Anti-atherogenic effect of Terminalia arjuna through suppressing adipocytokines and cardiac markers

Subasini Uthirapathy, Esra T. Anwer, Javed Ahamad, Omji porwal, and Muath Sh. Mohammed Ameen

Faculty of Pharmacy, Pharmacology Department, Ishik University, Iraq.

***Corresponding author (oral Presentar)**

Dr. Subasini Uthirapathy
Assistant Professor
Department of Pharmacology, Faculty of Pharmacy,
Ishik University, Erbil, Kurdistan Region, Iraq

ABSTRACT: Atherosclerosis results from slow deposition of fatty materials in media and large arteries leading to mortality worldwide. Terminalia arjuna is an herb of Combretaceae family which contains flavonoids, terpenoids, cardiac glycosides with high antioxidant properties. This study was conducted to determine the effect of hydroalcholic extract fraction of T. arjuna on blood lipids and atherosclerosis in hyperlipidemia Wistar rats model induced by atherogenic diet. In the hyperlipidemia animal model, the rats received hydroalcoholic extract of T. arjuna treatment exhibits noticeable reduction in total cholesterol, total triglycerides and elevation in high density lipoprotein cholesterol (HDL-C). A result reveals that T. arjuna considerably decreases TC, TG and increases antioxidant levels. Metabolic marker of homocysteine, pro-inflammatory (adipocytokines) markers such as C-reactive protein, leptin and IL6, anti-inflammatory marker like adiponectin, fibrinolytic factor such as plasminogen activator (PA) and plasminogen activator inhibitor (PAI) that are association with atherogenic diet consumption. Hence, T. arjuna extract can effectively prevent the progress of atherosclerosis. This is possible due to the effect of T. arjuna having triterpenoids, cardiac glycosides alkaloids and flavonoids. The hydroalcoholic extract of T. arjuna was found to possess remarkable hypolipidemic activity.

Keywords: Terminalia arjuna; leptin; interleukin -6; homocystine; C-reactive protein; adiponectin; plasminogen activator

INTRODUCTION:

Atherogenic diets have distinct proatherogenic effects on gene expression and suggest a strategy to study the contribution of acute inflammatory response and fibrogenesis independently through dietary manipulation. A vast body of literature is available to demonstrate the various causative factors of early atherosclerosis and coronary heart disease. Endothelial dysfunction is the result of early development of atherosclerosis. Pro-inflammatory cytokines like TNF-, low level of endothelial nitric oxide and elevated level of C-reactive protein and Interleukins have shown a positive correlation with adverse cardiac events [1].

In addition to inflammatory markers, the formation of atherothrombotic plaques due to genetic and environmental factors produces variety of metabolic, biochemical, and endocrine abnormalities among the prone individuals [2]. The tissue plasminogen activator (tPA) and urokinase are two important enzymes which convert plasminogen into plasmin. This enzyme is primarily produced from vascular endothelial cells. tPA is inhibited by PAI-I and hepatic clearance of tPA. The level of tPA is strongly associated with PAI-I activity. The tissue plasminogen activator inhibitor (tPAI) has been recently emphasized for playing an important role in the removal of thrombi from the vascular system. It has been repeatedly observed that increased fibrinolytic activity includes adrenogenic agonist, vasopressin, bradykinin and histamine. These factors significantly change the cardiac output, coronary blood flow, vascular elasticity and permeability of the essential constituents [3]. Further, it is also noticed that Indian population has high level of plasminogen activator inhibitor in comparison to western countries. Similarly those individuals who have hypercholesterolemia show elevated level of plasminogen activated inhibitor [4]. Both tPA and PAI-I have a strong correlation with triglycerides. Univariate

regression analysis shows elevated level of tPA and PAI-I. The limited demographic studies, conducted among Indian population have shown the high prevalence of coronary heart diseases (CHD) in the society where high levels of both enzymes are estimated [5].

It is also noticed that early atherosclerotic changes are more pronounced among the chronic diabetes cases and among cases of familial hypercholesterolemia and hyperglycemia, and hyperleptinemia. Therefore, it is considered important to identify the early cases of atherosclerosis.

Hypercholesterolemia is the presence of high level of cholesterol in the blood. It is not a disease but a metabolic de-arrangement that can be secondary to many diseases and can contribute too many form of disease, mostly notably cardiovascular disease [6]. "Atherosclerosis" is the principle underlying cause of coronary heart disease, which is commonest cause of death in industrialized world, and of stroke and pheripheral vascular disease, which is also a significant cause of morbidity and mortality [7, 8].

