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RESEARCH ARTICLE

SCREENING OF CARDIOPROTECTIVE AND ANTIOXIDANT ACTIVITY OF "DALBERGIA LATIFOLIA"

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ABSTRACT

The aim of the present study was to evaluate the possible cardio protective potency of Dalbergia latifolia leave against 5-FU-induced cardiotoxicity and oxidative stress in Albino rats.

The rats were divided into five groups. Rats in the normal group received saline daily for 8 days only. Rats in Disease control group received saline orally for 8 days, then I.P. injected with 5-FU (150 mg\kg B.W) on the 5th day. Rat in standard group receive Vit. E (100mg/kg) for 8 day and on the 5th day rats were administrated with the same previous dose of 5-FU. Rats in D L-treated group (low dose) were orally dosed with DL (250 mg\kg B.W\day) for 8 days, and on the 5th day rats were administrated with the same previous dose of 5-FU. Rats in DL-treated group (High dose) were orally dosed with DL (500 mg\kg B.W\day) for 8 days, and on the 5th day rats were administrated with the same previous dose of 5-FU.

Result: 5-FU induced cardiotoxicity was assessed by a significant increase in serum concentrations of lipid profile(Total cholesrtol, triglyceride, LDL). 5-FU significantly decreased serum HDL, and a moderate elevation of cardiac MDA and decrease in SOD,GLUTATHIONE PEROXIDASE and CATALASE.

The histopathological studies also showed that the plant extract significantly minimized the damage induced by 5-FU.

Conclusion: DL has a significant effect on the protection of the heart against 5-FU-induced cardiotoxicity through maintaining the cardio protective and antioxidant activity.

INTRODUCTION

CVD is a group of disorders/diseases of the heart and blood vessels, including heart attack and stroke. Cardiovascular diseases include: coronary heart disease (heart attacks), cerebrovascular disease, raised blood pressure (hypertension), peripheral artery disease, rheumatic heart disease, congenital heart disease, and heart failure [Vidhya Unnikrishnan and Nishteswar, 2015]. Atherosclerosis (also known as Arteriosclerotic Vascular Disease or ASVD) is the condition in which an artery wall thickens as the result of a build-up of fatty materials such as cholesterol. It is a syndrome affecting arterial blood vessels, a chronic inflammatory response in the walls of arteries, in large part due to the accumulation of macrophage white blood cells and promoted by low density (especially small particle) lipoproteins (plasma proteins that carry cholesterol and triglycerides) without adequate removal of fats and cholesterol from the macrophages by functional high density lipoproteins (HDL), is commonly referred to as a hardening or furring of the arteries.

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It is caused by the formation of multiple plaques within the arteries [Maton *et al.,* 1993]. Endothelial cell injury: The injury to endothelial vessel layer is the initial factor development of plaque formation. The possible causes for injury of the endothelial vessel layer are 1) exposure of endothelium to any toxic substances, which results in the damage eg: use of tobacco. 2) Due to mechanical stress associated with hypertension 3) Immune mechanisms and 4) Hyperlipidemia also play an active role in the pathogenesis of the atherosclerotic lesion. Lipoprotein deposition: When the endothelium is injured or disrupted, lipoprotein molecules can gain entry where they are then modified by oxidation (via free radicals or oxidizing enzymes) or glycation (diabetics). This modified lipoprotein (modified LDL) is inflammatory and able to be ingested by macrophages creating "foam cells" causing a "fatty streak" in the arterial wall (Srividya, 2017). Oxidative stress in cardiac and vascular myocytes describes the injury caused to cells resulting from increased formation of ROS and/or decreased antioxidant reserve. The increase in the generation of ROS seems to be due to impaired mitochondrial reduction of molecular oxygen, secretion of ROS by white blood cells, endothelial dysfunction, auto-oxidation of catecholamines, as well as exposure to radiation or air pollution

[Dhalla *et al.,* 2000]. An antioxidant can be broadly defined as any substance that delays or inhibits oxidative damage to a target molecule [Yamagishi and Matsui, 2011]. Normal biochemical reactions, increased exposure to the environment, and higher levels of dietary xenobiotics result in the generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) [Bagchi and Puri, 1998]. ROS and RNS are responsible for the oxidative stress in different pathophysiological conditions [Kim and Byzova, 2014]. Antioxidants can be categorized in multiple ways. Based on their activity, they can be categorized as enzymatic and non-enzymatic antioxidants. Enzymatic antioxidants work by breaking down and removing free radicals. The antioxidant enzymes convert dangerous oxidative products to hydrogen peroxide (H2O2) and then to water, in a multi-step process in presence of cofactors such as copper, zinc, manganese, and iron. Non-enzymatic antioxidants work by interrupting free radical chain reactions. Few examples of the non-enzymatic antioxidants are vitamin C, vitamin E, plant polyphenol, carotenoids, and glutathione [Shahidi and Zhong, 2010].

