

Boswellia serrata Resin Mitigates Doxorubicin-Induced Cardiac Oxidative Stress, Biomarker Leakage, and Myocardial Histopathological Injury in Rats

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ABSTRACT

Doxorubicin is a potent antineoplastic agent, but its clinical use is limited by dose-dependent cardiotoxicity. The resin of *Boswellia serrata* has antioxidant and anti-inflammatory properties and may confer cardio protection. The present study was planned to assess the protective effect of *Boswellia serrata* resin extract (BSE) on doxorubicin induced cardiac injury in rats. Adult male Wistar rats were divided into six groups (n = 48); control, BSE only, doxorubicin (DOX), DOX + BSE 250 mg/kg, DOX + BSE 500 mg/kg, and DOX + carvedilol. BSE was administered orally, and doxorubicin was administered intraperitoneally to induce cardiotoxicity. Serum CK-MB, LDH, cardiac troponin-I and AST were estimated. Myocardial MDA, GSH, SOD, CAT and GPx were determined. Cardiac histopathology was assessed semi-quantitatively. Doxorubicin markedly reduced body weight gain, elevated heart weight indices and serum cardiac injury biomarkers, myocardial MDA and reduced GSH and antioxidant enzyme activities. Histopathological signs of DOX included degeneration of myocardial fibres, sarcoplasmic vacuolation, fragmentation of myofibrils, inflammatory infiltration, vascular congestion, haemorrhage and necrosis. Co-treatment with BSE significantly attenuated these biochemical and histological alterations, and the protection was greater at 500 mg/kg than at 250 mg/kg. To summarize, attenuation of doxorubicin-induced cardiotoxicity by BSE was associated with reduction in cardiac injury biomarkers and lipid peroxidation, enhancement of antioxidant defences and preservation of myocardial architecture, supporting a potential cardioprotective effect of BSE, which may be related mainly to mitigation of oxidative and structural myocardial injury.

Keywords: *Boswellia Serrata*; Doxorubicin; Cardiotoxicity; Myocardial Injury; Cardioprotection.

راتنج البوسويلية المنشارية (*Boswellia serrata*) يخفف من الإجهاد التأكسدي القلبي الناجم عن الدوكسوروبيسين، وتسرب المؤشرات الحيوية، والضرر النسيجي القلبي لدى الجرذان

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الملخص

يُعد الدوكسوروبيسين (DOXORUBICIN) عاملاً قوياً ومضاداً للأورام، إلا أن استخدامه السريري يظل محدوداً بسبب سميته القلبية المعتمدة على الجرعة. ونظراً لما يمتلكه راتنج نبات البوسويلية المنشارية (*BOSWELLIA SERRATA*) من خصائص مضادة للأكسدة والالتهابات، فقد صُممت هذه الدراسة لتقييم تأثيره الوقائي على القلب ضد الإصابات المستحثة بالدوكسوروبيسين في الجرذان. شملت التجربة 48 من جرذان "ويستار" الذكور البالغة، والتي قُسمت إلى ست مجموعات: مجموعة ضابطة، مجموعة المستخلص وحده، مجموعة الدوكسوروبيسين، مجموعتين للعلاج المشترك بجرعات (250 و500 ملغم/كغم)، ومجموعة الكارفيديلول. أظهرت النتائج أن حقن الدوكسوروبيسين أدى إلى تدهور ملحوظ في وزن الجسم، وارتفاع مؤشرات وزن القلب والمؤشرات الحيوية لإصابة القلب في المصل (CK-MB, LDH, TROPONIN-I, AST)، فضلاً عن حدوث تغيرات نسيجية مرضية شديدة مثل تنكس الألياف العضلية، والارتشاح الالتهابي، والنخر. في المقابل، أدى العلاج المشترك بمستخلص البوسويلية إلى تخفيف هذه التغيرات البيوكيميائية والنسيجية بشكل ملحوظ، وكانت الحماية أكثر فاعلية عند الجرعة الأعلى (500 ملغم/كغم). وتؤكد الدراسة أن التأثير الوقائي للمستخلص يعود بشكل رئيسي إلى قدرته على تعزيز الدفاعات المضادة للأكسدة، وتقليل بيروكسيد الدهون، والحد من إصابة عضلة القلب التأكسدية والتركيبية.

