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Studies on e-pharmacophore based virtual screening and evaluation of hypolipidemic activity of leucocyanidin in hyperlipidemic induced rats

Dhivya Jensi V, Ananda Gopu P*

Department for Advanced Computing and Bioinformatics, PRIST University, Thanjavur-613403, Tamil Nadu, India

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ABSTRACT

The present study was designed to analyse energy-optimised structure primarily based pharmacophore virtual screening and high score compound was elect and used for hypolipidemic activity in rat fed with high-fat diet. Supported the e-pharmacophore virtual screening analysis discovered that the one in every of the compound particularly leucocyanidin has been elect for the hypolipidemic activities. In the treatment of Leucocyanidin group of animals fed with HFD was considerable reduction within the body weight compared to HFD fed cluster of animals. The enlarged the levels of TC, TG, phospholipids, LDL-C and VLDL-C were noticed in group 2 animals (HFD). When the activity of leucocyanidin (15mg per weight unit body weight per day) showed a major ($p<0.001$) decrement in plasma and TC, TG, phospholipids, LDL-C and VLDL-C in conjunction with an increment within the High-density lipoprotein-C compared with group 2 animals (HFD). Taking under consideration the outcomes, we tend to over that leucocyanidin may be a considerably hypolipidemic agent having preventive and curative activity against lipidemia.

* Corresponding Author

Name: Ananda Gopu P
Email: akottaimuthu@gmail.com

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INTRODUCTION

Atherosclerosis may be a complex sickness of the major and medium-sized muscular arteries and also the leading explanation for morbidity and mortality in industrial countries (Braunwald, 1997). It's characterised by epithelium dysfunction, vascular inflammation, the build-up of lipids, cholesterin (Ming-Shi *et al.,* 2008), metal and cellular debris within the intima of the vessel wall (Anuradha and Raji, 2009). This build-up end in plaque formation, vascular transforming, acute and chronic purple heart obstruction, abnormalities of blood flow and diminished elements provide to focus on organs (Bibave *et al.,* 2011). Depending on the location of the blocked arteries, hardening of the arteries might cause complications typically noted as vessel diseases (Coronary artery disease, arteria carotis sickness, peripheral artery sickness, aneurysms, heart failure and stroke). Hence, the target of the current study was to research the energy-optimised structure primarily based pharmacophore virtual screening and high score elect compound used for hypolipidemic activity in hyperlipidemic induced rats.

MATERIAL AND METHODS

E-pharmacophore based virtual screening

Energy-optimised structure primarily based pharmacophore grounded screening uses combined characteristic of structure and substance-based approach for the screening of substance info. For the screening, the E-pharmacophore hypothesis was generated from the Glide XP docked file of bioactive compounds of Terminalia Arjuna to the target macromolecule HMGCOA. The hypothesis was generated with most four pharmacophore options, as well as 2

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.

Evaluation of Hypolipidemic activity

Animals and Experimental Design

Male Wister rats of 17-20 weeks ago, weighing 150-180g were gotten from the Central Animal House, MNR pharmacy college, Sangareddy, Hyderabad, Telangana, India. The animals were kept in cages, 2 per confine, with 12:12 hr light and dark cycle at 25^0±2^0C. 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, Telangana CPCSEA/COP/07 dated 04-05-2017).

Experimental Design

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

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

Animal diet: The compositions of the two diets were as follows (Kottai Muthu A *et al.,* 2005).
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 was sacrificed by cervical dislocation after overnight fasting. Liver, heart and aorta were cleared of sticking fat, weighed precisely and utilized for the preparation of homogenate. Animals were sufficiently considered according to the Animal Ethical Committee's recommendations.

Biochemical estimation

Plasma samples were analysed for TC, HDL-cholesterol and TG were estimated using Boehringer Mannheim kits by Erba Smart Lab analyser USA. Low-density lipoprotein and very low-density lipoprotein were calculated by using the Friedwald *et al.,* 1972 method. EC (Sperry WM, 1950) and FC (Sperry WM, 1950) were analysed using digitonin. Parts of the tissues from liver, heart and aorta were marked, weighed and homogenised with methanol (3 volumes). The different cholesterol supernatant liquid was taken by the procedure of Folch *et al.,* 1957. The above extracts were used for the estimation of EC and FC (Varley H et al., 1991), triglycerides (Foster CS, 1973) and Free fatty acids (Falholt *et al.,* 1973).

