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EVALUATION OF HYPOGLYCEMIC, ANTI HYPERGLYCEMIC AND ANTI HYPERLIPIDEMIC ACTIVITY OF HYDROALCHOLIC EXTRACT OF CARICA PAPAYA *L.*IN ALLOXAN INDUCED DIABETIC RATS

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Abstract:

This study was undertaken to investigate the effect of hydroalcholic extract of –Carica papaya (caricaceae) fruit on blood glucose levels in diabetic and normal rats. The diabetic was induced by using alloxan (150 mg/kg b.wt.,i.p).The hyperlipidemic was induced by using high fat diet cocktail in rats. The treatment was given at doses of 200,300,400mg/kg. b.wt. for single doses to the animal and estimating the hypoglycemic ,antihypergycemic and antihyperlipidemic was performed. After the treatment a significant reduction was observed in fasting blood glucose levels in treated diabetic rats and normal rats. Carica papaya showed significant decrease ($p < 0.005$) in blood glucose levels. simultaneously, the alteration in lipid metabolism was partially attenuated as evidenced by decreased Serum Total Cholesterol (TC), Triglyceride (TG) And Low-Density Lipoprotein Cholesterol (LDL) levels and by increased High-Density Lipoprotein Cholesterol (HDL) concentration in diabetic rat ($p < 0.001$).. These results suggest that Carica papaya L possesses anti diabetic effects in alloxan induced diabetic rats

Keywords: *Hypoglycemic ,Antihypergycemic , Antihyperlipidemic Carica papaya Lipid Profile, Hydroalcholic Extract*

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INTRODUCTION:

Diabetes mellitus is a metabolic disorder affecting carbohydrate, fat and protein metabolism. Diabetes mellitus is a chronic disorder of metabolism caused by an absolute or relative lack of insulin. It is characterized by hyperglycemia in the postprandial and/or fasting state, and in its severe form is accompanied by ketosis and protein wasting1 Besides drugs classically used for the treatment of diabetes (insulin, sulphonylureas, biguanides and thiazolidine-diones), several species of plants have been described in the scientific and popular literature as having a hypoglycemic activity2,3, Because of their perceived effectiveness, minimal side effects in clinical experience and relatively low costs, herbal drugs are prescribed widely even when their biologically active compounds are unknown 4

Hyperlipidemia contributes significantly in the manifestation and development of atherosclerosis and coronary heart diseases (CHD). Atherosclerosis, are the most common cause of mortality and morbidity worldwide. Although several factors, such as diet high in saturated fats and cholesterol, age, family history,hypertension and life style play a significant role in causing heart failure, the high levels of cholesterol particularly TC, TG and LDL cholesterol is mainly responsible for the onset of CHDs (Choudhary M. I,etal,2005). A 20% reduction of blood cholesterol level can decrease about 31% of CHD incidence, and 33%of its mortality rate5.

The papaya is a large, tree -like plant with a single stem growing from 5 to 10 m (16 to 33 ft) tall, with spirally arranged leaves confined to the top of the trunk. The lower trunk is conspicuously scarred where leaves and fruit were borne. The leaves are large, 50–70 cm (20–28 in) in diameter, deeply palmately lobed, with seven lobes. Unusually for such large plants, the trees are dioecious. The tree is usually unbranched, unless lopped. The flowers are similar in shape to the flowers of the Plumeria, but are much smaller and wax -like. They appear on the axils of the leaves, maturing into large fruit - 15–45 cm (5.9–18 in) long and 10–30 cm (3.9–12 in) in diameter. The fruit is ripe when it feels soft (as soft as a ripe avacodo or a bit softer) and its skin has attained an amber to orange hue.
Carica papaya was the first transgenic fruit tree to have its genome deciphered

MATERIALS AND METHODS:

Collection and authentication of plant material:
The flower material i.e *CARICA PAPAYA* was collected in the month of May 2022 from a LB Nagar market,. Around 10 kgs of was collected. The plant material was taxonomically identified by Dr. (Mrs) B.Prathibha Devi, Professor and Head of Department of Botany, Osmania University,Hyderabad and a specimen was deposited in their herbarium against issue of Voucher no: 0144.

Preparation of powder:
The *CARICA PAPAYAL*(fruit) cut into pieces and were shade dried and then powdered with a mechanical grinder to form a coarse powder. The powder was passed through sieve no 40 and was stored in an air tight container until further use. The powder was used for the extraction process.

