



Research Article

Cardioprotective activity of Dasamula Arka in doxorubicin-induced cardiomyopathy in Wistar Albino Rats: An in-vivo study

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Abstract

Background: Cardiovascular diseases and cancer are the two leading causes of death globally, with chemotherapeutic drugs being a common contributor to the development of dilated cardiomyopathy. Dexrazoxane, a medication used to protect the heart from the cardiotoxic effects of chemotherapy, itself produces a range of side effects. As the incidence of cardiac complications continues to rise, there is an urgent need for the medical field to develop more effective and safer cardioprotective drugs. **Objective:** To evaluate the cardioprotective activity of *Dasamula arka* in doxorubicin induced cardiomyopathy on Wistar albino rats. **Materials and methods:** Cardiomyopathy was induced in animals via intraperitoneal doxorubicin injection (3 mg/kg) every other day for 2 weeks. The animals were divided into 6 groups (6 animals each): Vehicle control, Negative control (Doxorubicin 3 mg/kg), Positive control (Dexrazoxane 30 mg/kg), and treatment groups receiving *Dasamula arka* at 0.432 mg/kg (half dose), 0.864 mg/kg (therapeutic dose), and 1.728 mg/kg (double dose) for 28 days. *Dasamula arka* was administered alongside doxorubicin from days 14–28. After treatment, blood was collected for biochemical analysis, heart weight was measured, and hearts were histopathologically examined. **Result:** *Dasamula arka* significantly normalized biochemical parameters, relative heart weight and histology findings compared to the untreated negative control group. The double-dose group showed slightly better cardioprotective effects than the positive control and other *Dasamula arka* groups. **Conclusion :** The present data indicate that *Dasamula arka* exhibits significant cardioprotective activity, effectively mitigating doxorubicin-induced cardiac toxicity in Wistar albino rats.

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Keywords: Cardioprotective activity, Dasamula arka, Dexrazoxane, Doxorubicin, *Hridroga*

Introduction

Cardiovascular diseases and cancer are the 2 leading causes of death globally. An estimated 19.8 million people died from cardiovascular diseases in 2022, representing 32% of all global deaths and cancer accounted for nearly 10 million deaths in 2024, or nearly 1 in 6 deaths, according to the WHO.(1) (2)Cardiomyopathy is one of the reasons for heart failure. Dilated cardiomyopathy is the most common form.(3) Use of chemotherapeutic drugs is one of the common reasons for developing dilated cardiomyopathy.(4) Anthracyclines are widely used chemotherapeutic drugs. Doxorubicin, an antineoplastic

drug, is one of the strongest anthracycline drugs used in chemotherapy for various malignancies. It is found to induce cardiotoxicity.(5) Dexrazoxane is a cardioprotective agent used to protect the heart from the side effects caused by doxorubicin.(6) Even though dexrazoxane is effective in cardio protection, it produces many adverse reactions which is similar to the side effect profile of anthracyclines. Other adverse reactions include increased renal excretion of iron and zinc, hair loss, mucositis, myelosuppression etc.(7) Hence a more effective and less toxic pharmaceutical alternative or an adjuvant is necessary.

In the present study, *Dasamula arka* was tested for its cardioprotective role on animal model. The raw drugs in *Dasamula*, namely *Bilwa*, *Agnimantha*, *Shyonaka*, *Patala*, *Gambhari*, *Brihati*, *Kantakari*, *Salaparni*, *Prisniparni* and *Gokshura* when observed individually, exhibits cardioprotective action. Various studies conducted on each of them proves the statement to be true. *Dasamula* is used for the management of *hridroga*. It is widely used in many disorders due to its various

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pharmacological actions. It balances the excess *vata* in the biological system. This polyherbal formulation consists of various phytochemicals and exhibits both anti-inflammatory and antioxidant properties. (8) *Arka* is one of the important drug dosage forms in *Bhaishajya Kalpana*. It has reduced dosage, more shelf life, more potency and palatability in comparison to other *kalpanas*, which proves to be a better option for this study. *Dasamula arka* is based on the Ayurvedic treatise, *Ayurveda Sara Sangraha*. (9) The biomarkers of cardiomyopathy namely, total cholesterol, lipid profile, triglycerides, alkaline phosphokinase (ALP), creatine phosphokinase (CPK) and lactate dehydrogenase (LDH) were monitored. All the levels of the clinical biomarkers have been tested to confirm the cardioprotective activity of *Dasamula arka*.