Free radicals are atoms, molecules or ions with unpaired electrons, which are highly active to chemical reactions with other molecules. In the biology system, the free radicals are often derived from oxygen, nitrogen and sulphur molecules. These free radicals are parts of groups of molecules called reactive oxygen species (ROS), reactive nitrogen species (RNS) and reactive sulphur species (RSS). For example, ROS includes free radicals such as superoxide anion (O2−•), perhydroxyl radical (HO2•), hydroxyl radical (▪OH), nitric oxide and other species such as hydrogen peroxide (H2O2), singlet oxygen (1O2), hypochlorous acid (HOCl) and peroxynitrite (ONOO−) [Vajragupta *et al.,* 2004]. RNS are derived from nitric oxide through the reaction with O2−• to form ONOO−. RSS are easily formed from thiols by reaction with ROS [Giles and Jacob, 2002]. ROS are produced during cellular metabolism and functional activities, and have important roles in cell signalling, apoptosis, gene expression and ion transportation [Vajragupta *et al.,* 2004]. However, excessive amounts of ROS can have deleterious effects on many molecules including protein, lipid, RNA and DNA since they are very small and highly reactive. ROS can attack bases in nucleic acids, amino acid side chains in proteins and double bonds in unsaturated fatty acids, in which ▪OH is the strongest oxidant.

ROS attacking macromolecules is often termed oxidative stress. Cells are normally able to defend themselves against ROS damage through the use of intracellular enzymes to keep the homeostasis of ROS at a low level. However, during times of environmental stress and cell dysfunction, ROS levels can increase dramatically, and cause significant cellular damage in the body. Thus, oxidative stress significantly contributes to the pathogenesis of inflammatory disease, cardiovascular disease, cancer, diabetes, Alzheimer's disease, cataracts, autism and aging [Giles and Jacob, 2002; Ames *et al.,* 1993; Liu and Hotchkiss, 1995; Geier *et al.,* 2009 and Geier *et al.,* 2009]. Antioxidants may be molecules that can neutralize free radicals by accepting or donating electron(s) to eliminate the unpaired condition of the radical. The antioxidant molecules may directly react with the reactive radicals and destroy them, while they may become new free radicals which are less active, longer-lived and less dangerous than those radicals they They may be neutralized by other antioxidants or other mechanisms to terminate their radical status. For example, many antioxidants have aromatic ring structures and are able to delocalize the unpaired electron. Vitamin C (AscH−) in the aqueous phase and vitamin E (TOH) in the lipid phase will directly react with or neutralize hydroxyl, alkoxyl and lipid peroxyl (ROO▪) radicals and form H2O, alcohol and lipid hydroperoxides, respectively. Vitamin E itself becomes a phenyl radical and vitamin C turns to a very stable radical (Asc−•), due to its delocalized structure. Furthermore, vitamin C can also neutralize the radical form of other antioxidants such as glutathione radical and vitamin E radical, and regenerate these antioxidants [Hossain and Asada, 1985]. The antimetabolite 5-Fluorouracil (5-FU), an analogue of uracil, and its pro-drugs are widely used antineoplastic agents for the treatment of gastrointestinal cancers, breast, gynecological as well as head and neck tumors [Grem, 1997]. 5-fluorouracil (5-FU) is a key chemotherapeutic agent in the treatment of many gastrointestinal tract adenocarcinomas. Despite its proven therapeutic efficacy, 5-FU also possesses several undesired cardiac toxicities, including coronary vasospasm, coronary thrombosis, cardiomyopathy, and sudden cardiac death. This review addresses the incidence, mechanisms of action, clinical presentation, risk stratification, and management of 5-FU associated cardiotoxicity [Sorrentino *et al.,* 2012]. 5-FU also has numerous toxic effects. The most common toxicities associated with 5-FU include diarrhea, mucositis, myelosuppression, and thrombophlebitis of peripheral veins [Gianni *et al.,* 2003].

Endothelial dysfunction

Endothelial dysfunction and thrombus formation, independent of vasoconstriction, have also been shown to serve as potential mechanisms of the cardiotoxic effects of 5-FU administration. Several animal studies examined the direct effects of 5-FU on vascular endothelial cells and noted direct endothelial damage and platelet and fibrin accumulation with increased thrombus formation on both gross examination and electron microscopic evaluation [Cwikiel *et al.,* 1996 and Cwikiel *et al.,* 1995]. Myocarditis and HF are other manifestations of 5-FU cardiotoxicity [Calik *et al.,* 2012]. The mechanisms by which 5-FU produces these cardiac side effects are unknown, but the one most often suggested is ischemia to the myocardium. Ischemia could be due to a direct toxic effect on the vascular endothelium involving NO synthase, which leads to coronary vasospasms. The other mechanism of vasospasm endothelial vasoconstriction is via protein kinase C [Alter *et al.,* 2006]. 5-FU induces the endothelial damage and extravasation of blood with the drug into cardiac tissue resulting in an inflammatory reaction and myofibril necrosis. Another theory has suggested cardiotoxic impurities in the 5-FU formulation (fluoroacetaldehyde, generated in the alkaline solution of fluorouracil during storage, which may be converted to a cardiotoxic agent, fluoroacetate). Fluoroacetate enters the Krebs' cycle and converts into fluorocitrate, which inhibits the enzyme aconitase causing citrate accumulation, disruption of the tricarboxylic acid cycle and severe impairment of energy production within the myocytes. The pathogenesis of 5-FU induced cardiotoxicity may involve cellular damage due to the oxidative stress and the induction of apoptosis. Accordingly therapeutic interventions having antioxidant activity may be effective against oxidative stress associated with cardiovascular diseases. [Eman Taha Mohamed and Ghada Mohamed Safwat, 2016]

