International Journal of Advanced Pharmaceutical Sciences, Volume 1, Issue 07, Page 35-50
ISSN:2456-8147

Effect of Resveratrol and Fenofibrate in Triton WR 1339 Induced Dyslipidemic Wistar Rats

Sunny Sinha*, Dr. Priyanka Khurana[1] , Dr. Shreya Gupta [2], Dr. Deepa Iyer[3]

*M. Pharma in Pharmacology ,[1]BDS ,[2]MDS in Oral Pathology, [3]PhD in Pharmacognosy ,New Delhi - 110091, India.

An open access journal

Supporting Information:

Received: 19 June 2018
Accepted: 25 June 2018
Published: 06 July 2018

Competing Interests:
The authors have declared that no competing interests exist.

Corresponding author address

Dr. Priyanka Khurana
A88, First Floor, Gali no.16,
Pratap Nagar, Mayur Vihar
Phase 1, New Delhi - 110091,
India.

ABSTRACT

Aim: The aim of this research was to elucidate the antidyslipidemic and antioxidant activity of Resveratrol (RSV) and Fenofibrate (FB) combination in triton WR 1339 induced dyslipidemic wistar rats.

Materials and Methods: Albino wistar rats of either sex were used for the study with 4 animals per group divided into 5 groups. Antidyslipidemic activity was determined by Lipoproteins serum levels like TC, TG, LDL and VLDL decreasing and HDL increasing activity was evaluated using Triton WR 1339 as dyslipidemia enhancing agent. Antioxidant activity parameters like LPO and SOD in vitro assays was evaluated using Liver tissues homogenate.

Statistical Analysis: Statistical comparison between groups in each experiment was evaluated with One way analysis of Variance (ANOVA) followed by Dunnett's test.

Results: Resveratrol (RSV) and Fenofibrate (FB) combination showed significant ($P<0.01$) decrease in concentrations of serum lipoproteins TC, TG, LDL and VLDL in contrast to significant ($P<0.01$) increase in HDL level when compared to Negative control group animals. On the other hand, in antioxidant parameters there was significant ($P<0.01$) increase in SOD activity while, significant ($P<0.01$) decrease in LPO activity when compared to Negative control group.

Conclusion: Resveratrol (RSV) and Fenofibrate (FB) combination showed significant antidyslipidemic and antioxidant activities in triton induced dyslipidemic wistar rats.

***Keywords*:** Antidyslipidemic, Fenofibrate, Resveratrol, Triton Wr 1339, Antioxidant.

.

Introduction

Dyslipidemia is characterized by alternation occurring in serum lipid and lipoproteins profile due to increased concentration of Total cholesterol (TC), Total triglycerides (TG), Low density lipoprotein (LDL), Very low density lipoprotein (VLDL) with concomitant decrease in concentration of High density lipoprotein (HDL) in Blood circulation [1]. Disorders of Lipid metabolism oxidative stress are the prime risk factors for initiation and progression of these diseases [2].

Interest in the study of Phenolic compounds present in Red wine has grown since epidemiological studies have shown an inverse correlation between Red wine consumption and the incidence of Cardiovascular (CV) diseases [3]. In association with cardiovascular diseases it was also recently announced that various Phenolic compounds improve blood lipid components [4]. Since then numerous *in vivo* and *in vitro* studies have assessed the ability of Resveratrol in preventing multiple path physiological processes. Resveratrol has the ability to inhibit the peroxidation of Lipid membranes [5], to decrease the concentration of low & very low density lipoprotein [6] and to inhibit platelet aggregation [7].

PPAR (alpha), the first PPAR to be identified was named based on its ability to be activated by substances that drive peroxisome proliferation in rodents [8]. It has been known for several years that fibrates induce peroxisome proliferation in rodents [9]. Additionally the Sirtuin, SIRT-1 has been proposed to lie at the centre of a regulatory loop regulating the actions of PGC-1 (alpha) and PPAR, ultimately controlling muscle fatty acid oxidation [10]. Resveratrol is a potent activator of SIRT-1 (silencing information regulator-1) [11], a histone deacetylase that mediates the effects of Resveratrol in mice [12]. SIRT-1 is also reported to inhibit the formation of adipocytes via repression of PPAR (gamma) transcriptional activity [13].