Statistical analysis

Results were communicated as mean ± SE of 6 rats in every cluster. The statistical significance between the clusters was analysed by utilising a one-way analysis of variance (ANOVA), followed by Dunnet's multiple correlation tests. The significance level was fixed at 0.05.

RESULTS

Pharmacophore model evaluation

E-pharmacophore model was generated from the active Compound of Terminalia Arjuna. The hypotheses were validated by the virtual screening protocol using enrichment factor (EF) metrics calculations. The active compound quercetin was then combined to decoys set having 1000 drug-like compounds retrieved from Schrodinger (Friesner RA, 2004) to form an internal library of 1001 compounds. The validating protocol involves the ability of the e-pharmacophores to differentiate the active compound from the internal library.

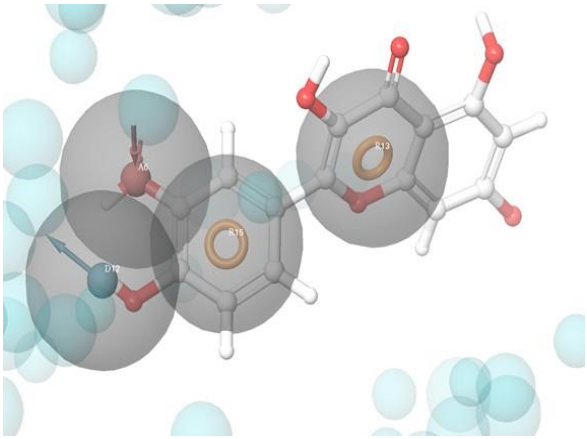

Figure 1: Generated E- Pharmacophore Hypotheses

Database screening

The above-resulted hypothesis was then used to screen the ZINC database containing 70, 00000 unique structure records; the obtained pharmacophoric 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

Table 1: Hypotheses feature

Rank	Feature_ label	Score	X	Y	Z	type	num	from_ chemscore	source
1	A6	-1.59	27.4495	-1.6873	5.3324	A	5	0	HBond
2	R15	-0.96	29.3949	-2.5184	3.5354	R	14	0	Ring Chemscore Hphobe
3	R13	-0.64	33.4796	-1.4603	4.0893	R	12	0	RingChemscore Hphobe
4	D12	-0.43	26.1945	-3.2908	3.8789	D	11	0	HBond

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.

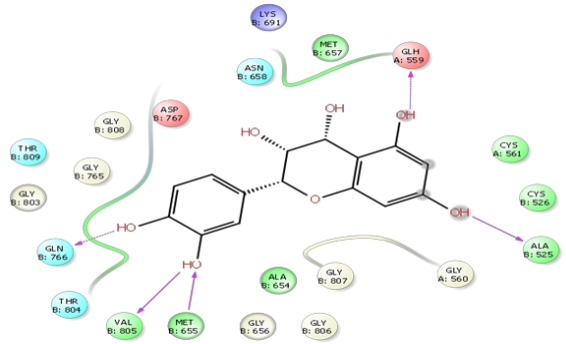

Figure 2: top scoring compound ligand interaction

Evaluation 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 cluster II HFD fed rats compared to normal control cluster I rats. A gradual increase within b.weight of all experimental animals was noted. The normal body weight was noted in the cluster I animals (control) as 43.04±1.54. The most increase in the body weight was recorded within the cluster II animals (High-fat diet) as 139.01±2.26. In cluster III animals once administration of Leucocyanidin, drastic decline in body weight gain was noted as 93.61 ± 1.93. In cluster IV animals once administration of the standard drugs, decrement in body weight was recorded as 71.90±2.30 compared to cluster II animals. The diet intake per animal per twenty-four hours was found to be 19.40 ± 2.0 g. Diet intake was an equivalent all told the AD animals.

