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Research Article

ANTIDIABETIC ACTIVITY OF NEW IMIDAZOLE DERIVATIVE (2-(2-benzylidenehydrazinyl)-5,5-diphenyl-1,5-dihydro-4H-imidazol 4-one(C22 H17 N4OCl)

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ABSTRACT

The new imidazole chloro derivative was synthesized and evaluated for the nti diabetic activity, by inducing diabetes using alloxan. The study was conducted using rats in four groups with 6 in each. group one served as control, second group served as diabetic control, third group as standard and fourth for test sample. Glibenclamide was used as standard drug . Lipid profile was also studied. The study was conducted for 14 days. Then blood samples were tested on 1st, 3rd, 7th and 14th day. The blood Glucose Levels decreased significantly after the administration of test sample from 449mg/dl to 164mg/dl with p<0. 01 . total cholesterol, LDL cholesterol, triglycerides and VLDL decreased. HDL cholesterol increased. SGPT, SGOT serum glucose levels reduced p<0.01 As the synthesized compound has reduced blood glucose levels and lipid lowering potential this can be developed into hypoglycemic drug.

Keywords: diabetes, alloxan, blood glucose level, lipids profile.

INTRODUCTION

According to WHO diabetics may increase by 35%. By 2025 number of diabetics may Increase to 300 millions. In India the number may increase to 57 millions from 15 millions in 1995. For various reasons number is increasing. There are two major types of diabetes type 1 which is insulin dependent and type 2 Diabetes which is non-insulin dependent. (sunil kumar,2010).[1]

Diabetes mellitus is the most common endocrine disorder characterized by disturbance in the glucose metabolism due to defect in the insulin secretion.

Diabetes mellitus is a disorder of glucose metabolism, where the blood glucose levels increase above normal. It results in disturbances of carbohydrate protein, fats metabolism which could be because of absolute or relatively lack of insulin.

Diabetes is classified into 4 different types .

1. Type 1 diabetes resulting from the destruction of beta cells leading to deficiency of insulin.
2. Type 2 results from defect in insulin secretion.
3. Diabetes due to genetic disorder
4. Gestational diabetes[2]

Vascular complications develop due to dislipidemia or hyperlipidemia. Post prandial glucose levels contribute to overall glycemic control and are correlated strongly with cardiovascular morbidity and mortality [3]. In type 2 diabetes Important risk factor is obesity. Obesity induces insulin resistance and beta cell dysfunction and also leads to weight gain as result

hyperglycemia increases. Weight management is important for glucose control in obese patients with type 2 diabetes[4].

Many synthetic and plant drugs have been tried in type 2 diabetes. Heterocyclic compounds are rich source of diverse physical, chemical and biological properties. Imidazoline derivatives have been reported to show anti hyperglycemic activity in vivo. (2-(2-benzylidenehydrazinyl)-5,5-diphenyl-1,5-dihydro-4H-imidazol 4-one was synthesized and found to have good antibacterial ,antifungal and anthelmintic property.[5] Genotoxicity studies were conducted on the same compound and found to free from genotoxicity ,(G.E.Suhasini , M.Nirmala etal ., 2012)[6]

MAINTENANCE OF ANIMALS

(experiments were conducted at institution with 1662/po/a/12/ CPCSEA)

Albino Wistar rats and Albino Wistar mice were purchased from mahaveer enterprises. Hyderabad. The animals were acclimatized to the conditions by maintaining them at the experimental conditions for about 7 days prior to dosing. Cage number and individuals making on the tail to identify the animals. The animals were housed six per cage of same sex in polypropylene cages with bedding of paddy. Pellet chew feed standard diet under good management conditions and water *ad libitum* was provided to the animals the temperature 20-25^{o}c and 12 hour each at dark and light cycle was maintained.

ACUTE TOXICITY STUDIES

The procedure was followed by using OECD guidelines (Organization of Economic Cooperation and Development) 423 (Acute Toxic Class Method).The acute toxic class method is a step wise procedure with three animals of single sex per step. Depending on the mortality and/or morbidity status of the animals, on average 2-4 steps may be necessary to allow judgement on the acute toxicity of the test substance. This procedure results in the use of a minimum number of animals while allowing for acceptable data based scientific conclusion.

The method used defined doses (5, 50, 500, 2000 mg/kg b.wt) and the results allow a substance to be ranked and classified according to the Globally Harmonised System (GHS) for the classification of the chemical which causes acute toxicity.

Six Rats weighing between 180-200 gms were used for toxicity. The starting dose level of Isatin derivative at dose of 50 mg/kg b.wt orally as most of the crude extract possesses LD50 value more than 4000 mg/kg b.wt per oral dose was administered to the rats, which were fasted overnight with water *ad libitum*, food was withheld for a further 3-4 hrs. After administration of drugs and observed for another 14 days.