Since Resveratrol and Fibrates (Fenofibrate) share a common pharmacological molecular target/receptor i.e. PPAR alpha (Peroxisome Proliferator Activated Receptor) in altering the lipid metabolism, as in case of dyslipidemia. So, the present research was designed on the basis of common therapeutic targets of both PPAR agonist against dyslipidemia and observation was made for complete lipid profile parameters like: HDL, LDL, TG, TC and VLDL along with

changes in SOD and LPO as *in vitro* assay depicting antioxidant parameters. We investigated the fixed dose combination of Resveratrol and Fenofibrate against Triton WR 1339 induced dyslipidemic Wistar rats of either sex. Besides latter point, Resveratrol as SIRT 1 activator used in Caloric restriction in mammals may possess synergistic antidyslipidemic activity with Fenofibrate

Materials and Methods:

Settings and Design

Wistar rats weighing 150 – 350 gm of either sex were divided into 5 different groups, in each group 4 rats were allotted, n = 4. Animals received treatment in the following manner:

S.no.	Group	Drug	Dose
1	Vehicle control	Carboxy methyl cellulose (CMC)	0.5 % p.o.
2	Negative control	Triton WR 1339	250 mg/kg p.o.
3	Standard	Fenofibrate	65 mg/kg p.o.
4	Treatment 1	Resveratrol	50 mg/kg p.o.
5	Treatment 2	Resveratrol + Fenofibrate	(65 + 50) mg/kg p.o.

The Vehicle treated group received a daily dose of 0.5% CMC solution orally considered as Group 1. Standard group received a daily dose of 65 mg/kg Fenofibrate orally considered as Group 2. Treatment 1 group received a daily dose of 50 mg/kg Resveratrol orally. Treatment 2 group received a daily fixed dose of combination of 65 mg/kg Fenofibrate and 50 mg/kg Resveratrol. Above mentioned treatment to all groups were administered orally for 7 days consecutively. On 8^{th} day 250 mg/kg triton WR 1339 was administered to each group animals through i.v. route. Before 10 minutes of triton injection to each group animals, blood were collected from each group of animals which served as blank sample of blood at 0 time point.

Then at time point of 1, 2, 4 and 6 hours, blood were collected through orbital plexus puncture of each group animals under mild ether anaesthetic condition. After blood collection from all the animals and the separated serum was subjected for the estimation of serum lipoproteins levels such as Triglycerides (TG), Total cholesterol (TC), High density lipoproteins (HDL), Low density lipoproteins (LDL) and Very low density lipoproteins (VLDL).

Animals

Healthy adult wistar rats of either sex weighing 150-350 gram housed in polypropylene cages, maintained under standard condition (12 hours Light Dark cycles) in VNS Faculty of Pharmacy, Bhopal, M.P., India were provide with standard pellet and had free access to purified drinking water. The guidelines for the committee for the purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Social Justice and Empowerment, Government of India were followed and prior permission was sought from IAEC (Institute for animal ethical committee) for conducting the study with approval No. (778-PO-a-03-CPCSEA).

Drugs and Chemicals

Resveratrol (Zenith Nutrition Pvt. Ltd. Bangalore), Fenofibrate as Fenolip (Cipla), Triton WR 1339 (Zydus), Carboxy methyl cellulose - CMC (Organic India), Superoxide dismutase kit (Sigma Aldrich), Lipid Peroxidation kit (Sigma Aldrich) were used in the present research work. Drug solutions were prepared in the freshly prepared CMC solution with distilled water stored at 4˚C. The doses prepared were based upon the previous experiments conducted and shown to be pharmacologically active [14] [15].

Triton WR 1339 induced dyslipidemia

250 mg/kg dose was administered to all the animals on the 8 th day in the tail vein of each rat for elevation of lipoproteins levels. Dose was decided according to the density of Triton WR 1339 i.e. 1.11 g/ml. Here, 1.11 ml of liquid Triton WR 1339 was diluted and volume was make up to 10 ml. with 0.5 % of CMC solution. Then according to individual animal's body weight, Triton was injected into tail vein under mild anesthesia of diethyl ether. However, all animals were kept at prior in fasting condition for 18 hours with access of drinking water before Triton injection.

