

# Effects of Long-term Nonylphenol Exposure on Myocardial Fibrosis and Cardiac Function in Rats

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## Research

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# Abstract

**Background:** Myocardial fibrosis is a critical pathological basis for the poor prognosis of cardiovascular diseases. Studies have found that myocardial fibrosis is closely associated with exposure to environmental estrogens such as nonylphenol (NP), as a representative of environmental estrogens. The aim of this study was to examine the effects of NP chronic exposure on myocardial fibrosis as well as cardiac structure and function. Forty Sprague Dawley rats were randomly divided into four groups (n = 10): control group (C), low NP dose (0.4 mg/kg, L), medium NP dose (4 mg/kg, M), and high NP dose (40 mg/kg, H) groups. The NP dose groups were gavaged with NP for 180 days.

**Results:** The NP level in the heart of the NP groups was significantly higher than those in the control group ( $F = 43.658, P < 0.001$ ). Serum aspartate aminotransferase (AST), creatine kinase (CK), creatine kinase isozyme (CK-MB), lactate dehydrogenase (LDH) and  $\alpha$ -hydroxybutyrate dehydrogenase ( $\alpha$ -HBDH) significantly increased in the NP groups compared with the control group (). Histopathological examination of the heart biopsy illustrates that in the medium and high NP groups, the fibrous connective tissue had a disordered and loose gridding shape, muscle fibers had fractured, and muscle fibers were loose with a widened gap. Extensive inflammatory cell infiltration and fibroblast proliferation in the myocardial interstitium were also found. With increasing NP dose, the degree of muscle fiber loosening and disorder became more significant in the NP treatment groups, and the collagen volume fraction (CVF) was higher than that in the control group ( $P < 0.01$ ). Compared with the control group, the expression of collagen I and collagen III increased significantly in the medium and high NP groups ( $P < 0.05$ ). The values of the systolic thickness of the left ventricular anterior wall (LVAWs), the diastolic thickness of the left ventricular posterior wall (LVPWd), the systolic thickness of the left ventricular posterior wall (LVPWs), and the left ventricular anterior wall (LVAWd) in the NP groups were slightly lower than those in of the control group. The values of left ventricular end systolic dimensions (LVIDs) in the NP groups increased compared with the control group.

**Conclusions:** Long-term NP exposure could lead to fibrosis in the rat myocardium, which is characterized by increased expressions of myocardial collagen I and collagen III, as well as elevated cardiac enzymes. In addition, the cardiac structure was affected and changes were observed in the thinner ventricular wall and as an enlarged ventricular cavity.