a →cluster I compared with clusters II, III and IV,
b →cluster II compared with clusters III and IV,
Cluster I: Standard chow pellets (Normal)
Cluster II: AD
Cluster III: AD and Leucocyanidin (15mg/kg B.wt)
Cluster IV: AD and Standard drug atorvastatin (1.2 mg/kg B.wt)

The activity of Leucocyanidin on plasma lipid levels was shown in Table 5. The Total cholesterol, Ester cholesterol, Free cholesterol, Free fatty acid, Phospholipid, and TG was noted in the cluster 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 was recorded in the cluster II animals (High-fat diet) as 179.36, 49.54, 129.49, 60.11, 151.98, 169.89. In cluster III animals after administration of Leucocyanidin, drastic decline in plasma Total cholesterol, 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 cluster IV animals after administration of the standard drugs, decrement in plasma lipid levels was recorded as 97.44, 23.93, 73.54, 39.55, 98.95, 69.32 compared to cluster II animals.

The traditional management of a cluster of animals Atherogenic Index (AI) was recorded as 2.90±0.01and was considerably ($p<0.001$) increased the AI value in AD fed animals was noted as 4.70±0.01and. Leucocyanidin treated rats were 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 Leucocyanidin on plasma lipoprotein in experimental rats. The cluster I receiving a normal diet showed a high level of HDL-cholesterol as 57.34 in comparison to cluster II. All the treated clusters of animals were compared to cluster II animals. HDL in the animal fed with atherogenic diet in cluster II as 37.38. The oral administration of leucocyanidin with atherogenic diet (cluster III animals) showed marked increased in the level of HDL-cholesterol as 57.32. Standard drug atorvastatin administered in cluster IV animals recorded a significant

Table 2: Selected compound through virtual screening

S. No	Compound	Name of the compound	Docking Score	XP Score	Glide g - score	Glide energy	glide e - model
1.	ZINC 04096940	Leucocyanidin	-9.321	-9.321	-9.321	-46.942	-65.624
2.	ZIN C01669608	3-bromo-1-[2-(3, 4-dihydroxyphenyl)-2-oxoethyl]quinolinium	-6.589	-6.605	-6.605	-46.255	-61.885
3.	ZINC 92786822	(2R)-2-(3-fluorophenyl)-2-[(4-hydroxy-5-methoxy -2-nitro-phenyl)methyl-methyl-amino]acetamide	-6.332	-6.453	-6.453	-50.664	-68.995
4.	ZINC 58168160	N-[4-[4-(3-carbamoyl-4-hydroxy-phenyl)thiazol-2-yl]phenyl]thiophene-2-carboxamide	-6.04	-6.061	-6.061	-52.513	-77.432
5.	ZINC 88608537	2-[(6-fluoro-2, 3-dihydro-1, 4-benzoxazin-4-yl)methyl]-5-hydroxy-pyran-4-one	-5.85	-5.85	-5.85	-33.892	-46.692
6.	ZINC 86454107	1-(4-chlorophenyl)-5-cyclopropyl-triazole-4-amine	-4.988	-4.988	-4.988	-37.484	-44.165
7.	ZINC 86454106	1-(4-fluorophenyl)-5-isopropyl-triazol-4-amine	-4.964	-4.964	-4.964	-33.563	-43.078
8.	ZINC 86454108	1-(4-chlorophenyl)-5-ethyl-triazole-4-amine	-4.875	-4.875	-4.875	-36.092	-42.643
9.	ZINC 86454105	1-(4-fluorophenyl)-5-propyl-triazol-4-amine	-4.864	-4.864	-4.864	-34.939	-42.718
10.	ZINC 86517463	4-chloro-5-(2-iodophenyl)isoxazol-3-amine	-4.774	-4.774	-4.774	-33.178	-41.998
11.	ZINC 86517461	5-(benzothiophene-3-yl)-4-chloro-isoxazol-3-amine	-4.175	-4.175	-4.175	-37.108	-45.713
12.	ZINC 04044733	5-(5-methoxy-2-methyl-1H-indol-3-yl)thiazol-2-amine	-4.094	-4.094	-4.094	-41.106	-50.898
13.	ZINC 74454786	1-[(1S)-1-[1-(4-fluorophenyl)-5-methyl-pyrazol-4-yl] ethyl]-3-methyl-urea	-4.076	-4.076	-4.076	-38.609	-49.147
14.	ZINC 86517462	4-chloro-5-(5-ethyl-2-furyl)isoxazol-3-amine	-3.797	-3.797	-3.797	-30.2	-34.2
15.	ZINC 05069417	N2-allyl-N6-(4-chlorophenyl)-5-nitro-pyrimidine-2, 4, 6-triamine	-3.383	-3.383	-3.383	-43.789	-56.636

increase in plasma HDL-cholesterol content as 56.20.

