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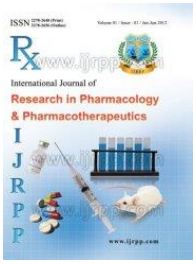

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Screening of antioxidant action of hesperidin in high cholesterol diet model in *Wistar albino* rats

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ABSTRACT

Background

Oxidative stress causes of various diseases in human. The present study aimed to evaluate the antioxidant effect of hesperidin in high cholesterol rats.

Aim

To evaluate the antioxidant action of hesperidin in high cholesterol diet model in Wistar Albino rats

Materials and Methods

Wister Albino rats weighing 200-250 gm were used in this study. 24 rats were divided into four groups each of 6 rats. G-A (Normal diet), G-B (High cholesterol diet), G-C (High cholesterol diet + Hesperidin 100 mg/kg) and G-D (High cholesterol diet+Hesperidin 200 mg/kg). Four groups tetrad with respective drugs for 90 days. At the end of experiment blood samples were collected and used for estimation of antioxidant enzymes like TBARS, SOD, GSH, GPx and CAT by standard biochemical methods. The results were expressed in mean and standard deviation. One way ANOVA used for statistical analysis.

Results

Group-B showed significant decrease in antioxidant enzymes compared to group-A ($p<0.05$). Group-C compared to group-D not showed significant difference ($p>0.05$). Group-C and D showed significant difference compared to group-B ($p<0.05$).

Conclusion

Hesperidin showed significant reduction in oxidative enzymes. Antioxidant effect hesperdin can be useful in the treatment of various diseases associated with oxidative stress.

Keywords: Antioxidants, Hyperlipidemia, High cholesterol, Hespiridin, oxidative stress, SOD

INTRODUCTION

Oxidative stress is an outcome of imbalance between reactive oxygen species (ROS) production and antioxidant defences which in turn evokes a series of events deregulating the cellular functions. [1] Oxidative stress in hyperlipidemiais considered as a factor in the development of atherosclerotic plaques. [2] Flavanoids prove to be highly effective and are gradually emerging as viable supportives to conventional drugs. [3] Flavanoids are polyphenolic compounds and constitute an important group of antioxidants, which can directly quench free radicals and inhibit enzymes of oxygen reduction pathways. [4] Hesperidin is an abundant and major flavanoid in sweet orange and lemon. Hesperidin provides strong cellular antioxidant protection against the damaging effects induced by peroxide hydrogen. [5] Studies showed marked protective effect against inflammatory disorders possibly through a mechanism involving antioxidant free radical scavenger activity. [6] Hesperidin treatment has been demonstrated to improve GSH levels in liver and kidneys of diabetic rats. [7] Hesperidin in combination with Diosmin has also been shown to inhibit the reactive oxygen radicals production in zymosan stimulated human polymorphonuclear nucleus. [8] Hesperidin has showed great scavenger activity and inhibition of formation on O_2^- radicals and a significant scavenging effect on OH radicals and an inhibitory action on non-enzymatic lipid peroxidation. [9] The present study aimed to evaluate the antioxidant effect of hesperidin in hyperlipidemia model.

MATERIALS AND METHODS

Animals

Wistar Albino male rats of 200-250g were included in the study. Animals were housed in well ventilated room (Temperature 23±2°C, humidity 65-70% and 12h light/dark cycle) at Central Animal House, Rajah Muthiah Medical College and Hospital, Annamalai University. This study was approved by Institutional Animal Ethical Committee (IAEC) (Register No.160/1999/CPCSEA), Annamalai University, Annamalai Nagar, India approved the experimental design (Proposal No.883, dated 10.01.2012). The study was conducted in accordance with Committee for the Purpose of Control and Supervision on Experiments on Animals (CPCSEA) norms and the National Institute of Health guidelines "Guide for the Care and use of Laboratory Animals".

Study groups

Group-A: Normal diet (n=6)
Group-B: High Cholesterol diet (1% Cholesterol, 0.5% Sodium Cholate, 1% Coconut Oil) (n=6)
Group-C: High Cholesterol diet+ Hesperidin (100 mg/kg orally OD) (n=6)
Group-D: High Cholesterol diet+ Hesperidin (200 mg/kg orally OD) (n=6)

PROCEDURE

Animals were divided into 4 groups of which 6 rats in each group. Wistar rats of 7 to 8 weeks old weighing about 200-250g fed with normal pellet diet and water in control group and high cholesterol diet (1% Cholesterol, 0.5% Sodium cholate, 1% Coconut oil mixed with normal pellet powder) into experimental group and water ad libitum throughout the study. 13 weeks drugs were administered to their respective groups. Hypercholesterolemia in rats was induced by administration of high cholesterol diet (1% Cholesterol, 0.5% Sodium cholate, 1% coconut oil) for 90 days in standard chow diet. After the study period, the animals in all groups were subjected to overnight fasting. Blood samples were drawn by retro orbital puncture under anesthesia. 3 ml of blood was collected and subjected to centrifuge (3000 RPM/ 15 min). Serum was collected and used for the estimation of TBARS, SOD, GSH, GPx and CAT enzymes by standard biochemical procedures. [10, 11]

STATISTICAL ANALYSIS

The data was expressed in mean and standard deviation. Statistical Package for Social Sciences (SPSS 16.0 version) used for analysis. One was ANOVA (Post hoc) followed by Dunnet t test applied to find the statistical significant between the groups. p value less than 0.05 ($p<0.05$) considered statistically significant at 95% confidence interval.

