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HYPOLIPIDEMIC AND ANTI-OXIDATIVE ACTIVITIES OF *TERMINALIA ARJUNA* BARKS AGAINST INDUCED HYPERLIPIDEMIC ALBINO RATS

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ABSTRACT

One of the preeminent factors of Coronary heart disease contemplated to be Hyperlipidemia. High cholesterol additives activates hyperlipidemia and Oxidative stress in rats eliciting biochemical and toxicological changes. Traditionally, *Terminalia arjuna* bark consumed as medicinal agents for various purposes, mainly as cardiac protectives. The present data experiments the influences of *Terminalia arjuna* ethanolic extract in chow(5% cholesterol+0.5% cholic acid) induced hyperlipidemia rats in compare with free plant additive control group rats. The hyperlipidemia aftermath assessed by evaluating the lipid profile and oxidative stress biomarkers. The test results showed that the *Terminalia arjuna* bark possessed significant cutback of the cholesterol level, Low density lipoprotein and elevated High density lipoprotein in Hyperlipidemia model rats. Free radicals cut off capabilities of *T. arjuna* has observed by significantly decreased levels of Malondialdehyde and Superoxide dismutase in induced hyperlipidemia rats. The blood inquiry of all tested groups revealed non-significant alteration by *T. arjuna* bark extract. The ethanolic extract of *Terminalia arjuna* bark (500 mg/kg body weight) possessed positive effect on the lipid profile and could serve as good antioxidant agent incorporating into Certain recipes as edible materials hyperlipidemia and high oxidative stress patients as they rely on chemical drugs drugs for too many periods.

*Keywords***:** Heart diseases, oxidative stress, Hyperlipidemia, *Terminalia arjuna*,

Introduction

Cardiovascular diseases are the main cause of disabilities and mortalities worldwide, majorly resulted from metabolic lipid disorder called Hyperlipidemia (Torben Jørgensen *et al.,* 2013). A disorder may be due to hereditary cause or dis functioning of kidney, endocrine and liver. To avert future snags of heart (atherosclerosis, coronary heart disease, and stroke), It's important to decrease Hyperlipidemia in virtue the elevated totalcholesterol, VLDL-cholesterol, triglyceride, LDL-cholesterol and declined HDL-cholesterol, as a consequence will head to ischemic heart disease or in more series cases heart failure (Davey Smith and Pekkanen, 1992)

Hyperlipidemia contributes to rising oxidative stress leading to significant production of oxygen free radicals, as scientists revealed that in long run oxidative stress occurs in virtue of excessive free radicals. Which will eventually head toward Heart problems and cardiovascular diseases if the symptoms not restrained (Mishra *et al.*, 2011). The superoxide dismutase (SOD) malondialdehyde (MDA) inquiry contemplated as a markers of oxidative stress and can rely on to quantify free radicals acquired by the body through many cause like hyperlipidemia (P. Kangari *et al.*, 2018).

Flavonoids and alkaloids are natural plant products can be consumed as alternative of drugs for treatment of hyperlipidemia because of synthetic drugs possessing further side effects (diarrhoea, gastric irritation, flushing, hyperuricemia, nausea, myositis and skin dryness (Speight and Avery's, 1977).

Terminalia arjuna Roxb. Is belonging to Family Combretaceae, its mainly effective components are triterpenoid, saponins (arjunolic acid arjunic acid, arjunglycosides and arjungenin), flavonoids (arjunone, luteolinand arjunolone), tannins, cardenolide, gallic acid, ellagic acid, oligomeric proanthocyanidins (OPCs), magnesium, zinc and copper, phytosterols, calcium (Miller, 1998). Traditionally consumed as medical agent for curing wounds, heart diseases and has been used as antioxidants, anticarcinogenics and anti-hypercholestrolemia. The prevailing inquiry targets to represent the interference of *T. arjuna* in reducing hyperlipidemia and oxidative stress markers in Chow induced hyperlipidemia albino rats (Dwivedi and Jauhari, 1997).

