 8 hours were 1.19±0.18, 1.43±0.17, 1.71±0.20 and 1.05±0.19 respectively (Table 2). The mean percent decreases in blood glucose levels produced by 15ml of water at 2, 4, 6 and 8 hours are insignificant (P>0.05).

Table-1

Effect of water (15 ml) on blood glucose levels of alloxan diabetic rabbits

Number of experiments	Blood glucose level in mg/dl of blood				
	Before administration of water (Control)	Time after administration of water			
		2 Hours	4 Hours	6 Hours	8 Hours
1	401.1	396.27	394.66	397.64	398.0
2	416.0	411.10	412.18	412.14	409.64
3	364.7	361.84	361.44	360.67	362.21
4	391.5	383.64	382.47	383.25	384.82
5	424.3	423.74	421.10	422.38	422.93
6	357.7	354.11	352.67	355.36	355.76

7	401.1	396.27	394.66	397.64	398.00
8	385	377.45	377.48	376.02	377.21
MEAN	**392.67**	**388.05**	**387.08**	**388.13**	**388.57**

Table-2

Percent decreases in blood glucose levels produced by water (15 ml) in alloxan diabetic rabbits

Number of experiments	2 Hours	4 Hours	6 Hours	8 Hours
1	1.20	1.60	0.86	0.77
2	1.17	0.91	0.92	1.52
3	0.78	0.89	1.10	0.68
4	2.00	2.30	2.10	1.70
5	0.13	0.75	0.45	0.32
6	1.00	1.40	0.65	0.54
7	1.30	1.70	0.96	0.87
8	1.96	1.95	2.33	2.02
MEAN	**1.19**	**1.43**	**1.71**	**1.05**
MEAN± S.E. P Value	**1.19±0.18 >0.05**	**1.43±0.17 >0.05**	**1.71±0.20 >0.05**	**1.05±0.19 >0.05**

Group-2

The effects on blood glucose levels of eight alloxan diabetic rabbits are shown in Table 3. The mean percent decreases in blood glucose levels at 2, 4, 6 and 8 hours were 1.31±0.11, 1.96±0.10, 2.54±0.10 and 2.18±0.19 respectively are shown in Table 4. The mean percent decreases in blood glucose levels produced by Vitis vinifera extract (50 mg/Kg) at 2, 4, 6 and 8 hours are insignificant (P>0.05).

Table-3

Effect of Vitis vinifera (50 mg/kg) on blood glucose levels of alloxan diabetic rabbits

Number of experiments	Blood glucose level in mg/dl of blood				
	Before administration of extract (Control)	Time after administration of extract			
		2 Hours	4 Hours	6 Hours	8 Hours
1	392.5	387.2	384.86	383.49	384.6
2	399.3	391.5	389.5	388.4	386.0
3	388.6	385.1	382.5	380.3	381.4
4	393.8	388.4	386.1	384.5	385.5
5	369.5	364.4	362.2	360.2	363.3
6	423.2	417.6	413.7	411.3	412.2
7	366.1	361.7	359.45	355.44	359.2
8	410.9	406.8	403.76	400.24	402.9
MEAN	**392.99±6.772**	**387.84±6.681**	**385.26±6.513**	**382.98±6.569**	**384.39±6.279**
P Value		**0.835^{NS}**	**0.522 ^{NS}**	**0.814 ^{NS}**	**0.542 ^{NS}**

Table-4

Percent decreases in blood glucose levels produced by

Vitis vinifera (50 mg/kg) in alloxan diabetic rabbits				
Number of experiments	2 Hours	4 Hours	6 Hours	8 Hours
1	1.35	1.94	2.29	2.01
2	1.95	2.45	2.72	3.33
3	0.90	1.56	2.13	1.85
4	1.37	1.95	2.36	2.10
5	1.38	1.97	2.51	2.21
6	1.32	2.24	2.81	2.59
7	1.20	1.81	2.92	1.88
8	0.99	1.73	2.59	1.94
MEAN	**1.31**	**1.96**	**2.54**	**2.18**
MEAN± S.E. **P Value**	**1.31±0.11** **>0.05**	**1.96±0.10** **>0.05**	**2.54±0.10** **>0.05**	**2.18±0.19** **>0.05**

Group-3

The effects on blood glucose levels of eight alloxan diabetic rabbits are shown in Table 5. The mean percent decreases in blood glucose levels at 2, 4, 6 and 8 hours were 1.78±0.17, 2.70±0.08, 2.94±0.13 and 2.53±0.11 respectively are shown in Table 6. The mean percent decreases in blood glucose levels produced by Vitis vinifera extract (100 mg/Kg) at 2, 4, 6 and 8 hours are insignificant (P>0.05).

