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Comparative Analysis of Quercetin and Leucocynidin against HMG-CoA reductase and their evaluation of hypolipidemic activity

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Abstract

The present study was designed to comparative analysis of quercetin and leucocynidin against HMG coA reductase and their evaluation of hypolipidemic activity. Computational methods has been used to identified the active molecule (quercetin) against HMG coA reductase , based on the pharmacophore features of quercetin the virtual screening analysis discovered that the one in every of the compound particularly leucocynidin has been elect for the hypolipidemic activities .ADME properties were predicted to confirm the safety profile of the identified virtual hits.. In treatment of quercetin and Leucocynidin group of animals fed with AD was considerably reduction within the body weight compared to AD fed Group of animals. The more levels of TC,TG, phospholipids, LDL-C and VLDL-C were considerably noticed in group II animals (AD). When the activity of quercetin and leucocynidin (15mg per weight unit body weigh per day) showed a major ($p<0.001$) decrement in plasma and tissues (liver,heart and aorta)TC,TG, phospholipids, LDL-C and VLDL-C in conjunction with an increment within the High density lipoprotein-C compared with group II animals (AD). Taking under consideration the outcomes, we tend to over that quercetin and leucocynidin may be a considerably hypolipidemic agent having preventive and curative activity against lipidemia.

Key words: Quercetin, Leucocynidin , rats, hypolipidemia

INTRODUCTION

HMG-CoA enzyme, a enzyme that rate-limiting the biogenesis of cholesterin through a feedback system[1]. In traditional class cells, the degradation of density conjugated protein (LDL) by the lipoprotein receptor brings regarding the biogenesis of cholesterin, that suppresses 5-hydroxy-3-methylglutaryl-coenzyme A reductase. The outflow of lipoprotein receptors within the liver is up regulated by the competitive inhibitors of 5-hydroxy-3-methylglutaryl-coenzyme A reductase, that builds the breakdown rate of plasma lipoprotein and leads to lower levels of cholesterin in plasma. Low LDL-cholesterol ultimately ends up in theatherosclerosis[2]. The current hostile to hyperlipidemic medication like statins and made cancer hindrance agents like probucol area unit broadly speaking wont to treatment of hyperlipidemic patients. Shockingly, these medications aren't freed from reactions. to provide novel medications to hyperlipoidemia, it's been focused round the common things that haven't terribly several reactions. the globe ethnobotanical information according completely different home adult medication from the herbs that area unit used for normalling arterial sclerosis and also the complexities in patients. Around eightieth of the collection populaces area unit whole dependent on standard medications. medicative Plants area unit contains sizable amount of medical specialty active phytoconstituents that may function lead for the event of activity, safe, low cost novel medication. variety of medicative plants have shown their useful activity on the disorder (CVD) by virtue of their hypolipidemic, antianginal, inhibitor and cardioprotective activitys[3,4].Hence, the target of the present study was to analysis the ADME properties of quercetin and leucocynidin against HMG CoA enzyme and their analysis of hypolidemic activity in hyperlipidemic induced rats.

MATERIAL AND METHODS

E-pharmacophore based virtual screening

Energy-optimized structure based pharmacophore grounded screening uses combined characteristic of structure and ligand based approach for the screening of ligand database. For the screening, the E-pharmacophore hypothesis was generated from the Glide XP docked file of bio active compounds of Terminalia Arjuna to the target protein HMGCOA. The hypothesis were generated with maximum four pharmacophore features, including two Rings, one hydrogen bond donors (D), one hydrogen bond acceptors (A), The hypothesis was generated with the selected features and was further used for database screening.

Database screening

The above resulted hypothesis was then used to screen the ZINC database containing 70, 00000 unique structure records, the obtained pharmocophoric features were then exported using find matches to hypotheses option in the 'Phase' tab. The unknown ligands with similar pharmacophoric features were identified and used for virtual screening.

Virtual screening

The structurally matched 1062 ligands were then taken for the virtual screening to pre filter the ligands through High Throughput Virtual Screening (HTVS), HTVS enables the primary screening SP Docking does the secondary screening. The selected compounds of these preliminary screening were then undergone to Glide XP docking is to find hydrogen-bond interactions, electrostatic interaction, hydrophobic enclosure, and pi–pi stacking interactions,the fitness score of the best-scoring pose to the known ligand were reported.

