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ANTI-ATHEROGENIC ACTION OF "CARDIPRO"- A HERBAL PROPRIETARY FORMULATION.

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ABSTRACT: *The objective of this study as to determine the anti-atherogenic effect of cardipro- a poly herbal cardiotonic which primarily contains the standardized extracts of Terminalia arjuna, Ocimum sanctum, Boerhaavia diffusa, Emblica officinalis and withania somnifera. For this purpose, 24 adult wistar albino rats were equally divided into 4 groups. Group I acted as control, Group 2 received individually cholesterol 100mg/kg dissolved in vegetable oil (4mg/ml) orally daily for 30 days. Group 3 received cardiPro 25 mg/kg body weight individually orally dissolved in distilled water daily for 30 days in combination with cholesterol as in group2, wile group 4 instead received Cardipro @ 50mg/kg body weight along with cholesterol. It was found that plasma total lipid, cholesterol, low density lipids, very low density lipids, triglycerides as well as aortic cholesterol contents were higher in cholesterol fed rats in comparison to health controls. Treatment with Cardipro significant; reduced the levels of these blood lipid profiles suggesting anti-atherogenic action of cardipro in rats. This was further strengthened b histopathological examination of Aorta in which the cholesterol fed rats treated with Cardipro @ 50% mg/kg body weight revealed only occasional presence of fat in the medial coat and intact elastic fibres in contrest to marked elevations and depressions I the tunica intima associated muscles of medical coat and disruption of elastic fibres in only cholesterol fed rats.*

INTRODUCTION :

Atherosclerosi is intimately associated with various cardiovascular disturbances which have emerged as a major world health problem. Atherosclerosis and associated heart diseases are not one of the principal causes of death in Western World and in al most every developing country (1). Extensive global research is continuing to develop pharmacological means for prevention and management of atherosclersis and allied cardiovascular problems. Cardipro is a polyherbal cardiotonic formulation which contains the standardized extract of : Terminalia arjuna, Ocimum sanctum, Boerhaavia diffusa, Emblica officinalis and wtihania somnifera.

Cardiopro is safe and non-toxic to experimental animals(2) Earlier studies have demonstrated that cardipro produced positive ionotropic and negative chronotrapic effect in addition to improvement n peripheral and coronary perfusion flow (3). In clinical trials, patients of angina pectoris responded well when treated with cardipro (4,5). The constituents

of cardipro were reported to produce hypocholesterolaemic action (6-10). The present study was carried out to investigate the anti atherogenic action of Cardipro in experimental animals.

MATERIALS & METHODS:

The stud was conducted in adult wistar albino rats twenty four rats were equally divided into 4 groups referred as

Group I (HC) : Healthy control.
Group II (AC) : Cholesterol (100mg/kg) dissolved in hyfrogenated vegetable oil(4mg.ml) per animal, orally, daily, for 30 days.

Group III (D-25) : Cardipro(25 mg/kg) pre animal, orally, dissolved in distilled water, daily for 30 days in combination with cholesterols as stated for group II.

Group (AD-50) : Same as group III but the dose of Cardipro was 50mg/kg pr animal.

At the end of 30 days. Blood samples were collected from each rat and plasma was separated for the estimation of total lipid, total cholesterol, high density lipids (HDL), low density lipids (LDL), very low density lipids (VLDL) and triglyceride concentrations using diagonostic kit (Span diagnostics). The animals were then sacrificed under overdoes of ether anaesthesia; the thoracic aorta of each rat was dissected out. A portion of aorta was preserved informal-saline for histopathology and another portion for estimation of tissue cholesterol content.

Statistical significance of data between groups in the present study was evaluated b employing student's test. A probability of less than 0.05 was considered significant.

RESULTS

Plasma total lipid, cholesterol, LDL, VLDL and triglyceride as well as aortic cholesterol contents were higher in cholesterol fed rats in comparison to healthy controls. Treatment with cardipro had reduced these blood lipid profiles in cholesterol fed rats (Table -1).

Gross examination of aortic tissues of the cholesterol fed rats (AC) showed wrinkling of tunica intima with occasional ulceration and dis-colouration. The arterial wall was moderately thickened in comparison the controls, Microscopically, There was gelatinous swelling and elevation and depressions (Fig I) of intima due to presence of structureless materials with karyorrhetic nuclei giving an appearance of microscopic mural thrombi and ulceration (Fig 3) with rough surface of tunica intima. In medial coat, there was hypertrophy of smooth muscles which was rich in lipoid materials (Fig2) calcium salts were deposited as fine granular material in the intima in vonkossas stain. In verhoeff's stained sections, there was disruption of elastic fibres due to fragmentation and also presence of discrete fat vacuoles (Fig 4).

In cardipro treated rats grossly the intima was less wrinkled and there was no evidence of microthrombi attached to the intimal surface and it was smooth. There were only occasional are droplets in medial coat (Fig 5) In verhoeff's stained sections intact and continuous elastic fibres were noted (Fig 6) No deposition of calcium salts was noticed.

The thickness of medical coat was more or less akin those in healthy control.