Drud used in CVS:

Diuretics [(e.g. Thiazides (Doxazosin, Amlodipine), Nonthiazide (Indapamide)]

- β-blockers
- Calcium channel blockers (Dihydropyridines (nifedepine), nondihydrophydines (Verampil and Diltiazem))
- Angiotensin converting enzyme inhibitors (e.g. Ramipril)
- Angiotensin receptor blockers (e.g. Losartan)
- Alpha blockers

WHO-ISH guidelines recommended that all the above drugs have equal efficacy in lowering BP in standard doses. Beta (β)-blockers Beta-adrenergic blockers (β-blockers) are major class of drugs for the treatment of various CVDs, including high blood pressure (BP), insufficiency of blood flow to the heart muscle, irregular heartbeat, thickened heart muscle, and decreased ability of the heart to empty or fill normally. β-blockers can also be used to cure migraine headache and glaucoma (increased pressure of the eye). No other class of man-made drugs has had such widespread applicability in clinical medicine [Andersson *et al.,* 2014].

Statins

By inhibiting the HMG-CoA-reductase activity in hepatocytes, statins reduce hepatic cholesterol synthesis, leading to lower intracellular cholesterol levels. This in turn, causes LDL-receptor upregulation on the hepatocyte surface, which results in increased uptake thereby further decreases the LDL-C levels in the circulation[Cholesterol Treatment Trialists *et al.,* 2010]. As a cholesterol absorption inhibitor, Ezetemibe inhibits intestinal cholesterol uptake and thereby reduces cholesterol transport to the liver. This causes the LDL-receptor upregulation which in turn, lowers the circulating LDL-C levels. Monotherapy with Ezetemibe results in lower LDL-levels, around 15-22%, while adding statin therapy causes a further 15-20% drop. In IMPROVE-IT, Ezetemibe was added to 40 mg Simvastatin in more than 18,000 patients after ACS, this led to an additional LDL-reduction, which resulted in another slight yet statistically significant reduction in cardiovascular events [Cannon *et al.,* 2015]. Dalbergia latifolia (Roxb) belonging to Family- Fabaceae. Is a large glabrous tree a single stem with characteristic smell.The tree has grey bark that peels in long fibers, compound leaves and bunches of small flowers. Traditionally various species are reported to be used as aphrodisiac, abortifacient, expectorant, anthelmintic, antipyretic, appetizer, allays thirst, vomiting, burning sensation, cures skin diseases, ulcers, diseases of the blood, reduces obesity, used in leucoderma, dyspepsia, dysentery, for diseases of the eye and nose, syphilis, stomach troubles, leprosy, leucoderma, scabies and ringworm[Saroj Kumar Yadav *et al.,* 2015]. Several phytoconstituents like isoflavonoids, neoflavonoids, glycosides, cinnamylphenols, quinones, and furans have been isolated from different species[Sanjib Saha1 *et al.,* 2013].

MATERIALS AND METHODS

Collection of plant material: The leaf of plant Dalbergia Latifolia was collected from Thirupati forest region, Thirupathi district,Andhra Pradesh, India in the month of September, 2017,the plant species were authenticated by Dr. K. Mahadev Chetty, Assistant Professor, Department of botany, Sri venkateswara university, Thirupati, Andhara Pradesh India. The plant was identified by a botanist and voucher specimen was deposited in Rajiv Gandhi University Of Health Science and copy has been preserved for, future reference at Karnataka College Of Pharmacy, Department Of Pharmacology, the collected leaf was washed thoroughly with water to remove adhering soil, mud and debries. Then the leaf was dried in shade at room temperature, then the plant material was powdered with blender, the powder was stored in an airtight container and protected from light**.**

Preparation of extract

250 gm powdered plant material was subjected to successive extraction in a reflux condenser using 1.5 litre methanol for 3 hour at temperature of 800c,separate the supernatant layer and remaining portion mixed with 1 litre of methanol and heated at 800c for another 1 and half hour again separate the supernatant layer and remaining portion is mixed with 1 litre methanol and heated at 800c for another 1 and half hour and separate the supernatant layer, finally mix all the three layers of extract and final product is evaporated to dryness to get constant weight.

Experimental animals

Wister albino rat having weight (150-200gm) were purchased from NIMHANS Bangalore. They were housed, six per poly propylene cage with paddy husk bedding. Animal will maintain under standard laboratory conditions at room temperature (25°C± 2°C) with 12 hr. light / dark cycle. The animals were provided with pellet chow and water. Ethical clearance was obtained from Institutional Animal Ethical Committee (IAEC) of Karnataka College of pharmacy, Bangalore.

