IJPSR (2012), Vol. 3, Issue 1 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 11 August, 2011; received in revised form 15 September, 2011; accepted 15 November, 2011

CARDIOPROTECTIVE EFFECT OF *TERMINALIA ARJUNA* ON CAFFEINE INDUCED CORONARY HEART DISEASE

S. Asha*[1] and G. Taju [2]

Department of Biochemistry, D.K.M., College for Women [1], (Autonomous), Vellore-632001, Tamil Nadu, India
Department of Aquaculture, Biotechnology, C. Abdul Hakeem College [2], Vellore-632001, Tamil Nadu, India

Keywords:
Terminalia arjuna,
Caffeine,
Cardioprotective,
Hypercholestrolemic effect,
Hypocholesterolemic effect

Correspondence to Author:

S. Asha

Assistant Professor, Department of Biochemistry, D.K.M., College for Women, (Autonomous), Vellore-632001, Tamil Nadu, India

ABSTRACT

The present study was aimed to investigate the effects of bark extract of *Terminalia arjuna* (6.75mg/kg of body weight) on caffeine (10 mg/kg body weight) induced coronary heart disease. Male wistar rats weighing about 120 and 160g were used as the experimental animal for the study. Caffeine dissolved in physiological saline (Nacl) with a pH of 7.0 administered orally to wistar rats continuosly for about 14 days. Thereafter, all the animals at the end of experiment showed a significant elevation in level of total cholesterol, LDL cholesterol, VLDL cholesterol and triglycerides and also a decreased level of HDL-cholesterol, ($P< 0.01$). When compared to the control rats, co-treatment of rats with caffeine and *Terminalia arjuna* resulted in an increase in HDL-cholesterol, decrease in serum total cholesterol, triglycerides, LDL cholesterol and VLDL cholesterol as compared to caffeine treated animals with a significant of $p<0.05$. These findings suggest that the bark extract of *Terminalia arjuna* has protective effects against caffeine induced coronary heart disease and may have potential as a cardioprotective agent.

INTRODUCTION: Caffeine is a trimethylxanthine, found in many everyday products like coffee, tea, kolanuts, chocolate, soda beverages, drugs etc. These are widely and immensely consumed. Its primary biological effect is the antagonism of the A1 and A2A subtypes of adenosine receptors [1, 2, 3] on the surface of heart muscle cells [4]. Caffeine has been found to have various pharmacological and cellular responses in biological systems [5].

These include stimulation of the central nervous system and cardiac muscle, increased urinary output, and relaxation of smooth muscles [6].

However, consumption of caffeine increases urinary calcium levels and also causes irregular heart beat in cartain people [7]. It has also found to cross the placenta and blood brain barriers [8].

From other studies, high caffeine intake during pregnancy is associated with a risk factor for low birth weight [9, 10] and also doubles the risk and spontaneous abortion [11, 12].

After ingestion of caffeine from coffee or other beverages, they are absorbed by the stomach and small intestine. Metabolism of caffeine takes place in the liver by the cytochrome P_{450} oxidase enzyme system. It results in the formation of three metabolite products [13] like paraxanthine, Theobromine and Theophylline. These are further metabolized and then excreted in the urine.

Some reported that these active chemicals are responsible for the increase in serum cholesterol level after coffee consumption [14].

Gordon *et al.,* [15] reported that increased total cholesterol concentration in blood increases the risk of coronary heart disease. It thus, implies that these chemicals (Caffeine) are responsible for the increased risk of coronary heart disease associated with consumption of caffeine products [16].

Several medicinal plants have been described to be beneficial for cardiac ailments. A few of them, for example, *Allium Sativum* L. (garlic) , *Cicer arietinum* L. (Bengal gram), *Curcuma longa* L. (turmeric), *Ocimum sanctum* L. (tulsi), *Terminalia arjuna* (arjuna) are identified and researched to have lipid lowering and cardioprotective activities [17]. Among these plant, the plant which has shown most promising and distinct results is *Terminalia arjuna*, popularly known as arjuna [18, 19].

Terminalia arjuna is a deciduous and evergreen tree found throughout India. It stands to about 20-30m above ground level, belongs to combretaceae family [20, 21]. Abundantly found throughout Indo-sub Himalayan tracts of Uttar Pradesh, South Bihar, Madhya Pradesh and Deccan regions near ponds and rivers. Also found in forests of Srilanka, Burma and Mauritius.

The bark, leaves and fruits of Terminalia arjuna are used in indigenous system of medicine for different ailments [22]. The bark powder has been found to possess cardioprotective properties, anti-ischaemic, antioxidant action [23], hypocholesterolaemic effect, fungicidal [24], antimicrobial [25], antibacterial [26], antifertility, treatment of ulcers, skin disorders and as antidote to poisons . It is also useful to cure obesity, hypertension and hyperglycemia [27].

This study was therefore, undertaken to study the cardioprotective effect of Terminalia arjuna on the risk of coronary heart diseases associated with the induction of caffeine in experimental animals.