Plant materials containing active compounds with chemically well-defined active substances, including chemically perfect isolated constituents of plants are not reflected to be herbal medicines [9]. Plant extracts isolated compounds are occasionally even more potent than known conventional drugs. It indicates that the researcher has stopped with just reporting the effect of plant chemical compounds and their outcomes are not interpreted into clinical research [10]. Taking these results advancing is compulsory to develop new drug molecule. Therefore further research into recognizing the active biomolecule, conducting preclinical and clinical studies is essential [7]. Recently, global attention has been focused towards the utilization of herbal remedies for the prevention and management of various risk factors for CHD. Early identification of various risk factors may be helpful in launching the preventive measures among the likely victims. The role of plant-based medicine has been recently emphasized by world health organization. This organization has provided guidelines for evaluation of safely and efficacy profile of plant based product. [11].

Terminalia arjuna (Roxb) is an ayurvedic and siddha plant with several medicinal values. It is commonly known as arjuna, bark, which is belongs to Combretaceae family comprising of nearly 200 species distributed around the world. Nearly 24 species of Terminalia have been reported from various parts of India, some selected species are T. arjuna, T. bellirica, T. bialata, T. catappa, T. elliptica, T. porphyrocarpa, T. mantaly etc. In India, T. arjuna is about 60 to 80 feet in height, buttressed trunk and horizontally spreading crown and drooping branches distributed in Burma, Mauritius, India and Sri Lanka.

It used for various complicated disease, treating wound healing, ulceration, lipid lowering, astringent effect, urinary tract infection, regulate hormone cycles, airway clear lung disease, used for all kinds of bleeding, cardiac tonic and antioxidant [4, 11, 12, 13, 14, 15]. The active phytoconstituents of fraction of T. arjuna include triterpenoids saponins, flavonoids, phenolic, and nutrients such as zinc, magnesium, copper and calcium. Administration of T. arjuna did not show any harmful adverse effect on hepatic, renal and haematological parameters (subasini et al., unpublished data) But the fraction of T. arjuna bark intense a high degree of anti-hyperlipidaemic and anti-atherogenic and anti-oxidant activities. Moreover, the hydroalocholic fraction of T. arjuna shows that better effects of multi targeted action of sitosterol as well as flavonoids action on the intestinal absorption of cholesterol and inhibiting HMG CoA enzyme respectively

MATERIALS AND METHODS:

Terminalia arjuna (TA) (Roxb) bark is collected from Tirunelveli, Tamil Nadu, India This plant barks are authenticated in Rabinat Herbarium, St. Joseph College, Trichy, Tamil Nadu, India. The voucher specimens are deposited in the CARISM herbarium and maintained as TA- 0048. All the TA barks are shade dried for 15 days and they are coarsely powdered using a pulverizer. Dried barks are subjected to hydroalcoholic extraction in the ratio of water: alcohol as 30:70, adopting cold percolation method. The extracts are then, dried in vacuum and stored in a refrigerator. The preliminary phytochemical analysis revealed that hydroalcoholic fractions contained tannins, penolics, sitosterol, anthraquinone glycosides, alkaloids and flavonoids.

Atherogenic diet

Atherogenic diet was rich in 30 % peanut oil and 5 % cholesterol. Atherogenesis is the formation of fatty materials plaque in the inner lining of epithelial cells of arteries and it is associated with primary and secondary atherosclerosis. Atherogenic diet promotes atheromas, it was induced inflammation of epithelial cells permeability, which leads to leakage of LDL-C to intima of arteries. Atheromas are the trademark of a cardiovascular disease called atherosclerosis.

Chemicals

Cholesterol, triglycerides, HDL cholesterol were procured from SRL SISCO laboratories, Mumbai. Leptin was procured from Randox laboratories and adiponectin chemicals were purchased from Sigma Chemical Co., St. Louis, MO, USA. Hs-CRP Apo-B Roche Diagnostic kits were purchased from SPINREACT and Himedia laboratories, Mumbai. All the other reagents used were of analytical grade. Standard drug - Atorvastatin's was purchased from pharmacy stop.

Animals & experimental protocol

Pre-clinical study has been carried out to evaluate the efficacy profile of TA in reducing the triglycerides. Accordingly 6 Albino rats of Wistar strain with an average body weight of 220.65 ±18.75 g are taken for the present trial. The age of the rats varied from 6-8 weeks. The rats are housed in polypropylene cages at room temperature. All animals are kept in one room and no other species being housed with them. The room is well ventilated with fresh air and normal temperature. The animals are distributed randomly into different groups as per protocol. Lipid profile and various pro-inflammatory markers like CRP, homocysteine, leptin, adiponectin, plasminogen activator and plasminogen activator inhibitor that are in association with atherogenic diet consumption are measured. All animals had free access to water and standard pelleted laboratory animal diet. This study was reviewed and approved by the Institutional animal ethical committee (Reg. No. 817/08/ac/cpcsea). The study is divided into 4 groups. First group normal control (normal laboratory diet), second group was atherogenic diet (rich in 30 % peanut oil and 5 % cholesterol) and third group was treated with atherogenic diet + hydroalcoholic extract fraction of TA (25 mg/kg/day). Fourth group was treated with atherogenic diet + atorvastatin drug (0.4 mg/kg/day).