Animals Are Divided Into 5 Groups Each Group Have Six Animals

Group I: Normal group: Will receive Vehicle (Normal Saline) for 8 days.
Group II: Diseased control: Will receive 5-FU on 5th day and normal saline for 8 days.
Group III: Standard group: Will receive Vit. E (for 8 days)1 hour before I.P injection of 5- FU(on 5th day).
Group IV: Will receive 5-FU(on 5th day) and low dose of Dalbergia latifolia leaf extract 1 hour before I.P injection of 5-FU(for 8 days).
Group V: Will receive 5-FU(on 5th day) and high dose of Dalbergia latifolia leaf extract 1 hour before I.P injection of 5-FU (for 8 days).

Here, to normal group nolmal saline was given at the dose of 10 ml/kg and to disease control group 5-FU was given at the dose of 150 mg/kg and to standard group vitamin-E was given at the dose of 100 mg/kg and to D L treatment group(low dose) D L was given and to D L treatment group(high dose) D L was given.

Blood sampling and tissue preparation [Eman Taha Mohamed and Ghada Mohamed Safwat, 2016]

Blood samples were collected 24 hours after the last dose, and all rats were sacrificed by cervical decapitation. The obtained

sera were monitored for lipid profile. Heart tissues were excised after dissection of the animals and designated for biochemical analysis. The excised heart tissue (0.5 g) was homogenized in ten volumes of ice cold phosphate buffer (pH:7) until a uniform suspension was obtained. The homogenate was then centrifuged at 20,000 × g for 10 min at 4 °C using high speed cooling centrifuge. The clear supernatant was used for the assay.

Biochemical Assays

On the 8th day, the rats were fasted overnight. On the 9th day the fasted rats were sacrificed under diethyl ether anesthesia and blood samples were collected into plain sample bottles. Blood samples were collected via retro-orbital puncture or by cardiac puncture with 21G needle mounted on 5ml syringe. The animals were analysed according to standard methods for effect of the extract on various biochemical parameters of rats such as TC, TG, LDL and HDL**.**

Statistical Analysis

Results were expressed as the Mean ±standard error means S.E.M.). The comparison of data within groups was performed by the analysis of variance using ANOVA test. Significant difference between control and experimental groups was assessed by Dunnett's test. A probability level of less than 1 % ($P < 0.001$) was considered significant. Statistical analysis was performed using Graph Pad prism.

Histopathological Analysis

On the 8th day, the rats were fasted overnight. On the 9th day the fasted rats were sacrificed under diethyl ether anesthesia and portion of heart of rats was collected from all group rats (normal, disease control, standard, low dose of DL, high dose of DL) and fixed in 10% formalin (10 ml of formaldehyde added to 90 ml of water). Then it was send for histopathological study to diagnostic centre.

RESULTS

Results of cardiac biomarkers was showed a significant increase in serum concentrations of Triglyceride, Total cholesterol, LDL in Disease control group in comparison to normal group. This elevation was significantly decreased in DL-treated group, and decrease in HDL in Disease control group in comparison to normal group. This elevation was significantly increase in DL-treated group, indicating the cardio protective role of plant. *Table 1:* Represented the effects of 5-FU and DL, vit. E treatment on serum lipid profile, including TAG, TC, HDL, LDL concentrations in different rat groups.5-FU treatment significantly increased the serum TAG and TC levels in Disease control group in comparison to normal group indicating hypertriglyceridemia and hypercholesterolemia. Serum LDL concentrations are significantly increased while the serum HDL concentration is significantly decreased in disease control group in comparison to normal group.

Table.1

SL.NO.	Group	Total cholesterol (mg/dl)	Triglyceride (mg/dl)	HDL(mg/dl)	LDL(mg/dl)
1	Normal	89±0.428	76.17±0.477	52.17±0.792	40.33±0.666
2	Disease control	156±0.494###	191.2±0.909###	37.5±0.562###	53.33±0.666###
3	Standard	106.2±0.477***	95.83±0.792***	45.83±0.307***	43.3±0.421***
4	Low Dose	116.3±0.494***	111.8±0.792***	41.83±0.401***	46±0.365***
5	High Dose	108.3±0.714***	102±2.543***	45.17±0.307***	43.17±0.654***

Value are expressed as mean±SEM and n=6. ###P<.001 when compared to normal.
***P<.001when compare to disease control.

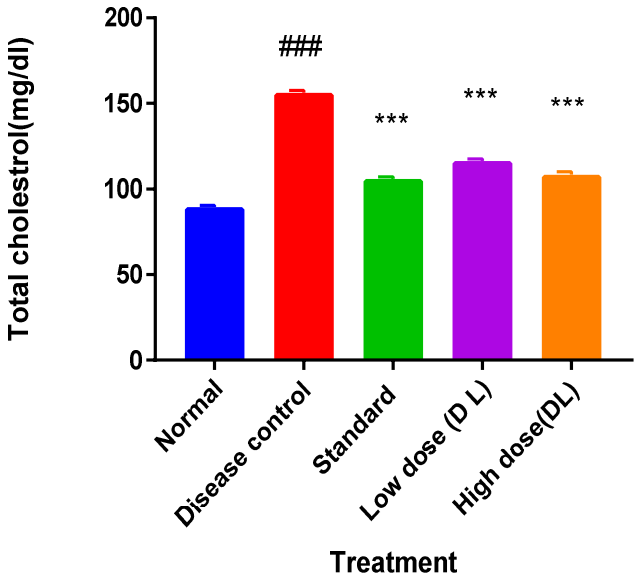

Fig.A.1.Effect of 5-FU,Vit.E and Dalbergia latifolia on serum Total cholestrol level