Evaluation of Hypolipidemic activity

Animals and Experimental Design

Male Wister rats of 17-20 weeks age, weighing 150-180g were gotten from the Central Animal House, MNR pharmacy college, Sangareddy,Hyderabad, Telugana, India. The animals were kept in cages, 2 per confine, with 12:12 hr light and dim cycle at $25^0 \pm 2^0$C. The animals were maintained on their separate diets and water *ad libitum.* Animal Ethical Committee's clearance was acquired for the study(MNR college of Pharmacy, Sangareddy,Hyderabad, Telugana CPCSEA/COP/07 dated 04-05-2017).

Experimental Design

Animals were divided into following four Groups of six rats each:

I Group : Standard chow pellet
II Group : Atherogenic Diet(AD)
III Group : AD plus treated with Quercetin (15mg/kg B.wt)
IV Group : AD plus treated with Leucocynidin (15mg/kg B.wt)
V Group : AD plus treated with Standard drug atorvastatin (1.2 mg/kg B.wt)

Animal diet

The compositions of the two diets were as follows [5].

Normal diet: Wheat flour 22.5%, simmered bengal gram powder 60%, skimmed milk powder 5%, casein 4%, refined oil 4%, salt blend with starch 4% and vitamin and choline blend 0.5%.

Atherogenic Diet: normal diet with coconut oil 9% and cholesterol 0.4%.

Toward the end of thirty one days every one of the animals were sacrificed by cervical dislocation after overnight fasting. Liver, heart and aorta were cleared of sticking fat, weighed precisely and utilizeded for the preparation of homogenate. Animals were sufficiently given consideration according to the Animal Ethical Committee's recommendations.

Biochemical estimation

Plasma samples were analyzed for TC, HDL-cholesterol and TG were estimated using Boehringer Mannheim kits by Erba Smart Lab analyzer USA. Low density lipoprotein and very low density lipoprotein were calculated by using Friedwald *et al* 1972 method. EC [6] and FC[6] were analyzed by using digitonin. Parts of the tissues from liver, heart and aorta were marked, weighed and homogenized with methanol (3 volumes). The different cholesterol supernant liquid was taken by the procedure of Folch *et al.*, 1957[7]. The above extracts were used for the estimation of EC and FC[8] , triglycerides[9] and Free fatty acids [10].

Statistical analysis

Results were communicated as mean ± SE of 6 rats in every Group. The statistical significance between the Groups was analyzed by utilizing one way analysis of variance (ANOVA), followed by Dunnet's multiple correlation test. Significance level was fixed at 0.05.

RESULTS

Virtual screening

The selected compounds(quercetin and leucocynidin) were then undergone to Glide XP docking is to find hydrogen-bond interactions, electrostatic interaction, hydrophobic enclosure, and pi–pi stacking interactions were reported.The docking results shows that leucocynidin has more interaction with HMG coA reductase, number of H bond and lenth of the H bond was also when compared with quercetin interaction. Quercetin has the interaction with GLY 765, and GLY 560, whereas Leucocyaninide has the interaction with GLN 766,VAL 805,MET 655,ALA 525, GLH 559 because of the leucocynidin has 4 more H atom when compared to quercetin.

Table 1: Top scoring compounds with its interaction analysis, and with the length.

S.No	Compound	Name of the compound	Docking Score	Interaction	H-Bond Length
1.	Quercetin	Quercetin	-8.31958	0-H…O=CGLY(560A) NH_2(GLY(560A)…O=C 0-H…O=C Gly (765B) 0-H…O=C Gly (765B)	2.114 2.416 2.381 2.146
2.	ZINC04096940	Leucocynidin	-9.321	O-H….0-HGLH (559A) O-H….O=C ALA(525B) O-H….O=C VAL(805B) NH_2(MET(655B)…OH O-H….O=C GLN(766B)	2.140 1.969 1.825 2.104 2.794

Table 2:

Molecular weight, in Da (range for 95% of drugs: 130–725 Da).
Molecular weight of the volume.
Van der waals surface areas of polar nitrogen and oxygen atoms.
No: of Hydrogen bonds donated by the molecule (range for 95% of drugs: 0–6).
No: of Hydrogen bonds accepted by the molecule (range for 95% of drugs: 2–20).