The cluster I receiving normal diet showed the level of LDL-C, VLDL-C as 35.04, 16.71 in comparison to cluster II. All the treated clusters of animals were compared to cluster II animals. There was marked increment in the amount of LDL-C, VLDL-C in the animal fed with atherogenic diet in cluster II as 98.97, 37.97. The oral administration of leucocyanidin with atherogenic diet (cluster III animals) showed marked exaggerated within the amount of LDL-C, VLDL-C as 31.67, 14.97 Standard drug atorvastatin administered in cluster IV animals recorded a significant increase in plasma LDL-C, VLDL-C content as 30.20 and 13.86.

The activity of Leucocyanidin on tissues ester and free cholesterol profile experimental rats were presented in Tables 7&8. The cluster I receiving a normal diet showed the level of tissues free and ester cholesterol as 1.99, 2.77, 2, 28 and 079, 070, 0.46 in comparison to cluster II. All the treated clusters of animals were compared to cluster II animals. There was marked increment in the level of tissues free and ester cholesterol in the animal fed with atherogenic diet in cluster II as 3.27, 6.93, 7.05 and 1.19, 0.99, 2.31. Administration of leucocyanidin with atherogenic diet (cluster III animals) showed marked increased in the level of

Table 3: Top scoring compound interaction table

S. No	Compound	Name of the compound	Docking Score	Interaction	H-Bond Length
1.	ZINC04096940	LEUCOCYANIDIN	-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
2.	ZINC01669608	3-bromo-1-[2-(3,4-dihydroxyphenyl)-2-oxoethyl]quinolinium	-6.589	O-H….O=C GLY(560A)	1.895
3.	ZINC92786822	(2R)-2-(3-fluorophenyl)-2-[(4-hydroxy-5-methoxy-2-nitro-phenyl)methyl-methyl-amino]acetamide	-6.332	O-H….O=C ASN(658B) NH_2(GLY(560A)…OH O=C…NH_2 (GLN(766B)	2.731 2.750 2.133
4.	ZINC58168160	N-[4-[4-(3-carbamoyl-4-hydroxyphenyl)thiazol-2-yl]phenyl]thiophene-2-carboxamide	-6.04	O-H….O=CVAL(805B) NH_2…O=CGLN(766B) NH_2 (ASP(766B)…O=C	1.712 1.980 2.220

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

Clusters	Initial Weight (g)	Final Weight (g)	Average Body weight gain (g)
Cluster 1	138.87±1.10 bNS	181.91±0.95 b*	43.04±1.54 b*
Cluster 2	136.25±1.54 aNS	275.26±1.56 a*	139.01±2.26 a*
Cluster 3	146.04 ± 1.98a*, bNS	239.65± 1.42a*, b*	93.61 ± 1.93 a*, b*
Cluster 4	144.01±1.08 aNS, b*	214.47±1.95 a*, b**	71.90±2.30 a*, b**

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

Table 5: Effect of Leucocyanidin on plasma lipid profile treated rats

Cluster	Total cholesterol (mg/dl)	Free cholesterol (mg/dl)	Ester cholesterol (mg/dl)	Free fatty acid mg/dl)	Phospholipid (mg/dl)	Triglyceride (mg/dl)	Athro-genic in-dex
Cluster 1	119.07± 0.77b*	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*
Cluster 2	179.36± 0.81a*	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*
Cluster 3	95.98± 0.75a**, b**	22.67± 0.77 a*, b*	73.34± 0.35a*, b*	37.38± 0.22a*,b*	102.30± 0.37 a*, b**	74.90± 0.35 a*, b**	1.66± 0.02a**,b**
Cluster 4	97.44± 0.29 a*, b*	23.93± 0.34 a*, b*	73.54± 0.39 a*, b*	39.55± 0.37a*,b*	98.95± 0.24 a*, b*	69.32± 0.38 a*, b*	1.73± 0.01a*,b*

tissues free and ester cholesterol as 1.89, 2.77, 2, 22 and 0.66, 0.60, 0.63, Atorvastatin administered

in cluster IV animals recorded a significant increase in tissues free and ester cholesterol content as 1.84, 2.49, 2.63 and 0.78, 0.55, 0.61.