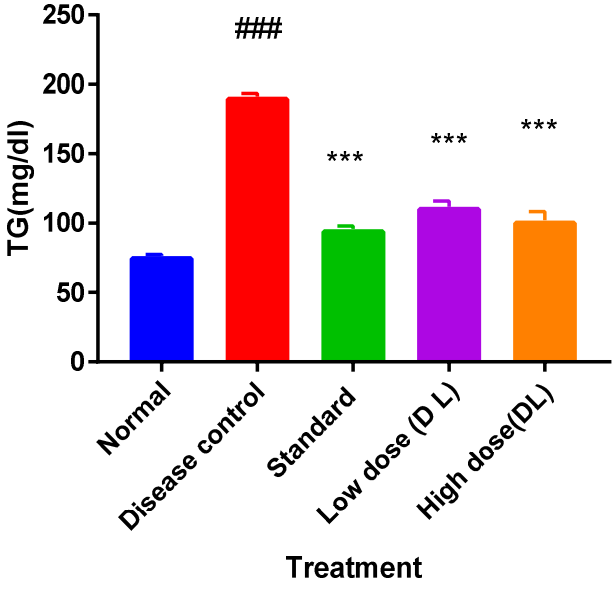

Fig.A.2. Effect of 5-FU,Vit.E and Dalbergia latifolia on Triglyceride

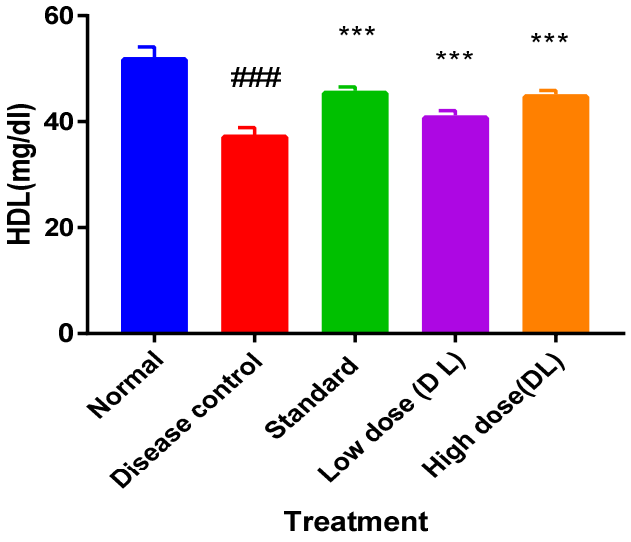

Fig. A.3. Effect of 5-FU,Vit.E and Dalbergia latifolia on HDL level

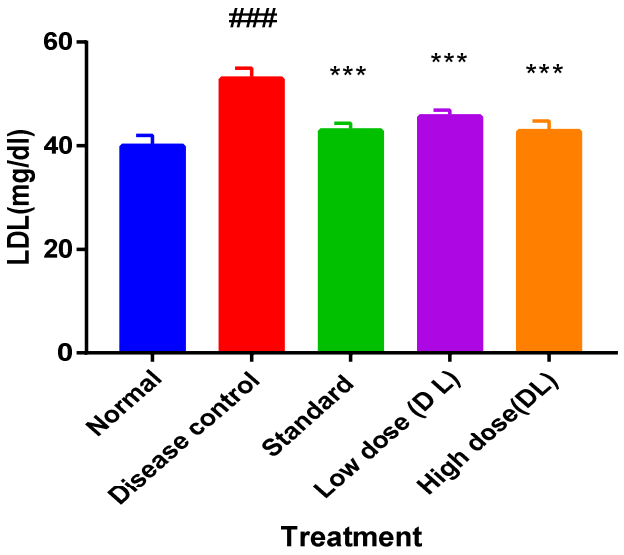

Fig.A.4. Effect of 5-FU,Vit.E and Dalbergia latifolia on LDL level

Histopathology of 5-FU induced myocardial necrosis

Normal (Heart)

Microscopy: Section studied from the myocardium shows intact arrangement of the cardiac muscle fibers [Fig.B.1, Arrow]. The cardiac muscle fibers show intact integrity of myocardial cell membrane, myofibrillar structure with striations and continuity with adjacent myofibrils [Fig.B.2, Arrow]. The interstitial space appears within normal limits.

