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COMPARATIVE CARDIOPROTECTIVE ACTIVITY ON THE LEAVES OF *SAPINDUS EMARGINATUS*

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ABSTRACT

The study investigates the cardio protective activity of ethanolic and water extracts of *Sapindus emarginatus* in doxorubicin induced myocardial infracted rats. Marked increase in the serum marker enzymes lactate dehydrogenase (LDH), SGOT, SGPT & CK-MB were observed in the doxorubicin treated rats when compared to extract treated and normal control rats. Administration of ethanol and water extract (500mg/Kg) for 30days and on 29th and 30th day with a single injection of doxorubicin showed a significant reduction in the elevated serum enzyme biomarkers levels. The histopathological study confirmed the results shown by the rats on reducing the elevated biomarker level by protecting the heart from the toxic effect of doxorubicin. But when compared to the ethanol extract, water extract showed a promising & significant cardio protective effect in the leaves of *Sapindus emarginatus*.

Key words: *Sapindus emarginatus*, Ethanol extract, Cardio protective.

INTRODUCTION

The plant *Sapindus emarginatus* is commonly known as soap nut tree. A deciduous tree found wild in north India, usually with 5-10 pairs of leaves, solitary with large drupes. This tree flourishes in deep clayey loam soil and does best in areas experiencing nearly 150 to 200 cm (60 to 80 in) of annual rainfall (Anonymous, 2004). The plant contains tannins& saponins in rich amount and flavonoid, carbohydrates was also found to contain (Kirtikar and Basu, 2004). Earlier literature review reveled that saponins can be used as an cardio protective agent. Hence an attempt has been made to evaluate the cardio protective effect of saponins present in the leaves of *Sapindus emarginatus*.

MATERIALS AND METHODS

Experimental Animals

Wistar albino rats (120-180gm) of either sex and of approximate same age used in the present studies were procured from listed suppliers of Sri Venkateswara Enterprises, Bangalore, India. The animals were fed with standard pellet diet (Hindustan lever Ltd. Bangalore) and water ad libitum. All the animals were housed in polypropylene cages. The animals were kept under alternate cycle of 12 hours of darkness and light. The animals were acclimatized to the laboratory conditions for 1 week before starting the experiment. The experimental protocols were approved by Institutional Animal Ethics Committee.

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Procedure

The animals were grouped as group-I (normal) rats, group-II doxorubicin induced myocardial infarcted rats without treatment (Induced Control) and group-III & IV pre treated with extracts and on day 29th & 30th with doxorubicin. Myocardial infarction was induced by a subcutaneous administration of doxorubicin (20mg/100g) twice at an interval of 24hrs (Osman *et al*., 2009; Shuai Y *et al*., 2007).

Group-I is given normal food and water throughout the study.
Group – II also has been treated in the same way but on 29th and 30th day were administered with doxorubicin at a dose of 20mg/100gm at an interval of 24hrs.
Group – III has been administered with the MESE at a dose of 500mg/kg for 28 days and on days 29 and 30th day the rats were administered with doxorubicin at a dose of 20mg/kg at an interval of 24hrs.
Group – IV has been administered with the AESE at a dose of 500mg/kg for 28 days and on days 29 and 30th day the rats were administered with doxorubicin at a dose of 20mg/kg at an interval of 24hrs.

Histopathological Examination

On day 30 1 hr after the injection, blood samples were collected through the orbital cavity for biochemical study and the hearts were subsequently removed and processed for histopathological examination. Histopathological examination of rat's heart section confirmed myocardial injury with doxorubicin.

To carry out histopathological examination the hearts were excised and immediately fixed in 10% buffered formalin. The ventricular mass was sectioned from the apex to the base of the heart, which was embedded in paraffin after being dehydrated in alcohol and subsequently cleared with xylene.

Five-micrometer thick serial histological sections were obtained from the paraffin blocks and stained with hematoxylin and eosin. The sections were examined under light microscope and photomicrographs were taken (Bodhankar SL *et al*., 2012).

Statistical Analysis

The results were presented as mean + standard deviation (SD). Student 't' test was used to analyze statistical significance.