Blood is taken by the heart puncture just prior to killing. The blood samples are centrifuged, and plasma is separated and frozen at – 80 ◦ C until needed for the assay.

Assay Methods

The total cholesterol, triglyceride, C-reactive protein assessed by immunoturbidometric method (using RANDOX, UK kits - catalogue no. CH 201) using cholesterol oxidase – PAP assay. Apolipo (B) and hs- CRP, assessed by immune assay method on a Hitachi modular analyzer. Serum adiponectin level, IL6 and leptin metabolism using ELISA assay, Homocysteine level were measure using DPC kits on immunlite – 2000 auto analyzer. Plasminogen activator inhibitor, tissue plasminogen antigen are measured by enzyme-linked immunosorbent assay (ELISA) (16)

Estimation of (TBARS) - The levels of lipid peroxidation in tissues were estimated by the method of (17). Assay of Catalase (CAT, EC. 1.11.1.6) - The activity of catalase was determined by the method of (18). Assay of glutathione peroxidase (GPX) (GPX, EC 1.11.1.9) - Glutathione peroxidase was estimated by the method of (19). Estimation of Reduced glutathione (GSH) was estimated by the method of (20).

Calculations

Statistical analysis is performed using students 't' test by SPSS software 9.05. Results are expressed as mean ± SD. from six rats in each group. P values <0.05, 0.01 are considered as significant.

RESULTS:

Lipid Profile

The efficacy profile of hydroalcoholic extract fraction of T. arjuna is evaluated in experimental animals. A comparative study is conducted with standard drug is given along with atherogenic diet in one group of 6 rats and 6 rats are treated with atherogenic diet along with T. arjuna for a period of 30 days. A group of 6 animals is served as normal control and 6 animals are kept on only atherogenic diet. This study has suggested that there is drastic reduction in the various contents of lipid profile i.e. total cholesterol and triglycerides following conventional treatment statin [21]. The pattern of reduction in total cholesterol, and triglycerides content following T. arjuna treatment along with atherogenic diet treated animals is also significant but the difference is not so marked, as it is in conventional treatment group (Table 1 and 2). But keeping the adverse effect of standard drug statin, we have to move the phytopharmaceuticals. Drugs, T. arjuna is a better choice of drug for the management of hyperlipidemia responsible for type 4 atherosclerosis and endothelial dysfunction manifesting in ischemic heart disease [18]. So many authors result displayed that T.arjuna having powerful hyperlipidemia and antioxidant properties due to rich constituents of secondary metabolites such as triperpenoids, tannins, flavonoids and glycosides.

Apolipo B & Homocysteinets

In the present experimental series, the apolipo B content was significantly increased following atherogenic diet group of animals. Following 30 days of T. arjuna and statin treatment which increase in the level of Apolipo B was not so significant changes when given along with atherogenic diet. Thus, the anti-atherogenic property of T. arjuna is proven in the Fig. 1A. The non-lipid factor of homocysteine level, when measured in experimental rats, has also shown elevated level in the group-II whereas atherogenic diet was given and the homocysteine level was increased significantly in group-III and IV where the animals were fed atherogenic diet and treated with the drug T. arjuna and statin. More beneficial effect was observed in statin treatment group of animals (Fig. 1B). Similar report was also published in the literature [22].

Antioxidant effect

Table 4 shows the antioxidant activity of the drug in heart homogenate after 30 days. The antioxidants such as catalase, GSH, and GST level were significantly decreased ($p<0.05$) in heart of disease induced rats when compared to normal group. Then these levels are significantly increased ($p>0.05$) in the drug (TA) treated groups. But the level of TBAR showed reverse effect of above parameters. The level is significantly decreased ($p<0.05$) after the administration of drug. The fourth group with statin showed significant results when compared with 2nd group of atherogenic diet. Specific enzymes such as superoxide dismutase, catalase and glutathione peroxidase can protect the organism against the reactive oxygen species effects [23].

