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Histopathological Evaluation of the Protective Effect of Nano-Curcumin on Adrenaline-Induced Myocardial Infarction in Rats

Hajar Fadhil Abed Alzahra[1*], Khamael Abdulsalam Abed[2], Hiba Jalil Turki[2]

[1]University of Al-Qadisiyah, College of Science, Unit of Environment Researches & Prevention of Pollution, Diwaniyah, Iraq
[2]University of Al-Qadisiyah, College of Science, Department of Environment, Diwaniyah, Iraq

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***Corresponding author:** Hajar Fadhil Abed Alzahra
University of Al-Qadisiyah, College of Science, Unit of Environment Researches & Prevention of Pollution, Diwaniyah, Iraq

Abstract | **Original Research Article**

Myocardial infarction (MI), also referred to heart attacks, as are the leading cause of cardiovascular death in the majority of nations worldwide. MI is caused by blockage of one or more coronary arteries that supply blood to the heart. This deprives a portion of the heart of oxygenated blood and nutrients, which ultimately results in myocardial necrosis. Curcumin is a poly-phenolic chemical which is largely produced from turmeric rhizome (Curcuma longa). The health benefits of curcumin are well-documented; notably, curcumin demonstrates anticancer, antiviral, antioxidant, anti-inflammatory, antibacterial, hypoglycemic, and ant rheumatic activities. The heart's Histopathological findings demonstrated how Nano-curcumin and Nano-turmeric preserve cardiac tissue and help to avoid major complications. Histopathological analysis revealed that the group treated with nano-curcumin at a dose of 300 mg/kg b.w. demonstrated the most significant protective effect ($P \leq 0.05$) compared to all other experimental groups. The cardiac tissue showed nearly normal myocardial architecture, with well-preserved and regularly arranged myofibers, minimal interstitial edema, absence of hemorrhage, and markedly reduced inflammatory cell infiltration, indicating effective attenuation of adrenaline-induced myocardial damage**.** The study shows the experimental parts endorsed conclusion that curcumin and turmeric may exhibit remarkable therapeutic effect in adrenaline induced myocardial infarction by improving a number of inflammatory markers linked with myocardial infarction.

Keywords: Myocardial Infarction, Curcumin Nanoparticle, Histopathology.

INTRODUCTION

According to pathology, myocardial infarction (MI) is defined as the death of cardiac cells brought on by extended myocardial ischemia, or inadequate oxygen delivery to the myocardium. (Banco *et al*., 2021).

In order to prevent the adverse effects of MI, including fibrosis, scarring, cardiac remodeling, and heart failure, timely and appropriate therapies that protect healthy cells must be used. (Kologrivova *et al*., 2021). Adrenaline was approved as a drug and was used first in human cardiopulmonary resuscitation. It also possesses other therapeutic applications in the treatment of cardiac arrest, allergic reactions, glaucoma, and asthma (Algoet, M *et al*., 2022). When there is high blood pressure or a MI, curcumin prevents left ventricular hypertrophy and heart failure.

Because of its rapid liver metabolism and poor water solubility, curcumin has been used safely in clinical studies and has positive pharmacological effects. Nanomaterial's may be able to address issues with distribution and bioavailability because of their potential ability to transport and deliver medications to target tissues. (Maleki Dizaj *et al*., 2022).

Curcumin prevents cardiac fibroblasts from differentiating and keeps the ratio of collagen synthesis and degradation in check (Gorabi *et al*., 2020).

MATERIAL AND METHODS

1. Experimental Animals

In this experiment 24 adult female Wister rats (each group 6 rats), about four month old, with average weight about 150±10 g.

2. Induction of Myocardial Infarction

Acute myocardial infarction was induced in female rats on days 8 and 9 of the experiment using two doses of adrenaline at 2 mg/kg. BW subcutaneous (El-Marasy, *S. A et al*., 2020)

3. Animal Grouping and Treatment

1. The first group (control negative): distilled wat er was given to the girls every day.
2. The second group (control positive, adrenaline group): The females were given normal saline for seven days and then given adrenaline (2 mg /kg/BW) for two days in a row for eight and ni ne days.
3. The third group (Nano CU 200 mg/kg. bw): The female rats received two consecutive days of injections of adrenaline (2 mg/kg. b.w.) on the eighth and ninth days, as well as 200 mg/kg. B.W. of Nano curcumin, which was given by gavage needle diluted in 1 ml distilled water for nine days.
4. The fourth group (Nano CU 300 mg/kg. bw): rats in this group received injections of adrenaline (2 mg/kg. bw) for two days in a row during the eighth and ninth days, as well as 300 mg/kg.BW of Nano curcumin by gavage needle diluted in 1 ml distilled water for nine days.