Title	stars	mol MW	volume	PSA	donorHB	accptHB
Quercetin	0	302.24	861.437	140.06	4	5.25
Leucocynidin	0	306.271	871.777	208.73	6	7.15

Table 3: Predicted octanol /water partition co-efficient log P (acceptable range: −2.0 to 6.5)

Predicted aqueous solubility; S in mol /L (acceptable range: −6.5 to 0.5)
Apparent Caco-2 permeability (nm/s) (<25 poor, >500 great)
Log HERG, HERG K+channel blockage (concern below −5)
Apparent MDCK permeability (nm/s) (25 poor, >500 great)
Percentage of human oral absorption (<25% poor and >80% is high)

Title	QPlogPo/w	QPlogS	QPPCaco	QPlogHERG	QPPMDCK	Percent Human Oral Absorption
Quercetin	0.387	-2.804	21.058	-4.981	7.624	52.9
Leucocynidin	-0.212	-3.192	-4.513	46.132	17.795	42.528

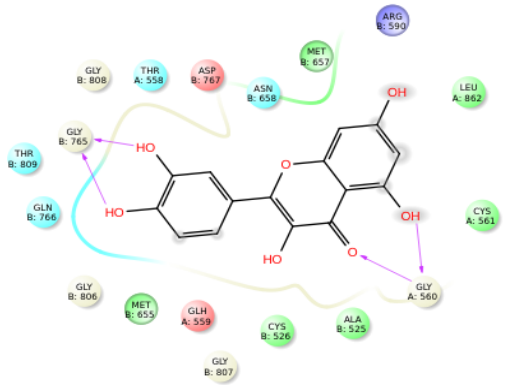

Fig 1- shows the interaction between HMG-CoA and Quercetin

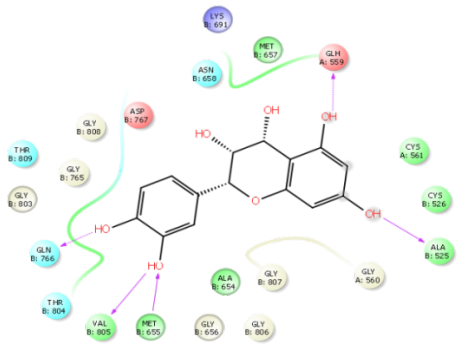

Fig 2- shows the interaction between HMG-CoA and Leucocynidin

ADMET profiling

The ADMET profiling were done using quickPro in Schrodinger software based on the "Lipinski's" rule of five and other drug like properties like absorption, distribution, metabolism, excretion and toxicity profile of the five ligands. The selection of the best among five ligands was based on the Lipinski rule and ADMET properties. All the ADME properties like volume , PSA, donorHB, aceptHB and Percent Human Oral Absorption were in the acceptable range and confirm the safety profile of the identified virtual hits. Hence the two active compounds (quercetin and leucocynidin) were selected for the hypolipidemic activity.

Comparative study of Hypolipidemic activity

Table 4 illustrates the typical body weight changes in control and experimental rats. A major increase in b.weight was detected in Group II HFD fed rats compare to normal control Group I rats. A gradual increase within b.weight of all experimental animals was noted. The normal body weight was noted in the Group I animals (control) as 43.04±1.54 . The most increase in the body weight was recorded within the Group II animals (High fat diet) as 139.01±2.26. In Group III animals once administration of quercetin,drastic decline in body weight gain were noted as 76.06 ± 0.36 . In Group IV animals once administration of Leucocynidin ,drastic decline in body weight gain were noted as 73.61 ± 1.93. Group V animals once administration of the standard drugs, decrement in body weight was recorded as 71.90±2.30 compared to Group II animals. The diet intake per animal per twenty four hours was found to be 18.30 ± 1.5 g. Diet intake was an equivalent all cluster of animals.