Pro-inflammatory markers

The result was obtained out of the study indicates that the inflammatory markers like C-reactive protein and interleukin-6 significantly increased after 15th and 30th days following atherogenic diet consumption among the rats. But the level of CRP and IL6 was quite less in the group III where the atherogenic diet was given along with T. arjuna and standard drug [20,28]. The trend of increase in the level of CRP was significantly less in standard group of drug when compared to T. arjuna group of animals (Fig. 2A & B).

Leptin

Fig. 2C summarizes the blood leptin level in the atherogenic diet was given for 30 days continuously to the experimental rats. A significant reduction of leptin level was measured in group III and group IV. Whereas, the II group of animals have high level of leptin when compared with normal group of animals. This results were suggested that T. arjuna have a potential anti-obesity and anti- atherogenic effect [24, 25].

Anti-inflammatory markers

Adiponectin when estimated in this series of experimental study has exerted an inverse relationship with atherogenic diet consuming rats. A decrease in the level of adiponectin was noticed following atherogenic diet that has increased under the influence of T. arjuna and standard group of animals. Result shows that decrease in adiponectin is significantly less where the animals were treated with drugs along with atherogenic diet. More beneficial role was noticed in statin group of animals than the T. arjuna treated animals (Table 3). T. arjuna having antioxidant property which stimulate the protein hormone, it may be leads to increase the level of Adiponectin which might be reduce the inflammation [26].

Fibrinolytic factors

The fibrinolytic factors like tissue plasminogen activator and plasminogen activator inhibitor have shown elevated level among hyper-triglyceridemic animals. T. arjuna slightly reduces the elevated level of TPA and PAI at 30 days' treatment. T.arjuna treatment group animals does not show any significant value for PAI at 30 days. Both T. arjuna and standard drug statin treatment does not reduce the rise in the level of TPA at 15 days which was displayed in Fig. 3A & B.

Table 1: Role of hydro alcoholic fraction of TA on TGL level among experimental animals.

Groups	No. of Animals	Triglyceride (mg/dl)		
		Initial	After 15 days	After 30 days
Normal control	6	39.60±7.98 a	37.80±8.60 a	41.11±5.26 a
Atherogenic diet	6	44.58±7.80 b	589.66±88.95 d	648.65±92.01 d
Atherogenic diet+ TA	6	40.82±6.85 a	180.54±30.01 c	210.25±36.30 c
Atherogenic diet+ Statin	6	47.68±6.80 c	85.75 ±14.82 b	90.75±16.85 b
a, b, c, d, values not sharing a common letter are significant different between the groups ($p < 0.05$)				

Table 2: Role of Hydro alcoholic extract of TA on TC level among the experimental animals.

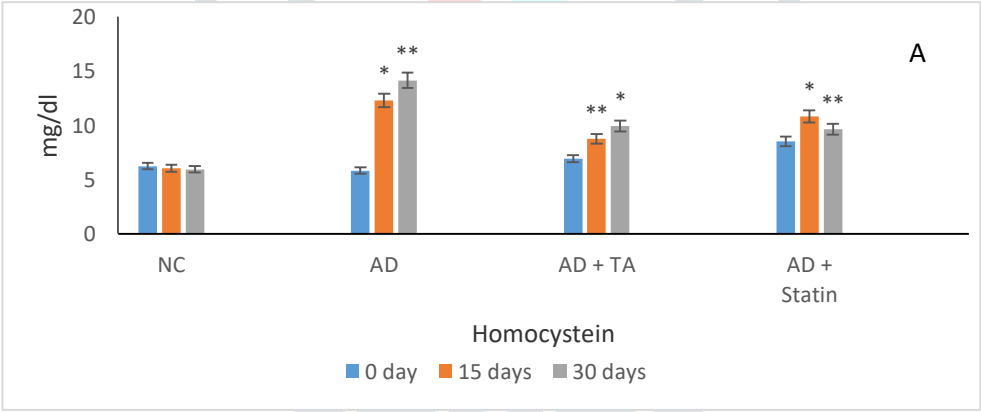
Groups	No. of Animals	Total cholesterol level (mg/dl)		
		Initial	After 15 days	After 30 days
Normal control	6	64.95±8.52 a	70.51±6.38 a	78.62±7.66 a
Atherogenic diet	6	70.10±6.90 b	120.35±19.88 d	180.42±20.90 d
Atherogenic diet+ TA	6	68.46±5.01 ab	110.85±20.60 c	130.65±30.85 c
Atherogenic diet+ statin	6	78.77±7.82 c	90.32±11.11 b	100.40±22.38 b
a, b, c, d, values not sharing a common letter are significant different between the groups ($p< 0.05$)				