Body weight of the rats before and after treatment were noted and any changes in skin and fur, eyes and mucous membranes and also autonomic, central nervous systems, somatomotor activity and behavior pattern were observed and also signs of tremors, convulsions, salivation, diarrhea, lethargy, sleep and coma were noted. The onset of toxicity and signs of toxicity was also to be noted (OECD 423)

MATERIALS AND METHODS

Materials

Glibenclamide (Hetero chemicals), Alloxan (SD fine chemicals) , Glucometer (Thyrocare), Cholesterol Kit (Span diagnostics ltd) , Triglycerides Kit (Span diagnostics ltd), SGPT-SGOT Kit, GOD kit

METHODS FOR ANTIDIABETIC ACTIVITY

Induction of diabetes mellitus in experimental animals [(1662/PO/a/12/CPC SEA) Wistar albino rats were selected weighing 150-250g of either sex and fasted overnight. 130mg/kg of alloxan monohydrate was freshly prepared and administered by s.c route within 5min of preparation to prevent degradation at 130mg/kg dose. To prevent hypoglycemic shock 5% glucose solution was given for 72 hrs . Animals had access to feed and water . Glucose was estimated for development of hyperglycemia by fasting serum glucose estimation 72hr after Alloxan monohydrate injection. Animals were fasted again for 14hrs before blood collection . Rats which were found to have fasting serum glucose level of above 200mg/dl at 72 hr were diabetic and considered for the study.(Rai P K etal .,2007)[7]

Experimental Design

- Normal wistar rats of either sex (150-250g) were used in the present study.
- Animals were provided with standard diet and water ad libitum.

- The rats were divided into 4 different groups containing 6 each.
- Group I- Control, administered vehicle (ethanol) at a dose of 50mg/kg.
- Group II- Diabetic control, administered alloxan monohydrate at a dose 130 mg/kg b. wt. intraperitoneally.
- Group III- Administered standard drug at oral dose of 10 mg/kg b. wt.
- Group IV- Administered with imidazole derivative at oral dose of 50mg/kg b. wt.

Preparation of test drug

Test drug was suspended in 10% ethanol and each rat received a daily 1 ml as suspension at a dose of 50mg/kg body weight orally by oral gavage throughout the experimental period.

Determination of the blood glucose levels

Blood was collected from the tip of the tail vein and fasting blood glucose levels were measured using single touch Glucometer (Thyro care) based on glucose oxidase method.

Oral glucose tolerance test

The Animals were fasted for 16hrs over night , the blood glucose levels of rats were determined and treated with test samples and standard. Test samples and standard were given immediately after the collection of initial blood samples. The blood glucose levels were determined in the following pattern: 15 and 30 min to access the effect of test samples on normoglycaemic animals. The rats were then loaded orally with 2g/kg glucose and the glucose concentrations were determined at 30, 60, 120, 180min, after glucose load[8] .

Determination of single dose treatment of imidazole derivative on blood glucose level in Alloxan-induced diabetic rats

The test animals were divided into 4 groups. Group I consists of normoglycaemic rats and the remaining 3 groups consisted of six Alloxan-induced diabetic rats, each. In a single dose treatment study, all surviving diabetic animals were fasted overnight. Blood samples were collected from the fasted animals prior to the treatment with dosage schedule and after drug administration at 0, 1, 2, 3 hr time intervals to determine the blood glucose level, by glucometer [9] .

Determination of sub-acute treatment of Imidazole derivative on changes in body weight in Alloxan-induced diabetic rats

The body weight changes of the control, diabetic control, standard, test groups treated rats were measured throughout the study. The rats were weighed at the beginning of the experiment and then subsequently 1st, 3rd, 7th, 14thday[10].

Determination of sub-acute treatment of imidazole derivative on blood glucose level in Alloxan-induced diabetic rats

The Animals were divided into 4 groups. Group I consists of normoglycaemic rats and the remaining 3 groups consisted of six Alloxan - induced diabetic rats, each. The treatment schedule was followed for the respective group of animals for 14 days. Blood samples were collected from overnight fasted animals on 1st, 3rd, 7th and 14th day to estimate blood glucose levels using glucometer. On the final day of the study, blood was collected from the retro-orbital plexus [11]