Curcumin Extraction and Nano Particle Preparation

Dried turmeric rhizomes (Curcuma longa) were obtained from a local market, ground for 20 minutes, and sieved using a 212-micron mesh to remove coarse fibers. A total of 250 grams of the sieved powder was used for extraction. Fifty grams at a time were placed in an extraction thimble and subjected to Soxhlet extraction using 500 ml of 99% ethanol at 60°C for 8–12 hours. After extraction, the solvent was evaporated, and the residue was dried in Petri dishes in an oven at 50°C. The dried material was then scraped and ground to obtain the final turmeric powdered extract (Patil *et al*., 2019).

Liposomes were prepared using the dried thin lipid film method. A lipid mixture containing 0.25 g of L-α phosphatidylcholine and 0.25 g of cholesterol was dissolved in 15 ml of a chloroform: methanol (2:1) solution and vortexes at 1500 rpm for 30 minutes. The mixture was warmed in a 40°C water bath for 15 minutes, then transferred to a rotary evaporator at 80 rpm and 40°C under vacuum. The flask was kept in a thermostatic water bath at 40°C for 2 hours to ensure complete drying of the thin lipid film on its inner walls. The resulting dry lipid film was then hydrated with phosphate buffer to form empty liposomes.

Animal Sacrificing

All animals were anesthetized by intra-peritoneal of Ketamine and xylazin (9mg/kg/B.W and 10mg/kg/B.W) respectively scarified, then heart will be taken for Histopathological study.

Histological Study

The heart was removed and preserved in 10% formalin until histological processing. Tissue slices were prepared following (Holmes *et al*., 2000), buffered for 48 hours at 4–8°C, then fixed, dehydrated in graded alcohols, cleared in two stages of xylene, and embedded in liquid paraffin at room temperature for two hours. Sections were cut at 5 µm thickness using a microtome, then de-waxed and stained with Eosin and Harris Hematoxylin (E&H). The slides were examined under a light microscope using X4, X10.

RESULT

Histopathological Change

Control Negative: Rats in the control negative group had cardiac tissue with normal histological architecture. The cardiac myofibers in the heart parenchyma seemed to be arranged neatly and oriented in a single direction.

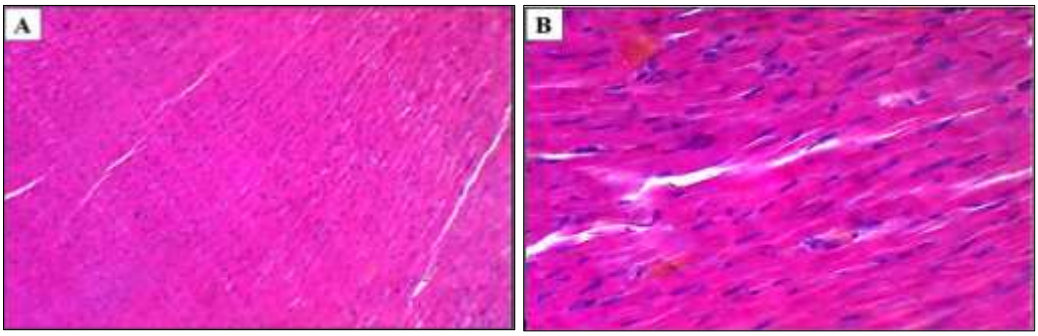

Figure 1: Photomicrographs of heart tissue from the control negative group.
A: Normal histological structure of cardiac muscle (H&E, 100x).
B: Well-aligned cardiac myofibers in the parenchyma (H&E, 400x).

Control Positive (Adrenaline 2 mg/kg b.w.): Rats in the control positive group had substantial pathological alterations in their heart tissue.

A: Severe cardiac myocyte necrosis accompanied by bleeding (blue arrow), inflammatory cell infiltration (yellow arrow), and the creation of gaps (black arrow).

B: Necrotic cardiac myocytes with tissue disruption (black arrow) and inflammatory infiltration (yellow arrow).