الكلمات المفتاحية: بوسويليا سيراتا؛ دوكسوروبيسين؛ السمية القلبية؛ تلف عضلة القلب؛ حماية القلب.

1. Introduction

Doxorubicin is one of the most frequently used anthracycline anti-cancer drugs and is still clinically useful in the treatment of several solid tumors and hematologic malignancies. Its antitumor activity correlates with DNA intercalation, topoisomerase II inhibition and blockade of DNA replication and transcription. However, its therapeutic significance is limited by cardiotoxicity, which is cumulative and sometimes irreversible, and can lead to subclinical myocardial dysfunction, dilated cardiomyopathy or heart failure [1], [2].

Doxorubicin-induced cardiotoxicity is mediated by complex and overlapping mechanisms. Experimental and clinical studies showed that formation of reactive oxygen species, lipid peroxidation, mitochondrial dysfunction, calcium dysregulation, inflammatory activation and regulated cell-death pathways interact to lead to cardiomyocyte damage [2]-[4]. The heart is especially vulnerable because of its high mitochondrial density, substantial oxygen demand, and relatively limited antioxidant reserve compared with some other tissues. In experimental models, doxorubicin commonly increases malondialdehyde (MDA), depresses glutathione (GSH), and reduces antioxidant enzyme activities such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), changes that are often paralleled by leakage of CK-MB, LDH, cardiac troponins, and AST into the circulation [1], [2].

Structural myocardial injury provides an important tissue-level correlate of these biochemical disturbances. Doxorubicin-induced cardiotoxicity is frequently characterized by myocardial fiber degeneration, cytoplasmic vacuolation, myofibrillar disorganization, interstitial edema, inflammatory infiltration, vascular congestion, hemorrhage, necrosis, and loss of normal myocardial architecture. These changes reflect cardiomyocyte membrane disruption, microvascular disturbance, inflammatory stress, and progressive impairment of myocardial integrity [2], [4].

Boswellia serrata Roxb. ex Colebr., commonly known as Indian frankincense, produces an oleo-gum resin enriched with pentacyclic triterpenic acids, including beta-boswellic acid, keto-beta-boswellic acid, acetyl-beta-boswellic acid, and acetyl-11-keto-beta-boswellic acid. These constituents are associated with anti-inflammatory and antioxidant activities mediated through pathways that include inhibition of 5-lipoxygenase, modulation of NF-kappaB-related

inflammatory signaling, and reduction of oxidative tissue injury [5]-[7]. Previous experimental work also suggests that boswellic acids can reduce doxorubicin-associated cardiac damage while preserving or enhancing antitumor activity in tumor-bearing models [8], [9].

Although *Boswellia*-derived compounds have shown promising tissue-protective effects, additional experimental evidence is needed to define how *Boswellia serrata* resin influences the combined physiological, biochemical, oxidative, and histopathological manifestations of doxorubicin cardiotoxicity. This study was designed to evaluate the cardioprotective effects of *Boswellia serrata* resin against doxorubicin-induced cardiac injury through assessment of body and heart weight indices, serum cardiac injury markers, myocardial oxidative stress indices, antioxidant defenses, and histopathological alterations.

2. Materials and Methods

2.1. Study Design

The plant material of *Boswellia serrata* was obtained from the local markets and was authenticated by Prof. Dr. Khamas Eidan Mohammedat the Department of Biology, College of Science, Tikrit University. A voucher specimen has been deposited in the Herbarium of the College under the reference number (TU-Edu-Bio-2026-042).

A controlled experimental animal study was conducted to evaluate whether *Boswellia serrata* resin extract (BSE) protects against doxorubicin (DOX)-induced cardiac injury. The study included six groups: control, *Boswellia* only, DOX only, DOX + BSE low dose, DOX + BSE high dose, and DOX + carvedilol. The experimental design allowed comparison of normal cardiac status, BSE safety in non-injured animals, DOX-induced cardiotoxicity, two BSE dose levels, and a reference cardioprotective drug.