Table-5	
Effect of Vitis vinifera (100 mg/kg) on blood glucose levels of alloxan diabetic rabbits	
	Blood glucose level in mg/dl of blood

Number of experiments	Before administration of extract (Control)	Time after administration of extract			
		2 Hours	4 Hours	6 Hours	8 Hours
1	394.5	388.09	385.05	383.26	385.20
2	367.11	360.4	358.0	357.5	357.7
3	389.1	381.0	377.5	377.0	377.2
4	379.4	370.1	369.5	368.7	369.1
5	409	400.78	396.6	393.73	398.6
6	369.1	366.3	359.4	359.0	359.2
7	383.2	376.16	372.10	371.67	374.2
8	365.7	359.68	356.27	356.02	358.47
MEAN **P Value**	**382.14±5.341**	**375.31±5.036** **0.835^{NS}**	**371.80±5.025** **0.522 ^{NS}**	**370.86±4.742** **0.814 ^{NS}**	**372.46±5.127** **0.542 ^{NS}**

Table-6

Percent decreases in blood glucose levels produced by Vitis vinifera (100 mg/kg) in alloxan diabetic rabbits

Number of experiments	2 Hours	4 Hours	6 Hours	8 Hours
1	1.62	2.39	2.84	2.35
2	1..82	2.48	2.61	2.56
3	2.08	2.98	3.10	3.05

4	2.45	2.60	2.82	2.71
5	2.00	3.03	3.73	2.54
6	0.75	2.62	2.73	2.68
7	1.83	2.89	3.00	2.34
8	1,64	2.57	2.64	1.97
MEAN	**1.78**	**2.70**	**2.94**	**2.53**
MEAN± S.E. **P Value**	**1.78±0.17** **>0.05**	**2.70±0.08** **>0.05**	**2.94±0.13** **>0.05**	**2.53±0.11** **>0.05**

Group-4

The effects on blood glucose levels of eight alloxan diabetic rabbits are shown in Table 7. The mean percent decreases in blood glucose levels at 2, 4, 6 and 8 hours were 2.04±0.10, 2.51±0.15, 2.85±0.09 and 2.59±0.14 respectively are shown in Table 8. The mean percent decreases in blood glucose levels produced by Vitis vinifera extract (150 mg/Kg) at 2, 4, 6 and 8 hours are insignificant (P>0.05).

Table-7

Effect of Vitis vinifera (150 mg/kg) on blood glucose levels of alloxan diabetic rabbits

Number of experiments	Blood glucose level in mg/dl of blood				
	Before administration of extract (Control)	Time after administration of extract			
		2 Hours	4 Hours	6 Hours	8 Hours
1	417.0	407.3	405.1	404.6	404.7
2	401.1	393.4	391.6	390.5	391.0
3	396.3	388.4	385.5	384.8	385.0
4	367.5	361.4	359.5	358.1	359.2

5	411.4	401.0	398.4	397.7	398.1
6	376.0	368.07	365.57	365.0	366.43
7	360.2	353.22	353.0	350.14	351.45
8	371.0	364.02	363.53	361.07	363.75
MEAN±SE P Value	**387.56±7.622**	**379.60±7.191 0.835 NS**	**377.78±6.973 0.522 NS**	**376.49±7.206 0.814 NS**	**377.45±6.979 0.542 NS**

Table-8

Percent decreases in blood glucose levels produced by Vitis vinifera (150 mg/kg) in alloxan diabetic rabbits

Number of experiments	2 Hours	4 Hours	6 Hours	8 Hours
1	2.32	2.85	2.97	2.94
2	1-91	2.36	2.64	2.51
3	1.99	2.72	2.90	2.85
4	1.65	2.17	2.55	2.25
5	2.52	3.15	3.33	3.23
6	2.10	2.77	2.92	2.54
7	1.93	1.99	2.79	2.42
8	1.88	2.01	2.67	1.95
MEAN	**2.04**	**2.51**	**2.85**	**2.59**
MEAN± S.E.	**2.04±0.10**	**2.51±0.15**	**2.85±0.09**	**2.59±0.14**