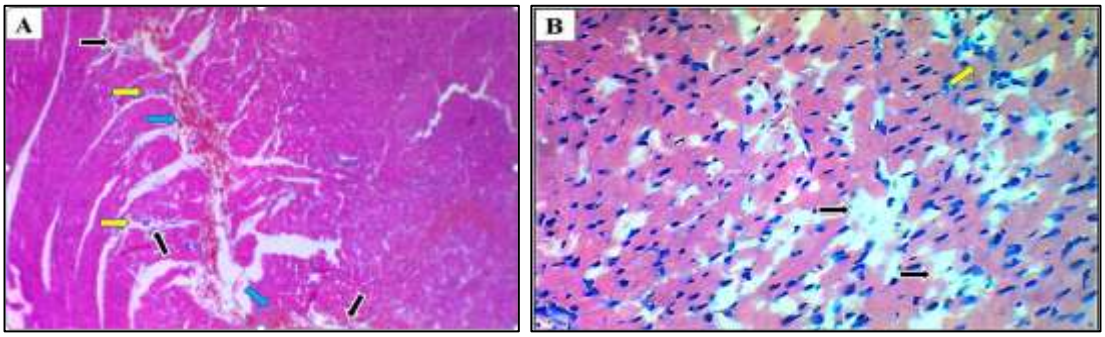

Figure 2: Photomicrographs of heart tissue from the control positive group.
A: Severe myocardial damage with necrosis, inflammation, and hemorrhage (H&E, 100x).
B: Necrosis and inflammatory cell infiltration in cardiac tissue (H&E, 400x).

Nano-Curcumin 200 mg/kg b.w. Group:

Rats' heart tissue that had been pretreated with nano-curcumin (200 mg/kg b.w.) for nine days and then given adrenaline (2 mg/kg b.w.) on days eight and nine displayed normal histological characteristics.

A and B: The intact myocardial architecture and well-arranged cardiac myofibers suggested that the reduced nano-curcumin dosage had a protective effect.

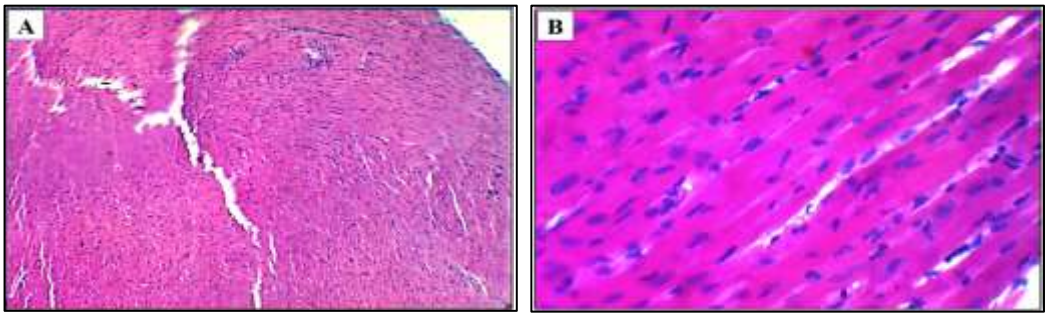

Figure 3: Photomicrograph of heart of 200 mg/kg of curcumin NPs treated rat.
A: Normal cardiac structure (H&E, 100x).
B: Well-organized cardiac myofibers (H&E, 400x).

Nano-Curcumin 300 mg/kg b.w. Group:

The heart tissue of rats pretreated with nano-curcumin (300 mg/kg b.w.) for 9 days, followed by adrenaline administration (2 mg/kg b.w.) on days 8 and 9, exhibited preserved normal histological architecture.

A & B: Cardiac myofibers were well arranged, indicating effective myocardial protection at the higher nano-curcumin dose.

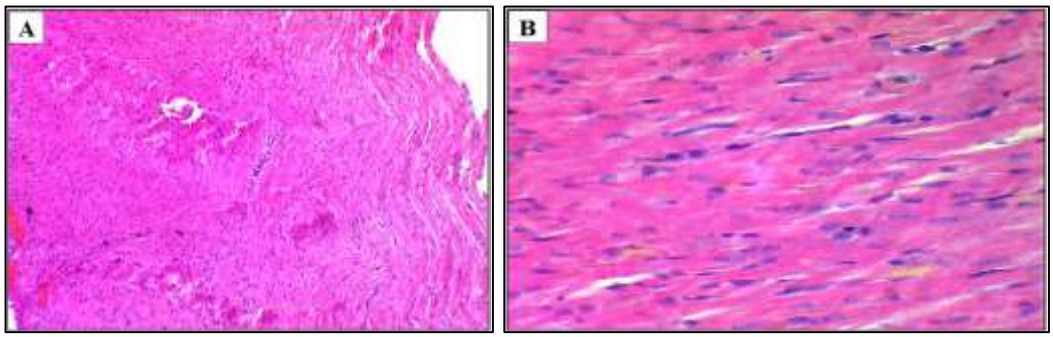

Figure 4: Photomicrographs of heart tissue from the nano-curcumin 300 mg/kg b.w. group.
A: Normal cardiac morphology (H&E, 100x).
B: Well-organized myofiber arrangement (H&E, 400x).