Table 4: Average B.weight changes in normal and active compounds treated animals

Groups	Initial Weight (g)	Final Weight (g)	Average Body weight gain (g)
Group I	138.87±1.10 ^{bNS}	181.91±0.95 ^{b*}	43.04±1.54 ^{b*}
Group II	136.25±1.54 ^{aNS}	275.26±1.56 ^{a*}	139.01±2.26 ^{a*}
Group III	144.3 ± 1.12$^{a*, b**}$	220.56± 1.33$^{a*, b*}$	76.06 ± 0.36 ^{a*,b*}
Group IV	146.04 ± 1.98^{a*,} ^{bNS}	219.65± 1.42$^{a*, b*}$	73.61 ± 1.93 $^{a*, b*}$
Group V	144.01±1.08 $^{aNS, b*}$	214.47±1.95 $^{a*, b**}$	71.90±2.30 $^{a*, b**}$

Values are mean ± SE of half-dozen rats;*P* values: *<0.001, **<0.05;NS : Non significant a →Group I compared with Groups II, III and IV.;b →Group II compared with Groups III and IV. Group I : Standard chow pellets (Normal); Group II : AD; Group III : AD and Quercetin (15mg/kg B.wt) Group IV : AD and Leucocynidin (15mg/kg B.wt) ;Group V : AD and Standard drug atorvastatin (1.2 mg/kg B.wt)

Activity of active compounds on plasma lipid levels were shown in Table 5. The Total cholesterol, Ester cholesterol,Free cholesterol, Free fatty acid , Phospholipid, and TG was noted in the Group I animals (control) as 119.07± 0.77, 33.23±0.88, 88.84±0.27 ,40.41±0.30, 105.97,83.38. The maximum increase in the Total cholesterol, Ester cholesterol,Free cholesterol, Free fatty acid , Phospholipid, and TG were recorded in the Group II animals (High fat diet) as 179.36,49.54,129.49,60.11,151.98,169.89. In Group III animals after administration of quercetin ,drastic decline in plasma Total cholesterol, Ester cholesterol,Free cholesterol, Free fatty acid , Phospholipid, and TG were noted as 103.77,38.85,64.91,39.05,103.38,89.08.In Group IV animals after administration of Leucocynidin ,drastic decline in plasma TC, Ester cholesterol,Free cholesterol, Free fatty acid , Phospholipid, and TG were noted as 95.98,22.67,73,34,37,38,102.30,74.90 . In Group V animals after administration of the standard drugs, decrement in plasma lipid levels were recorded as 97.44,23.93,73.54,39.55,98.95,69.32 compared to Group II animals.

The control Group of animals Atherogenic Index (AI) was recorded as 2.90±0.01and was was considerably ($p<0.001$) increased the AI value in AD fed animals was noted as 4.70±0.01and supplementation of Quercetin animals was considerably reduced the atherogenic index was recorded as 1.63 ±0.02. Leucocynidin treated rats was considerably reduced the atherogenic index was recorded as 1.66 ±0.01and standard drug treated animals were recorded as 1.66 ±0.01.

Table 6 illustrates the effect of active compounds on plasma lipoprotein in experimental rats. The Group I receiving normal diet showed high level of HDL-cholesterol as 57.34 in comparison to Group II. All the treated Groups of animals were compared to Group II animals. HDL in the animal fed with atherogenic diet in Group II as 37.38. Supplementation of quercetin with AD (Group III animals) showed marked increased in the level of HDL-cholesterol as 56.27. The oral administration of leucocynidin with atherogenic diet (Group IV animals) showed marked increased in the level of HDL-cholesterol as 57.32. Atorvastatin administered in Group V animals recorded significant increase in plasma HDL-cholesterol contentas 56.20.

The Group I receiving normal diet showed level of LDL-C, VLDL-C as 35.04,16.71 in comparison to Group II. All the treated Groups of animals were compared to Group II animals. There was marked increment in the amount of LDL-C, VLDL-C in the animal fed with atherogenic diet in Group II as 98.97,37.97. Administration of quercetin with AD (Group III animals) showed marked exaggerated within the amount of LDL-C, VLDL-C as 30.42,18.69. The oral administration of leucocynidin with atherogenic diet (Group IV animals) showed marked exaggerated within the amount of LDL-C, VLDL-C as 31.67,14.97. Atorvastatin administered in Group V animals recorded significant increase in plasma LDL-C, VLDL-C content as 30.20 and 13.86..