Dasamula arka has shown significant activity in cardio protection in an in-vitro study conducted recently. (10) To explore the cardioprotective action from the proven evidence of its action in-vitro, this pre-clinical study will allow more translatable results for humans with minimal side effects.

Table 1: Ingredients of *Dasamula arka*

Ingredients	Botanical name	Family	Part used	Ratio
<i>Bilwa</i>	<i>Aegle marmelos</i> (L.) Corrêa	Rutaceae	Root	1 part
<i>Agnimantha</i>	<i>Premna serratifolia</i> L.	Verbanaceae	Root	1 part
<i>Shyonaka</i>	<i>Oroxylum indicum</i> (L.) Kurz	Bignoniaceae	Root	1 part
<i>Gambhari</i>	<i>Gmelina arborea</i> Roxb.	Verbanaceae	Root	1 part
<i>Brihati</i>	<i>Solanum indicum</i> L.	Solanaceae	Root	1 part
<i>Kantakari</i>	<i>Solanum xanthocarpum</i> Schrad. & H. Wendl.	Solanaceae	Root	1 part
<i>Shaalaparni</i>	<i>Desmodium gangeticum</i> (L.) DC.	Fabaceae	Root	1 part
<i>Prisniparni</i>	<i>Uraria picta</i> (Jacq.) Desv. ex DC.	Fabaceae	Root	1 part
<i>Gokshura</i>	<i>Tribulus terrestris</i> L.	Zygophyllaceae	Root	1 part
Water				10 parts

Method of manufacturing *Arka Yantra*

A large, round-shaped earthen vessel with a neck measuring more than three *angulas* (approximately 5.85cm) was selected to hold the crude drugs for the distillation process. A matching lid was placed to cover the mouth of the pot, ensuring a three-*angula* rim. *Jeernasthi mruttika* (aged earthen clay) was applied to seal the edges, rendering the apparatus airtight. Two bamboo tubes were utilized: one small tube and another double the length of the first. The tubes were inserted four *angulas* (approximately 7.8 cm) into the pot and sealed firmly with clay. An *arka patra* (collection vessel) was positioned beneath the larger tube. The vapor emerging from the pot was collected in this vessel, which was maintained in cold water. Consequently, condensed vapour was collected in the form of *arka*.

Preparation of *Dasamula arka*

According to the method for preparing *Arka* described in *Rasatantrasara va sidhaprayoga sangraha*, one part of the drug was soaked in water 10 times its weight. (11) Hence, about 40gm each of powdered samples of *Bilwa*, *Agnimantha*, *Shyonaka*, *Patala*, *Gambhari*, *Brihati*, *Kantakari*, *Shaalaparni*, *Prisniparni* and *Gokshura* was placed in an earthen pot submerged in 2 litres of sterilized distilled water for soaking and left undisturbed for a duration of 24 hours. After 24 hours, it was poured into the *Arka yantra* and the remaining 2 litres of water

Aim

Evaluate the cardioprotective activity of *Dasamula arka* in doxorubicin induced cardiomyopathy in Wistar Albino rats.