Estimation of Biochemical parameters

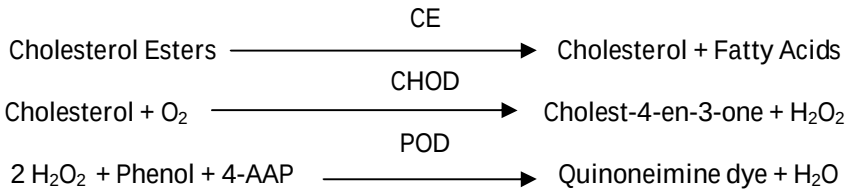
Estimation of total cholesterol

a)Method

PEG-CHOD-PAP Method

b)Principle

Cholesterol esters are hydrolysed by cholesterol esterase (CE) to give free cholesterol and fatty acids. In subsequent reaction, Cholesterol Oxidase (CHOD) oxidises the 3-OH group of free cholesterol to liberate Cholest-4-en-3-one and Hydrogen Peroxide. In presence of Peroxidise (POD), Hydrogen Peroxide couples with 4-Aminoantipyrine (4-AAP) and phenol to produce Red Quinoneimine dye. Absorbance of coloured dye is measured at 505 nm and is proportional to amount of total cholesterol concentration in the sample.



c) Procedure

Pipette into tubes marked	Blank	Standard	Test
Serum/Palsma	----	----	10 µl
Reagent 2	----	10 µl	-----
Reagent 1	1000 µl	1000 µl	1000 µl

Mix well. Incubate at 37°C for 10 minutes at room temperature (15 to 30°C) for 30 minutes.
Program the analyzer as per assay parameters.
1. Blank the analyzer with reagent blank
2. Measure absorbance of standard followed by test.

d)Calculation

$$\text{Cholesterol Concentration (mg/dL)} = \frac{\text{Absorbance of Test}}{\text{Absorbance of Standard}} \times 200$$

Estimation of HDL Cholesterol

a)Method

CHOD-PAP method

b)Principle

Low Density Lipoprotein (LDL) Cholesterol, Very Low Density Lipoprotein (VLDL) Cholesterol and Chylomicron fractions are precipitated by addition of Polyethylene Glycol 6000 (PEG). After centrifugation, the high density lipoprotein (HDL) fraction remains in the supernatant and is determined with CHOD-POD method.

c)Procedure

Step 1: HDL-Cholesterol separation

Pipette into tubes marked	Test
Serum/Plasma	200 µl
Reagent 3	200 µl

Mix well and keep at room temperature (15 to 30°c) for ten minutes. Centrifuge for 15 minutes at 2000 rpm and separate clear supernatant. Use the supernatant for HDL cholesterol estimation.

Step 2: HDL-Cholesterol estimation

Pipette into tubes marked	Blank	Standard	Test
Supernatant from step 1	----	----	100 µl
Reagent 4	----	100 µl	-----
Reagent 1	1000 µl	1000 µl	1000 µl

Mix well. Incubate at 37°C for 10 minutes at room temperature (15 to 30°C) for 30 minutes.
Program the analyzer as per assay parameters.
1. Blank the analyzer with reagent blank
2. Measure absorbance of standard followed by test.
3. Calculate results as per given calculation formula.

d)Calculation

$$\text{HDL- Cholesterol Concentration (mg/dL)} = \frac{\text{Absorbance of Test}}{\text{Absorbance of Standard}} \times 50 \times 2^{*}$$

*(2 = dilution factor, as Sample is diluted 1:1 in step 1)

LDL-Cholesterol using Friedewald's equation**

$$\text{LDL-Cholesterol} = \text{Total Cholesterol} - \frac{\text{Triglycerides}}{5} - \text{HDL Cholesterol}$$

VLDL-Cholesterol

$$\text{VLDL-Cholesterol} = \text{Total Cholesterol} - \text{HDL} - \text{LDL.}$$

Estimation of Triglycerides

a)Method

GPO- PAP Method.

b) Principle

Triglycerides are hydrolysed by Lipoprotein Lipase (LPL) to produce Glycerol and Free Fatty Acid (FFA). In presence of Glycerol Kinase (GK), Adenosine Triphosphate (ATP) phosphorylates Glycerol to produce Glycerol 3-Phosphate and Adenosine Diphosphate (ADP).Glycerol 3-Phosphate is further oxidised by Glycerol 3-Phosphate Oxidase (GPO) to produce Dihydroxyacetone Phosphate (DAP) and H_2O_2. In presence of Peroxidase (POD), hydrogen peroxide couples with 4-Aminoantipyrine and 4-Chlorophenol to produce red Quinoneiminedye. Absorbance of coloured dye is measured at 505nm is proportional to triglycerides concentration in the sample.

$$\text{Triglycerides} \xrightarrow{\text{LP}} \text{Glycerol + Free Fatty Acid}$$

$$\text{Glycerol + ATP} \xrightarrow{\text{GK}} \text{Glycerol 3-Phosphate + ADP}$$

$$\text{Glycerol 3-Phosphate + } O_2 \xrightarrow{\text{GPO}} \text{DAP + } H_2O_2$$

$$2\,H_2O_2 + \text{4-Chlorophenol + 4-AAP} \xrightarrow{\text{POD}} \text{Quinoneimine dye +} 4H_2O$$