Table 5 : Effect of active compounds on plasma lipid profile treated rats

Group	Total cholesterol (mg/dl)	Free cholesterol (mg/dl)	Ester cholesterol (mg/dl)	Free fatty acid mg/dl)	Phospholipid (mg/dl)	Triglyceride (mg/dl)	Athrogenic index
Group I	119.07± 0.77^{b*}	33.23± 0.88 ^{b*}	88.84± 0.27 ^{b*}	40.41± 0.30 ^{b*}	105.97± 0.43 ^{b*}	83.38± 0.27 ^{b*}	2.90± 0.01 ^{b*}
Group II	179.36± 0.81^{a*}	49.54± 0.64 ^{a*}	129.49± 0.53 ^{a*}	60.11± 0.30 ^{a*}	151.98± 0.52 ^{a*}	169.89± 0.45 ^{a*}	4.79± 0.01 ^{a*}
Group III	103.77± 0.95$^{a**, b*}$	38.85± 1.93 $^{a*, b*}$	64.91± 1.41 $^{a**, b*}$	39.05± 0.57 $^{a*, b**}$	103.38± 0.78 $^{a*, b**}$	89.08± 0.57 $^{a*, b**}$	1.63± 0.02 $^{a**, b**}$
Group IV	95.98± 0.75$^{a**, b**}$	22.67± 0.77 $^{a*, b*}$	73.34± 0.35$^{a*, b*}$	37.38± 0.22 $^{a*, b*}$	102.30± 0.37 $^{a*, b**}$	74.90± 0.35 $^{a*, b**}$	1.66± 0.02 $^{a**, b**}$
Group V	97.44± 0.29 $^{a*, b*}$	23.93± 0.34 $^{a*, b*}$	73.54± 0.39 $^{a*, b*}$	39.55± 0.37 $^{a*, b*}$	98.95± 0.24 $^{a*, b*}$	69.32± 0.38 $^{a*, b*}$	1.73± 0.01 $^{a*, b*}$

Values square measure mean ± SE of half-dozen rats , *P* values : * < 0.001, ** < 0.05

Table 6: Effect of active compounds on plasma lipoprotein in experimental rats

Groups	HDL cholesterol (mg/dl)	LDL cholesterol (mg/dl)	VLDL cholesterol (mg/dl)
Group I	57.34±0.25^{b*}	35.04±0.20^{b*}	16.71±0.05^{b*}
Group II	37.38±0.22^{a*}	98.97±0.17^{a*}	33.97±0.09^{a*}
Group III	56.27±0.54$^{a*, b*}$	31.42±0.62$^{a*, b*}$	18.69±0.12$^{a*, b*}$
Group IV	57.32±0.08$^{a**, b*}$	30.67±0.18$^{a*, b*}$	14.97±0.07$^{a*, b*}$
Group V	56.20±0.19$^{a*, b*}$	30.20±0.19$^{a*, b*}$	13.86±0.19$^{a*, b*}$

Values square measure mean ± SE of half-dozen rats , *P* values: * < 0.001, ** < 0.05.

Activity of active compounds on tissues ester and free cholesterol profile experimental rats were presented in Tables 7&8. The Group I receiving normal diet showed level of tissues free and ester cholesterol as 1.99,2.77,2,28 and 079,070,0.46 in comparison to Group II. All the treated Groups of animals were compared to Group II animals. There was marked increment in the level of tissues free and ester cholesterol in the animal fed with atherogenic diet in Group II as 3.27,6.93,7.05 and 1.19,0.99,2.31. Supplementation of quercetin with AD (Group III animals) showed marked increased in the level of tissues free and ester cholesterol as 1.98,2.88,2,64 and 0.92,0.82,0.79 .The oral administration of leucocynidin with atherogenic diet (Group IV animals) showed marked increased in the level of tissues free and ester cholesterol as 1.89,2.77,2,22 and 0.66,0.60,0.63. Atorvastatin administered in Group V animals recorded significant increase in tissues free and ester cholesterol content as 1.84,2.49,2.63 and 0.78,0.55,0.61.