Intravenous injection of non-ionic detergent such as Triton WR 1339 in experimental animals results in a progressive increase in the concentration of lipids in the blood [16]. The concentration of Triglycerides (TG) in the plasma rises linearly for 3 hours after the i.v. injection of the non-ionic detergent, Triton 1339 in Rat [17].

Antioxidant activity

1. **Lipid peroxidation (LPO) assay:** The lipid peroxidation product in liver tissues was determined by TBARS, expressed as the extent of malondialdehyde (MDA) production. Briefly, tissue homogenates were centrifuged at 10,000 g for 10 min at 4℃ to sediment cell debris. The liver homogenate were suspended in PBS at pH 7.4, mixed with BHT – TCA solution (1% w/v BHT dissolved in 20% w/v TCA) and centrifuged at 1000 g for 5 min. Supernatant fluid was then mixed with 0.5 N HCl and 120 mM TBA in 26 mM Tris buffer solution, heated in a water bath at 80℃ for 10 min. After cooling the absorbance of the resulting chromophore was determined at 532 nm using a SHIMADZU UV-Visible spectrophotometer and MDA production was determined by using an extinction coefficient of 1.56 X 10^5 $M^{-1}cm^{-1}$. Tissue protein were estimated in aliquots of diluted membranes fractions using a calorimetric reaction with Folin's phenol reagent. The colour developed measured at 640 nm. Values were expressed as mg protein / gm wet tissue [18].

2. **Superoxide dismutase (SOD) assay:** The liver homogenates were prepared in Tris (ethylenediamine tetraacetic acid) buffer centrifuged for 40 min at 10000 r.p.m at 4°C, the supernatant was used for the enzyme assay. 2.8 ml Tris-EDTA and 100 µl Pyrogallol (2mM) were taken in the cuvette and scanned for 3 min at 420 nm wavelength. Then 2.8 ml Tris-EDTA buffer (pH -8.0), 100 µl Pyrogallol and 50 µl tissue homogenate were taken and scanned for 3 min at the same wavelength. One unit of SOD activity is the amount of the enzyme that inhibits the rate of auto oxidation of pyrogallol by 50% and was expressed as Units/mg protein/min [19].

Biochemical Estimation

Blood collected were given for diagnosis of Complete lipid profile parameters like: Triglycerides (TG), Total cholesterol (TC), Low density Lipoprotein (LDL), High density lipoprotein (HDL) and Very low density lipoprotein (VLDL) in the Nidaan Pathology, Beema Kunj, Kolar, Bhopal, M.P., India.

Reference range of Lipid Profile parameters:

- Total cholesterol (TC) = 200 mg/dl
- Triglycerides (TG) = 150 mg/dl
- High density lipoprotein (HDL) = 35 – 70 mg/dl
- Low density lipoprotein (LDL) = 130 mg/dl
- Very low density lipoprotein (VLDL) = 30 mg/dl

Statistical Analysis

Analysis of variance (ANOVA) on experimental datas was analyzed using Standard error mean (±SEM). Statistical significance was assessed using One way ANOVA followed by Dunnett's test. **P<0.01 was considered as significant by Instat graph Pad software version 3.1.

Results

Triton WR 1339 induced dyslipidemia:

Serum Total Cholesterol (TC) level: Animals showed significant (P<0.01) decrease in the level of serum total cholesterol (TC) compared to Triton treated group. Dyslipidemic rats with Fenofibrate (FB-65 mg/kg p.o.) and Resveratrol (RSV-50 mg/kg p.o.) showed significant (P<0.01) decrease in levels of serum total cholesterol (TC) as compared to Triton treated group on day 8 of study.

Serum Triglycerides (TG) level: Animals showed significant (P<0.01) decrease in the level of serum triglycerides (TG) compared to Triton treated group. Dyslipidemic rats with Fenofibrate (FB-65 mg/kg p.o.) and Resveratrol (RSV-50 mg/kg p.o.) showed significant (P<0.01) decrease in levels of serum triglycerides (TG) as compared to Triton treated group on day 8 of study.