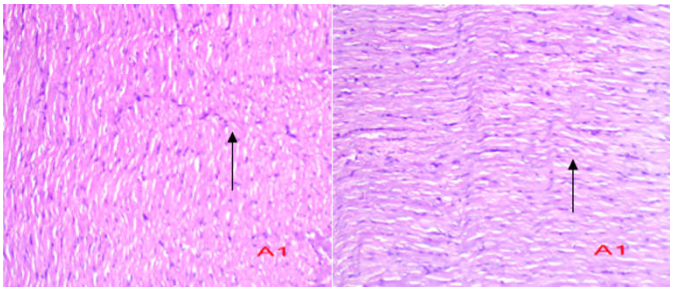

Fig.B.1 [H&E, x200] Fig.B.2 [H&E, x200]

Disease control

Microscopy

Section studied from the myocardium shows focally haphazard arrangement of the cardiac muscle fibers [Fig.B,3, Arrow]. The cardiac muscle fibers show focal loss of integrity of myocardial cell membrane, myofibrillar structure with focal loss of striations and loss of continuity with adjacent myofibrils [Fig.B,4, arrow]. The interstitial space appears increased at focal areas.

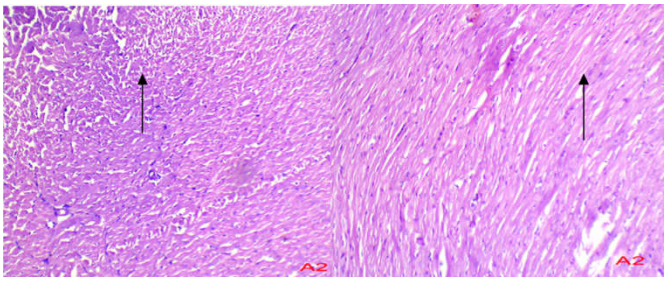

Fig.B,3 [H&E, x200] Fig.B,4 [H&E, x200]

Standard Group

Microscopy

Section studied from the myocardium shows intact arrangement of the cardiac muscle fibers [Fig.B,5, Arrow]. The cardiac muscle fibers show intact integrity of myocardial cell membrane, myofibrillar structure with focal loss of striations and loss of continuity with adjacent myofibrils [Fig.B,6, arrow]. The interstitial space appears increased at few areas.

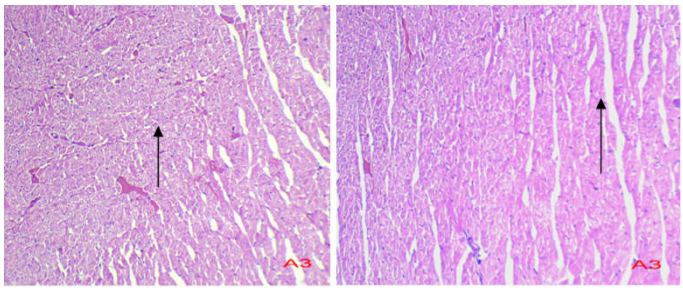

Fig.B,5 [H&E, x200] Fig.B,6 [H&E, x200]

Low Dose

Microscopy

Section studied from the myocardium shows intact arrangement of the cardiac muscle fibers [Fig.B,7, Arrow]. The cardiac muscle fibers show intact integrity of myocardial cell membrane, myofibrillar structure with focal loss of striations and loss of continuity with adjacent myofibrils [Fig.B,8, arrow]. The interstitial space appears increased at few areas.

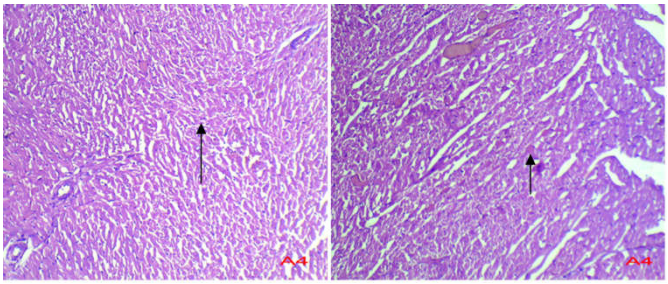

Fig.7[H&E, x200] Fig.8[H&E, x200]

Table.2. Show the antioxidant activity of 5-FU, D L and Vit. E

Sl.No	Group	Catalase (unit/mg protein/min)	Superoxide dismutase (unit)	LPO (MDA nmol/mg protein)	GLUTATHIONE PEROXIDASE (mmol/min/mg protein)
1	Normal	20.5±0.50	1.46±0.040	3.165±0.045	42.15±0.95
2	Disease control	12±0.5##	0.85±0.05###	4.75±0.05###	31.51±0.49##
3	Standard	17±1.00**	1.35±0.010***	3.5±0.40***	39.15±1.15**
4	Low dose	15.5±0.50**	1.205±0.015***	4.15±0.15***	38.78±0.37**
5	High dose	17±1.00**	1.43±0.02***	3.5±0.10***	38.6±1.60**

Value are expressed as mean±SEM and n=6. ***P<0.001, ###P=<.001,##P=0.006,and**P=0.006 when compared to normal.

High Dose

Microscopy

Section studied from the myocardium shows intact arrangement of the cardiac muscle fibers. These cardiac muscle fibers show intact integrity of myocardial cell membrane, myofibrillar structure with striations and continuity with adjacent myofibrils [Fig.B,9, Arrow]. The interstitial space appears intact [Fig.B,10, Arrow].