P Value	**>0.05**	**>0.05**	**>0.05**	**>0.05**

Group-5

The effects on blood glucose levels of eight alloxan diabetic rabbits are shown in Table 9. The mean percent decreases in blood glucose levels at 2, 4, 6 and 8 hours were 1.77±0.22, 2.45±0.20, 2.71±0.019 and 2.42±0.24 respectively are shown in Table 10. The mean percent decreases in blood glucose levels produced by Vitis vinifera extract (200 mg/Kg) at 2, 4, 6 and 8 hours are insignificant (P>0.05).

Table-9

Effect of Vitis vinifera (200 mg/kg) on blood glucose levels of alloxan diabetic rabbits

Number of experiments	Blood glucose level in mg/dl of blood				
	Before administration of extract (Control)	Time after administration of extract			
		2 Hours	4 Hours	6 Hours	8 Hours
1	411.4	401.2	398.4	397.7	398.1
2	379.2	376.1	374.0	373.5	374.3
3	401.1	393.4	391.6	390.5	391.0
4	396.3	388.4	385.5	384.8	385.0
5	417.0	407.3	405.1	404.6	404.8
6	373.5	366.0	363.08	362.33	363.0
7	385.3	378.60	376.56	374.51	378.57
8	391.0	387.48	383.06	381.05	383.29
MEAN	**394.35**	**387.31**	**384.66**	**383.62**	**384.76**
MEAN±SE P Value	**394.35±5.363**	**387.31±4.793 0.835^{NS}**	**384.66±4.824 0.522 ^{NS}**	**383.62±4.878 0.814 ^{NS}**	**384.76±4.709 0.542 ^{NS}**

Table-10

Percent decreases in blood glucose levels produced by Vitis vinifera (200 mg/kg)in alloxan diabetic rabbits

Number of experiments	2 Hours	4 Hours	6 Hours	8 Hours
1	2.47	3.15	3.33	3.23
2	0.81	1.37	1.50	1.29
3	1.91	2.36	2.64	2.51
4	1.99	2.72	2.90	2.85
5	2.32	2.85	2.97	2.92
6	2.00	2.78	2.99	2.81
7	1.73	2.26	2.80	1.74
8	0.90	2.03	2.54	1.97
MEAN	**1.77**	**2.45**	**2.71**	**2.42**
MEAN± S.E. **P Value**	**1.77±0.22** **>0.05**	**2.45±0.20** **>0.05**	**2.71±0.19** **>0.05**	**2.42±0.24** **>0.05**

The effect of different doses of Vitis vinifera are shown in Table 11, while mean percent decreases caused by various doses of Vitis vinifera are shown in Table 12.

Table-11

Effect of different doses of Vitis vinifera on blood glucose levels of alloxan diabetic rabbits

Time interval	Blood glucose level in mg/dl	
		Vitis vinifera Extract

(Hours)	(Control)				
		50mg/Kg	100mg/Kg	150mg/Kg	200mg/Kg
0	392.67±10.28 (8)	392.99±6.772 (8)	382.14±5.341 (8)	387.56±7.622 (8)	394.35±5.363 (8)
2	388.05±10.13 (8)	387.84±6.681 (8)	375.31±5.036 (8)	379.60±7.191 (8)	387.31±4.793 (8)
4	387.08±10.04 (8)	385.26±6.513 (8)	371.80±5.025 (8)	377.78±6.973 (8)	384.66±4.824 (8)
6	388.13±10.12 (8)	382.98±6.569 (8)	370.86±4.742 (8)	376.49±7.206 (8)	383.62±4.878 (8)
8	388.57±10.01 (8)	384.39±6.279 (8)	372.46±5.127 (8)	377.45±6.979 (8)	384.76±4.709 (8)
P Value		0.835^{NS}	0.522 ^{NS}	0.814 ^{NS}	0.542 ^{NS}

Table-12

Mean percent decrease in blood glucose by various doses of Vitis vinifera extract in alloxan diabetic rabbits