Table 7: Effect of active compounds on EC(liver,heart, Aorta)levels in animals

Groups	Ester cholesterol (mg/g tissue)		
	Liver	Heart	Aorta
Group I	1.99 ± 0.01^{b*}	2.77± 0.01^{b*}	2.28±0.02^{b*}
Group II	3.27±0.01^{a*}	6.93±0.01^{a*}	7.05±0.04^{a*}
Group III	1.98±0.02$^{a*, b**}$	2.88±0.02$^{a*, b**}$	2.64±0.02$^{a*, b**}$
Group IV	1.89±0.02$^{a*, b*}$	2.77±0.02$^{a*, b**}$	2.22±0.12$^{a*, b**}$
Group V	1.84±0.01$^{a*, b*}$	2.49±0.01$^{a*, b*}$	2.63±0.04$^{a*, b*}$

Values square measure mean ± SE of half-dozen rats ,
P values : * < 0.001, ** < 0.05.

Table 8: Effect of active compounds on FC(liver,heart, Aorta)levels in animals

Groups	Free cholesterol (mg/g tissue)		
	Liver	Heart	Aorta
Group I	0.79±0.01^{b*}	0.70± 0.01^{b*}	0.46±0.01^{b*}
Group II	1.19±0.01^{a**}	0.99±0.01^{a*}	2.31±0.06^{a*}
Group III	0.92±0.02^{a**,b**}	0.82±0.01^{a*,b**}	0.79±0.05^{a*,b**}
Group IV	0.66±0.02^{a**,b*}	0.60±0.01^{a*,b**}	0.63±0.05^{a*,b**}
Group V	0.78±0.01^{a*,b*}	0.55±0.01^{a*,b*}	0.61±0.04^{a*,b*}

Values square measure mean ± SE of half-dozen rats ,
P values : * < 0.001, ** < 0.05.

Table 9 illustrates the effect of active compounds on tissues Triglyceride level experimental rats.. The Group I receiving normal diet showed tissues (liver,heart,aorta) triglyceride levels as 7.85,8.50,8.96 in comparison to Group II. All the treated Groups of animals were compared to Group II animals. There was marked increment in the tissue triglyceride levels in the animal fed with atherogenic diet in Group II as 26.33,21.74,26.08. Treatment oif quercetin with AD (Group III animals) showed marked increased in the tissue triglyceride levels as 14.41,17.57,19.23.Administration of leucocynidin with atherogenic diet (Group IV animals) showed marked increased in the tissue triglyceride levels as 12.16,12.06,18.93. Atorvastatin administered in Group V animals recorded significant increase in tissue triglyceride levels content as 10.97,10.60,16.98..

Table 9: Effect of active compounds on TG(liver,heart, Aorta)levels in animals

Groups	Triglyceride (mg/g tissue)		
	Liver	Heart	Aorta
Group I	7.85±0.06^{b*}	8.50±0.03^{b*}	8.96±0.06^{b*}
Group II	26.33±0.15^{a*}	21.74±0.23^{a*}	26.08±0.18^{a*}
Group III	14.41 ± 0.59^{a*,b**}	17.57±0.50$^{a**, b**}$	19.23±0.27$^{a*, b**}$
Group IV	12.16 ± 0.21^{a*,b*}	12.06±0.21$^{a*, b**}$	18.93±0.17$^{a*, b**}$
Group V	10.97±0.08^{a*,b*}	10.60±0.22$^{a*, b*}$	16.98 ± 0.20$^{a*, b*}$

Values square measure mean ± SE of half-dozen rats ,
P values : * < 0.001, ** < 0.05.

Table 10 illustrates the activity of active compounds on tissues free fatty acids level experimental animals . The Group I receiving normal diet showed level of tissues free fatty acid as 10.74,13.69,11.49 in comparison to Group II. All the treated Groups of animals were compared to Group II animals. There was marked increment in the level of tissues free fatty acid in the animal fed with atherogenic diet in Group II as 30.76,44.59,31.33. Treatment of quercetin with AD (Group III animals) showed marked increased in the level of level of tissues free fatty acid as 12.13,15.30,13.08. The oral administration of leucocynidin with atherogenic diet (Group IV animals) showed marked increased in the level of level of tissues free fatty acid as 11.43,14.66,12.77. Atorvastatin administered in Group V animals recorded significant increase in plasma level of tissues free fatty acid content as 12.28,13.50,12.45.