2.2. Experimental Animals

Forty-eight adult male Wistar rats, weighing approximately 200-220 g, were used. Animals were housed in polypropylene cages under standard laboratory conditions (22 ± 2 °C, 50-60% relative humidity and a 12 h light/dark cycle) with free access to a standard pellet diet and water. Rats were acclimatized for 7 days prior to treatment.

2.3. Preparation of *Boswellia serrata* Resin Extract

The *Boswellia serrata* resin extract was prepared following the method described by Javdani et al. [10]. *Boswellia serrata* gum resin was cleaned, dried and

Table 1. Body weight, heart weight, and relative heart weight

Parameter	Control	Boswellia only	DOX only	DOX + BSE low	DOX + BSE high	DOX + carvedilol
Initial body weight (g)	215.66 ± 13.34	216.26 ± 10.77	213.86 ± 8.50	207.00 ± 11.71	210.62 ± 11.18	217.22 ± 10.52
Final body weight (g)	247.80 ± 18.22	246.16 ± 9.04	198.19 ± 12.96***	230.21 ± 8.16*####	234.58 ± 8.37###	241.61 ± 10.11###
Body weight change (g)	32.14 ± 21.98	29.90 ± 15.88	-15.68 ± 13.92***	23.21 ± 12.78###	23.95 ± 15.50###	24.39 ± 12.96###
Absolute heart weight (g)	0.79 ± 0.02	0.77 ± 0.04	0.94 ± 0.03***	0.84 ± 0.01###	0.82 ± 0.04###	0.79 ± 0.06###
Relative heart weight (mg/g)	3.22 ± 0.32	3.12 ± 0.22	4.74 ± 0.30***	3.65 ± 0.15*####	3.52 ± 0.21###	3.29 ± 0.34###

Data are presented as mean ± SD, n = 8 rats/group. *, **, and *** indicate $p < 0.05$, $p < 0.01$, and $p < 0.001$ versus the control group, respectively; ### indicates $p < 0.001$ versus the DOX-only group; † and †† indicate $p < 0.05$ and $p < 0.01$ versus the DOX + BSE low-dose group, respectively.

coarsely powdered. The powdered resin was macerated with 70% ethanol for 72 h with intermittent shaking for extraction of the resin. The extract was filtered, concentrated under reduced pressure with a rotary evaporator and dried to give a semisolid residue. The dried extract was stored at 4 °C in an airtight container and freshly suspended in 0.5% carboxymethylcellulose before oral administration. For treatment, BSE was administered at 250 mg/kg as the low dose and 500 mg/kg as the high dose.

2.4. Drugs and Chemicals

Doxorubicin hydrochloride (DOX; product No. D1515, Sigma-Aldrich, Merck KGaA, Darmstadt, Germany) was used for induction of experimental cardiotoxicity and was prepared freshly in sterile normal saline before injection. Carvedilol (CAR; product No. C3993, ≥98% purity, Sigma-Aldrich, Merck KGaA, Darmstadt, Germany) was used as the reference cardioprotective treatment. Carvedilol was used as the reference cardioprotective drug and was suspended in 0.5% carboxymethylcellulose for oral administration. All biochemical assay reagents were of analytical grade and were used according to the manufacturers' instructions.

2.5. Experimental Groups and Treatment Protocol

Forty-eight rats were randomly divided into six groups (n=8/groups): control, BSE 500 mg/kg, DOX 2.5 mg/kg i.p. on alternate days for six injections (cumulative dose 15 mg/kg), DOX + BSE 250 mg/kg, DOX + BSE 500 mg/kg and DOX + carvedilol 30 mg/kg. During the 14 days of the experiment, a single daily dose of BSE and carvedilol was given orally. All procedures were approved by the Institutional

Animal Care and Use Committee, College of Veterinary Medicine, University of Mosul (Ref. UM. VET. 2026. 157, February 12, 2026). The study comprised 48 rats housed at the College of Veterinary Medicine animal facility. Animals were monitored daily for clinical condition, distress, treatment related toxicity and mortality and the study was reported in compliance with ARRIVE 2.0 guidelines.