Hydro alcoholic extract :
The powder was stored in airtight container which was used for extraction. About 70 gm of air dried powdered material was soaked in mixture of water and alcohol (ethanol) 60:40%v/v and placed it separately for 72 hrs Separated filtrate extract is filtered by using muslin cloth .and the liquid was evaporated. At the end of the extraction process the marc was taken out and it was dried. After drying, the powdered marc was weighed & again packed. The yield obtained is 9 gms.
The phytochemical screening is estimated .

Drugs:
Alloxone monohydrate was purchased from sigma chemicals (St. Louis, U.S.A). Glucometer purchased from Microgene (Accusure). Simvastatin was obtained as gift sample from Dr.Reddys lab, Hyderabad. Diagnostic kits for estimation of Cholesterol (Span Diagnostics), triglyceride (Biolab diagnostics), HDL-C (Coral Clinical) were used. High-cholesterol diet was prepared in college lab. All other chemicals used for this study were analytical grade

Animals:
Wister Albino Rats (150–200g) were obtained from the Animal House, Hyderabad. Rats were maintained on standard pellet diet and tap water *ad libitum*. They were kept in clean cages under a 12 hour light/dark cycle and room temperature 22–24C and were acclimatized to the environment for 2 weeks prior to experimental use. This study was conducted according to the guidelines approved by the Institutional Animal Ethics Committee.

EXPERIMENTAL DESIGN:
Hypoglycemic Activity8:
On the previous day of experimentation, the food was withdrawn 12-hours advance. However water was allowed *ad libitum*. The fasting was continued

till the completion of the experiment. On next day, the blood samples were withdrawn from tail vein for determine of basal glucose concentration. Then the animals were administered with plain 0.5% w/v CMC suspension Thereafter the blood sample each were collected at 0,1,2,3,4,5,6 hours and analyzed for the determining the glucose concentration using glucometer.

Wister albino rats (150-200g) and healthily 36 rats were selected. The rats were divided in to six groups each having six animals. Group 1 consisted of normal rats, Group 2 contained treated rats that served as control rats, Group 3 Glibenclamide (50mg/kg) treated rats, Group 4, 5 and 6 groups were treated with hydroalcholic extract of *HIBISCUS ROSA-SINENSIS L*at doses of 200,300 and 400 mg/kg respectively according to the body weight . All the doses were administered orally.

Ant diabetic activity9:
Induction of diabetes
Diabetes was induced by injection of a single intra-peritoneal dose of Alloxan monohydrate (freshly prepared in 0.1% normal saline). Overnight fasted rats were injected with Alloxan (alloxan; 150 mg/kg body wt., *i.p*) to induce diabetes. Diabetes was confirmed by glucose estimation. Animals with plasma glucose level > 200 mg / dl were selected for the study. Diabetic induced Animals were grouped for further study. After 3 days (50, 50,50mg respectively) of alloxan induction, treatment was started.

The serum glucose level was estimated in overnight fasted controls, diseased controls (DC) and drug treated diabetic animals at a dosage of 200, 300 and 400mg/kg, body weight. Blood samples were withdrawn from tail vein and glucose concentration was estimated by using glucometer for 12 hrs.

Antihyperlipidemia:
Composition of high fat diet (hcd)10,11,12
High fat diet cocktail was prepared by mixing cholesterol (100g), cholic acid(50g) in 1 liter of coconut oil supplemented with egg

Experimental procedure:
The animals were fed a high-cholesterol diet for 10 days. To confirm the induction of hyperlipidemia, blood samples were collected by retroorbital vein. The TC concentration of the blood samples was then determined using a standard diagnostic kit. The rats were then divided into 5 groups of 6 animals based on their cholesterol levels, after which the treatments were administered orally once daily for 10 days.

Group 1 consisted of normal rats, Group 2 contained treated rats that served as control rats, Group 3 Glibenclamide (50mg/kg) treated rats, Group 4, 5 and 6 groups were treated with hydroalcholic extract of *CARICA PAPAYA* at doses of 200,300 and 400 mg/kg respectively according to the body weight . All the doses were administered orally

Biochemical assay:
At the end of the experimental period Blood was withdrawn from retro-orbital plexus of rat under ether anesthesia and centrifuged at 2000 rpm for 30min so at to get serum. Serum total cholesterol,triglyceride HDL-C was estimated by using diagnostic kits. Low and respectively. Atherogenic index was calculated from TC and HDL-C. Cholesterol was measured by a direct colorimetric method13.