Time interval (Hours)	Extract of vitis vinifera			
	50mg/Kg	100mg/Kg	150mg/Kg	200mg/Kg
2	1.31±0.11 (8)	1.78±0.17 (8)	2.04±0.10 (8)	1.77±0.22 (8)
4	1.96±0.10 (8)	2.70±0.08 (8)	2.51±0.15 (8)	2.45±0.20 (8)
6	2.54±0.10 (8)	2.94±0.13 (8)	2.85±0.09 (8)	2.71±0.19 (8)
8	2.18±0.19 (8)	2.53±0.11 (8)	2.59±0.14 (8)	2.42±0.24 (8)
P Value	>0.05	>0.05	>0.05	>0.05

DISCUSSION

In 1918, an oral effective antidiabetic drug was discovered that was a derivative of guanidine. The two other compounds i.e. Synthalin A and B were discovered in 1926, but withdrawn from the market within in a few years due to their toxic adverse effects. Their pharmacological action resembles biguanides, now in current use. The hypoglycemic activity of sulphonamides was first noted during 1942 and the sulphonylureas were marketed in 1956 to treat patients of type 2 diabetes

mellitus.[21] The miglitol and acarbose are oral antidiabetic drugs belonging to α-glucosidase inhibitors. The α-glucosidases cause breakdown of complex carbohydrates into monosaccharides, which are then absorbed from the small intestine. The acarbose and miglitol inhibit these enzymes and thus prevent absorption of carbohydrates from the small intestine. The adverse effects related to this group are diarrhea, abdominal bloating and flatulence.[22]

Insulin and the synthetic oral antidiabetic drugs are the main treatment to control diabetes mellitus, but they cannot reverse the complications and also show the prominent adverse effects like drug resistance and having no effect to control hyperlipidemia. This is the main force for discovering alternative sources of hypoglycemic drugs. There is potential need of new hypoglycemic drugs which are free from toxic effects, favorably hypoglycemic agents from plant kingdom. The World Health Organization identified 21,00 plants, which are used to treat medical ailments around the world.[23,24]

The research workers have studied hundreds of plant species for their potential to reduce blood glucose levels. The plants with significant hypoglycemic activity include Eugenia jambolana[25], Allium sativum[26], Allium cepa[27], Momordica charantia[28], Mangifera indica[29], Cuminum cyminum[30], Eriobotrya japonica[31], Ficus religiosa[32], Tinospora cordifolia[33], Azadirachta indica[34], Aegle marmelos[35], Gymnema sylvestre[36], Canscora decussata[24] and Pterocarpus Marsupium.[37]

The present work deals with the study of the effects of alcoholic extracts of Vitis vinifera on the blood glucose levels of alloxan diabetic rabbits. The water used as solvent in these experiments did not produce any significant change ($P>0.05$) on blood glucose levels of diabetic rabbits. This finding is in accordance with the finding of Shoaib and Ali.[38]

The mean percent decreases in blood glucose levels produced by 50 mg/Kg, 100 mg/Kg, 150 mg/Kg and 200 mg/Kg of Vitis vinifera are not significant ($P>0.05$). This study reveals that the extract of Vitis vinifera in various doses have no significant effect on blood glucose levels of alloxan diabetic rabbits. The extract of Vitis vinifera, however, causes remarkable reduction in blood glucose levels of normal experimental animlas.[39]

Insulin causes a reduction in blood glucose levels in both normal and alloxan diabetic rabbits.[41] This shows that mechanism of action of Vitis vinifera is different from insulin as it reduces blood glucose levels in normal experimental animals only.

In view of the similarity between the action of sulphonylureas and Vitis vinifera, it may be likely that the action of Vitis vinifera to reduce blood glucose levels in normoglycemic experimental animals may be caused by release of insulin from pancreatic β-cells[40]. A similar mechanism has been proposed to explain the blood glucose lowering action in normoglycemic rabbits of other medicinal herbs such as Eriobotrya japonica[41], Canscora decussata[24], Emblica officinalis[42], Mangifera indica[43] and Acacia Arabica[44].

CONCLUSION

The research has revealed that the extract of the leaves of Vitis vinifera cause hypoglycemia in normoglycemic and but not in alloxan diabetic experimental. The mechanism of action of Vitis vinifera seems to be same as sulphonylureas that cause hypoglycemia in normoglycemic animals.

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