Materials and Methods

Collection and drying of plant materials

For the preparation of the test formulation *Dasamula arka*, the ingredients [Table 1] namely *Bilwa*, *Agnimantha*, *Shyonaka*, *Patala*, *Gambhari*, *Brihati*, *Kantakari*, *Shaalaparni*, *Prisniparni* and *Gokshura* drugs was collected from different vendors across the state. The collected roots was authenticated in the Pharmacognosy lab of Department of *Dravyaguna Vigyana*, Government Ayurveda College, Tripunithura. The collected roots were washed with water thoroughly to remove physical impurities and thoroughly dried in the shade. Later they were crushed and then powdered using electric blender to make a coarse powder.

was added and subjected to distillation. Initial drops of condensed vapors were discarded and the later formed were collected in the *arka patra*. The total yield was 70%.

Animal selection

A total of 36 healthy adult (8-12 weeks old) Wistar albino rats was procured from Small Animal Breeding Station, College of Veterinary and Animal Sciences, Mannuthy. The experiment was conducted in conformity with the internationally accepted principles for laboratory animal use and the experimental protocols were approved by the Institutional Animal Ethical Committee (IAEC), Small Animal Breeding Station, College of Veterinary and Animal Sciences, Mannuthy, Thrissur, Kerala, India, (328/GO/ReBt-S/Re-L/01/CPCSEA). The animals were maintained in the Department of Veterinary Pharmacology and Toxicology under controlled climatic conditions of 23-25 °C and 70 per cent humidity. They had free access to standard rat feed & ample water. Blood was collected prior to experimentation on the first day and on the last day before sacrificing.

Animals were randomly divided into 6 groups of 6 animals each. Each animal was marked and kept in 6 cages for observation. They were acclimatized for one week to laboratory conditions before starting the experiment. Weight of each animal was noted and dose was calculated.

Dose fixation

In the present work, the fixed human dose of *Dasamula arka* is 48 ml. The effective dose of the test drug for rats will be calculated using the formula given by M.N.Ghosh in Fundamentals of experimental pharmacology.(12) The doses of the drugs are calculated by deducing the therapeutic dose to rat dose on the basis of the body surface area (conversion factor 0.018 for rats).

1. *Dasamula arka* (Test drug):

Animal dose = Human dose x 0.018 for rat weighing 200gm.

= 48 x 0.018 = 0.864ml (X)

For cardioprotective study,

X dose (therapeutic dose) is taken as 0.864ml/Kg.bw, 1/2 X dose as 0.432 ml/Kg.bw (Half dose) and 2 X as 1.728 ml/Kg.bw. (Double dose)

2. Doxorubicin: 3mg/Kg.bw

3. Dexrazoxane: 30mg/Kg.bw

Grouping of animals

- Group 1: Normal control, given with normal saline
- Group 2 : Negative control, Cardiomyopathy induced with Doxorubicin (DOXO) in the dose of 3mg/Kg body weight of animal
- Group 3 : Positive control. Administered with Dexrazoxane (DEXA) in the dose of 30mg/Kg body weight of animal
- Group 4 : Test group Half dose DA (LD), administered with *Dasamula arka* in the dose 0.432 ml/Kg body weight of animal
- Group 5 : Test group Therapeutic dose DA (TD), administered with *Dasamula arka* in the dose 0.864 ml/Kg body weight of animal
- Group 6 : Test group Double dose DA (DD), administered with *Dasamula arka* in the dose 1.728 ml/Kg body weight of animal

Experimental protocol

The grouped animals were kept in separate cages and marked for their easier observation. They were kept on fasting for around 12hrs. Following the period of acclimatization, Group 1 was given normal saline throughout the experimental days. Doxorubicin was injected intraperitoneally on alternate for 2 weeks on group 2. Whereas, dexrazoxane was injected intraperitoneally 30 minutes prior to doxorubicin injection for 2 weeks on alternate days for group 3. The test drug was given to respective groups at morning hours for 4 weeks from day 0. After the administration of test drug for 2 weeks, Doxorubicin was co administered as injection intraperitoneally for 2 more weeks on alternate days for group 4, 5 & 6. Blood from retro orbital plexus was collected by capillary puncturing & send to laboratory for estimation of serum biochemical parameters. Then these animals were sacrificed by overdose of anaesthesia. Abdomen was opened by midline incision & heart was dissected & cleaned for extraneous tissue. Heart was weighed, & transferred to 10% formalin solution & send for histopathological studies.