Statistical analysis:
One way analysis of variance (ANOVA)followed by Dunnets t-test was carried out and $P<0.005$ was considered significant

RESULTS:

I.phytochemical screening:
Table: 1

Sr. No.	Chemical constituents	Hydroalcholic extract
1.	Alkaloids	+
2.	Sterols	-
3.	Proteins	-
4.	Tannins	+
5.	Amino acid	-
6.	Glycosides	+
7.	Mucilage	+
8.	Flavonoids	+

9.	Reducing sugar	+
10.	Saponin	-

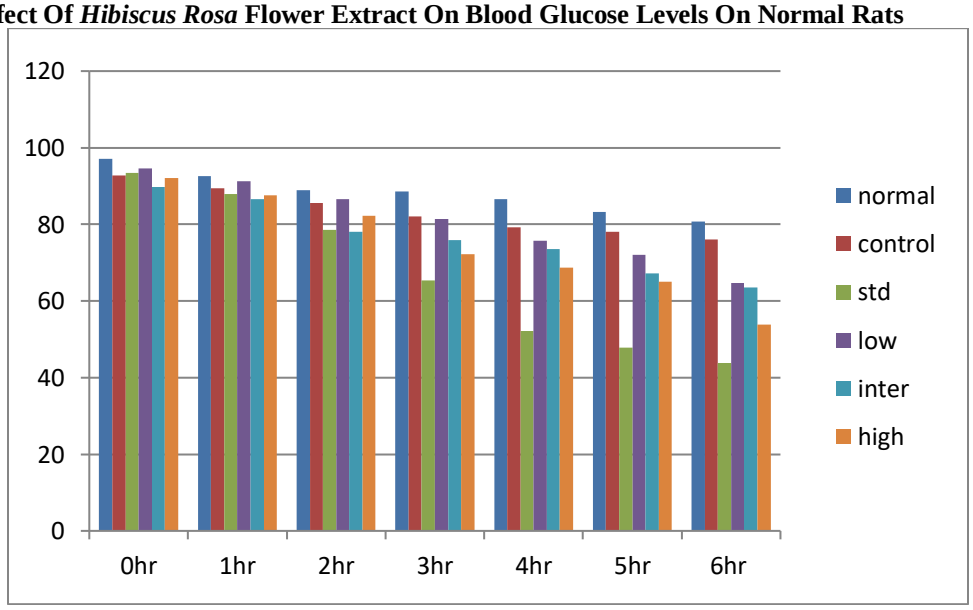
II. HYPOGLYCEMIC ACTIVITY:
Table:2

Effect Of *Hibiscus Rosa* Flower Extract On Blood Glucose Levels On Normal Rats

Sl.no	Groups	0^{TH} HR	1^{ST} HR	2^{ND} HR	3^{RD} HR	4^{TH} HR	5^{TH} HR	6^{TH} HR
1	Normal	97.1±4.38	96.6±5.8	94±8.3	90.66±7.63	85.6±10.8	83.3±3.43	81.66±7.63
2	Control(cmc)	97.83±10.9	97.5±5.68	93.66±7.5	89.1±7.29	82.16±7.4	80±7.77	79±7.18
3	Std 10mg	93.5±4.46	88±4.85	78.5±7.39	65.33±5.16	52.16±4.9	47.83±6.2	43.83±6.9
4	Low200	94.6±4.63	91.83±6.01	86.66±5.3	81.33±5.8	75.8±3.8	72±8.7	64.66±8.6
5	Inter300	89.83±3.3	86.5±2.01	78±3.08	75.83±4.4	73.5±3.2	67.16±4.7	63.5±7.58
6	high 400	92.1±7.16	87.66±5.4	82.16±8.5	72.16±6.49	68.66±6.6	65±5.72	53.8±9.76

Value expressed as mean ±sem where n=6 * P< 0.05.**Effect of *hibiscus rosa* flower extract on blood glucose levels on normal rats**

Graph:1 Effect Of *Hibiscus Rosa* Flower Extract On Blood Glucose Levels On Normal Rats