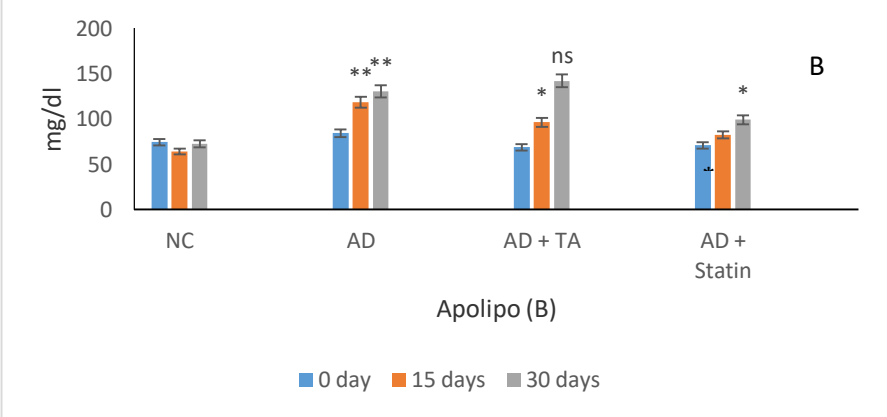
Table 3: Anti- inflammatory markers - adiponectin level on TA treatment in atherogenic diet induced rats.

Groups	No. of Animals	Adiponectin (µg/L)		
		Initial	After 15 days	After 30 days
Normal control	6	48.95±10.80 c	53.32±9.01 c	50.35±8.33 c
Atherogenic diet	6	42.53±12.85 b	30.75±8.01 a	24.50±5.48 a
Atherogenic diet + TA	6	48.75±10.85 c	40.75±9.95 b	48.20±8.35 c
Atherogenic diet + statin	6	39.85±7.82 a	38.85±8.01 b	43.85±10.85 b
a, b, c, d, values not sharing a common letter are significant different between the groups ($p< 0.05$)				

Table: 4 Effect of TA fraction in heart antioxidants of atherogenic diet induced hyperlipidemic rats

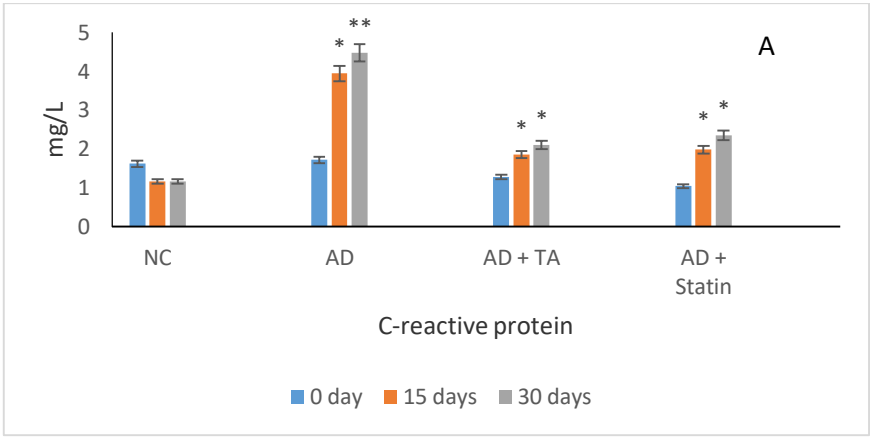
Groups	**TBARS** (nM of malondialdehyde/ mg of protein)	**Catalase** (nM of H_2O_2 used/min/mg of protein)(µM of GSH consumed/min/mg of protein	**GSH** (µg of GSH/mg of protein)	**GST** (nM of of H_2O_2 used/min/mg of protein) (nM CDNB-GSH conjugate formed/min/mg of protein)
Normal control	0.34±0.15 b	33.39±3.35 c	2.3 ± 0.02 d	1.2 ± 0.01 c
Atherogenic diet	1.16±0.01 d	1.34 ± 0.01 a	1.5 ± 0.01 a	0.6 ± 0.03 a
Atherogenic diet + TA	0.49±0.03 c	12.56 ± 9.65 b	1.8 ± 0.02 b	0.9 ± 0.01 b
Atherogenic diet + Statin	0.25±0.061 a	42.90 ± 4.05 d	2.1 ± 0.03 c	1.1 ± 0.02 c
a, b, c, d, values not sharing a common letter are significant different between the groups (p< 0.05)				