Statistical Analysis

SPSS version 21 was used to analyse the data, which were gathered in Microsoft Excel. The frequencies, percentages, means, and standard deviations of the data were analysed. Kruskal Wallis

test was used for comparative statistics and p0.05 is regarded as the level of significance.

Results

Effect of *Dasamula arka*

Effect on serum biochemical parameters: On comparison with the normal group, there was drastic and significant increase in the serum Lactate dehydrogenase – LDH, Creatine Phosphokinase – CPK, Serum Alkaline Phosphatase and Lipid Profile in the group treated with Doxorubicin. Dexrazoxane treated groups showed significant reduction in the above-mentioned biochemical parameters. The same trend was followed by the group treated with *Dasamula arka*, but the effect was augmented at a dose of 1.728ml/Kg when compared to 0.432ml/Kg and 0.864ml/Kg.

Effect on histopathology of heart: On comparison with the normal group, the histopathological studies revealed an extensive cardiac damage in the group treated with doxorubicin. Dexrazoxane and test groups showed a protective effect by decreasing the extent of necrosis and degenerative changes in the myocardium, infiltration of inflammatory cells, haemorrhages as well as congestion in the blood vessels. The protective effect was intense at 0.864ml/Kg dose of *Dasamula arka*.

Effect on heart weight: On comparison with the normal group, both the groups treated with dexrazoxane and test drug revealed reduction in the heart weight. But when the test drug groups were compared, those which received double dose of *Dasamula arka* showed highly significant results.

Cardioprotective studies of raw drugs in *Dasamula*

Gambhari: Ethanolic extract of *Gmelina arborea* Roxb. has shown potential protective effect against doxorubicin (DOX) induced cardiotoxicity by increasing cardiac markers activities in plasma.(13) The result of the experimental study reveal that both *Ksheerapaka* and aqueous extract provide an adequate protection from free radical scavengers and oxidative stress and help them in maintaining the endogenous anti-oxidant levels. They were also contributory in the structural integrity of the cardiac cells thereby preventing any leakage of enzymes into the serum.(14)

Kantakari: Pharmacological studies on the herb have shown that aqueous and alcoholic extracts of the plant possess hypotensive. The glycoalkaloid fraction of the drug seems to possess cardiotonic effects worth investigating clinically.(15)

Prisniparni: In carrageenan – induced inflamed rats, administration of the root extract prior to reperfusion showed better antioxidant status in myocardial tissue homogenate and mitochondrial, complemented by the levels of cardiac specific marker proteins in myocardial tissue and perfusate.(16) The free radical elimination activity from the leaves, stems, and roots of *U. picta*. Antioxidant activity being the highest, prevents cardiovascular diseases.(17)

Salaparni: In vivo study in rats, the extract produced antioxidant activity. Scavenge the free radicals generated during ischaemia and ischaemia reperfusion thereby preserving the mitochondrial respiratory enzymes that eventually lead to cardio-protection.(18) Possesses the ability to scavenge the free radicals generated during ischaemia and ischaemia reperfusion thereby preserving the mitochondrial respiratory enzymes that eventually lead to cardio-protection. Showed better antioxidant status in myocardial tissue homogenate and mitochondrial, complemented by the levels of cardiac specific marker proteins in myocardial tissue and

perfusate. It maintains the normal vasculature of channels, keeps the myocardium healthy and helps in its proper functioning. (19)