2.6. Sample Collection

At the end of the experiment, rats were fasted overnight and deeply anesthetized with intraperitoneal ketamine/xylazine. Blood was collected by cardiac puncture, allowed to clot and centrifuged at 3000 rpm for 10 min to obtain serum that was stored at -20°C until analysis. The specific terminal euthanasia procedure could not be verified retrospectively from the available experimental records and was therefore not included in the revised methodology. Hearts were immediately removed, washed in ice-cold saline, blotted dry and weighed. Relative heart weight was calculated as heart weight/final body weight × 100. Biochemical assays were performed on cold homogenized portions of myocardial tissue, and representative samples were fixed in 10% neutral-buffered formalin for histopathology.

2.7. Biochemical Assessment

Serum cardiac injury was evaluated by measuring creatine kinase-MB (CK-MB; E-EL-R1327) and cardiac troponin-I (cTnI; E-EL-R1253) using rat-specific ELISA kits obtained from Elabscience Biotechnology Co., Ltd. (Wuhan, Hubei, China). Lactate dehydrogenase (LDH; A020-2-2) and aspartate aminotransferase (AST; C010-1-1) activities were determined using commercial assay kits from

Table 2. Serum cardiac injury biomarkers

Parameter	Control	Boswellia only	DOX only	DOX + BSE low	DOX + BSE high	DOX + carvedilol
CK-MB (U/L)	135.59 ± 20.93	140.50 ± 14.31	591.65 ± 57.01***	364.49 ± 26.95***###	234.47 ± 32.85***###††	229.31 ± 23.48***###††
LDH (U/L)	434.71 ± 43.78	430.52 ± 38.15	1334.04 ± 108.88***	866.45 ± 89.45***###	614.20 ± 48.81***###††	545.34 ± 58.94***###††
Cardiac troponin-I (ng/mL)	0.05 ± 0.02	0.06 ± 0.01	0.87 ± 0.07***	0.43 ± 0.07***###	0.20 ± 0.05***###††	0.20 ± 0.04***###††
AST (U/L)	76.66 ± 8.20	73.74 ± 4.44	163.09 ± 22.30***	120.47 ± 14.18***###	95.29 ± 10.16***###††	86.98 ± 5.74***###††

Data are presented as mean ± SD, n = 8 rats/group. *, **, and *** indicate $p < 0.05$, $p < 0.01$, and $p < 0.001$ versus the control group, respectively; ### indicates $p < 0.001$ versus the DOX-only group; † and †† indicate $p < 0.05$ and $p < 0.01$ versus the DOX + BSE low-dose group, respectively.

Nanjing Jiancheng Bioengineering Institute (Nanjing, China). Cardiac malondialdehyde (MDA; A003-1-2), reduced glutathione (GSH; A006-2-1), superoxide dismutase (SOD; A001-3-2), catalase (CAT; A007-1-1), and glutathione peroxidase (GPx; A005-1-2) were measured in cardiac tissue homogenates using commercial assay kits from Nanjing Jiancheng Bioengineering Institute (Nanjing, China), according to the manufacturers' instructions.

Stress parameters were normalized to tissue protein content where applicable.

2.8. Histopathological Examination

Formalin-fixed heart samples were processed routinely, dehydrated through ascending ethanol concentrations, cleared in xylene, embedded in paraffin, and sectioned at 5 µm. Sections were stained with haematoxylin and eosin and examined under a light microscope. Myocardial injury was graded on an ordinal scale from 0 to 4, according to the severity of cardiomyocyte degeneration, vacuolation, myofibrillar disruption, necrosis, infiltration of inflammatory cells, edema, and vascular congestion, where 0 represents no detectable injury and 4 represents severe injury.

2.9. Statistical Analysis

Data for the Continuous variables were expressed as mean ± SD and were analysed by one-way ANOVA followed by Tukey's post-hoc multiple-comparison test. Histopathological scores were expressed as median [IQR] and analysed by Kruskal–Wallis test followed by Dunn's multiple-comparison test.