## Full Text

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## Figures

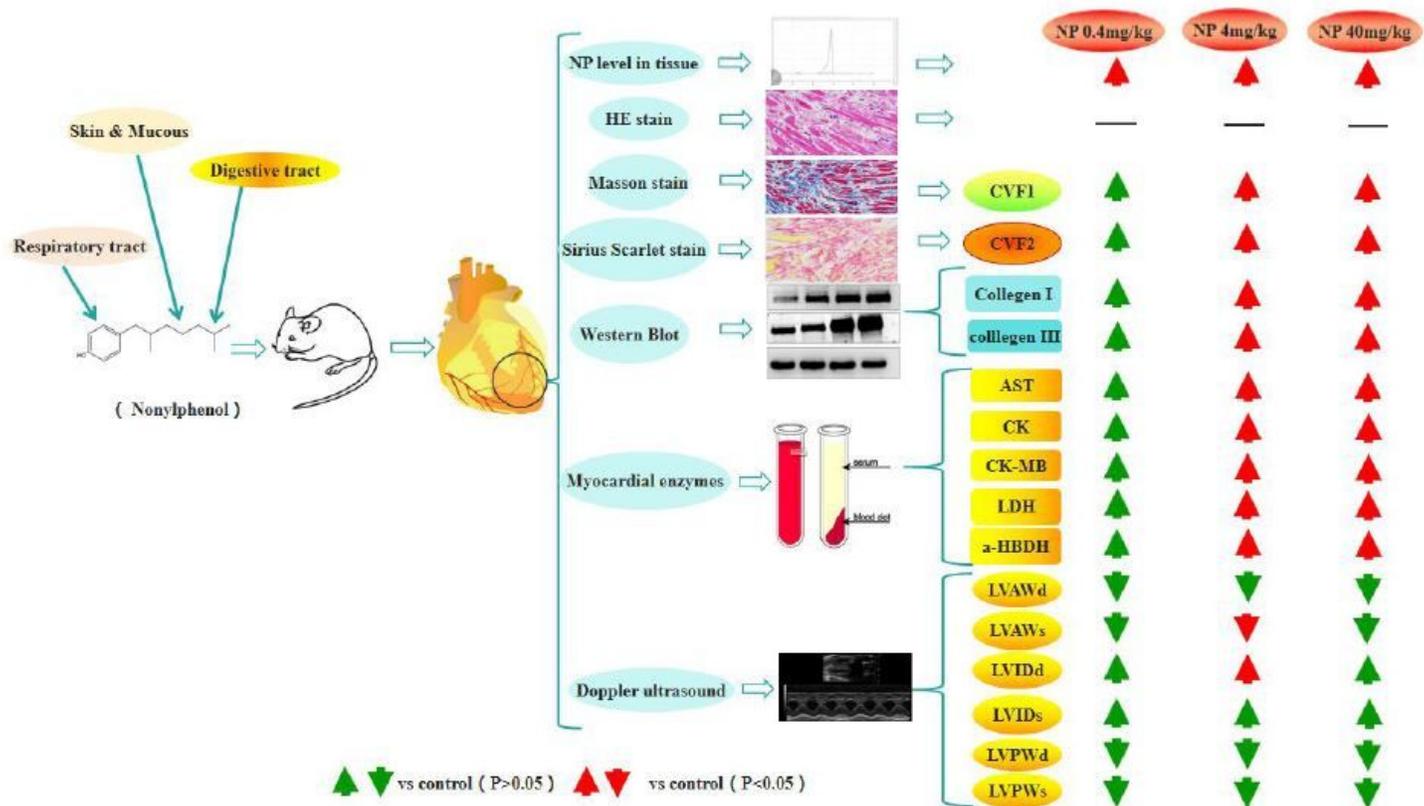


Figure 1

Flowchart depicting exposure protocols and time 194 duration of exposure.