RESULTS

Heart weight, Body weight and ratio of heart weight to body weight

The animal's body weight and heart weight were recorded for all the groups and is found that the ratio of heart weight to body weight is less in drug treated groups as compared to doxorubicin treated groups. The results were tabulated in Table-3.

The doxorubicin induced control group rats showed significant elevation in serum SGOT, SGPT, LDH and CK-MB levels is an indicator for cardiac toxicity. The serum enzyme viz SGOT and SGPT serves as sensitive indices to assess the severity of myocardial infarction. CK-MB and LDH cardiac enzymes found primarily in the myocardium are used to evaluate the existence and extent of myocytes injury. The increase of these biomarkers in serum and extracellular fluids suggests an increased leakage of these enzymes from mitochondria was due to the treatment with doxorubicin. Both the extracts had shown significant inhibition of elevated serum biomarkers such as CK-MB, SGOT, SGPT and LDH.

Histopathological Examination

Abbreviation and Description

C	=	Congestion
DC	=	Degenerative Changes
ID	=	Intercalated Disks
MF	=	Myocardial Fibers
N	=	Nuclei

Normal Control:

- The normal architecture of the myocardial tissue with lower magnification (10X); And Higher magnification (40X).

Induced control:

- The degenerative changes in myocardial tissue with congestion in the doxorubicin induced rats with lower magnification (10X); And Higher magnification (40X).

EESE

- Regeneration of heart tissue takes place and shows similar to normal cyto-architecture with lower magnification (10X); And Higher magnification (40X).

WESE:

- Regenerative changes in heart tissues shows similar to normal cyto-architecture of myocardial tissue with lower magnification (10X); And Higher magnification (40X).

Table 1. Heart to Body weight ratio of the animals

Groups	Treatment	Body weight (gms)	Heart weight (gms)	Heart / Body weight ratio (10^{-3})	Mortality
I	Normal Control	185	0.85	4.5	0/3
II	Induced Control	185	0.99	5.3	0/3
III	Drug treated (EESE)	190	0.68	3.5	0/6
IV	Drug treated (WESE)	186	0.71	3.7	0/6

EESE – Ethanol extract of *Sapindus emarginatus*
WESE – Water extract of *Sapindus emarginatus*

Table 2. Effect of Extracts on Serum Biomarkers in Normal and Doxorubicin Exposed Rats

Groups	**Treatment**	**CK-MB**	**LDH**	**SGOT**	**SGPT**
GROUP I	Normal Control	128±2.01	126.16±4.16	82.33±2.812	54.33±3.52
Group II	Induced Control	264.66±4.06	308.33±15.14	203±4.13	115.66±4.65
Group III	EESE	186±2.39**	199.33±5.81**	177.83±3.81**	85.16±1.44**
Group IV	WESE	161.5±4.81**	161.83±3.88**	94.5±6.07**	59.5±2.32**

The values are mean±SEM, n=6 when compared with induced control **p<0.01.

Figure 1. Effect of Extracts on Serum Biomarkers in Normal and Doxorubicin Exposed Rats