DISCUSSION

An increased risk of atherosclersis is always associated with high blood concentrations of total lipid, LDL, VLDL, triglycerides and total cholesterol wit low concentration of HDL (11). As has been noticed in this stud, Significant reduction in blood concentration of cholesterol, total lipid, LDL, VLDL and triglycerides brought about b cardipro in cholesterol fed rats as compared to untreated cholesterol fed (AC) group rats, observed herein, was considered extremely beneficial, particularly in rats treated with higher dose. Lower levels of LDL due to Cardipro in the present stud suggest that this herbal product is a potential agent for reducing or controlling atherogensis and cholesterol deposition in peripheral tissues including blood vessels which is further strengthened by reduction in the levels of VLDL – a precursor of LDL.

Hypertriglyceridaemia as a possible risk factor for development of ischaemic heart disease is well documented and atherogenic property of triglycerides is related to its lipoprotein transport and metabolism. In hypertriglyceridaemia, these is marked reduction in clearance of VLDL and LDL, which are highly atherogenic. Hypertriglyceridaemia is also associated with hypercoagulability due to decreased fibrinolytic activity (12).Most hypercholesterolaemic drugs do not decrease blood triglyceride levels but cardipro lowered the concentration of blood triglyceride even in cholesterol fed rats, though the same was still above the healthy control values, in the present experiment.

Accumulation of lipids and lipoprotenins is the most important event in the pathogenesis of atherosclerotic plaque formation in blood vessels. In the present stud, accumulation of cholesterol and other lipoid materials in the aorta was found to be significantly less in cardipro treated rats as compared to untreated cholesterol fed rats, as evident from both biochemical and histological studies of aortic tissues. This shows significant anti-atherogenic action of cardipro. Arterial thrombotic occlusion, as seen in cholesterol fed rat aorta, complicated atherosclerosia causing myocardial infarction. Treatment of the rats with cardipro did not show any presence of microthrombi attached to the intimal surface of aorta which is in accordance with chaturvedi who stated that T. arjuna, which forms as important component of cardipro. Possesses anticoagulant and anti-thrombotic activity (13).

Cardipro also effectively prevented the deposition of calcium salts in the aortic tissues leading the prevention of atherogenesis as clacification of aortic tissue plays a ital role I the pathogenesis of atherosclerosis (14).

Although the exact mechanism of action of cardipro can not be clearly defied at this stage, it is possible that E. officinalis and T arjuna which form important components of cardipro increase the fecal excretion of cholesterol and enhance the plasma lecithine-cholesterol acyl transferase (LCAT) activity in addition to stimulation of receptor medicated catabolism of LDL as indicated by shaila & coworkers (&) and mathur and coworkers (9).

It has been concluded from this study that cardipro can be used effectively for amelioration of atherosclerosis and associated cardiac problems to a certain extent. Therefore, it is recommended that large scale clinical trials in hyperlipidaemic

patients may be undertaken using cardipro, as it has been much higher than the recommended dose.

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TABLE -1: EFFECT OF CARDIPRO ON LIPID PROFILE OF EXPERIMENTALANIMALS

Group	Total lipid (mg/dl)	Cholesterol (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/gm)	VLDL-C (mg/dl)	Trigyceride (mg/dl)	Aortic cholesterol (mg/gm)	RF#
Control (HC)	** 193.39 ± 7.81	** 96.75 ± 3.72	34.42 ± 1.12	** 56.02 ± 3.59	** 7.32 ± 0.28	** 36.64 ± 1.43	** 1.72 ± 0.09	2.81
Cholesterol fed (AC)	342.78 ± 7.22	185.35 ± 3.73	35.64 ±4.07	128.63 ± 0.98	21.08 ± 5.05	105.43 ± 0.11	3.92 ± 5.20	
Cholesterol Fed+CardiPro (25mg/kg) (AD-50)	* 286.10 ± 10.43	* 144.77 ± 5.06	32.77 ± 1.45	* 94.14 ± 3.97	* 17.86 ±0.63	* 89.33 ± 3.17	* 2.95 ± 0.15	4.41
Cholesterol Fed+CardiPro (50mg/kg) (AD-50)	** 222.08± 9.37	** 115.60 ± 4.71	35.45 ± 1.79	** 67.65 ± 4.47	** 12.50 ± 0.71	** 62.51 ± 3.57	** 2.13 ± 0.12	3.26

RF = Risk Factor (Cholesterol/HDL –C).
* Significant (P £ 0.05) difference with cholesterol fed (AC) rats.
** Significant (P £ 0.01) difference with cholesterol fed (AC) rats.

LEGENDS OF THE FIGURE:

Fig.1 Section of aorta (AC) showing gelatinous swelling of intima, hypertrophy of medical muscles and presence of fat vacuoles (H&E x83).

Fig.2 Section of aorta (AC) showing hypertrophy of medical coat and appearance of microthrombi. (H&E x83).

Fig.3 Section of aorta (AC) showing rough surface of tunica intima and presence of vacuoles(H&E x83).

Fig.4 Section of aorta (AC) showing disruption of elastic fibres and presence of discreate fat vaculoes (Verhoeff's x34).

Fig.5 Section of aorta (AC-50) with intact, smooth intima and absence of fat droplets (H&E x83).

Fig.2 Section of aorta (AC-50) with intact elastic fibres (Verhoeff's x34).