Gokshura: In an in vivo study in rats, evaluated the protective effect of tribulosin from TT against cardiac ischemia/reperfusion injury to study the underlying mechanism in rats. Its results showed that Tribulosin protected myocardium against ischemia/reperfusion injury through protein kinase C epsilon activation. (20) Methanolic and aqueous extracts of TT are shown to possess significant antihypertensive activity by direct arterial smooth muscle relaxation and membrane hyperpolarization in spontaneously hypertensive rats in an in vitro study. (21) It protects the heart cells and may even improve the heart function following a heart attack. (22)

Bilwa: The leaf extract of *Bilwa* has a preventing effect in isoprenaline-induced myocardial infarction in rats. Use of *Bilwa* as a cardiac depressant and in palpitation has also been reported. (23) Fresh fruit juice of *Bilwa* with different dilution were used for cardiotonic activity. The activity was tested by using isolated frog heart assembly. (24) In an in vivo study, *Aegle marmelos* (L.) Corrêa, effectively prevented tissue damage by decreasing the oxidative stress and restoring the antioxidant status in doxorubicin-induced myocardial toxicity in albino rats. (25)

Patala: *Patala* has different therapeutic properties like Diuretics, anti-inflammatory, cardiac tonic. It is also used in the management

of *Tridosha*, as it is useful in the balance of *vata*. Flowers of *Patala* used in the management of blood-related disorders. (26)

Shyonaka: The cardioprotective effect of 70% methanol extract of root bark of *Sonapatha* was studied in doxorubicin-treated Sprague Dawley rats. The serum marker enzymes significantly reduced by methanol extract of *Sonapatha*. *Sonapatha* extract administration reduced focal degeneration, fragmentation, disorganization of myofibrils, and necrotic changes in the heart tissue in murine models, which was produced due to doxorubicin administration. Thus *Oroxylum indicum* (L.) Kurz root bark extract prevents doxorubicin-induced cardiac damage by restoring redox balance. (27)

Brihati: Root is diaphoretic and stimulant, useful in catarrhal affections, dropsy, toothache, dyspepsia, colic, verminosis, diarrhea, pruritus, leprosy, skin diseases, bronchitis, cardiac disorders and vomiting. (28)

Agnimantha: Cardioprotective effect of ethanol extract of stem-bark and stem-wood of *Premna serratifolia* L. were tested on isoproterenol-induced experimental myocardial infarction in rats. The ethanol extract of stem-bark and stem-wood of *Premna serratifolia* L. produced cardiotonic effect and aqueous extract of stem-bark and stem-wood of *Premna serratifolia* L. produced β -adrenergic effect. The cardioprotection was confirmed. (29)

Table 2: Comparative evaluation of serum biochemical parameters among experimental groups on the 28th day (Mean $\pm$ SD)

Biochemical parameter	Normal	Doxo	Dexra	LD	TD	DD
Toal cholesterol	79.77 $\pm$ 13.75	100.84 $\pm$ 3.67	73.80 $\pm$ 6.52	117.71 $\pm$ 22.66	96.78 $\pm$ 4.96	94.08 $\pm$ 3.26
Triglycerides	102.71 $\pm$ 11.51	108.73 $\pm$ 20.73	107.27 $\pm$ 2.87	127.73 $\pm$ 15.79	121.00 $\pm$ 19.13	87.03 $\pm$ 30.63
VLDL	20.54 $\pm$ 2.30	33.58 $\pm$ 3.26	22.79 $\pm$ 1.49	27.71 $\pm$ 2.80	24.20 $\pm$ 3.82	23.74 $\pm$ 1.61
HDL	39.55 $\pm$ 8.78	70.08 $\pm$ 24.47	39.61 $\pm$ 4.48	41.87 $\pm$ 14.82	28.74 $\pm$ 3.83	21.33 $\pm$ 2.09
LDL	71.97 $\pm$ 24.93	112.90 $\pm$ 9.50	80.73 $\pm$ 10.54	102.35 $\pm$ 3.91	80.45 $\pm$ 13.57	73.13 $\pm$ 16.99
ALP	99.80 $\pm$ 9.11	747.15 $\pm$ 261.79	447.88 $\pm$ 30.92	524.77 $\pm$ 80.24	217.98 $\pm$ 38.44	95.33 $\pm$ 9.90