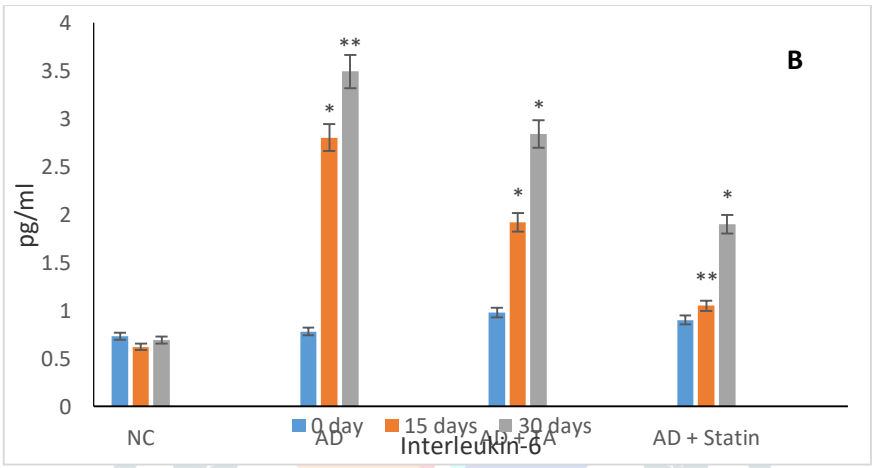


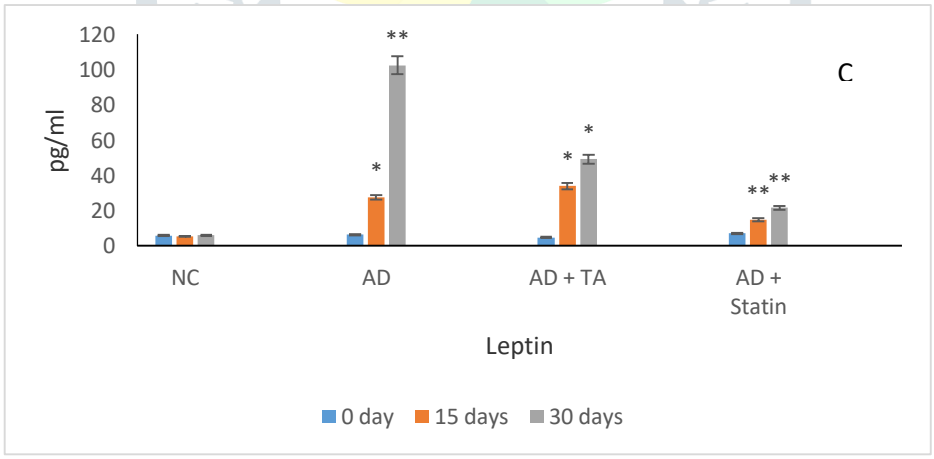


Student t test – P < 0.05*, P < 0.01**

Fig. 1. Effect of TA on homocysteine level (A) & Apolipo B (B) among atherogenic diet treated rats