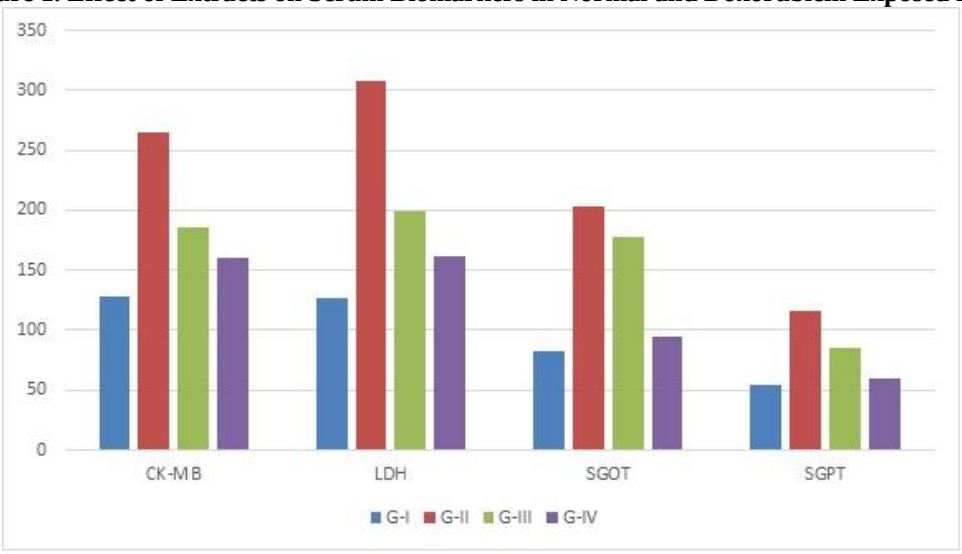
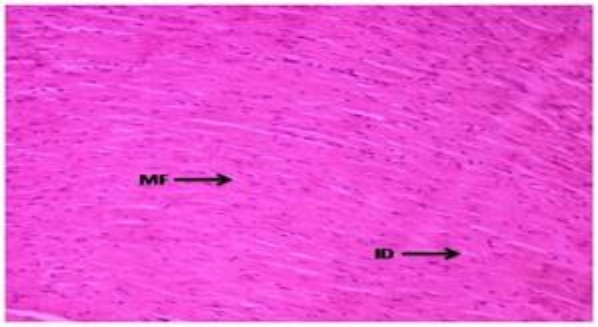
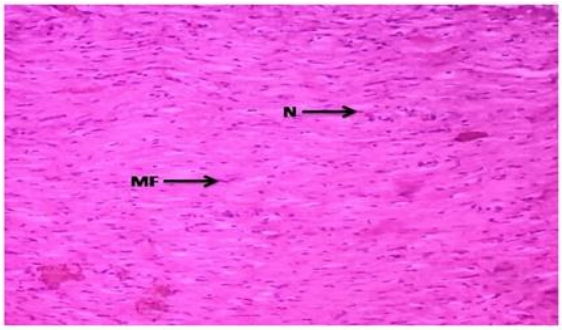


Figure 2. Diagram showing structure of heart of Normal Control



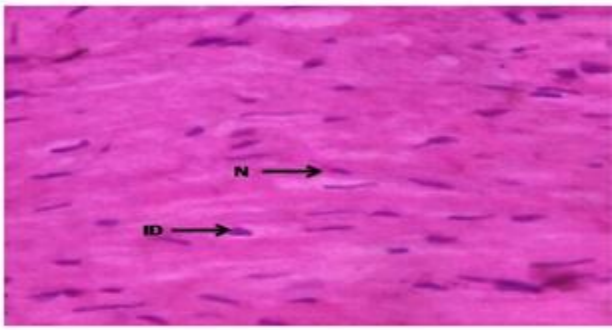
NORMAL CONTROL 40X

Figure 3. Diagram showing structure of heart of Induced Control rats



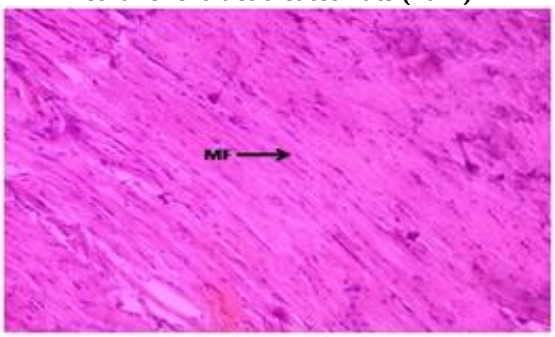
INDUCED CONTROL 2 10X

Figure 4. Diagram showing structure of heart of Induced Control rats



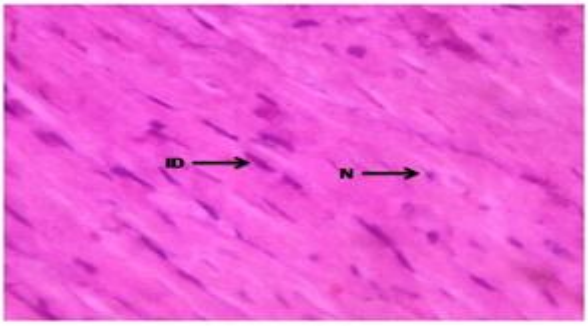
INDUCED CONTROL 2 40X

Figure 5. Diagram showing structure of heart of ethanol extract treated rats (10 X)