Table 9 illustrates the effect of Leucocyanidin on tissues Triglyceride level experimental rats. The cluster I receiving normal diet showed tissues (liver, heart, aorta) triglyceride levels as 7.85, 8.50, 8.96 in comparison to cluster II. All the treated clusters of animals were compared to cluster II animals. There was marked increment in the tissue triglyceride levels in the animal fed with atherogenic diet in cluster II as 26.33, 21.74, 26.08. Administration of leucocyanidin with atherogenic diet (cluster III animals) showed marked increased in the tissue triglyceride levels as 12.16, 12.06, 18.93. Atorvastatin administered in cluster IV animals recorded a significant increase in tissue triglyceride levels content as 10.97, 10.60, 16.98.

Table 10 illustrates the activity of Leucocyanidin on tissues free fatty acids level experimental

Table 6: Effect of Leucocyanidin on plasma lipoprotein in experimental rats

Clusters	HDL cholesterol (mg/dl)	LDL cholesterol (mg/dl)	VLDL cholesterol (mg/dl)
Cluster 1	57.34±0.25^{b*}	35.04±0.20^{b*}	16.71±0.05^{b*}
Cluster 2	37.38±0.22^{a*}	98.97±0.17^{a*}	33.97±0.09^{a*}
Cluster 3	57.32±0.08$^{a**, b*}$	31.67±0.18$^{a*, b*}$	14.97±0.07$^{a*, b*}$
Cluster 4	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

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

Clusters	Ester cholesterol (mg/g tissue)		
	Liver	Heart	Aorta
Cluster 1	1.99 ± 0.01^{b*}	2.77± 0.01^{b*}	2.28±0.02^{b*}
Cluster 2	3.27±0.01^{a*}	6.93±0.01^{a*}	7.05±0.04^{a*}
Cluster 3	1.89±0.02 $^{a*, b*}$	2.77±0.02$^{a*, b**}$	2.22±0.12 ^{a*,b**}
Cluster 4	1.84±0.01 ^{a*,b*}	2.49±0.01 ^{a*,b*}	2.63±0.04 ^{a*,b*}

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

Clusters	Free cholesterol (mg/g tissue)		
	Liver	Heart	Aorta
Cluster 1	0.79±0.01 ^{b*}	0.70± 0.01 ^{b*}	0.46±0.01^{b*}
Cluster 2	1.19±0.01^{a**}	0.99±0.01 ^{a*}	2.31±0.06^{a*}
Cluster 3	0.66±0.02^{a**,b*}	0.60±0.01 ^{a*,b**}	0.63±0.05^{a*,b**}
Cluster 4	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: Effect of Leucocynidin on TG (liver, heart, Aorta) levels in animals

Clusters	Triglyceride (mg/g tissue)		
	Liver	Heart	Aorta
Cluster 1	7.85±0.06^{b*}	8.50±0.03^{b*}	8.96±0.06^{b*}
Cluster 2	26.33±0.15^{a*}	21.74±0.23^{a*}	26.08±0.18^{a*}
Cluster 3	12.16 ± 0.21 ^{a*,b*}	12.06±0.21$^{a*, b**}$	18.93±0.17$^{a*, b**}$
Cluster 4	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: Effect of Leucocynidin on free fatty acids (liver, heart, Aorta) levels in animals