Results

2.10. Body Weight, Heart Weight, and Relative Heart Weight

As shown in Table 1, initial body weight was

comparable across the experimental groups, indicating similar baseline conditions before treatment. DOX exposure markedly reduced final body weight and body weight change, reflecting systemic toxicity and impaired weight gain. In contrast, rats treated with BSE during DOX exposure showed improved final body weight and a positive body weight change compared with the DOX-only group. DOX also significantly increased absolute heart weight and relative heart weight, consistent with cardiac injury and tissue stress. BSE suppressed the absolute and relative heart weight compared to DOX alone. The high-dose BSE group had a stronger trend of protection than the low-dose group and was close to the carvedilol-treated group for these indices.

2.11. Serum Cardiac Injury Biomarkers

As shown in Table 2, DOX significantly increased serum CK-MB, LDH, cardiac troponin-I and AST compared with the control group. This pattern suggests injury to the cardiomyocyte membrane and subsequent leakage of intracellular enzymes and contractile injury markers into the circulation. BSE co-treatment significantly reduced all measured cardiac injury biomarkers compared with the DOX-only group. The high-dose BSE group showed greater improvement than the low-dose group for CK-MB, LDH, cardiac troponin-I, and AST, and its effect was broadly comparable to carvedilol for several markers.

2.12. Cardiac Oxidative Stress and Antioxidant Defenses

Cardiac oxidative stress and antioxidant markers are summarized in Table 3. DOX markedly increased myocardial MDA and reduced GSH, SOD, CAT, and GPx, demonstrating enhanced lipid peroxidation and depletion of enzymatic and non-enzymatic antioxidant

Table 3. Cardiac oxidative stress and antioxidant markers

Parameter	Control	Boswellia only	DOX only	DOX + BSE low	DOX + BSE high	DOX + carvedilol
MDA (nmol/mg protein)	2.27 ± 0.15	2.08 ± 0.15	7.08 ± 0.68***	4.52 ± 0.47***###	3.26 ± 0.31***###††	3.13 ± 0.30***###††
GSH (μmol/g tissue)	7.81 ± 0.85	7.95 ± 0.19	2.95 ± 0.22***	5.08 ± 0.48***###	6.53 ± 0.28***###††	6.37 ± 0.74***###††
SOD (U/mg protein)	15.43 ± 1.48	15.27 ± 0.78	6.96 ± 0.37***	10.52 ± 0.97***###	12.90 ± 0.95***###††	12.79 ± 0.51***###††
CAT (U/mg protein)	57.39 ± 4.22	57.31 ± 3.65	25.56 ± 3.11***	39.90 ± 2.88***###	47.84 ± 3.45***###††	50.46 ± 2.34***###††
GPx (U/mg protein)	34.75 ± 3.22	35.81 ± 3.19	15.93 ± 1.92***	25.62 ± 1.74***###	29.77 ± 2.43***###†	30.09 ± 2.07***###†

Data are presented as mean ± SD, n = 8 rats/group. *, **, and *** indicate $p < 0.05$, $p < 0.01$, and $p < 0.001$ versus the control group, respectively; ### indicates $p < 0.001$ versus the DOX-only group; † and †† indicate $p < 0.05$ and $p < 0.01$ versus the DOX + BSE low-dose group, respectively.

defenses. BSE administration attenuated these oxidative disturbances. The low-dose BSE group partially reduced MDA and partially restored GSH, SOD, CAT, and GPx compared with the DOX-only group, whereas the high-dose BSE group produced stronger restoration across the antioxidant profile. Although the values did not fully return to control levels, high-dose BSE showed a pattern close to that observed with carvedilol.

2.13. Histopathological Findings

Histopathological scoring supported the biochemical evidence of myocardial injury. As presented in Table 4 and Figure 1, the control and Boswellia-only groups had minimal lesion scores, indicating preserved myocardial architecture. The DOX-only group showed severe myocardial injury, with high scores for myocardial fiber degeneration, sarcoplasmic vacuolation, myofibrillar fragmentation, interstitial edema, inflammatory infiltration, vascular congestion, hemorrhage, necrotic changes, and loss of myocardial architecture. BSE co-treatment significantly reduced lesion severity and total injury score compared with DOX alone. The high-dose BSE group showed greater histological preservation than the low-dose group, particularly for edema, inflammatory infiltration, hemorrhage, necrotic changes, and loss of myocardial architecture. Carvedilol produced a similar reduction in total injury score, supporting its role as a positive cardioprotective reference treatment.