PERCENTAGE INHIBITION OF GLUCOSE ON NORMAL RATS

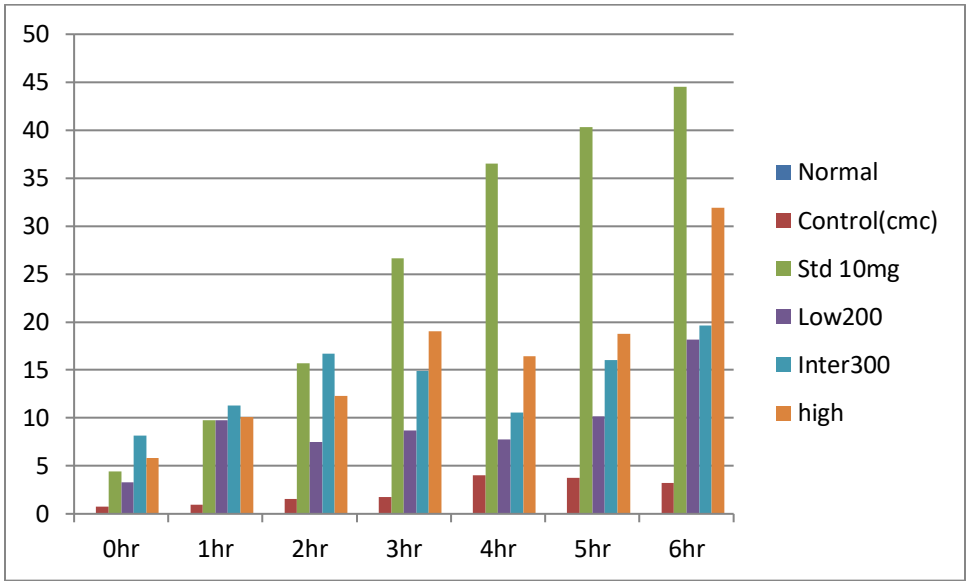
Table:3

Percentage Inhibition

		0hr	1hr	2hr	3hr	4hr	5hr	6hr
1	Normal	-	-	-	-	-	-	
2	Control(cmc)	0.75	0.93	1.52	1.72	4.01	3.72	3.25
3	Std 10mg	4.42	9.74	15.73	26.65	36.51	40.30	44.51
4	Low200	3.30	9.74	7.47	8.72	7.74	10.13	18.15
5	Inter300	8.17	11.28	16.72	14.89	10.54	16.05	19.62
6	high 400	5.85	10.09	12.27	19.01	16.43	18.75	31.89

Value expressed as mean ±sem where n=6 * P< 0.05. **Percentage inhibition of glucose on normal rats**

Graph:2
PERCENTAGE INHIBITION OF GLUCOSE ON NORMAL RATS



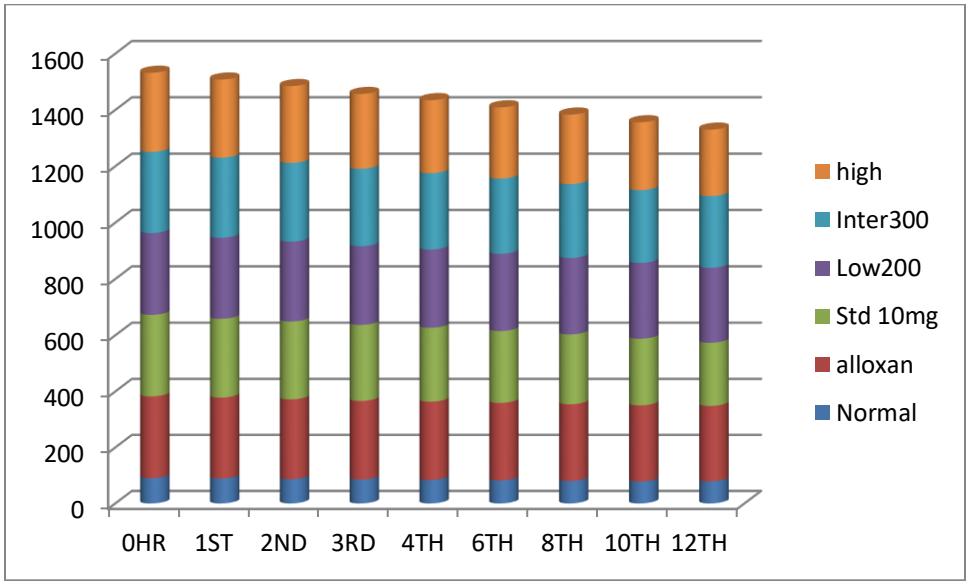
ANTIHYPERGLYCEMIC ACTIVITY:Table:4
Effect of hibiscus rosa flower extract on blood glucose levels on alloxan induced diabetic rats