C) **Procedure**

Pipette into tubes marked	Blank	Standard	Test
Serum/Plasma	----	----	10 µl
Reagent 2	----	10 µl	-----
Reagent 1	1000 µl	1000 µl	1000 µl

Mix well. Incubate at 37°C for 10 minutes.
Program the analyzer as per assay parameters.
1 Blank the analyzer with Reagent Blank
2 Measure absorbance of Standard followed by Test.
3 Calculate results as per given calculation formula.

d)Calculation

$$\text{Triglycerides (mg/dL)} = \frac{\text{Absorbance of Test}}{\text{Absorbance of Standard}} \times 200$$

Estimation of SGPT

a)Method

2,4-DNPH method

b)Principle

Alanine aminotransferase (ALT) catalyses the transamination of L-alanine and α-Ketoglutarate (α-KG) to form Pyruvate and L-Glutamate. Pyruvate so formed is coupled with 2,4-Dinitrophenyl hydrazine (2,4-DNPH) to form a corresponding hydrazone, a brown coloured complex in alkaline medium and this can be measured colorimetrically.

α- KG + L-Alanine ⟶ Pyruvate + L-Glutamate

Pyruvate + 2,4-DNPH ⟶ Corresponding Hydrazone (browncolour)

c)Procedure

Pipette into tubes marked	**Blank (Volume in ml)**	**Standard (Volume in ml)**	**Test (Volume in ml)**	**Control (Volume in ml)**
Reagent 1	0.25	0.25	0.25	0.25
Serum	----	----	0.05	----
Standard	----	0.05	----	----

Mix well and incubate at 37°C for 30 minutes

Reagent 2	0.25	0.25	0.25	0.25
Deionised water	0.05	----	----	----
Serum	----	----	----	0.05

Mix well and allow to stand at Room Temperature (15-30°C) for 20 minutes.

Solution 1	2.5	2.5	2.5	2.5

Mix well and read the O.D against Purified Water in a Colorimeter using Green filter or on Photometer at 505nm, within 15 minutes.

d)Calculation

$$\textbf{ALT (GPT) activity (in IU/L)} = \frac{\textbf{Absorbance of Test} - \textbf{Absorbance of Control}}{\textbf{Absorbance Of Standard} - \textbf{Absorbance of Blank}} \times \textbf{Conc. Of Standard}$$

Estimation of SGOT

a) Method

2,4-DNPH method

b) Principle

Aspartate aminotransferase (AST) catalyses the transamination of L-Aspartate and α-Ketoglutarate (α-KG) to form Oxaloacetate and L-Glutamate.

Oxaloacetate so formed is coupled with 2,4-Dinitrophenyl hydrazine (2,4-DNPH) to form a corresponding hydrazone, a brown coloured complex in alkaline medium and this can be measured colorimetrically.

α- KG + L-Aspartate ⟶ Oxaloacetate + L-Glutamate

Oxaloacetate + 2,4-DNPH ⟶ Corresponding Hydrazone (browncolour)

c)Procedure

Pipette into tubes marked	**Blank (Volume in ml)**	**Standard (Volume in ml)**	**Test (Volume in ml)**	**Control (Volume in ml)**
Reagent 1	0.25	0.25	0.25	0.25
Serum	----	----	0.05	----
Standard	----	0.05	----	----

Mix well and incubate at 37°C for 60 minutes

Reagent 2	0.25	0.25	0.25	0.25
Deionised water	0.05	----	----	----
Serum	----	----	----	0.05

Mix well and allow to stand at Room Temperature (15-30°C) for 20 minutes.

Solution 1	2.5	2.5	2.5	2.5

Mix well and read the O.D against Purified Water in a Colorimeter using Green filter or on Photometer at 505nm, within 15 minutes.

d) Calculation

$$\text{AST (GOT) activity (in IU/L)} = \frac{\text{Absorbance Of Test} - \text{Absorbance of Control}}{\text{Absorbance Standard} - \text{Absorbance of Standard Blank}} \times \text{Conc. Of}$$

RESULTS

The results obtained after the experiment are presented in the form of tables 1 - table 6.