Serum High density lipoprotein (HDL) level: Animals showed significant (P<0.01) decrease in the level of serum High density lipoprotein (HDL) compared to Triton treated group. Dyslipidemic rats with Fenofibrate (FB-65 mg/kg p.o.) and Resveratrol (RSV-50 mg/kg p.o.) showed significant (P<0.01) decrease in levels of serum High density lipoprotein (HDL) as compared to Triton treated group on day 8 of study.

Serum Low density lipoprotein (LDL) level: Animals showed significant (P<0.01) decrease in the level of serum Low density lipoprotein (LDL) compared to Triton treated group. Dyslipidemic rats with Fenofibrate (FB-65 mg/kg p.o.) and Resveratrol (RSV-50 mg/kg p.o.) showed significant (P<0.01) decrease in levels of serum Low density lipoprotein (LDL) as compared to Triton treated group on day 8 of study.

Serum Very low density lipoprotein (VLDL) level: Animals showed significant (P<0.01) decrease in the level of serum Very low density lipoprotein (VLDL) compared to Triton treated group. Dyslipidemic rats with Fenofibrate (FB-65 mg/kg p.o.) and Resveratrol (RSV-50 mg/kg p.o.) showed significant (P<0.01) decrease in levels of serum Very low density lipoprotein (VLDL) as compared to Triton treated group on day 8 of study.

Antioxidant parameters

SOD (Superoxide Dismutase) level: Animals showed significant (P<0.01) increase in the level of SOD (IU/mg of Protein value) compared to Triton treated group. Dyslipidemic rats with Fenofibrate (FB-65 mg/kg p.o.) and Resveratrol (RSV-50 mg/kg p.o.) showed significant (P<0.01) increase in levels of SOD as compared to Triton treated group on day 8 of study.

LPO (Lipid Peroxidation) level: Animals showed significant (P<0.01) decrease in the level of LPO (MDA nmol/mg of Protein value) compared to Triton treated group. Dyslipidemic rats with Fenofibrate (FB-65 mg/kg p.o.) and Resveratrol (RSV-50 mg/kg p.o.) showed significant (P<0.01) decrease in levels of LPO as compared to Triton treated group on day 8 of study.

Discussion

The aim of the present study was to elucidate the role of fixed dose combination of Resveratrol and Fenofibrate during dyslipidemia induced by Triton WR 1339 in Wistar rats of either sex. Triton WR 1339 was used to induce acute dyslipidemia. It is well known fact that Triton WR 1339 elevates total TC and TG in blood by altering the hepatic lipid metabolism (Freidman M et al 1963). Moreover, this could be associated with a down regulation in LDL receptors by the cholesterol and saturated fatty acids in the Triton which could also explain the elevation of serum LDL levels either by changing hepatic LDL receptors activity, the LDL production rate or both.

The activity of cholesteryl ester transfer protein (CETP) a key enzyme in reverse cholesterol transport and HDL metabolism increase in Triton and mediates the transfer of cholesteryl esters from HDL to TG rich particles in exchange for TG. This leads to increased plasma concentrations of TG and decreased concentrations of HDL. Lipid profile of dyslipidemic control rats in our study revealed higher levels of serum TG, TC, LDL and VLDL accompanied by decrease of serum HDL as compared to Normal control group animals.

Treatment dyslipidemic rats with individual Fenofibrate, Resveratrol and combination of Resveratrol and Fenofibrate showed a significant ($P<0.01$) decreasae of serum TG, TC, LDL and VLDL in contrast to significant ($P<0.01$) increase of serum HDL levels compare to Negative group. The potential of antidyslipidemic and antioxidant effect may be due to the PPAR activation which plays a key role in lipid metabolism alteration.