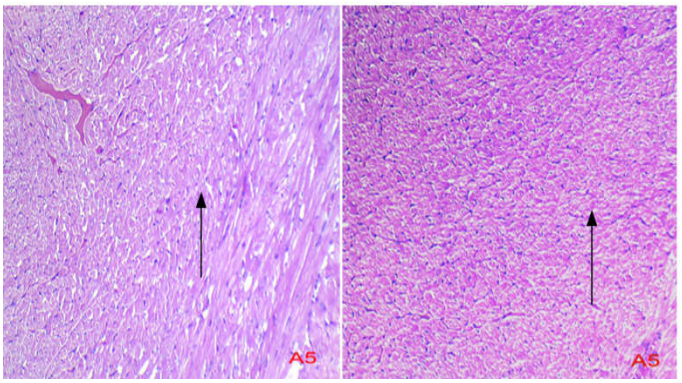

Fig.B,9[H&E,x200] **Fig.B,10[H&E, x200]**

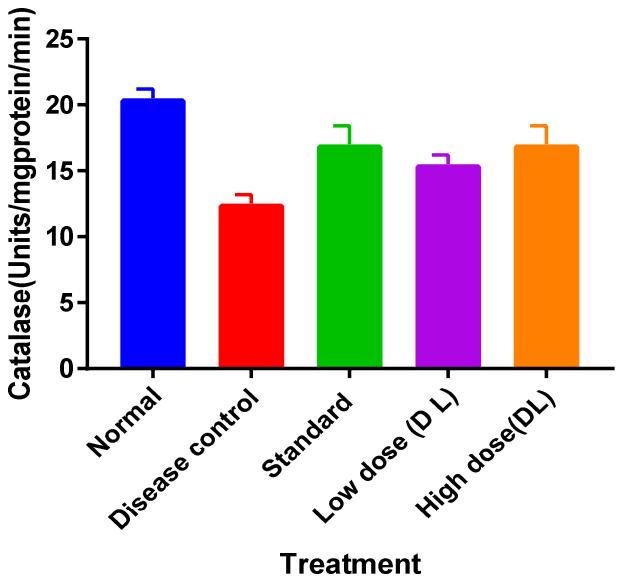

Fig.C.1 Effect of 5-FU,Vit.E and Dalbergia latifolia on catalase activity

Antioxidant activity of Superoxide dismutase

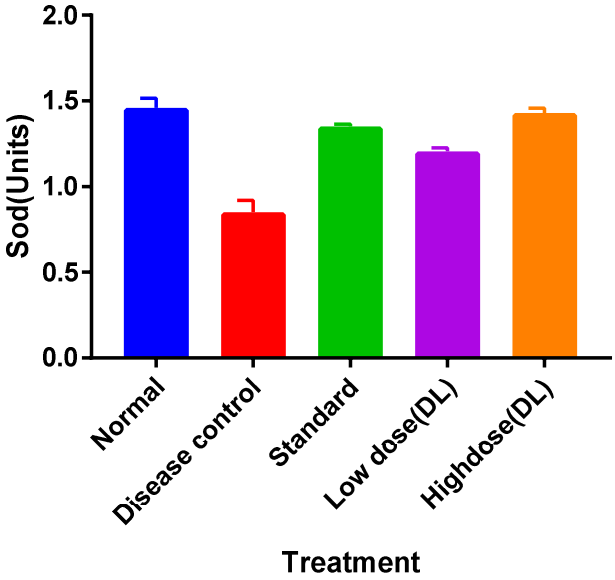

Fig.C.2. Effect of 5-FU,Vit.E and Dalbergia latifolia on sod

Antioxidant activity of lipid peroxidation

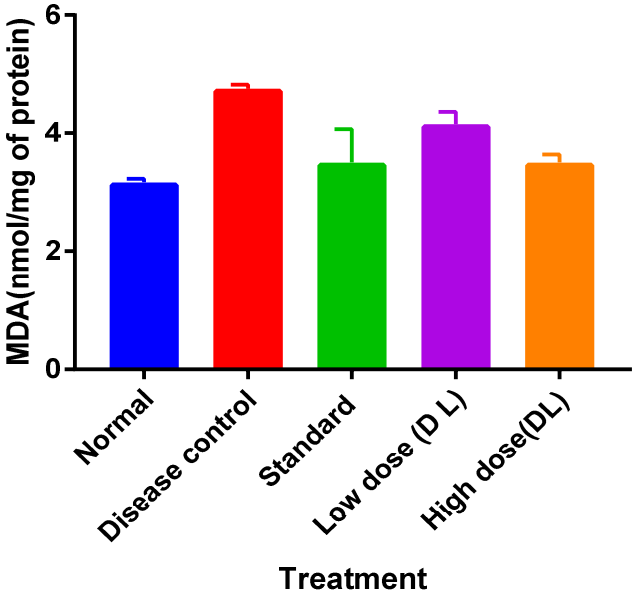

Fig.C.3. Effect of 5-FU, Vit.E and Dalbergia latifolia on lipid peroxidation

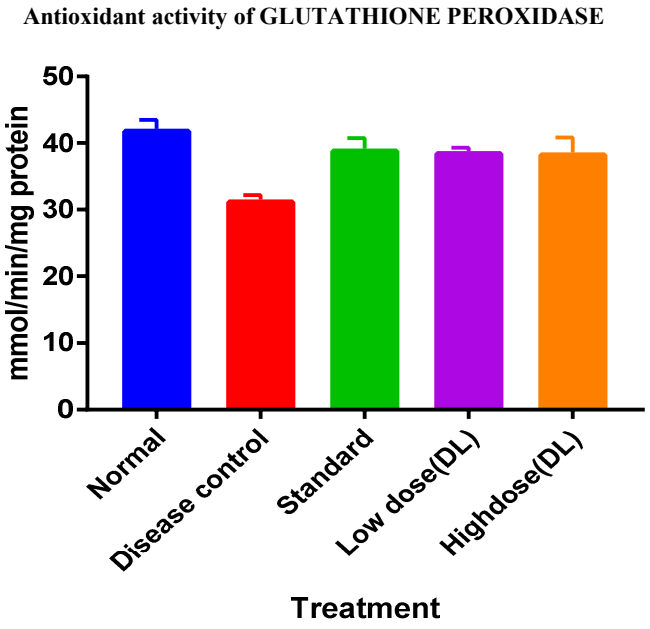

Fig.C.4 .Effect of 5-FU,Vit.E and Dalbergia latifolia on GLUTATHIONE PEROXIDASE.

DISCUSSION

CVD includes high blood pressure, coronary heart disease, congestive heart failure, stroke and accounts Myocardial infarction is the interruption of blood supply to part of the heart, causing heart cells to die, commonly due to blockage of coronary artery [Amit Kumar *et al.,* 2017]. Dalbergia latifolia Leaves extract was used as antidiabetic, antioxidant anticancer, analgesic, antipyretic and for jaundice. Flowers were used for Skin problems, as blood purifier and immunity Booster [Khare, 2007].

FU- induced myocardial necrosis in rats

In this study animal feed with normal diet for 8 days. Then 5-FU is given on 5th day, On the 9th day the fasted rats were sacrificed under diethyl ether anesthesia and blood samples were collected into plain sample bottles. Blood samples were collected via retro-orbital puncture or by cardiac puncture with 21G needle mounted on 5ml syringe. The animals were analysed according to standard methods for effect of the 5-FU, vit-E, and extract on various biochemical parameters of rats such as TC, TG, LDL and HDL. Administration of 5-FU in control rats showed a significant increase serum Total Cholesterol (TC), Triglycerides (TG), low density lipoprotein (LDL) and decrease in High density lipoprotein (HDL). Rats treated with vit-E (100 mg/kg), methanolic extract of Dalbergia latifolia(250mg/kg and 500 mg/kg) showed decreased TC, TG, LDL and increases HDL levels. Many studies have shown that free radicals cause several damages to the human body. The free radicals such as reactive oxygen species (ROS) and reactive nitrogen species (RNS) are continuously generated inside the human body. Reactive oxygen species (ROS) such as superoxide anion radical, hydroxyl radical, and H2O2, can cause oxidative damage of DNA, proteins, lipids, and small cellular molecules. Increasing evidence has suggested that many human diseases, such as cancer, cardiovascular disease, neurodegenerative disorders and also the process of aging, are the results of oxidative damage by reactive oxygen species [Zhao *et al.,* 2006].