Table 1: Effect of Chloro derivatives on body weight changes in Alloxan induced diabetic rats

Group	Treatment	Dose (Kg^{-1}Body Weight)	Body Weights(gms)				
			Intial Weight	1st Day	3rd Day	7th Day	14th Day
I	Control (Water)	0.4ml	177.5± 8.342	175.8333± 8.207	173.5± 8.036	163.333± 7.923	160.833± 7.002
II	Diabetic control (Alloxan)	130mg	160± 5.164^{ns}	155.5± 5.045^{ns}	152.833± 5.449^{ns}	147.6± 5.308^{ns}	145.5± 4.856
III	Standard(GBC+Alloxan)	10mg	156.666± 6.412^{ns}	156.66± 4.944^{ns}	160.5± 4.425^{ns}	168.33± 3.33*	171.66± 2.789**
IV	Test +Alloxan	50mg	136.66± 5.110*	137.01± 4.830^{ns}	141.5± 4.972^{ns}	169.166± 3.962*	169.16± 3.005**

Values are expressed as Mean ± S.E.M; n=6, *p<0.05. **p<0.01.
Diabetic control values are compared with control group.
Experimental group values are compared with diabetic control group.

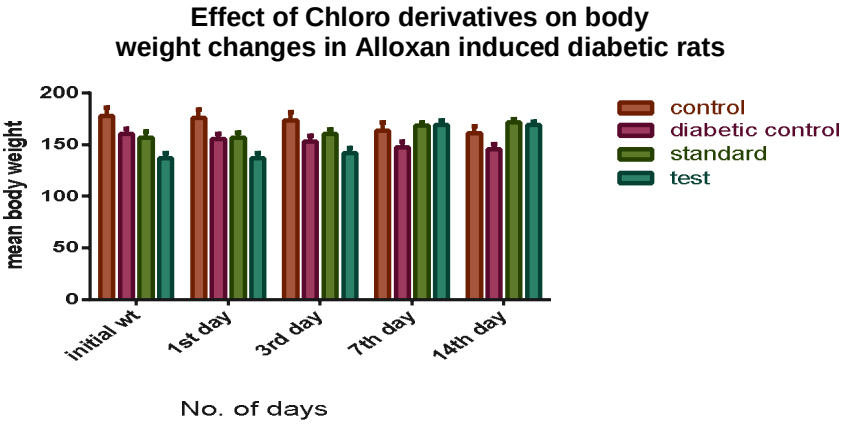


Table 2: Effect of Chloro derivative on blood glucose of initial day of drug given in Alloxan induced diabetic rats

Group	Treatment	Dose (Kg^{-1}Body Weight)	Blood Glucose Levels(mg/dl)			
			0 min	60 min	120 min	180 min
I	Control(ethanol)	0.4ml	87.5±3.612	87.166±3.361	87.833±2.725	86.833±2.651
II	Diabetic control (Alloxan)	130mg/kg	572.166±4.799**	571.66±3.748**	568.833±4.895**	569.166±5.816**
III	Standard(GBC+Alloxan)	10mg/kg	445.0±27.988**	432.5±26.825**	436±27.334**	426.33±25.126**
IV	Test +Alloxan	50mg/kg	542.5±20.299ns	532.33±17.441ns	519.166±21.215ns	506.66±24.737 ns

Values are expressed as Mean ± S.E.M; n=6, *p<0.05. **p<0.01.
Diabetic control values are compared with control group.
Experimental group values are compared with diabetic control group

Effect of Chloro derivative on blood glucose of initial day of drug given in Alloxan induced diabetic rats

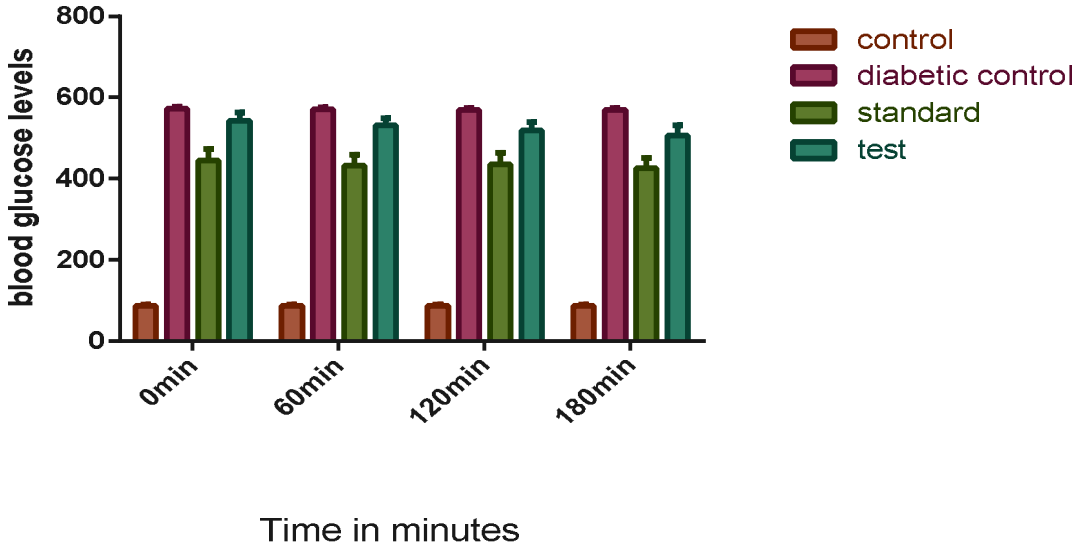


Table 3 : Effect of Chloro derivative on blood glucose in Alloxan induced diabetic rats