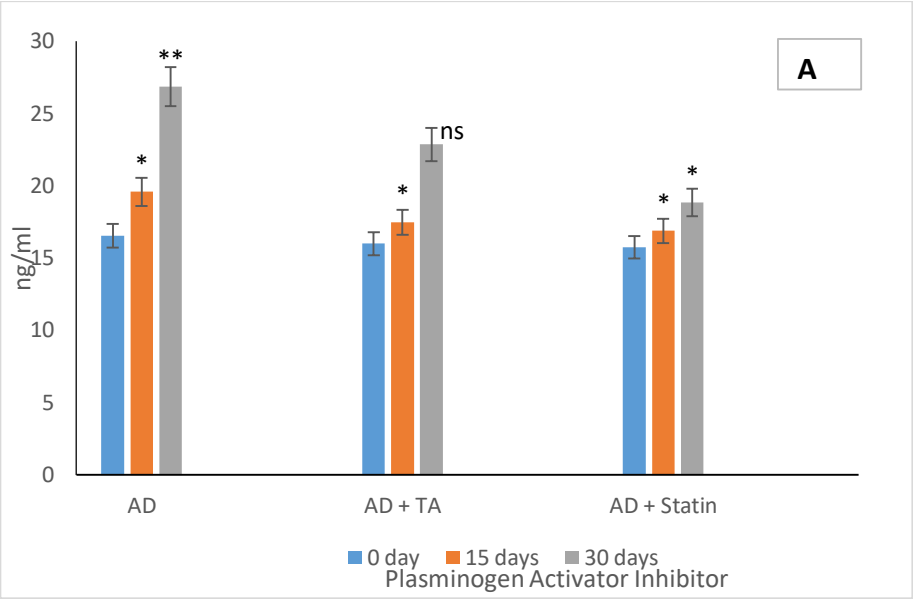


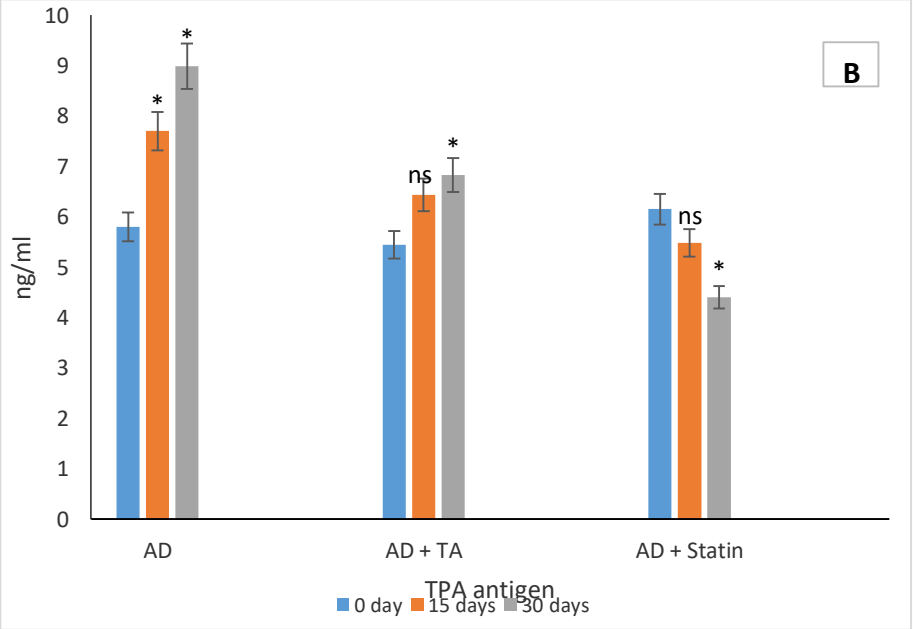




Student t test – P < 0.05*, P < 0.01**

Fig. 2. Effect of TA on pro- inflammatory markers (A, B & C) among atherogenic diet induced rats





Student t test – P < 0.05*, P < 0.01**

Fig. 3. Effect of TA on PAI (A) & TPA (antigen) level (B) among experimental animals

DISCUSSIONS:

The experimental study demonstrated that diet induced hypertriglyceridemic animals have an elevated level of homocysteine and pro-inflammatory markers like C-reactive protein, Leptin and Interleukins (IL6). The release of leptin from adipose tissue is a negative feedback mechanism to quash the appetite and reduction in weight gain. The cardiac markers including total cholesterol, triglycerides and C-reactive protein levels are maintained normal. We have also estimated the level of TBARS the marker of antioxidants in atherogenic diet administered animals. Since oxidative stress is the major factor responsible for the development of age related diseases and other cardiovascular diseases. The antioxidant activity was increased by increasing the activity of enzymatic antioxidants like GST and catalase, non-enzymatic antioxidants like GSH along with the decrement of TBARS.

Atherogenic dyslipidemia is a part of complex cluster of abnormalities called the metabolic syndrome which has a direct correlation with coronary artery disease (CAD) events. In recent years, Indian population have increasing incidence of atherosclerosis disease (AD) and CAD as compared to western population, which may be due to a life style changes such as physical inactivity, unhealthy diet and a higher genetic predisposition. Despite large reduction in LDL-C levels, significant residual cardiovascular risk due to low HDL-C, high TG and non-HDL-C levels exists. Their management with the therapeutic lifestyle changes with statins or statins combination with niacin and/or fibrates has considerably reduced the incidences of cardio vascular disease (CVD) events. Apo B/ApoA-1 ratio has been considered as an accurate predictor of (CVD) risk, however several studies have reported LDL-C/HDL-C ratio to be more accurate.

The hydro-alcoholic fraction of T. arjuna fraction has shown significant effect on triglycerides, and inflammatory markers particularly involved in endothelial dysfunction resulting in atherosclerosis, hypertension and ultimately leading to myocardial infraction and cerebro-vascular accidents. Currently the following atherosclerotic factors have been recognized by the genetic inheritance particularly lipoprotein (a) and leptin has been recently recognized as one of the important hormones responsible for insulin resistance, endothelial dysfunction and, the extra formation and deposition of adipose tissues.

Hyper-leptinemia has shown significant metabolic effect particularly on the lipid metabolism. Elevated level of leptin is responsible for high production of glucocorticoids resulting in elevated level of plasma cortisol. The endocrine effect starts from hypothalamus involving complete hypothalamo-hypophysial neuro-endocrine axis. Leptin plays an important role in the regulation food intake, energy expenditure, lipid metabolism and immune function. It is associated with metabolic syndrome, dyslipidemia and inflammatory markers. Interleukin is a novel adipokine pro-inflammatory marker, IL6 concentration raises with weight gain of atherogenic animals. IL6 concentration reduced with weight loss of atherogenic animals, which disturb appetite and energy intake through action in the hypothalamus.