Materials and Methods

Collection and Identification of Plant Materials

The bark of *Terminalia arjuna* was obtained from the Southern part of India (Madurai District, Tamil Nadu), and the Pharmacognostic authentication was done by the Department of Plant Sciences, University of Madras [vide voucher no 031].

Ethanolic extraction of *Terminalia arjuna*

The bark was air dried under shade. The dried and pulverized bark powder was extracted with ethyl alcohol (90%) by hot continuous percolation over 72 hours by using Soxhlet apparatus. The alcoholic extract was filtered and concentrated to a dry mass by using vacuum distillation and evaporation. A dark brownish red shiny crystal-like residue of 13.89% (w/w) yield was obtained (Kaur *et al.*, 2001).

Collection and Maintenance of Test Animals

Forty male albino rats were used in this study. All rats were 8-10 weeks of age and weighting about 200-250 grams. The experiment was achieved between (25-july-2018 and 2-February-2019). Animals were bred and housed in the animal house of Biology Dept. College of Education, Salahaddin University. During the experimental period four or five animals were kept in each cage. The animals were housed under laboratory conditions of 22±2 ºC and 12h light: 12h dark (Coskun *et al.*, 2004). At the beginning of the experiment the animals were given standard rat pellet and tap water ad libitum. The standard pellet has following composition: wheat 66.6%, soya 25.6%, oil sun flower 4.4%, limestone 1.5%, salt 0.63%, methionine 0.15%, choline chloride 0.06% and trace elements 0.05% (George, 2000). To induce hyperlipidemia in rates chow is given (5% cholesterol+0.5% cholic acid) for six week which is one of the most commonly used animal models for the screening of hypolipidemic property of the drugs (Xie *et al.*, 2012).

Experimental design

The rats have been distributed into five groups, each of eight individuals. First group received standard diet throughout the experimental period (Control). The second group represented the model, as the laboratory rats were given chow (5% cholesterol+0.5% cholic acid) for six weeks (Model). The third group received standard diet chow (5% cholesterol+0.5% cholic acid) and diet containing *Terminalia arjuna* bark extract at the concentration of 500 mg/kg body weight.

Determination of Serum Lipid Profiles

Detection of Serum Total Cholesterol, Serum LDL-C, Serum Triglyceridem, Serum HDL-Cholesterol done using Biolabo reagent kit/France/Cobas C111- Roche/Germany based on method at which the color intensity of the dye formed is directly proportional to the concentration of tested parameters (Thomas, 1998).

Hematological Analysis

Red blood cells (RBCs) count, haemoglobin (Hb) concentration, packed cell volume (PCV), white blood cells (WBCs) count, platelets (PLTs) count, mean corpuscular volume (MCV), mean corpuscular haemoglubin (MCH), mean corpuscular haemoglobin concentration (MCHC) and mean platelet volume (MPV) were determined automatically by automated hematology analyzer (System model: K-1000, Japan) (Greisenegger, 2004).

Oxidative Stress Evaluation

MDA reacts with TBA to produce a pink colored end product when heat and acid exist. The intensity of the color at 532 nm corresponds to the level of lipid peroxidation in the sample. The level of serum MDA was determined of spectrophotometrically with a thiobarbituric acid solution the kit assay Rat SOD-1 level is used and the color change is measured spectrophotometrically at a wavelength of 450 nm. After that concentration of Rat SOD-1 in the samples is detected by comparing the O.D. of the samples to the standard curve (Kangari *et al.,* 2018).

Statistical Analysis

All data are expressed as mean ± standard. The software (SPSS Version 19) was used to find the error of means and statistical analysis. Statistically the p<0.05 was considered to be significant at which changes in the statistics were found using Duncan test for multiple comparisons after ANOVA.