3. Discussion

We observed a consistent pattern of cardiac injury induced by doxorubicin characterized by systemic weight loss, increased indices of heart weight, leakage of biomarkers of cardiac injury, lipid peroxidation, depletion of antioxidant defences, and extensive histopathological injury of the myocardium. BSE attenuated these alterations in a dose related manner, the high dose producing greater improvement than the low dose and a profile often close to carvedilol. Overall, the data suggest that Boswellia serrata resin produced significant cardioprotection in this experimental model.

The decrease in final body weight and body weight gain after DOX exposure is in agreement with systemic toxicity generally seen in animals treated with anthracyclines. Doxorubicin can interfere with food intake, metabolism, tissue repair, and organ function, thus limiting normal weight gain. The increase in absolute and relative heart weight in the DOX-only group likely reflects myocardial stress, edema, vascular congestion, inflammatory infiltration, and tissue injury. The partial normalization of these indices in BSE-treated animals is therefore biologically consistent with the histological reduction in edema, congestion, inflammation, and necrosis.

The elevations of CK-MB, LDH, cardiac troponin-I, and AST confirm cardiomyocyte injury at the biochemical level. CK-MB and LDH are released

Table 4. Histopathological scoring of myocardial injury

Parameter	Control	Boswellia only	DOX only	DOX + BSE low	DOX + BSE high	DOX + carvedilol
Myocardial fiber degeneration	0.00 ± 0.00	0.00 ± 0.00	3.88 ± 0.35***	1.88 ± 0.35***###	1.38 ± 0.52***###	1.12 ± 0.64***###†
Sarcoplasmic vacuolation	0.00 ± 0.00	0.00 ± 0.00	3.38 ± 0.52***	1.75 ± 0.46***###	1.12 ± 0.35***###	1.00 ± 0.76***###†
Myofibrillar fragmentation	0.25 ± 0.46	0.00 ± 0.00	3.50 ± 0.53***	1.88 ± 0.64***###	1.25 ± 0.46***###	1.00 ± 0.53***###††
Interstitial edema	0.12 ± 0.35	0.00 ± 0.00	3.25 ± 0.71***	1.50 ± 0.53***###	0.62 ± 0.52###†	1.00 ± 0.53***###
Inflammatory infiltration	0.00 ± 0.00	0.00 ± 0.00	3.38 ± 0.52***	1.62 ± 0.52***###	0.75 ± 0.71*###†	1.12 ± 0.64***###
Vascular congestion	0.12 ± 0.35	0.12 ± 0.35	3.50 ± 0.53***	1.62 ± 0.52***###	1.25 ± 0.46***###	1.25 ± 0.46***###
Hemorrhage	0.00 ± 0.00	0.00 ± 0.00	2.88 ± 0.64***	1.12 ± 0.35***###	0.50 ± 0.53###	0.62 ± 0.74###
Necrotic changes	0.00 ± 0.00	0.00 ± 0.00	3.38 ± 0.52***	1.75 ± 1.04***###	1.00 ± 0.00***###	0.75 ± 0.71###††
Loss of myocardial architecture	0.00 ± 0.00	0.12 ± 0.35	3.38 ± 0.74***	1.88 ± 0.64***###	0.75 ± 0.46###††	1.00 ± 0.53***###†
Total injury score	0.50 ± 0.76	0.25 ± 0.46	30.50 ± 3.59***	15.00 ± 3.55***###	8.62 ± 2.20***###††	8.88 ± 4.52***###†

Data are presented as mean ± SD, n = 8 rats/group. *, **, and *** indicate $p < 0.05$, $p < 0.01$, and $p < 0.001$ versus the control group, respectively; ### indicates $p < 0.001$ versus the DOX-only group; † and †† indicate

when membrane integrity is compromised, whereas cardiac troponin-I is a more specific marker of cardiomyocyte injury. The reduction of these markers by BSE suggests preservation of cardiomyocyte membrane integrity and attenuation of cellular damage. Similar reductions in cardiac biomarkers have been reported with antioxidant and anti-inflammatory interventions in doxorubicin cardiotoxicity models [11]-[14].