Resveratrol is a SIRT 1 activator and SIRT-1 is located in between the PGC-1 (alpha) and PPAR (alpha) so, in this research work Resveratrol may have somewhere activated PPAR agonist property like Fenofibrate, which acts as a enhancer of cellular mitochondrial oxidative phosphorylation in the cell. Since both Resveratrol and Fenofibrate acts on PPAR (alpha) and PGC-1 (alpha) receptor in the liver of mammals and share a common pharmacological target, so this therapeutic activity against dyslipidemia may be due to this very point. Fenofibrate produces a notation of an antioxidant capacity by lowering Malondialdehyde (MDA) an indicator of lipid peroxidation and stimulating the expression of Superoxide dismutase (SOD), a major antioxidant enzyme [20]. This claims that Fenofibrate makes apo B containing lipoproteins more resistant to

oxidative modifications [21]. Resveratrol has been reported to be a good antioxidant against the peroxidation of low density lipoproteins [22]. On the other hand presence of natural polyphenol in Resveratrol may possess antidyslipidemic property. The decreased level of TBARS in LPO and increased level of SOD may results due to antioxidant activity of combined Fenofibrate and Resveratrol in inhibiting LDL oxidation in the liver tissues of rats.

So the present research was designed on the basis of common Pharmacological target i.e. PPAR agonist against dyslipidemia and observation was made for complete lipid profile parameters like HDL, LDL, TC, TG and VLDL along with Antioxidant parameters like LPO (Lipid peroxidation) and SOD (Superoxide dismutase) *in vitro* assays.

In the near future, it is expected that we will be able to better understand the physiological role of PPAR's agonists like Fenofibrate and Resveratrol in altering lipid metabolism as in Dyslipidemia and other metabolic diseases. Attention is required in exploration of PPAR agonist which may be helpful in combating against metabolic diseases like Obesity, Atherosclerosis, Diabetes mellitus and many others.

Acknowledgement

The authors are grateful to Dr. Vipin V Dhote and Dr. Rajesh Pawar for providing guidance, resources and facilities which were of utmost importance for completion of our research work in the campus of Pharmacology department of VNS Faculty of Pharmacy, Bhopal, Madhya Pradesh, India.

References

1. Jayabalan S, Palayan M. Antihyperlipidemic activity of Sapindus emarginatus in Triton WR 1339 induced albino rats. Res J Pharm Tech 2009; 2: 319-323

2. Sharma N, Garg V. Antidiabetic and antioxidant potential of ethanolic extract of Butea monosperma leaves in alloxan induced diabetic mice. Ind J Biochem Biophys 2009; 46: 99-105

3. Nanji AA, French SW. Alcoholic beverages and coronary heart diseases. Atherosclerosis 1986; 60: 189-197

4. Yugarani T, Tan BK, The M, Das NP. Effects of polyphenolic natural products on the lipid profiles of rats fed high fat diets. 1992; 27: 181-186

5. Fauconneau B, Waffo P, Hugent F, Barrier L, Decentit A & Merillon JM. Comparative study of radical scavengers and antioxidant properties of Phenolic compound from vitis vinefera cell cultures using in vitro tests. Life Sci 1997; 61: 2103-2110

6. Frankel EN, Waterhouse AL & Kinsella JE. Inhibition of human LDL oxidation of Resveratrol. 1993; 341: 1103-1104

7. Kimura Y, Okuda H & Arichi S. Effects of stilbenes on arachidonate metabolism in leucocyte. Biochem Biophys Acta 1985; 834: 275-278

8. Andrew C & Christopher K. PPAR and LXR dependent pathways controlling lipid metabolism and the development of atherosclerosis. J Lip Res 2004; 45: 2161-2169

9. Schoojans K, Staels B, Auwerx J. Role of PPAR in mediating effects of fibrates and fatty acids on gene expression. J Lipid Res 1996; 37: 907-925

10. Sugden MC, Caton PW, Holness MJ. PPAR control : its SIRTainly as easy as PGC. Jour of Endo 2010; 2: 93-104

11. Miles PD, Barak Y, Evans RM, Olefsky JM. Effects of heterozygous PPAR gamma deficiency and TZD treatment on insulin resistance associated with age and high fat feeding. Am Jour Physio Enocr Metab 2003; 284: 18-26

12. Lagouge M *et al*. Resveratrol improves mitochondrial function and protects against metabolic diseases by activating SIRT-1 and PGC-1α. Cell 2006; 127: 1109-1122

13. Picard F *et al*. SIRT-1 promotes fat mobilization in white adipocytes by repressing PPAR-γ. Nature 2004; 429: 771-776