Results

Serum total cholesterol was significantly (p<0.01) increased (134.86±9.83 mg/dl) in hyperlipidemic rats when compared to the control group (61.42±3.18 mg/dl). Also treatment of hyperlepidemic rats with *Terminalia arjuna* bark (77.14±2.61 mg/dl). Hyperlipidemic rats were associated with significantly elevated (p<0.01) levels of serum triglyceride (164.86±8.37 mg/dl) in comparison to the control group (57.00±2.51 mg/dl). This elevation decreased significantly by treatment of hyperlipidemic rats with *Terminalia arjuna* (85.29±9.62 mg/dl) Figure(1).There was no significant difference between hyperlipidemic rats and treated groups on serum HDL levels. The hyperlipidemic rats had significantly elevated (p<0.01) levels of serum VLDL (32.97±1.67 mg/dl) in comparison to the control group (11.40±0.50 mg/dl)Figure(1). This elevation decreased significantly by treatment of hyperlipidemic rats with *Terminalia arjuna* (17.05±1.92 mg/dl)(table 1).

Table 1 : Effects of Terminalia arjuna on Serum Lipid profiles in Hyperlipidemic Rats

Parameters / Tested Groups	Cholesterol (mg/dl)	Triglyceride (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)	VLDL-C (mg/dl)
G1 (Control)	61.42±3.18 bc	57.00±2.51 C	22.54±2.14 a	9.14±0.40 c	11.40±0.50 C
G2 (Hyperlipidemic) Rats	134.86±9.83 a	164.86±8.37 a	25.33±1.81 a	23.22±1.80 a	32.97±1.67 A
G3 (*Terminalia arjuna*)	77.14±2.61 b	85.29±9.62 b	33.37±1.96 a	15.28±1.13 b	17.05±1.92 B

The same letters within column mean no significant differences and the different letters mean significant differences.
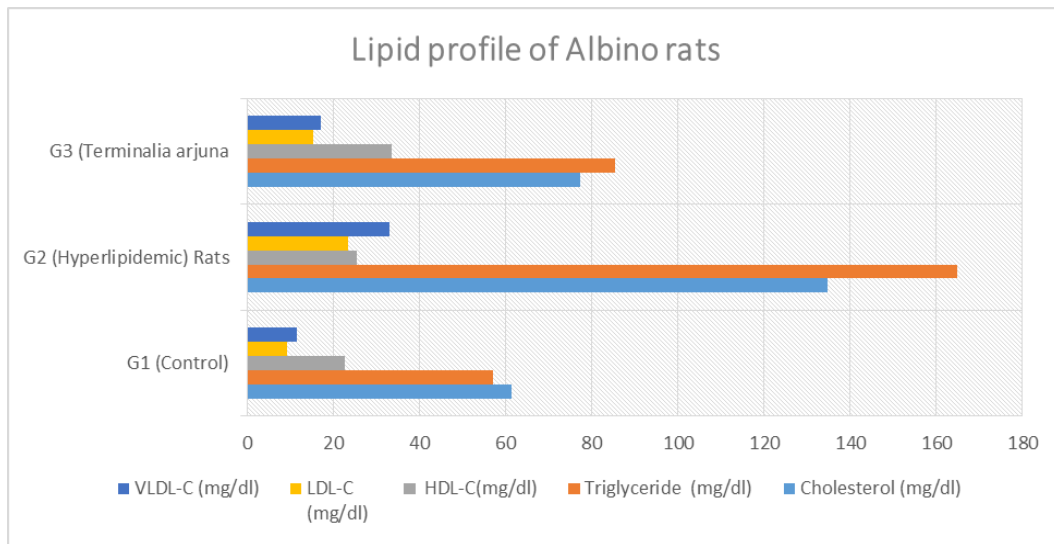
Fig. 1 : Effects of *Terminalia arjuna* on Serum Lipid profiles in Hyperlipidemic Rats.

The present data showed that serum levels of MDA in hyperlipidemic group (5.64±0.30μmol/L) were significantly different in compare with control group rats (3.28±0.19 μmol/L) and *Terminalia arjuna* treated group (3.66±0.12 μmol/L) (Table 3). The SOD levels in hyperlipidemic group (4.01±0.19 U/ml)were found to be Significantly different in compare with control group (2.14±0.18 mg/dl) and *Terminalia arjuna* treated groups (2.82±0.24 U/ml).