Table 3: Comparative evaluation of relative heart weight among experimental groups on the 28th day (Mean $\pm$ SD)

Parameter	Normal	Doxo	Dexra	LD	TD	DD
Values	3.994 $\pm$ 0.214	6.807 $\pm$ 0.528	4.042 $\pm$ 0.081	6.921 $\pm$ 0.769	4.860 $\pm$ 0.345	3.920 $\pm$ 0.225

The effect of the test drugs on lipid profile, biochemical parameters and heart rate was evaluated in comparison with the doxorubicin-treated group. The results are expressed as mean $\pm$ SD.

Total cholesterol: The normal group showed a mean total cholesterol level of 79.76 $\pm$ 13.75, which increased to 100.84 $\pm$ 3.66 in the doxorubicin-treated group. Treatment with dexrazoxane reduced the level to 73.79 $\pm$ 6.53 ($p = 0.009$). Among the test drug groups, TD showed an increase in total cholesterol to 117.71 $\pm$ 22.66 ($p = 0.014$), whereas LD and DD showed values of 96.78 $\pm$ 4.96 ($p = 0.020$) and 94.08 $\pm$ 3.30 ($p = 0.013$), respectively. All the treatment groups showed statistically significant differences in comparison with the doxorubicin group.

Triglycerides: The mean triglyceride level was 102.71 $\pm$ 11.51 in the normal group and increased to 128.72 $\pm$ 20.73 following doxorubicin administration. Dexrazoxane treatment resulted in a reduction to 107.26 $\pm$ 2.86 ($p = 0.035$). The DD, TD and LD groups showed mean values of 105.73 $\pm$ 15.79 ($p = 0.034$), 121.00 $\pm$ 19.12 ($p = 0.036$), and 117.03 $\pm$ 30.62 ($p = 0.045$), respectively.

The differences observed between the treatment groups and the doxorubicin group were statistically significant.

Alkaline phosphatase: A marked elevation in alkaline phosphatase was observed in the doxorubicin group (747.15 $\pm$ 261.78) compared with the normal group (99.80 $\pm$ 9.10). Dexrazoxane significantly reduced the level to 447.88 $\pm$ 30.92 ($p = 0.001$). The TD, DD and LD groups showed values of 524.76 $\pm$ 80.24 ($p = 0.002$), 217.98 $\pm$ 38.43 ($p = 0.001$), and 95.33 $\pm$ 9.90 ($p = 0.003$), respectively. All treatment groups demonstrated statistically significant differences compared with the doxorubicin group, with the DD and LD groups showing a marked reduction in alkaline phosphatase.

Creatinine: The normal group exhibited a mean creatinine value of 236.50 $\pm$ 39.83, which increased to 414.18 $\pm$ 49.19 in the doxorubicin group. Dexrazoxane treatment reduced the value to 361.96 $\pm$ 49.13 ($p = 0.002$). The LD, TD and DD groups showed mean values of 439.38 $\pm$ 45.47 ($p = 0.003$), 301.57 $\pm$ 25.13 ($p = 0.001$), and 186.50 $\pm$ 36.44 ($p = 0.001$), respectively. The differences between each treatment group and the doxorubicin

group were statistically significant, with the DD group showing the greatest reduction.

Lactate dehydrogenase (LDH): The mean LDH level increased from 146.78 ± 18.65 in the normal group to 291.63 ± 63.96 in the doxorubicin group. Dexrazoxane reduced the level to 245.43 ± 9.81 ($p = 0.003$). The LD, TD and DD groups showed values of 245.73 ± 26.64 ($p = 0.003$), 225.43 ± 31.03 ($p = 0.002$), and 194.58 ± 26.99 ($p = 0.002$), respectively. All treatment groups demonstrated statistically significant reductions compared with the doxorubicin group, with the DD group showing the most pronounced reduction.