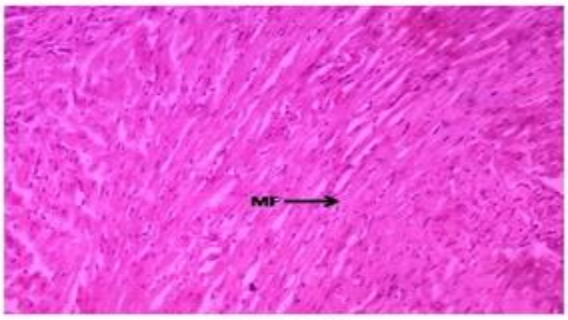
DOSE 1 10X

Figure 6. Diagram showing structure of heart of ethanol extract treated rats (40 X)



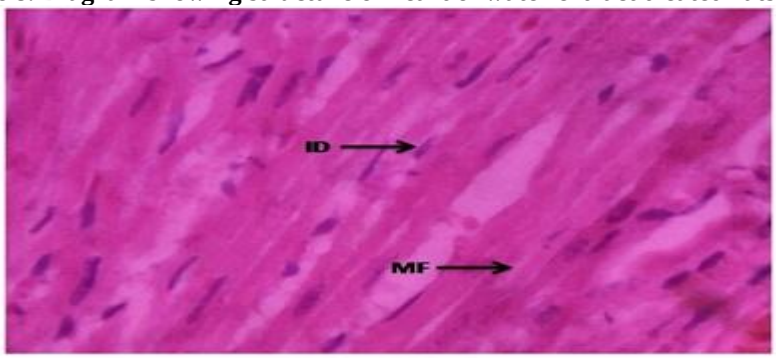
DOSE 1 40X

Figure 7. Diagram showing structure of heart of water extract treated rats (10 X)



DOSE 2 10X

Figure 8. Diagram showing structure of heart of water extract treated rats (40 X)



DOSE 2 40X

DISCUSSION

Doxorubicin, a potent anti tumour agent cures several types of cancer and lymphomas but provides acute and chronic toxicities (Zhon S *et al*., 2001). Acute cardiotoxicity may cause arrhythmiasis while chronic toxicity may leads to irreversible cardio myopathy. The elevation of the levels of different enzymes by doxorubicin treatment is probably denotes that the drug induces cardio toxicity and an elevation in CK-MB level specifically denotes myocardial damage (Adel RA Abd-Allah *et al*., 2002; Naidu MUR *et al*., 2002).

In our study, the ethanol and water extracts of the *Sapindus emarginatus* leaf were injected at a dose of 500mg/kg for 30 days and on 29th and 30th day, doxorubicin was injected. After a hour of doxorubicin injection on 30th day, blood sample were collected and the hearts were isolated for histopathological examination (Daoud SS, 1992; Murat Y *et al*., 2003).

The body weight of the drug treated rats had increased while the body weight for the doxorubicin had decreased has decreased. The estimation of serum enzyme biomarkers in the collected blood sample sharply indicated that the doxorubicin produced severe myocardial damage which has been confirmed by the marked increase in the CK-MB level in those rats and also by its histopathology specimen (Bristow MR *et al*., 1980; Antonio A *et al*., 2005).

The drug treated rats showed remarkably reduced levels of the biomarkers and less myocardial damage. But when compared to the ethanol extract, the water extract of the leaves of *Sapindus emarginatus* had restored the elevated serum enzyme levels to its normal levels.

CONCLUSION

It is concluded that the leaves of *Sapindus emarginatus* has showed a potential cardio protective activity by reducing the doxorubicin induced cardiac damage.

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