Sl.no	Groups	0HR	1ST	2ND	3RD	4TH	6TH	8TH	10TH	12TH
1	Normal	90.16±6.64	89±4.33	86.33±5.84	84.83±3.86	83.33±1.94	82±1.41	80.33±1.50	78.16±1.32	78.83±1.94
2	alloxan	292.16±10.10	289.16±10.06	285.33±10.53	281.16±9.06	280±6.22	276.83±5.77	273.83±4.62	272±4.33	269.33±4.17
3	Std 10mg	290.16±8.61	283.83±8.37	277.33±8.82	270.83±8.03	263.33±7.84	256.33±8.45	249±8.00	237.66±6.50	225.33±6.43
4	Low 200	290.83±4.79	287.66±5.64	283.5±5.61	279.5±5.35	277.66±4.63	274±3.40	271.33±3.66	269.16±3.65	266.33±3.32

5	Inter 300	288± 6.22	284.5 ±5.78	279.66 ±5.68	274.8 3±4.2 1	271±2.6 0	267.16±2. 85	262.66 ±2.16	258.16±3 .06	254.33±3.3 8
6	high	281± 8.50	277.1 6±8.6 3	272.5± 9.0	265.5 ±5.85	259.33± 5.42	252.83±5. 03	246.83 ±4.07	241.16±4 .26	236±3.94

Value expressed as mean ±sem where n=6 * P< 0.05. **Effect of hibiscus rosa flower extract on blood glucose levels on alloxan induced diabetic rats .**

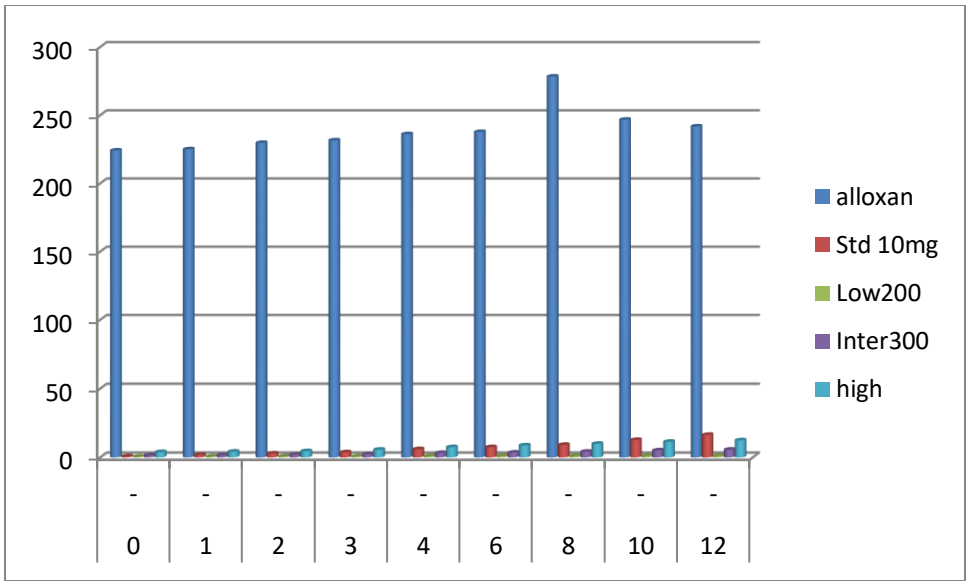
Graph:3



Percentage Inhibition Of Glucose On Alloxan Induced Diabetic Rats
Table:5

	Percentage inhibition of hibiscus in hours									
Sl.no	**Groups**	**0**	**1**	**2**	**3**	**4**	**6**	**8**	**10**	**12**
1	Normal	-	-	-	-	-	-	-	-	-
2	alloxan	224.04	224.89	229.6	231.43	236.01	237.59	278.22	246.61	241.65
3	Std 10mg	0.68	1.84	2.8	3.67	5.95	7.41	9.07	12.63	16.34
4	Low200	0.45	0.51	0.64	0.59	0.83	1.02	0.91	1.04	1.11
5	Inter300	1.42	1.61	1.98	2.25	3.21	3.49	4.07	5.08	5.56
6	high	3.82	4.15	4.5	5.57	7.38	8.67	9.86	11.34	12.38