MATERIALS AND METHODS:

Plant Material: The bark of *Terminalia arjuna* (TA) obtained from the southern part of India. The dried 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 was obtained. The chemical constituents of the extract were identified by quantitative analysis for the presence of flavonoids, alkaloids, glycosides, carbohydrates, amino acids, proteins and tannins. The extracts were stored in a vacuum dessicator and the weighed dose was used for the experiment by dissolving in the distilled water.

Chemical: Caffeine was obtained from Sigma Chemical Company. U.S.A and diluted in physiological saline (Nacl) with a pH of 7.0.

Animals: Twelve male Wistar rats weighing between 120 and 160g were used. The rats were housed for atleast one week before the start of the experiment. They were maintained in a 12-h light /dark cycle and fed with regular laboratory diet and water *ad libitum*. The twelve male rats used for this study were randomly divided into three experimental groups (A, B and C). Group A served as the control while groups B and C where administered caffeine (dissolved in saline) orally at dosage of 10mg/kg body weight respectively for fourteen days. In addition Group C animals were treated with bark powder of *Terminalia arjuna* at the dosage of 6.75 mg/kg of body weight after induction of caffeine. This treatment was carried out once a day for 4 weeks [6days/week]. The animals were used as per Ethical Committee No.-1282/ac/09/CPCSEA.

Sample Collection and Preparation: Twenty four hours after the last administration, the animals were sacrificed and blood from each animal collected by cardiac puncture into clean sample bottles. This was allowed to clot and then centrifuged at 3000 rpm for five minutes. The serum was separated and stored away for further analysis.

Determination of Serum Lipid Parameters: Serum Total Cholesterol concentration was estimated according to Chod-Pap method reported by Fredrickson *et al*., [28] and Allain *et al.* [29].

The determination of the serum triacylglycerol concentration was carried out using the glycerol-phosphate oxidase method described by Trinder [30]. HDL cholesterol was determined by the phosphotungstate precipitation method adopted by Richmond [31].

The VLDL cholesterol content of serum was estimated, by dividing the serum triglyceride value by the factor 5 [32]. The concentration of LDL cholesterol was derived from the difference between total cholesterol and sum of HDL and VLDL cholesterol according to Friedwald *et al*., relationship [33].

Statistical Analysis: Statistical Analysis was performed using the Turkey Multiple comparison test, all values were expressed as mean ± S.E (n=4 in each group). A value of $p<0.05$ was considered statistically significant.

RESULTS AND DISCUSSION: Terminalia arjuna is a plant, well known for its cardioprotective properties in the ancient Indian system of medicine. In the present study cardioprotective effects of oral administration of *Terminalia arjuna* against caffeine induced coronary heart disease were evaluated in male Wistar rats. Experimental values of *Terminalia arjuna* suggests its benefits in the treatment of coronary artery diseases, heart failure, and hypercholesterolemia [34]. Reported work obtained from [35] on *Terminalia arjuna* shows that its cardioprotective activity was due to its free radical scavenging activity. The effect of caffeine and bark powder of *Terminalia arjuna* on the serum lipid profile in male Wistar rats was presented in **table 1**.

TABLE 1: EFFECT OF CAFFEINE AND BARK EXTRACT ON SERUM LIPID PROFILE IN RATS

Groups	Biochemical parameters				
	Cholesterol	Triglyceride	HDL	LDL	VLDL
Group 1	161.25±4.26*	54.25±4.04*	57.50±3.22*	96.25±1.75*	10.50±1.29*
Group 2	246.32±6.25	187.00±12.17	29.50±2.10**	179.40±6.32	38.85±4.96
Group 3	178.50±1.32*	83.00±0.91*	48.50±2.25*	106.28±1.49*	21.75±1.25*

Results are mean ± S.E. * Significantly different from control ($p<0.05$). ** Significantly different from control ($p<0.001$).

The results indicate that oral administration of caffeine in induced animals produced an increase in total serum cholesterol, Triglyceride, LDL-cholesterol and VLDL cholesterol with a decrease in HDL cholesterol level relative to the control (Group I) Animals. It shows the significance of ($p<0.001$) when compared to control.

Since the level of HDL cholesterol concentration has decreased and LDL cholesterol concentration has increased, these have been associated with increased risk of coronary heart disease [36, 37].

This hypercholestrolemic and hyper triglyceridemic effects in rats, following the oral administration of caffeine may be due to the presence of some constituents like theobromine and theophylline as the metabolite [38].

It was also found that the rats receiving *Terminalia arjuna* (Treated animals) had a marked reduction in total cholesterol [39, 40], triglycerides, LDL cholesterol [36], and VLDL cholesterol. However, it also showed an increased HDL cholesterol with a significance of $p<0.05$ when compared to the induced animals.

Hence, treated rats showed a significant prevention to the risk of coronary heart disease [41]. Thus, *Terminalia arjuna* was observed to be the most potent hypolipidemic, hypotriglycemic agent and also raised high density lipo-cholesterol. All these observations from our present study clearly indicated the cardioprotective effect of Terminalia arjuna against the damage caused by caffeine administration.

ACKNOWLEDGEMENT: The author would like to thank Miss A. Kavitha, Department of Biochemistry, D.K.M. College for Women, Vellore, India, for her technical assistance.

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