HDL: The mean HDL level was 39.55 ± 8.77 in the normal group and increased to 70.07 ± 24.47 in the doxorubicin group. Dexrazoxane showed a mean value of 43.61 ± 4.47 ($p = 0.019$). The LD, TD and DD groups showed mean values of 49.87 ± 14.82 ($p = 0.038$), 40.74 ± 3.82 ($p = 0.002$), and 39.33 ± 2.08 ($p = 0.001$), respectively. Statistically significant differences were observed between all treatment groups and the doxorubicin group.

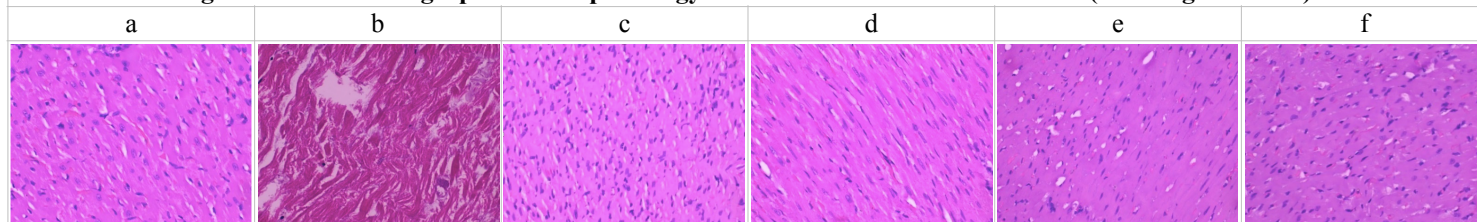
LDL: The mean LDL level increased from 71.97 ± 24.93 in the normal group to 112.89 ± 9.50 in the doxorubicin group. Dexrazoxane treatment reduced the LDL level to 80.73 ± 10.54 ($p = 0.003$). The DD, TD and LD groups showed mean values of 102.35 ± 3.91 ($p = 0.002$), 80.44 ± 13.57 ($p = 0.003$), and $73.13 \pm$

16.98 ($p = 0.005$), respectively. All treatment groups showed statistically significant differences compared with the doxorubicin group, with TD and LD producing greater reductions in LDL.

Heart weight: The mean heart weight was 3.994 ± 0.214 in the normal group and increased to 6.807 ± 0.528 in the doxorubicin group. Dexrazoxane treatment resulted in a reduction to 4.042 ± 0.080 ($p = 0.003$). The LD and DD groups showed mean values of 6.921 ± 0.768 ($p = 0.003$) and 4.860 ± 0.344 ($p = 0.001$), respectively, while the TD group showed a value of 3.919 ± 0.225 ($p = 0.003$). Statistically significant differences were observed between all treatment groups and the doxorubicin group. Among the test drug groups, TD showed the greatest normalization of heart weight, with a mean value close to that of the normal group.

Overall, doxorubicin administration produced significant alterations in total cholesterol, triglycerides, alkaline phosphatase, creatinine, LDH, HDL, LDL and heart rate. Treatment with dexrazoxane and the test drug groups resulted in statistically significant changes in these parameters compared with the doxorubicin group. Among the test drug groups, DD demonstrated a pronounced reduction in alkaline phosphatase, creatinine and LDH, while TD showed greater improvement in heart rate and triglycerides. LD showed a marked reduction in LDL and alkaline phosphatase.