Value expressed as mean ±sem where n=6 * P< 0.05. **Effect of hibiscus rosa flower extract on blood glucose levels on alloxan induced diabetic rats**
Graph:4



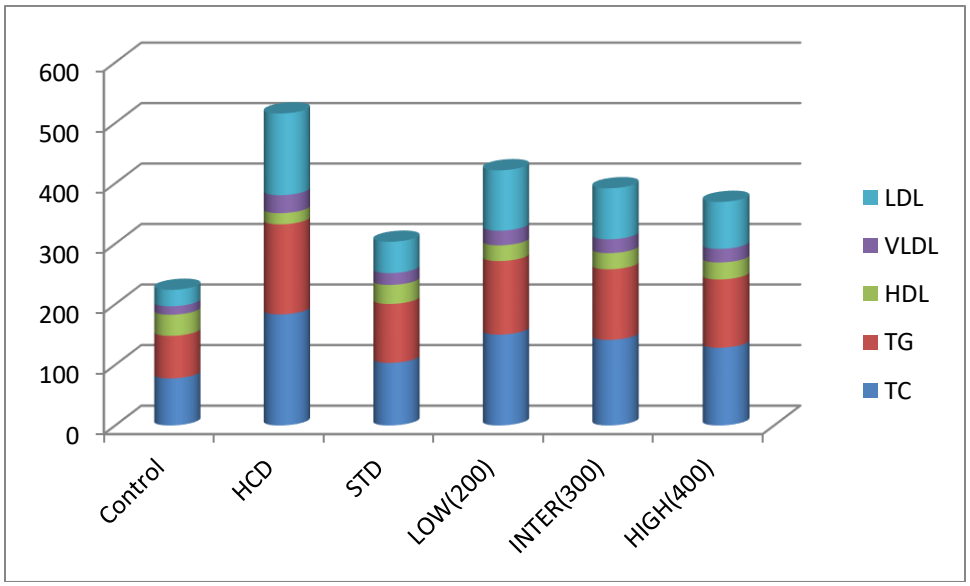
ANTI HYPER LIPDEMIC ACTIVITY :

Table-6

Groups	TC	TG	HDL	VLDL	LDL
Control	77.77±4.05	70.15±6.16	34.81±1.58	14.03±1.23	27.08±2.91
HCD	183.33±6.67	148.92±6.53	18.51±1.36	29.77±1.30	135.04±5.47
STD	103.33±7.13	97.22±5.28	31.47±2.54	19.60±1.03	51.80±3.97
LOW(200)	150±10.33	121.54 ±3.29	25.92 ±2.58	24.41 ±0.75	99.77±9.85
INTER(300)	141.31±4.15	116.54±3.10	26.74±2.7	22.94±1.4	84.34±1.9
HIGH(400)	128.33±6.01	112.74±5.56	28.10±2.19	22.51 ±1.12	77.67±3.97

Value expressed as mean ±sem where n=6 * P< 0.05. **Effect of hibiscus rosa flower extract on blood lipid levels on High fat diet rats**