Clusters	Free fatty acids (mg/g tissue)		
	Liver	Heart	Aorta
Cluster 1	10.74±0.21^{b*}	13.69 ±0.22^{b*}	11.49±0.22^{b*}
Cluster 2	30.76±0.24^{a*}	44.59±0.21^{a*}	31.33± 0.18^{a*}
Cluster 3	11.43± 0.19^{a*,b*}	14.66±0.22^{a*,b*}	12.77 ± 0.20$^{a*, b*}$
Cluster 4	12.28±0.10^{a*,b*}	13.50±0.21^{a*,b*}	12.45± 0.19$^{a*, b*}$

animals. The cluster I receiving a normal diet showed the level of tissues free fatty acid as 10.74,

13.69, 11.49 in comparison to cluster II. All the treated clusters of animals were compared to cluster II animals. There was marked increment in the level of tissues free fatty acid in the animal fed with atherogenic diet in cluster II as 30.76, 44.59, 31.33. The oral administration of leucocyanidin with atherogenic diet (cluster III animals) showed marked increased in the amount of tissues free fatty acid as 11.43, 14.66, 12.77. Standard drug atorvastatin administered in cluster IV animals recorded a significant increase in plasma level of tissues free fatty acid content as 12.28, 13.50, 12.45.

DISCUSSION

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 (Ohlorge *et al.,* 1981). Once treatment of leucocyanidin reduced considerably within the b.weight. Results show that treatment with AD considerably enhanced the amount of plasma and tissue lipids as revealing that significant elevation of plasma and tissue lipid parameters in response to atherogenic diet and cholesterol feeding (Chandar *et al.,* 1997; Guido and Joseph *et al.,* 1997). This observation was in agreement with the report that polyphenolic compounds are possessing anti-hyperlipidemic properties (Solomon, 2012).

Both plasma free and ester cholesterol reduced remarkably on treating the HFD rats with

leucocyanidin. This lipid-lowering activity of leucocyanidin is also because of inhibition of internal organ cholesterogenesis or because of the rise in excretion of faecal as according to by Purohit and Vyas *et al.,* 2006. Studies have involved the amount 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 (Choi *et al.,* 2001; Xu *et al.,* 2006).

Several results discovered that reduction within the good lipoprotein made by the cluster of animals fed with AD, this result's extremely considerably therein low good lipoprotein was thought about because of the most vital risk issue for hardening of the arteries (Gordan and Rifkind, 1989; Brewer, 2004). Supplementation of the AD with leucocyanidin considerably accrued the HDL–Cholesterol level compared to HFD rats (cluster II). Many studies show that a rise in HDL-cholesterol is related to a decrease in coronary risk (Harrison *et al.,* 2003). Waggemans et al., 2003 according to that flavonoid's intake diminished LDL-C and accrued HDL-C in hypercholesterolaemic people who will hasten the removal of steroid alcohol from peripheral tissue to the liver for catabolism and excretion.

AD treated rats showed considerably increment the amount of LDL-C and VLDL-C. Yakubu and Afolayan et al., 2009 investigated that top level of LDL and triglycerides are related to arterial illness.

Treatment with leucocyanidin markedly reduced the amount of plasma LDL – C and VLDL -C compared to HFD rats (Cluster II). Reduced levels of LDL and VLDL on AD fed rats perhaps probably because of increase with catabolism of LDL. Earlier studies indicated the extent reduction of CHD incidence is directly associated with the magnitude of reduction in LDL-C and VLDL-C levels (Pekkanen *et al.,* 1990). HFD rats considerably increase within the level of plasma triglycerides was because of a decrease in the activity of lipoprotein lipase (Kavitha *et al.,* 2001). Recent studies additionally implicate that triglycerides square measure severally associated with a coronary heart condition and most of the antihyper cholesterolemic medicine don't decrease triglycerides levels (El-Hazmi and Warsy, 2001). However, leucocyanidin lowered it considerably during this study, and this result may well increase the uptake of triglycerides from plasma by striated muscle and fatty tissue (El-Hazmi, 2001).

CONCLUSION

The leucocyanidin were considerably reduced the plasma lipid and lipoprotein profile and reduced the atherogenic index. It additionally the considerably reduced the tissues free cholesterol, ester cholesterol, triglycerides and phospholipids compared to the medicine of statin drug. The findings thus support the therapeutic use of leucocyanidin within the management of heart diseases complications like hardening of the arteries.

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