Table 2 : Effects of *Terminalia arjuna* on Serum MDA and serum SOD in Hyperlipidemic Rats

Parameters / Tested Groups	MDA (μmol/L)	SOD (U/ml)
G1 (Control)	3.28±0.19 b	2.14±0.18 b
G2 (Hyperlipidemic) Rats	5.64±0.30 a	4.01±0.19 a
G3 (*Terminalia arjuna*)	3.66±0.12 b	2.82±0.24 b

The same letters within column mean no significant differences and the different letters mean significant differences.

Cholesterol and cholic acid diet given to the animals for six weeks insignificantly changed RBC count (6.63±0.17 x106/μL) when compared to control group (6.87±0.17 x106/μL). However, *Terminalia arjuna* (7.24±0.05 x106/μL) treatments produce a significant change in the mean value of RBC count (Table 3). Hemoglobin concentration (Hb) of hyperlipidemic rats did not alter hemoglobin concentration significantly (11.85±0.28 g/dl) when compared with control group (12.80±0.25 g/dl). Additionally, treatments of hyperlipidemic rats with *Terminalia arjuna* (14.30±0.20 g/dl)

showed a significant alteration in comparison to untreated hypercholesterolemic rats. Packed Cell Volume (PCV) Hyperlipidemias in rats (36.40±1.25 %) significantly differed when compared with control group (40.38±0.94 %). *Terminalia arjuna* (45.11±0.49 %) administration have produced significant increase (p<0.05) in PCV value in comparison to hyperlipidemic rats. The results showed that PLTs did not significantly changed in hyperlipidemia rats and hyperlipidemia group treated with *Terminalia arjuna*, when compared with control group (Table 3).

Table 3 : Effects of *Terminalia arjuna* on BCs, Hb, PCV and PLTs in Hyperlipidemic Rats

Parameters / Test Groups	RBCs (x10⁶/μL)	Hb (g/dl)	PCV (%)	PLTs (x10³/μL)
G1 (Control)	6.87±0.17 bc	12.80±0.25 b	40.38±0.94 b	455.42±21.57 a
G2 (Hyperlipidemic) Rats	6.63±0.17 c	11.85±0.28 b	36.40±1.25 c	469.28±24.42 a
G3 (*Terminalia arjuna*)	7.24±0.05 ba	14.30±0.20 a	45.11±0.49 a	460.71±23.03 a

The same letters within column mean no significant differences and the different letters mean significant differences.
The hyperlipidemic rats and hyperlipidemic group treated with *Terminalia arjuna* did not showed
Significant differences in the level of MCV, MCH and MPV when compared with control group.
The level of MCHC in hyperlipidemia in rats (6.14±0.30 g/dl) changed significantly when compared to the control group (5.15±0.24 g/dl). Also The MCHC value significantly changed in hyperlipidemia treated with *Teminalia arjuna* group (4.04±0.13 g/dl) in compared to the untreated hyperlipidemic group.

Table 4 : Effects of Terminalia arjuna onMCV, MCH, MCHC and MPV in Hyperlipidemia Rats

Parameters Test Groups	MCV (fl)	MCH (Pg)	MCHC (g/dl)	MPV (Pg)
G1 (Control)	18.58±0.16 b	31.74±0.30 a	5.15±0.24 b	58.65±0.62 a
G2 (Hyperlipidemic) Rats	19.30±0.11 a	31.90±0.15 a	6.14±0.30 a	60.52±0.17 a
G3 (*Terminalia arjuna*)	19.09±0.11 a	3146±0.15 a	4.04±0.13 d	60.02±0.27 a

The same letters within column mean no significant differences and the different letters mean significant differences.

Discussion

Hyperlipidemia contemplated as one of central initiative of atherosclerosis and other related health problems like ischemic cerebrovascular disease, coronary heart disease. Hypercholesterolemia mainly elevated Low density lipoprotein cholesterol (LDL) has known to play role in the imitation and complications of heart diseases (R. H. Nelson, 2013).