Graph:5

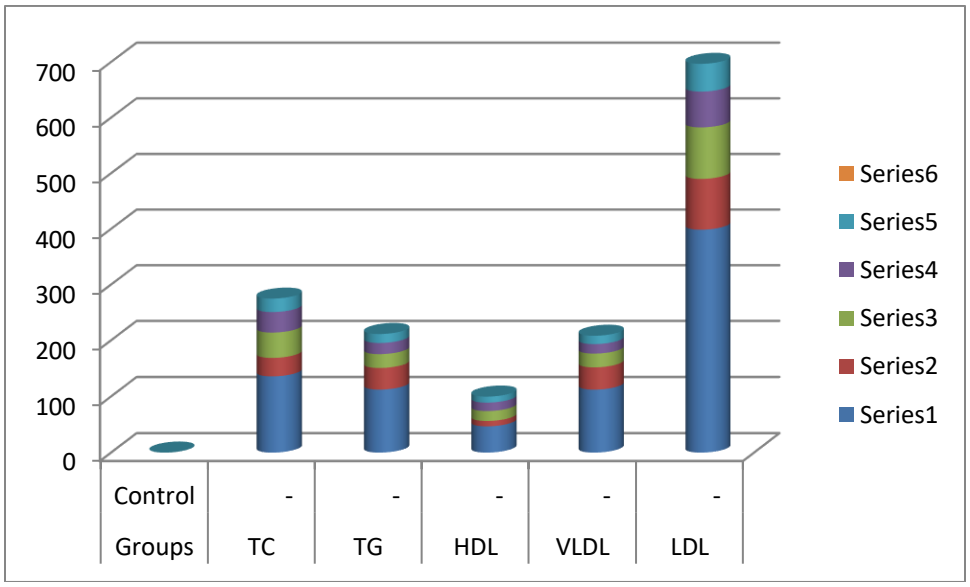


PERCENTAGE INHIBITION OF HIBISCUS

Groups	TC	TG	HDL	VLDL	LDL
Control	-	-	-	-	-
Hcd	135.83	112.28	46.82	112.18	398.6
Std	32.86	38.5	9.59	39.7	91.28
Low (200)	45.16	24.67	17.63	24.54	92.6
Inter (300)	36.75	19.87	15.03	16.88	64.36
High(400)	24.19	15.96	10.70	14.84	49.94

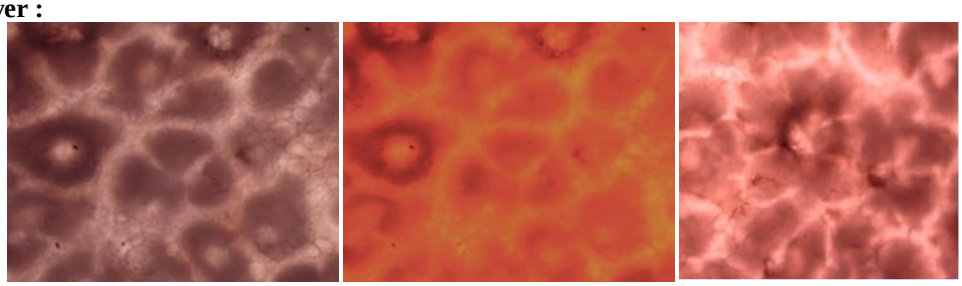
Value expressed as mean ±sem where n=6 * P< 0.05. **Effect of hibiscus rosa flower extract on blood lipid levels on High fat diet rats**

Graph:6

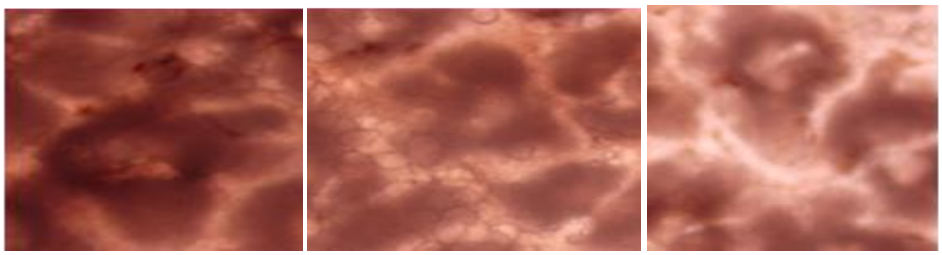


Histopathological studies:

Images of liver :



Control **HCD treated** **std**



Low dose(200) **Intermediate(300)** **high dose(400)**

DISCUSSION:

Hydro Alcoholic Extract of *CARICA PAPAYA* obtained is 9 gms.

From the table-1-The hydroalcholic extract of hibiscus rosa flowers shows the presents of alkaloids, tannins, glycosides, mucilage,flavonoids,reducing sugars in the extract.

From the table-2,3-After 6hrs of study on hypoglycemic active we come to know that *Papaya* shows a significate reduced in blood glucose levels with increasing in dose.the percentage inhibition of blood glucouse level on normal rats was to be found std 43.99%,test(200,300,400)19.22%,29.%,42.22%.

From the table-3,4-the diabetis was induced by alloxan and the study was carried on for 12hrs study on antihyperglycemic activity . *Papaya* shows a significate reduced in blood glucose levels with increasing in dose.

From the table-4,5-the hyperlipidaemic was induced by High fat diet cocktail was prepared by mixing cholesterol (100g), cholic acid(50g) in 1 liter of coconut oil supplemented with egg for 10 days .the plant extract shows an significant dcrease the levels of total cholestrol,triglyceriad,VLDL,LDL but increase in HDL.

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