The antioxidants are known to play an important role in protection against disorders caused by oxidative damage. Antioxidants can delay or inhibit the initiation or propagation of oxidative chain reaction [Tiwari and Tripathi, 2007]. Studies demonstrated that higher intake of antioxidants in the human diet reduces the complexity in such diseases [Aljadi and Kamaruddin, 2004]. Synthetic antioxidants such as butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA) and tert- butylhydroxyquinone (TBHQ) are usually used as food additives by the food industry to prevent lipid peroxidation. However, their applications have been limited because they exhibit toxicity and carcinogenic potential, show lower efficiency than natural antioxidants, and require high manufacturing costs. Thus, there is a need to identify natural and possibly more economic and effective antioxidants [Mathew and Abraham, 2006]. Natural antioxidants are also in high demand for application as nutraceuticals as well as food additives because of consumer's preferences [Zielinski and Kozlowska, 2000]. Natural products from microbial origin have played and still playing an invaluable role in drugdiscovery, which counts for more than 30% of worldwide human pharmaceutical sales [Schmid *et al.,* 1999]. Moreover, natural products and their derivatives constituted about 50% of the approved drugs over the period 1981-2002 [Newman *et al.,* 2003]. Administration of Dalbergia latifolia and Vit. E resulted in a significant correction in Cardioprotective and antioxidant activity when compared to the normal.

Conclusion

From the experimental studies carried out, extract of leaves of Dalbergia latifolia at two different administered doses (250 mg/kg and 500 mg/kg) showed dose dependent cardioprotective and antioxidant activity. The higher dose 500 mg/kg showed significant protection compared to lower dose 250 mg/kg. The cardioprotective and antioxidant effect may be due to the presence of flavonoids. Further studies need to be carried out to isolate the potential chemical constituents of flavonoid of leaves of Dalbergia latifolia and to find its mechanism of action in the treatment.

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