14. Kumar D, Parcha V, Maithani A. Combined effect on antihyperlipidemic activity of *Bauhinia variegate* and *Salradora oleoides* in Triton WR 1339 induced hyperlipidemic rats. World Jour Pharm Sci 2014; 2: 428-435

15. Marier JF, Vachon P, Gritsas A, Zhang J, Moreau JP, Ducharme MP. Metabolism and disposition of Resveratrol in rats: Extent of absorbtion, gluuronidation and enterohepatic recirculation evidenced by a linked rat model. Jorn Pharmacol Exp Therap 2002; 302: 369-373

16. Byers SO, Freidman M, Sugiyama T. Triton hypercholesterolemia: Cause or consequence of augmented cholesterol synthesis. Am Jour Physio 1963; 204: 1100-1102

17. Otway S, Robinson D. The use of a non ionic detergent (Titon WR 1339) to determine rates of Triglycerides entry into the circulation of the Rat under different Physiological conditions. Jour Physio 1967; 190: 321-332

18. Marklund S, Marklund G. Involvement of the superoxide anion radical in the autoxidation of pyrogallol and a convenient assay for superoxide dismutase. Eur J Biochem 1974; 47: 469-474

19. Draper HH, Hadley M. Malondialdehyde (MDA) determination as index of lipid peroxidation. Methods Enzymol 1990; 186: 421-431

20. Olukman M, Sezer ED, Ulker S, Sazmen EY, Cinar GM. Fenofibrate treatment enhances antioxidant status and attenuates endothelial dysfunction in Streptozotocin induced diabetic rats. Exp Diabetes Res 2010

21. Sliwa A, Jozwik A, Fronczyk W, Guszkiewicz A, Kolataj A. Effect of lysosomal system in subcellular fractions of mouse kidney. Anim Sci Pap Rep 2004; 22: 237-245

22. Tadolini B, Julian C, Piu L, Franconi F, Cabrini L. Resveratrol inhibition of lipid peroxidation. Free Radical Research 2000; 33: 105-114

Tables

Table 1: Comparative effect of Fenofibrate and Resveratrol combination on Total cholesterol (TC) and Triglycerides (TG) in Triton WR 1339 induced dyslipidemic rats of each group on day 8.

Sl. No.	GROUPS	(TC) mg/dl ±SEM	(TG) mg/dl ±SEM
1	Normal (CMC-0.5%)	76.85±0.71	70.81±0.74
2	Negative (Triton WR 1339-250 mg/kg)	87.00±0.96**	84.94±1.11**
3	Standard (Fenofibrate-65 mg/kg)	65.55±0.99	67.01±1.19
4	Treatment 1 (Resveratrol-50 mg/kg)	67.86±0.97	68.35±0.89
5	Treatment 2 (Fenofibrate + Resveratrol)	62.58±0.83**	61.78±0.69**

TC & TG levels were estimated by Standard methods. Values are expressed as mean ± SEM for 4 animals in each group. **P<0.01 was considered as statistically significant, when Negative Triton WR 1339 treated groups was compared with Treatment 2 group (Fenofibrate + Resveratrol).

Table 2: Comparative effect of Fenofibrate and Resveratrol combination on High density lipoprotein (HDL), Low density lipoprotein (LDL) and Very low density lipoprotein (VLDL)

in Triton WR 1339 induced dyslipidemic rats of each group on day 8.

Sl. No.	Group	Normal (0.5% CMC)	Negative (TR-250)	Standard (FB-65)	Treatment 1 (RSV-50)	Treatment 2 (FB+RSV)
1	HDL	40.11±0.70	32.87±0.90**	46.57±1.16	45.26±0.78	48.30±0.82**
2	LDL	29.79±1.40	35.77±0.82**	25.96±1.02	26.74±0.81	23.48±0.93**
3	VLDL	13.22±0.72	15.20±0.90**	11.90±0.64	12.36±0.54	11.60±0.54**

HDL, LDL & VLDL levels were estimated by Standard methods. Values are expressed as mean ± SEM for 4 animals in each group. **P<0.01 was considered as statistically significant, when Negative Triton WR 1339 treated groups was compared with Treatment 2 group (Fenofibrate + Resveratrol).