RESULTS

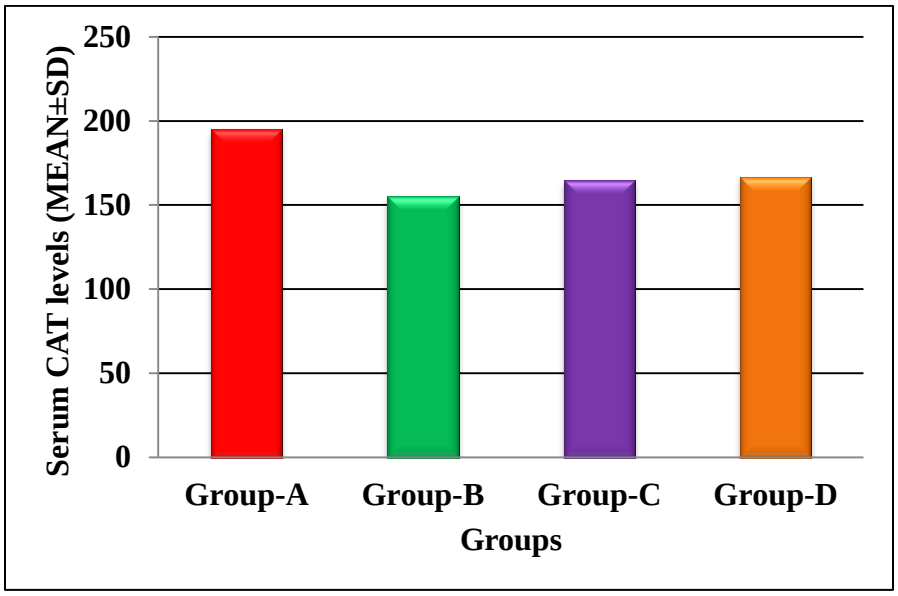
Group-B showed significant increase in TBARS compared to group-A ($p<0.05$). Group-C and D showed significant difference in TBARS levels

compared to group-B ($p<0.05$). Group-C and D not showed any significant difference in TBARS levels ($p>0.05$). SOD, GSH, GPx and CAT levels were significantly ($p<0.05$) reduced in group-B compared to group-A. Group-C and D showed significant increase antioxidant enzymes levels compared to group-B ($p<0.05$). There is no significant difference observed between group-C compared to group-D (Table-1 and Gram-1).

Table-1: Effect of hesparidin on serum antioxidant levels

Groups	TBARS (mmol/dl) (MEAN±SD)	SOD (U/mg Hb) (MEAN±SD)	GSH (mg/dl) (MEAN±SD)	GPx (µmol/min/mg Hb) (MEAN±SD)
Group-A	0.16±0.01	6.55±0.27	31.75±3.58	17.09±1.16
Group-B	0.54±0.03*	5.06±0.31*	22.81±3.43*	10.22±1.00*
Group-C	0.33±0.04*,#	6.07±0.26*,#	25.81±1.33*,#	13.16±1.41*,#
Group-D	0.27±0.03*,#	6.29±0.36*,#	27.18±1.70*,#	14.85±1.50*,#

(*p<0.05 significant compared Group-A with other groups, #p<0.05 significant compared Group-B with other groups, p>0.05 no significant difference compared Group-C with Group-IV)



Graph-1: Effect of hespiriadin on serum CAT levels

DISCUSSION

Increased intracellular generation of reactive oxygen species (ROS) plays an important role in chronic inflammatory responses to atherosclerosis. Enzymic superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) and nonenzymic antioxidants play an important role in alleviating tissue damage due to the formation of free radicals. [12] Studies have found that serum MDA are higher in subjects with hyperlipidemia and decrease following dietary supplementation with antioxidants.[13] Elevated levels of TBARS in plasma are a clear manifestation of excessive formation of free radicals and activation of lipid peroxidation system. [14] In the present study also TBARS were significantly increased in hypercholesterolemic rats. Hesperidin significantly reduced the TBARS level in a dose dependant manner. Antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidise (GPx) are first line defensive enzymes against free radicals and also known to contol oxidative damage. [15] In our study, administration of High cholesterol diet showed a decreased activity of SOD, CAT, GPx and GSH. This may probably be due to increased utilization of antioxidants by the hepatocytes to counteract the increased formation of

lipid peroxides. Nutritional antioxidants like Vitamin C, Vitamin E, beta carotene and butylated hydroxytoluene have significant antioxidant effects to prevent cholesterol oxidation and atherosclerosis. [16] In the present study also Hesperidin by preventing the lipid peroxidation induced by high cholesterol diet had restored the activities of enzymatic and non enzymatic antioxidants. Hence this study showed the antioxidant and free radical scavenging properties of Hesperidin.

CONCLUSION

Oxidative stress is one of the major causes to develop various chronic disorders in humans. Lipid peroxidation leads to formation of free radicals which increase the oxidative stress. Antioxidants plays major role to prevent the free radicals induced diseases. It can be concluded that hesperidin showed significant antioxidant effect in high fat diet model. It can be used as food supplement to prevent the free radical induced diseases.

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