Group	Treatment	Dose (Kg^{-1}Body Weight)	Blood Glucose Levels(mg/dl)			
			1st Day	3rdDay	7thDay	14thDay
I	Control(ethanol)	0.4ml	91.00±3.215	96.833±3.468	89±3.011	90.166±2.903
II	Diabetic control (Alloxan)	130mg/kg	568±7.234**	564.166±6.580**	564.833±6.030**	570.833±5.974**
III	Standard(GBC+Alloxan)	10mg/kg	505±29.467ns	438.66±57.307*	246.66±54.078**	164.166±13.442**
IV	Test +Alloxan	50mg/kg	449.166± 22.829**	296.166±15.723**	209.16±4.902**	164.16±8.983**

Values are expressed as Mean ± S.E.M; n=6, *p<0.05. **p<0.01.
Diabetic control values are compared with control group.
Experimental group values are compared with diabetic control group.

Effect of Chloro derivative on blood glucose in Alloxan induced diabetic rats

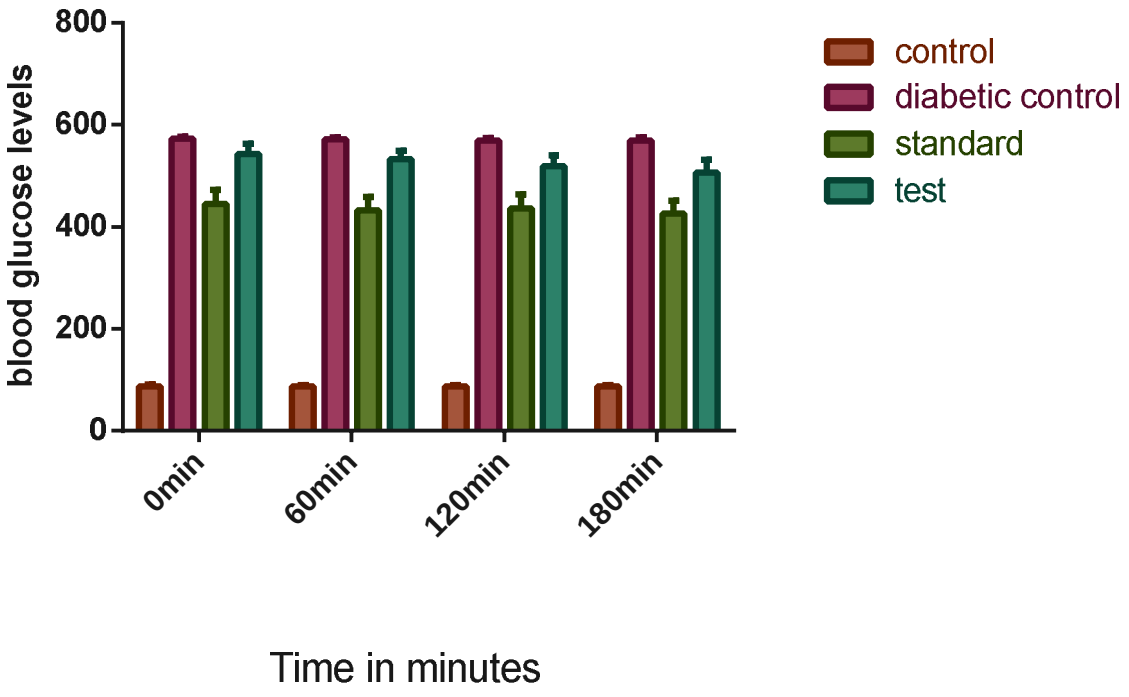


Table 4: Effect of Chloro derivative on normoglycaemic and glucose fed-hyperglycemic rats