DISCUSSION

The effects of nano-curcumin on the histopathology of cardiac tissue after an adrenaline-induced myocardial infarction (MI) in rats were investigated in this work. Four groups participated in the experiment: two treatment groups received 200 mg and 300 mg dosages of Nano-curcumin for nine days prior to receiving 2 mg of adrenaline on days eight and nine; a negative control group received standard saline treatment; and a positive control group received 2 mg of adrenaline to induce MI.

According to the study's findings, Nano-curcumin, at both 200 and 300 mg/kg doses, clearly has a cardio protective effect against adrenaline-induced myocardial damage. Histological investigation demonstrated relative preservation of cardiac architecture in treated groups compared to the untreated adrenaline group, which displayed typical pathological alterations such as myocyte enlargement, cellular degeneration, and localized bleeding.

These outcomes align with prior research that has validated cur cumin's cardio protective effectiveness. Sarawi *et al*., (2021) showed that via modulating the TLR4/NF-κB and MAPK signaling pathways, Nano-curcumin reduces inflammation and oxidative stress, thereby attenuating heart damage. Cur cumin's antioxidant qualities are probably essential for reducing the cardio toxic effects of catecholamine's like adrenaline, which cause heart damage by producing inflammatory mediators and reactive oxygen species (Rameshrad *et al*., 2011).

The 300 mg/kg dose in this trial was superior to the 200 mg/kg dose in terms of maintaining the organization of cardiac fibers and lowering inflammatory alterations. This implies a dose-response connection and could be explained by Nano-cur cumin's higher tissue permeability than that of regular curcumin, as noted by Zhou *et al*., (2024).

Furthermore, our findings are corroborated by Li *et al*., (2023), who found that curcumin prevents fibrosis and inhibits oxidative stress, thereby protecting against myocardial ischemia/reperfusion injury. Soni & Kuttan (2008) also showed the cardio protective effect of curcumin in a similar experimental model using isoproterenol.

According to some theories, the mechanisms behind this protective effect include neutralizing free radicals, stabilizing cardiomyocyte membranes, inhibiting pro-inflammatory cytokines like TNF-α and IL-6, and better intracellular calcium control, which lowers mitochondrial permeability transition pore (mPTP) opening, as shown by Rameshrad *et al*., (2011).

These findings imply that nano-curcumin significantly prevents heart damage brought on by adrenaline. Despite being exposed to adrenaline, the preservation of cardiac architecture suggests that nano-curcumin may be able to successfully stop the chain reaction of oxidative damage and inflammation brought on by too many catecholamines. According to earlier research, curcumin's antioxidant, anti-inflammatory, and membrane-stabilizing qualities are what give it its cardioprotective impact (Boarescu *et al*., 2019; Lv *et al*., 2016).

The therapeutic promise of nano-curcumin as a preventative measure against chemically induced myocardial infarction is strengthened by these histological enhancements, which further support its function in regulating cellular damage pathways and maintaining heart integrity.

According to these result, one possible treatment for catecholamine-induced myocardial injury may be Nano-curcumin. especially in settings linked with acute stress or hormone-induced cardiac events.

Also, the use of nano-formulation in this study is very relevant and could lead to greater therapeutic efficacy because it boosts curcumin's bioavailability and cellular uptake. Similar histological results across the 200 mg and 300 mg groups suggest that both doses are sufficient to decrease tissue damage at the histological level, suggesting a threshold effect.

CONCLUSIONS

1. Nano-curcumin successfully guards against cardiac damage brought on by adrenaline.
2. The architecture of the heart was maintained by both the 200 mg/kg and 300 mg/kg doses, however the 300 mg/kg dose provided superior protection.
3. Its anti-inflammatory, antioxidant, and membrane-stabilizing qualities probably provide protection.

Recommendation

1. Investigate the mechanisms underlying the cardio protective benefits of Nano-curcumin by doing molecular studies.
2. To evaluate its efficacy in treating chronic heart damage, conduct long-term research.
3. Compare Nano-curcumin with standard cardiovascular therapies.

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