Oxidative stress appears to be a central mechanism in the observed injury. DOX increased cardiac MDA, indicating lipid peroxidation of myocardial membranes, and at the same time reduced GSH and inhibited SOD, CAT and GPx activities. Such a combination is expected, as doxorubicin undergoes redox cycling and promotes generation of reactive oxygen species, while cardiomyocytes have limited antioxidant reserve and high mitochondrial oxygen flux [1], [2]. The enhancement of MDA and antioxidant enzymes in BSE-treated groups is indicative of the extract's ability to reduce oxidative burden and to help preserve the endogenous antioxidant capacity.

The histopathological findings provide important structural support for the biochemical data. Severe myocardial fiber degeneration, sarcoplasmic

vacuolation, myofibrillar fragmentation, edema, inflammatory infiltration, vascular congestion, hemorrhage, necrosis, and loss of architecture in DOX-treated rats reflect widespread myocardial injury. These lesions are compatible with oxidative membrane damage, inflammatory stress, microvascular dysfunction, and cardiomyocyte degeneration. The decrease in lesion scores following BSE treatment suggests that the biochemical protection was reflected in the preservation at the tissue level. The increased protection seen with the high dose BSE also supports a dose responsive pattern.

Pharmacological activity of BSE is probably related to its boswellic acid content. In experimental settings, boswellic acids and related triterpenoids are reported to inhibit inflammatory mediators, to modulate 5-lipoxygenase and NF-kappaB associated pathways [5]-[7], and to decrease oxidative injury [8]. These properties provide a plausible explanation for the observed lower levels of MDA, partial restoration of antioxidant enzymes and decrease in inflammatory and degenerative histological scores observed in the present study. The mechanisms described here should be considered biologically plausible rather than directly proven, as we did not measure inflammatory cytokines, apoptotic proteins, mitochondrial function