The result of these inquiry exhibits that *Terminalia arjuna* bark extract capable of reducing serum total cholesterol, triglyceride, LDL and VLDL level of hyperlipidemia rats. These inquiry was acknowledged by previous probes (Sharma *et al.*, 2012) declaring significant cutback in serum total cholesterol and triglyceride of hyperlipidemia rats consuming *Terminali arjuna* barks. In contrast, a study on Triton WR-1339 induced hyperlipidemia rats explained the influences of *T. arjuna* on the lipid profile at which alteration fixed up to 30h and at end of48h, lipid level normalized (Chander *et al.,* 2004). Previously, Lipid lowering Efficacy and capturing free radicals by the *T. arjuna* has been studied by (Subramaniam *et al.,* 2011) in PX-407 model rats for longer durations. Our result also agreed with the findings done by (Patil *et al.*, 2011). In contrast with our findings, a research by (Asha and Taju, 2011) demonstrated that bark extract of *Terminalia arjuna* (6.75 mg/kg of body weight) significantly increased of HDL-cholesterol and decreased of serum total cholesterol, triglyceride, LDL-cholesterol and VLDL. In accordance, a significant Hypolipidemia effect of *Terminalia arjuna* in chow induced hyperlipidemia rabbits was declared by (Shaila *et al.*, 1997). Researchers have explained the hypolipidemia role and heart preserving role might be contributed to the presence of a plant sterols mainly beta sitosterol (Becker *et al.*, 1993).

The present data demonstrated that bark extract of Terminalia plant significantly reduced malondialdehyde level of hyperlipidemic rats. These results are agreed with the study of (Bindu Sharma and Farhan Ahmad Khan, 2014) concluded that extract of *Terminalia arjuna* bark significantly decreased lipid peroxidation and malondialdehyde (MDA) levels in Benzo[a] pyrene induced lung toxicity rats, also declaredthat the antioxidant activity of the extract performed by the amendment of oxidative stress. A research work by (Asha and Taju, 2012) also showed that Lipid peroxidase levels of patients suffer from coronary heart diseases decreased significantly by consuming (500mg) Terminalia bark extracts. Similarly, The antioxidant activity of the ethanolic extract of *T.arjuna* in rates with alloxan induced oxidative stress has been declared by (Raghavan and Kumari, 2006). The current inquiry delivered a significant cutback for the SOD levels in *T.arjuna* treated rats. The data

showed accompanied by previous research work (Shivananjappa, 2006) declaring the antioxidant role of *T.arjuna* through reducing SOD and other oxidative stress markers in induced oxidative stress for HepG2 cell model. Similarly, (Mahima and Begum, 2013) showed the decreasing of Lipid peroxidation by antioxidant effect of *T.arjuna* bark in rats with N-nitrosodiethylamine induced oxidative stress. A scientific probe by (Mahima and Begum, 2013) verified that *T.arjuna* barks are full of polyphenols may play as pro oxidant, which could deteriorate the activities of SOD. Previously researchers (S.K. and U.R, 2010) showed that presence of flavonoids and Triterpenoids as main antioxidant constituents of *T.arjuna* play vital role in reducing oxidative stress in patients with cardiovascular diseases.

Hematological parameters (RBCs, Hb, PCV, PLTs, MCV, MCH, MCHC and MPV) of hyperlipidemic rats was not significantly changed by daily administration of *Terminalia arjuna* bark extract, this result was agreed by a study reported mentioning that orally administration of plant extract at specific dosage according to body Wight for a period of six months, didn't possessed significant alteration on hematological parameters of rats (Talwar *et al.,* 2013). Previously scientists verified that extraction of *T.arjuna* in constantly changed of the heamatological parameters in the *T.arjuna* treated fishes (Suely *et al.*, 2016).

Conclusion

The Performed research can conclude that the ethanolic extract of *Terminalia arjuna* barks can serve as effective hypolipidemidic agents as shown to be efficient in reducing (total cholesterol Triglycerides, LDL, VLDL) and notably increased good cholesterol (HDL) in induced hyperlipidemia rates. *T. arjuna* as active agent seem to have antioxidant potentiality in virtue of its role in cutback of MDA and SOD levels as shown in induced hyperlipidemia rats. The current probe suggests further exploring on mentioned genotypes for potentiality of being used as active medicinal agent bearing positive less side effects on drug based peoples suffering from elevated lipid profile and increased oxidative stress.

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