Adiponectin is the important adipocyte complement related protein regulating the glucose and adipose tissue homeostasis. It is also responsible for anti-atherogenic effects and anti-inflammatory effects, neutralizing the adverse effect of hyperleptinemia and hyperglycaemia. In a series of experimental studies, it has been observed that atherogenic heart animals have low level of adiponectin. Similarly, adiponectin is also responsible for enhancing the pro-inflammatory cytokines like leptin level increased in experimental models. Adiponectin is a cardiovascular protector, it also inhibits endothelial cell, ventricular walls, smooth muscles, production of adhesion molecules responsible for endothelial damage.

The level of homocysteine, a sulfydryl-containing amino acid has shown to be predictive of future coronary heart disease (CHD). There is also evidence that the elevated range of homocysteine has a significant association with atherosclerosis and formation of atherothrombotic plaque responsible for ischemic heart disease.

It has been observed in several cases and also among the patient suffered from vascular disease that genetic factor influences plasma homocysteine concentration. It is also reported that plasma homocysteine rise with age in both men and women and its concentration are higher in men than women. This may be due to difference in muscle mass and renal function. Sex hormones may also influence homocysteine concentration in plasma [29].

The elevated plasma homocysteine is a known factor for atherosclerotic vascular disease. Homocysteine level increased with decreasing concentration of vitamin B6, vitamin B12 and folate. Further, it increases due to impaired metabolism by the kidneys and liver which enhances the risk of myocardial infraction and stroke [30]. Certain drugs like combination of colestipol and niacin, metholrexate, phenytoin carbomazepine and nitrous oxide may increase homocysteine concentration in plasma. Further, it is pointed out that patients with inherited defects of methionine metabolism can develop severe hyperhomocysteinemia and can have premature atherothrombosis. Though, mild to moderate elevations of homocysteine are common among general population, due to insufficient dietary intake of folic acid, vitamin B6 and B12 level, if the condition is not treated, it may cause endothelial dysfunction and formation of atherothrombotic plaque.

Recently, hyperhomocysteinemia has been recognized as an independent risk factor for cardiovascular disorders [31]. It is further, noticed that hyperhomocysteinemia is three fold more common in cases suffering from type-II diabetes mellitus [32]. More recently, several studies have been demonstrated in such a way to attest that elevated level of homocysteine are responsible for endothelial dysfunction, formation of atherothrombotic plaque and also responsible for neurodegeneration. In the present thesis, the researchers had included the role of hyperhomocysteinemia in the causation of atherosclerosis and the remedial measure for its prevention.

Early estrogen deficiency in females is responsible for abnormal lipid profile as well as increased atherosclerotic process. Hormone replacement therapy may significantly prevent the abnormal elevation of lipids as well as reduction in the vascular inflammatory process responsible for rapid progression of atherosclerotic changes [33]. But prolong administration of HRT may precipitate the breast and endometrial cancer.

Oxidative stress is responsible for endothelial dysfunction in different age and sex group. In type-II diabetes mellitus, oxidative stress occurs through the formation of reactive oxygen species and lowers the anti-oxidant concentration [34]. The mechanism of oxidative injury responsible for endothelial dysfunctions are complex and varied but in different experimental and clinical studies [35], it is observed that oxidative stress may accelerate the information process and responsible for rapid atherosclerotic changes. A vast body of evidence is available to indicate the role of anti-oxidant in the prevention and management of endothelial dysfunction in type-II diabetes mellitus [36].

CONCLUSION:

In the present experimental studies, the researcher has observed that the herb T. arjuna has adiponectin enhancing property among atherogenic diet induced rats. Atherogenic diet is responsible for hyper-triglyceridemia leading to endothelial dysfunction due to enhanced vascular inflammatory process. High level of C-reactive protein, interleukin-6 has a significant effect in reducing the adiponectin and thus, enhances the atherosclerotic process that may be manifested in a future cardiac event. T. arjuna has shown significant elevation of adiponectin among the animals showing evidence of hypertriglyceridemia. T. arjuna has shown potential effect on total cholesterol by acting on cholesterol receptors as well as reducing the oxidized high LDL cholesterol. Likewise, the same T. arjuna fraction also displays the antioxidant activity by increasing the activity of enzymatic antioxidants like GST and Catalase, non-enzymatic antioxidants like GSH along with the decrement of TBARS. It increases adiponectin level and decreases pro-inflammatory adipokines, proving its antiatherogenic property. The reduction in inflammation and cell damage may be due to antioxidant and antilipid peroxidative effect

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