Table 9- Effect of active compounds on free fatty acids (liver,heart, Aorta)levels in animals

Groups	Free fatty acids (mg/g tissue)		
	Liver	Heart	Aorta
Group I	10.74±0.21^{b*}	13.69 ±0.22^{b*}	11.49±0.22^{b*}
Group II	30.76±0.24^{a*}	44.59±0.21^{a*}	31.33± 0.18^{a*}
Group III	12.13± 0.21^{a**,b*}	15.30±0.36^{a**,b*}	13.08 ± 0.36$^{a*, b**}$
Group IV	11.43± 0.19^{a*,b*}	14.66±0.22^{a*,b*}	12.77 ± 0.20$^{a*, b*}$
Group V	12.28±0.10^{a*,b*}	13.50±0.21^{a*,b*}	12.45± 0.19$^{a*, b*}$

Values square measure mean ± SE of half-dozen rats ,
P values : * < 0.001, ** < 0.05.

DISCUSSION

Statin derivatives, has a lot of facet effects like headache, hoarseness, lower back or facet pain, loss of appetence, pyrosis and stomach upset etc. therefore we've selected herbs extract for medication with none facet impact compared with artificial medication. hese days, hyperlipidemia, particularly hypercholesterolemia is related with a danger for the occurrence of coronary heart disease and fatty liver[11].Recently, varied analysis work have targeting the therapeutic capability of plant constituents for treating varied very important common diseases, notably fatness and its complications[12].

A significant increase in b.weight was detected in AD fed rats. The gain in b.weight of those rats was because of deposition of

excess lipide that loose the body's threshold metabolism[13]. Plasma lipid profiles are elevated in the group receiving atherogenic diet; earlier studies reveal significant elevation of lipid parameters in plasma and tissue response to atherogenic diet or high fat diet[14].The reduction within the HDL made by the cluster of animals fed with HFD, this result's extremely vital in this low HDL-cholesterol is currently thought-about because the most vital risk issue for coronary-artery disease[15]. when administration of Quercetin and leucocynidin were showed considerably enlarged the HDL-C concentration. it's accepted that enlarged HDL-cholesterol levels have a protecting role in arteria sickness.[16].

The elevated levels of LDL and VLDL-cholesterol in rats fed with HFD, Clinical and epidemiological studies have proved that individuals with elevated LDL show an increased risk for cardiovascular diseases[17]. The level of LDL-C and VLDL-C were significantly reduced by administration of active compounds can be helpful to reduce the risk of atherosclerosis, cardiovascular diseases, and fatty liver. There is strong evidence from several studies that the extent of reduction in the incidence of CHD is directly related to the magnitude of reduction in LDLc and VLDLc levels[18].

Both plasma free and ester cholesterol reduced remarkably on treating the HFD rats with leucocynidin . This lipide lowering activity of quercetin and leucocynidin is also because of the inhibition of internal organ cholesterogenesis or because of the rise in excretion of fecal as according by Purohit and Vyas *et al* 2006[19]. Studies have involved the concentration of plasma cholesterol may be regulated by steroid alcohol biogenesis, removal of steroid alcohol from the circulation, absorption dietary steroid alcohol and excretion of steroid alcohol via excrement[20] .

AD rats considerably increase within the level of plasma triglycerides was because of decrease in activity of lipoprotein lipase [21]. Recent studies additionally implicate that triglycerides are severally associated with coronary heart condition and most of the antihypercholesterlemic medicine don't decrease triglycerides levels [22]. However, active compounds treated animals lowered it considerably ($P < 0.001$) during this study and this result may well be increase the uptake of triglycerides from plasma by striated muscle and fatty tissue [22].

CONCLUSSION

The active compounds(quercetin and leucocynidin) were considerably reduced the plasma lipid and lipoprotein profile and reduced the atherogenic index. But the leucocynidin treated animals were considerably reduced the plasma and tissues free cholesterol, ester cholesterol,triglycerides and phospholipids in comparison to quercetin treated animals group as well as statin drug. The findings thus support the therapeutic use of quercetin and leucocynidin as natural agents for management of heart diseases complications like hardening of the arteries.

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