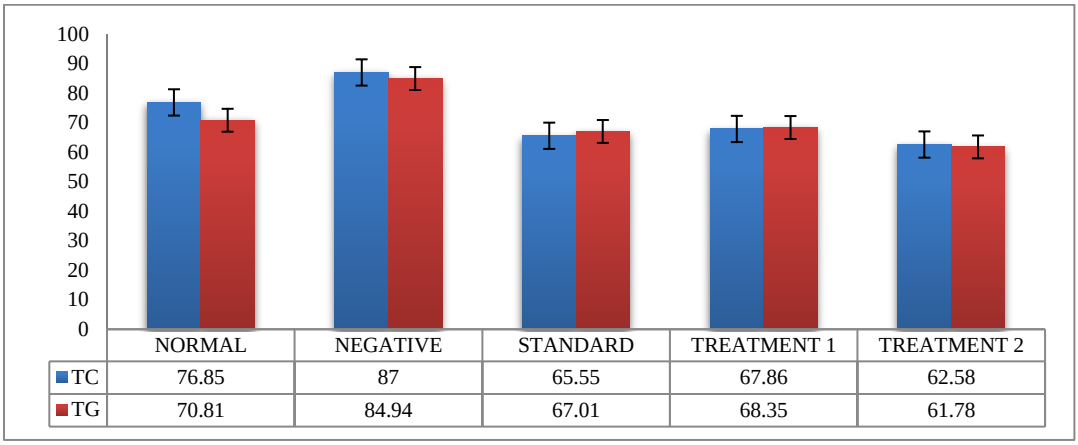
Table 3: SOD (Superoxide dismutase) and LPO (Lipid peroxidation) level of Liver tissue homogenate.

Sl. No.	Groups	SOD (IU/mg of Protein)	LPO (MDA nmol/mg of Protein)
01	Normal (0.5%CMC)	19.06±1.06	0.19±0.06
02	Negative (Triton WR 1339)	11.86±1.25**	0.30±0.01**
03	Standard (Fenofibrate-65 mg/kg)	20.67±1.43	0.18±0.06
04	Treatment 1 (Resveratrol-50 mg/kg)	17.74±1.85	0.24±0.05
05	Treatment 2 (Fenofibrate + Resveratrol)	19.84±1.58**	0.18±0.01**

SOD and LPO levels were estimated by Standard methods. Values are expressed as mean ± SEM for 4 animals in each group. **P<0.01 was considered as statistically significant, when Negative Triton WR 1339 treated groups was compared with Treatment 2 group (Fenofibrate + Resveratrol).