Group	Treatment	Dose (Kg¹Body Weight)	Blood glucose levels(mg/dl)					
			0 min	15 min	30 min (glucose)	60 min	120 min	180 min
I	Control (Ethanol)	50mg (0.4ml)	81.666± 1.406	81.106± 1.167	81.666± 1.476	108..66± 4.470	98.33.± 4.088	80.66± 2.155
II	Standard (GBC)	10mg	80.416± 1.129^{ns}	70.766± 2.703**	66.166± 2.688**	91.33± 1.229**	71.166± 0.7032**	60.5± 1.176**
III	Test(chloro derivative)	10mg	84.333± 1.116^{ns}	77.833± 0.9098*	72.666± 0.4944*	112.5± 2.291**	97.66± 1.256**	76.666± 2.578**
IV	Test(chloro derivative)	50mg	85.333± 1.585*	74.± 1.155^{ns}	68.16± 1.759ns	107.5± 1.875**	78± 0.8944^{ns}	62.166±2.257**

Values are expressed as Mean ± S.E.M; n=6, *p<0.05. **p<0.01.
Diabetic control values are compared with control group.
Experimental group values are compared with diabetic control group.

Effect of Chloro derivative on normoglycaemic and glucose fed-hyperglycemic rats

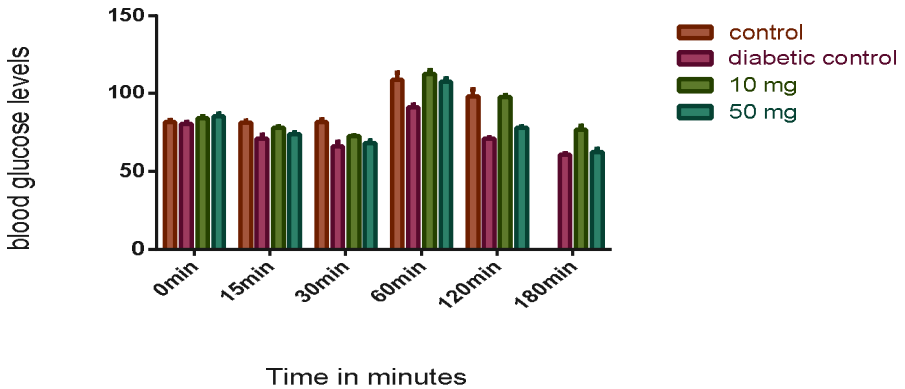


Table 5: Effect of Chloro derivatives on serum lipid profiles in Alloxan induced diabetic rats

Group	Treatment	Dose (Kg^{-1}Body Weight)	Lipid Profiles(mg/dl)				
			Total Cholesterol	Triglycerides	HDL	LDL	VLDL
I	Control(ethanol)	50mg (0.4ml)	49.9983± 2.635	78.78± 3.499	17.17903± 1.795	13.96± 1.420	17.5579± 0.4802
II	Diabetic control	130mg	109.9366± 4.116**	97.1455± 3.548**	39.726± 4.675**	47.564± 2.113**	23.6373± 1.586**
III	Standard (GBC+Alloxan)	10mg	96.9521± 3.219*	76.0866± 4.537**	30.2188± 1.046*	39.2190± 2.824*	18.1246± 0.6287**
IV	Test(chloro derivative +Alloxan)	50mg	89.283± 2.672**	82.1466± 3.447*	29.872± 0.7271*	37.1383± 2.316**	16.788± 1.182**

Values are expressed as Mean ± S.E.M; n=6, *p<0.05. **p<0.01.
Diabetic control values are compared with control group.
Experimental group values are compared with diabetic control group.

Effect of Chloro derivatives on serum lipid profiles in Alloxan induced diabetic rats