Figure 3: Photomicrographs of histopathology of the heart of Wistar albino rats ($\times 40$ magnification).



a) Control group rats shows heart tissue with normal architecture. Normal endocardium and myocardium with branching cardiac muscle fibres having central nuclei b) Doxorubicin treated group rats with necrosis, vacuolar degenerative changes, infiltration of inflammatory cells and haemorrhages. c) Dexrazoxane treated group rats with normal branching of cardiac muscle fibres with central nuclei and endocardium. d) Rat group treated with half dose of *Dasamula arka* showing multifocal areas of vacuolar degenerative changes in the myocardium, mild congestion and infiltration of inflammatory cells. e) Rat group treated with therapeutic dose of *Dasamula arka* showing mild levels of vacuolar degenerative changes and normal endocardium. f) Rat group treated with double dose of *Dasamula arka* showing normal endocardium and myocardium.

Discussion

Cardiovascular disease, particularly cardiomyopathy, remain one of the leading cause of mortality worldwide, often caused by the chemotherapy drug Doxorubicin.(4) Dexrazoxane is used as a standard and proven medicine for cardiomyopathy for patients who are undergoing anthracycline chemotherapy.(6) Various other medicines are available in the market for the same. But the fact remains that all these medicines have adverse effects on the body, highlights the need for safer and more effective therapies. *Dasamula arka* is a proven Ayurvedic formulation which has cardio tonic property. Present experiments conducted, demonstrated a promising degree of cardioprotective activity of *Dasamula arka* in doxorubicin-induced cardiomyopathy when compared with the standard drug Dexrazoxane. The decreased levels of CPK, LDH, ALP, improved lipid profile indicates preservation of myocardial cell membrane integrity and reduced leakage of intracellular enzymes into the circulation created by doxorubicin treatment. Dexrazoxane only outperforms the double dose of *Dasamula arka* in triglycerides. It could be suggested here that patients undergoing chemotherapy which induce

cardiomyopathy with the standard medicines can also be suggested to use *Dasamula arka* as a supportive cardio tonic.

Histopathological examination revealed normal cardiac architecture in the control group, whereas doxorubicin caused marked myocardial damage characterized by necrosis, vacuolar degeneration, inflammatory infiltration and haemorrhage. Dexrazoxane and *Dasamula arka* treatment attenuated these pathological changes, with the double-dose group showing near-normal cardiac architecture.

The cardioprotective activity of *Dasamula arka* may be attributed to the diverse phytoconstituents present in its ingredients, including flavonoids, tannins, triterpenoids, and steroids. These phytoconstituents possess antioxidant, anti-inflammatory, lipid-lowering, and tissue-protective properties. Also the antioxidant potential of these phytoconstituents, reduce oxidative stress through free radical scavenging, inhibition of lipid peroxidation, preservation of myocardial architecture, and maintenance of normal cardiac function. Furthermore, Anticoagulant properties identified in specific herbs within *Dasamula* aid in preventing the

formation of blood clots, reducing the risk of heart attacks or strokes.

Conclusion

The outcomes of this research suggest that *Dasamula arka* has potential as an adjunctive cardioprotective therapy during anthracycline chemotherapy. The *Arka* dosage form may offer additional advantages due to its rapid absorption, improved bioavailability, and ease of administration. The results of cardiomyopathy in rat model reveal that the higher dose of *Dasamula arka* (1.728 ml/Kg) showed higher cardio protective effects which is very much comparable with the standard drug Dexrazoxane (30mg/Kg) with reference to CPK, LDH, ALP, improved lipid profile levels. Dexrazoxane only outperforms the double dose of *Dasamula arka* in triglycerides. These results were well reflected in the improvement of histological parameters which were comparable with standard drug treatment for cardiomyopathy.

Nevertheless, the present investigation was conducted in an experimental animal model, and extrapolation of these findings to clinical practice should be made with caution. Further studies involving detailed phytochemical characterization, toxicity evaluation, mechanism of action of *Dasamula arka* for controlling the various parameters and well-designed clinical trials are required to establish its safety, efficacy, and therapeutic applicability in humans. It can be concluded that *Dasamula arka* is found to be a potent herbal formulation for cardiomyopathy for patients undergoing anthracycline chemotherapy and as a general cardio tonic.

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Nil

Conflict of interest

There are no conflicts of interest

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