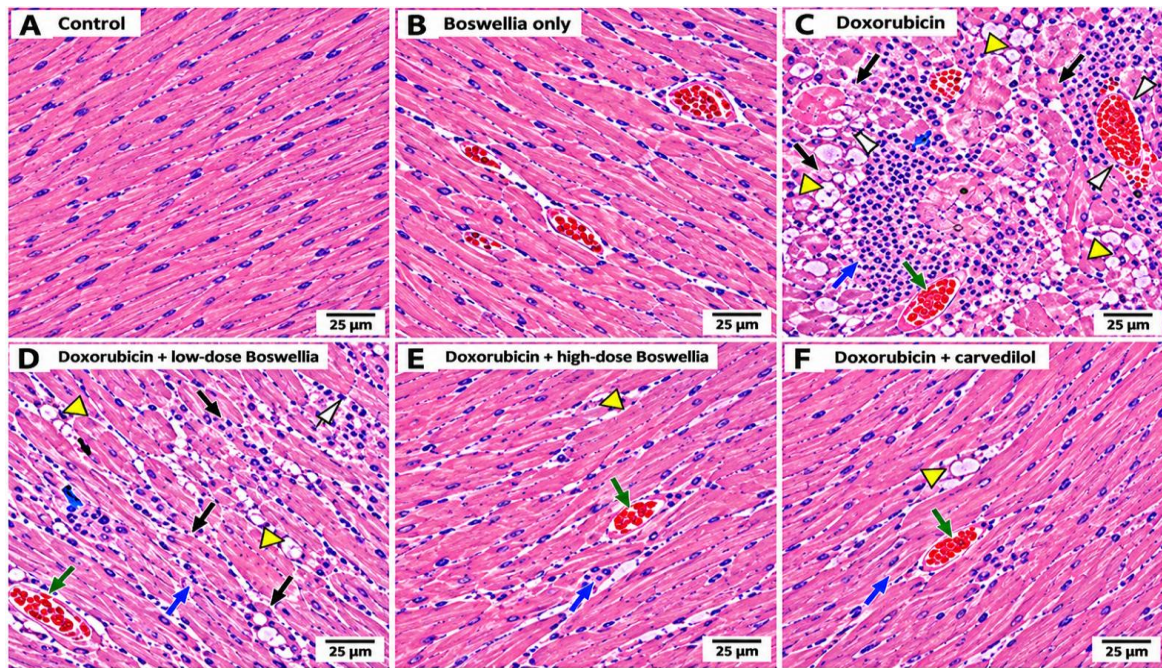


Figure 1. Representative H&E-stained cardiac sections from the experimental groups. A. Control and B. Boswellia serrata resin-only groups show preserved myocardial architecture. C. The doxorubicin-only group shows severe myocardial injury characterized by fibre degeneration, interstitial edema, inflammatory infiltration, haemorrhage, and necrosis. D. Treatment with low-dose Boswellia serrata resin partially attenuates these lesions, whereas high-dose Boswellia serrata resin E. shows greater preservation of myocardial structure. F. The carvedilol-treated group shows comparable improvement against doxorubicin-induced myocardial injury. Black arrows: myocardial fiber degeneration; yellow arrowheads: sarcoplasmic vacuolation; white arrows: myofibrillar fragmentation; asterisks: interstitial edema; blue arrows: inflammatory infiltration; green arrows: vascular congestion; red arrows: hemorrhage; white arrowheads: necrotic changes; dashed outlines: loss of myocardial architecture. H&E, 400X.

or specific signalling pathways.

The comparison with carvedilol is consistent with the interpretation of the model. Carvedilol is a beta-blocker with antioxidant and anti-inflammatory properties and has been demonstrated to be protective in experimental doxorubicin cardiotoxicity [11]. Carvedilol in this study reduced leakage of cardiac biomarkers, oxidative stress, depletion of antioxidants and histopathological injury. The effects for several endpoints were broadly similar for high-dose BSE, indicating meaningful protection by the resin extract, although it is not possible to claim direct equivalence without a study designed and powered for non-inferiority.

The overall pattern indicates that BSE attenuated doxorubicin induced myocardial injury mainly through attenuation of oxidative stress and preservation of tissue architecture. These results are in agreement with previous studies showing that boswellic acids may protect against doxorubicin-induced cardiotoxicity [8], [9]. The present data extend this evidence by combining measurements of body and heart weight, serum injury biomarkers, cardiac redox status and antioxidant enzyme activity, and histopathological

scoring within the same experimental setting.

4. Conclusion

Boswellia serrata resin extract attenuated doxorubicin-induced cardiac injury in rats. The protective effect was reflected by improved body and heart weight indices, reduced serum CK-MB, LDH, cardiac troponin-I, and AST, lower cardiac MDA, partial restoration of GSH, SOD, CAT, and GPx, and reduced myocardial histopathological injury. The findings support the cardioprotective potential of BSE against doxorubicin-induced oxidative and structural myocardial damage, with stronger effects observed at the higher dose.

5. Limitations

The study was carried out only on adult male Wistar rats; thus, the results may not completely reflect sex related differences. Second, the Boswellia serrata resin extract was tested at two dose levels, but the extract was not chemically characterized or quantitatively standardized for individual boswellic acids or other potential active constituents. Third, cardioprotection was evaluated by assessing serum cardiac injury biomarkers, indices of myocardial oxidative stress and

antioxidant status, and histopathological examination without direct functional evaluation by echocardiography, electrocardiography or hemodynamic measurements. Therefore, future studies should include detailed phytochemical profiling of the extract, functional cardiac assessments, molecular mechanistic endpoints, longer-term experimental models, and inclusion of both sexes to strengthen the mechanistic interpretation, reproducibility, and translational relevance of these findings.

6. Funding Statement

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7. Conflict of Interest Statement

The authors declare no conflict of interest.

8. Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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