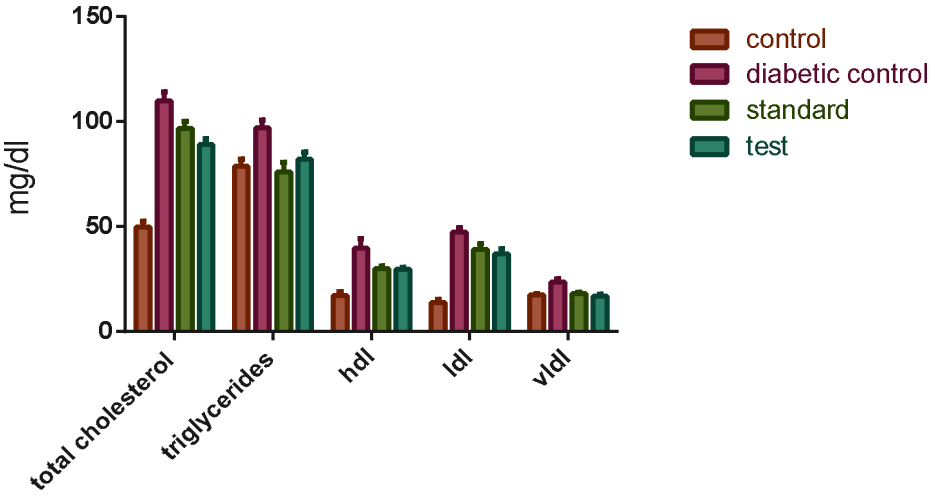
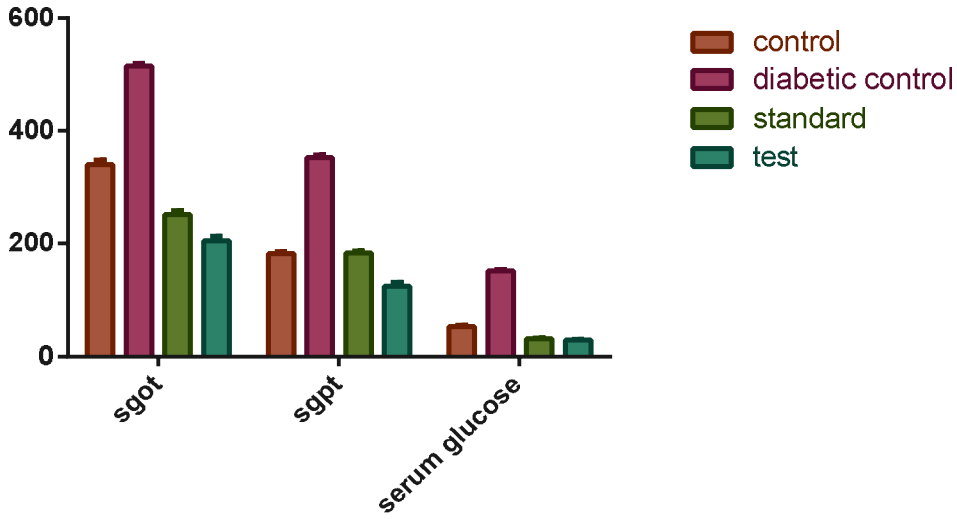


Table 6: Effect of Chloro derivative on SGOT, SGPT and serum glucose in Alloxan induced diabetic rats

Group	Treatment	Dose (Kg^{-1} Body Weight)	SGOT(IU/L)	SGPT(IU/L)	Serum glucose (mg/dl)
I	Control(Ethanol)	50mg (0.4ml)	339.765±7.935	182.1250±3.682	53.95025±1.174
II	Diabetic Control	130mg	517.293± 3.237**	352.453±4.697**	152.1666±1.831**
III	Standard (GBC+Alloxan)	10mg	252.3160± 6.4132**	183.228±3.536**	32.075166±0.7659**
IV	Test(chloro+Alloxan)	50mg	205.277± 7.473**	124.671±6.440**	29.8788±0.5458**

Values are expressed as Mean ± S.E.M; n=6, *p<0.05. **p<0.01.
Diabetic control values are compared with control group.
Experimental group values are compared with diabetic control group.

Effect of Chloro derivative on SGOT, SGPT and serum glucose in Alloxan induced diabetic rats



DISCUSSION

Test sample was given to the diabetic rats in the dose of 10mg and 50mg. changes in fasting blood glucose levels were noted.

In diabetes mellitus levels of serum lipids are usually elevated and become a risk factor for coronary artery diseases. Hyperlipidemia a consequence of diabetes could be because of action of lipolytic hormones on the fat deposits. Low concentration of serum lipid by drug therapy or by dietary control was found to be associated with reduced risk of coronary vascular diseases. . Total cholesterol , HDL cholesterol , LDL cholesterol and Triglycerides were studied along with blood glucose Levels.

When the changes in the body weight were studied test sample increased the body weight from day 1 to day 14days and also in standard whereas body weight decreased in diabetic control and control. After the administration of 50mg of the test sample the blood glucose levels were decreased Significantly from day 1 to 14th day from 449mg/dl to 164mg/dl with $p<0.01$.

The diabetogenic action of alloxan is through the generation of reactive oxygen species. Alloxan and its reduced product dialuric acid with the formation of superoxide

Radicals establish a redox cycle. Radicals undergo dismutation to hydrogen peroxide. Hydroxyl radicals which are highly reactive are formed by Fenton reaction. Rapid destruction of B cells take place with the action of reactive oxygen species with a simultaneous increase in cytosolic calcium concentration. [12]

Total cholesterol triglycerides HDL, LDL. VLDL were found to be less than the diabetic control $p<0.01$. SGPT, SGOT serum glucose levels reduced significantly $p<0.01$.

STATISTICAL ANALYSIS

All the results are analysed with Anova (Dunnet 's t method)

CONCLUSION

Our present study showed that the new imidazole derivative has reduced the blood glucose levels significantly and also the lipid levels . Further research on the compound may develop the compound into lead molecule.

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