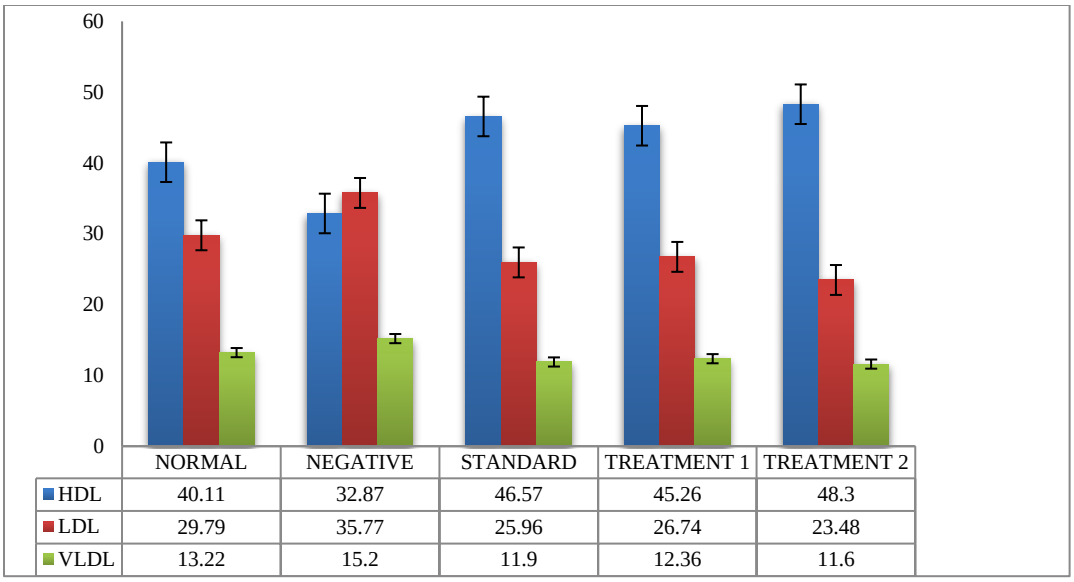
Figures

Figure 1: Effect of Fenofibrate and Resveratrol on serum Total cholesterol (TC) and Triglycerides (TG) in Triton WR 1339 induced dyslipidemic rats on day 8. (n=4. All data subjected to one way analysis of variance followed by Dunnett's test. **P<0.01 considered significant as compared to Negative group.



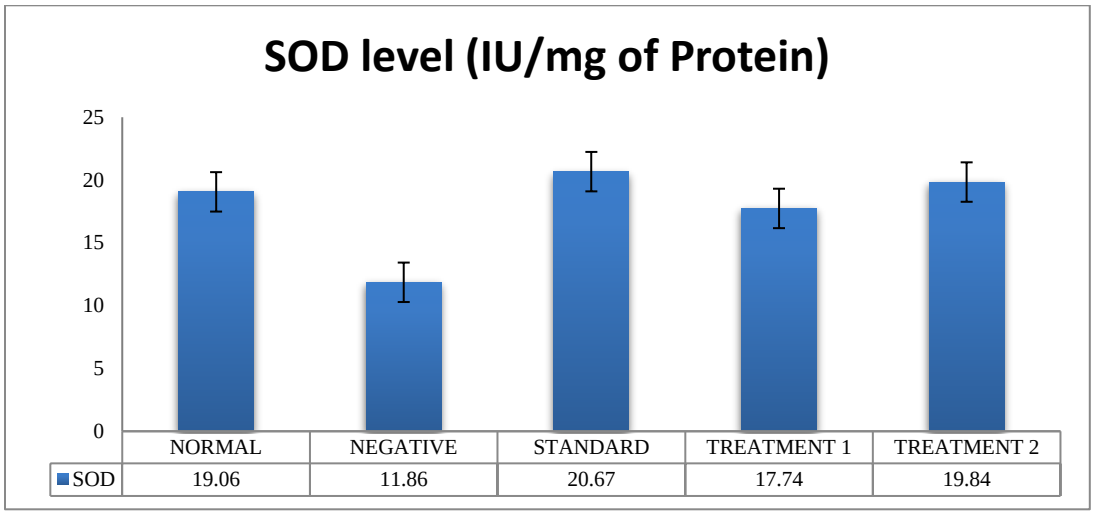
	NORMAL	NEGATIVE	STANDARD	TREATMENT 1	TREATMENT 2
TC	76.85	87	65.55	67.86	62.58
TG	70.81	84.94	67.01	68.35	61.78

Figure 2: Effect of Fenofibrate and Resveratrol on serum High density lipoprotein (HDL), Low density lipoprotein (LDL) and Very low density lipoprotein (VLDL) in Triton WR 1339 induced dyslipidemic rats on day 8. (n=4. All data subjected to one way analysis of variance followed by Dunnett's test. **P<0.01 considered significant as compared to Negative group).



	NORMAL	NEGATIVE	STANDARD	TREATMENT 1	TREATMENT 2
HDL	40.11	32.87	46.57	45.26	48.3
LDL	29.79	35.77	25.96	26.74	23.48
VLDL	13.22	15.2	11.9	12.36	11.6

Figure 3: Effect of Fenofibrate and Resveratrol on SOD level in Triton WR 1339 induced dyslipidemic rats on day 8. (n=4. All data subjected to one way analysis of variance followed by Dunnett's test. **P<0.01 considered significant as compared to Negative group).



	NORMAL	NEGATIVE	STANDARD	TREATMENT 1	TREATMENT 2
SOD	19.06	11.86	20.67	17.74	19.84

Figure 4: Effect of Fenofibrate and Resveratrol on LPO level in Triton WR 1339 induced dyslipidemic rats on day 8. (n=4. All data subjected to one way analysis of variance followed by Dunnett's test. **P<0.01 considered significant as compared to Negative group).