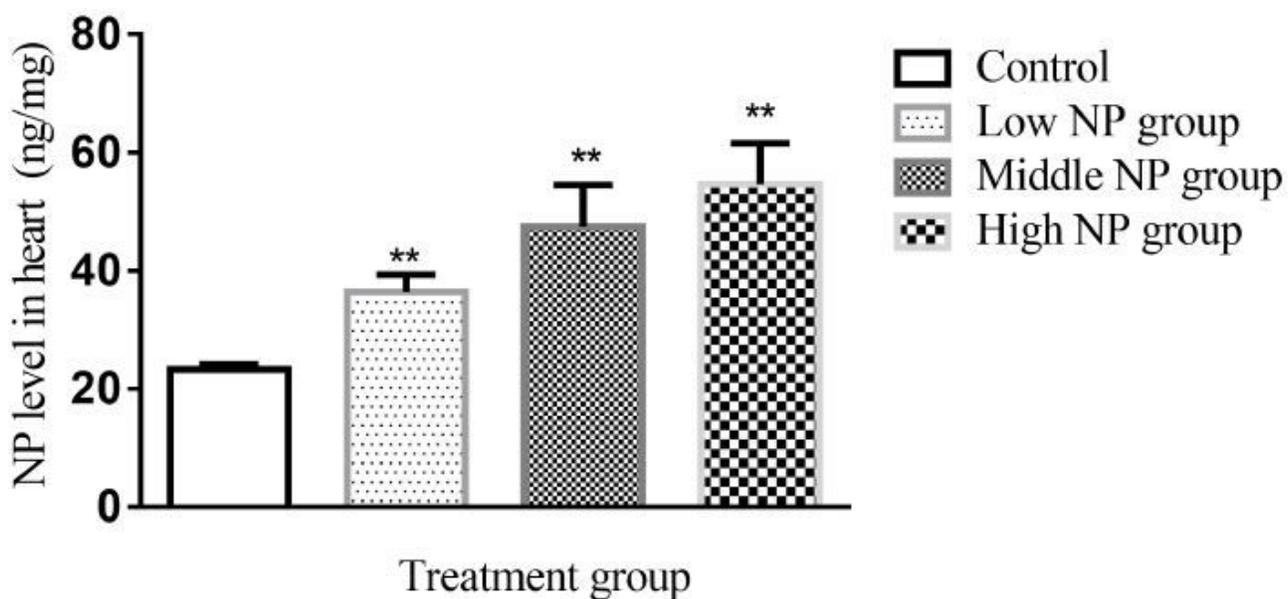
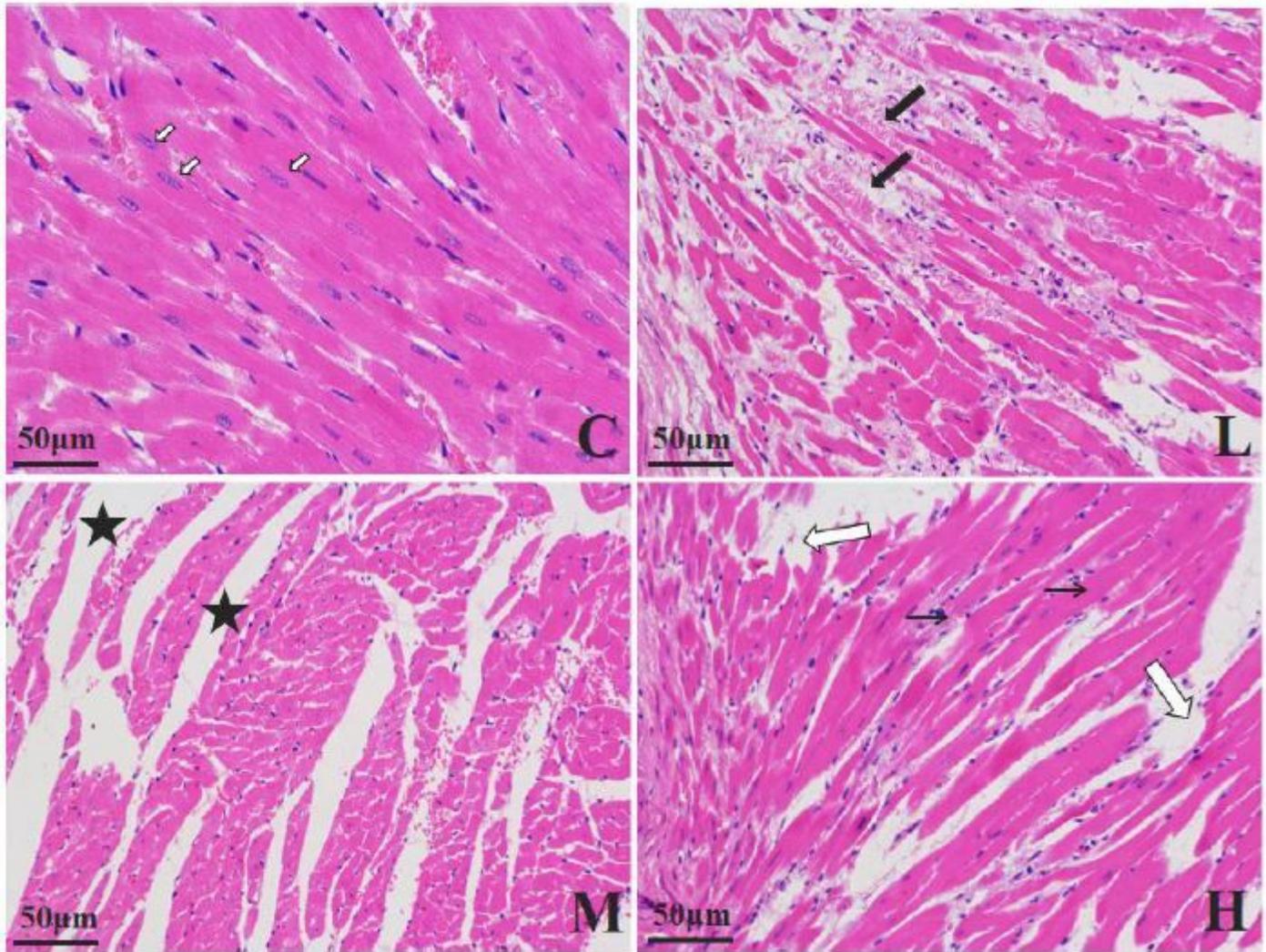


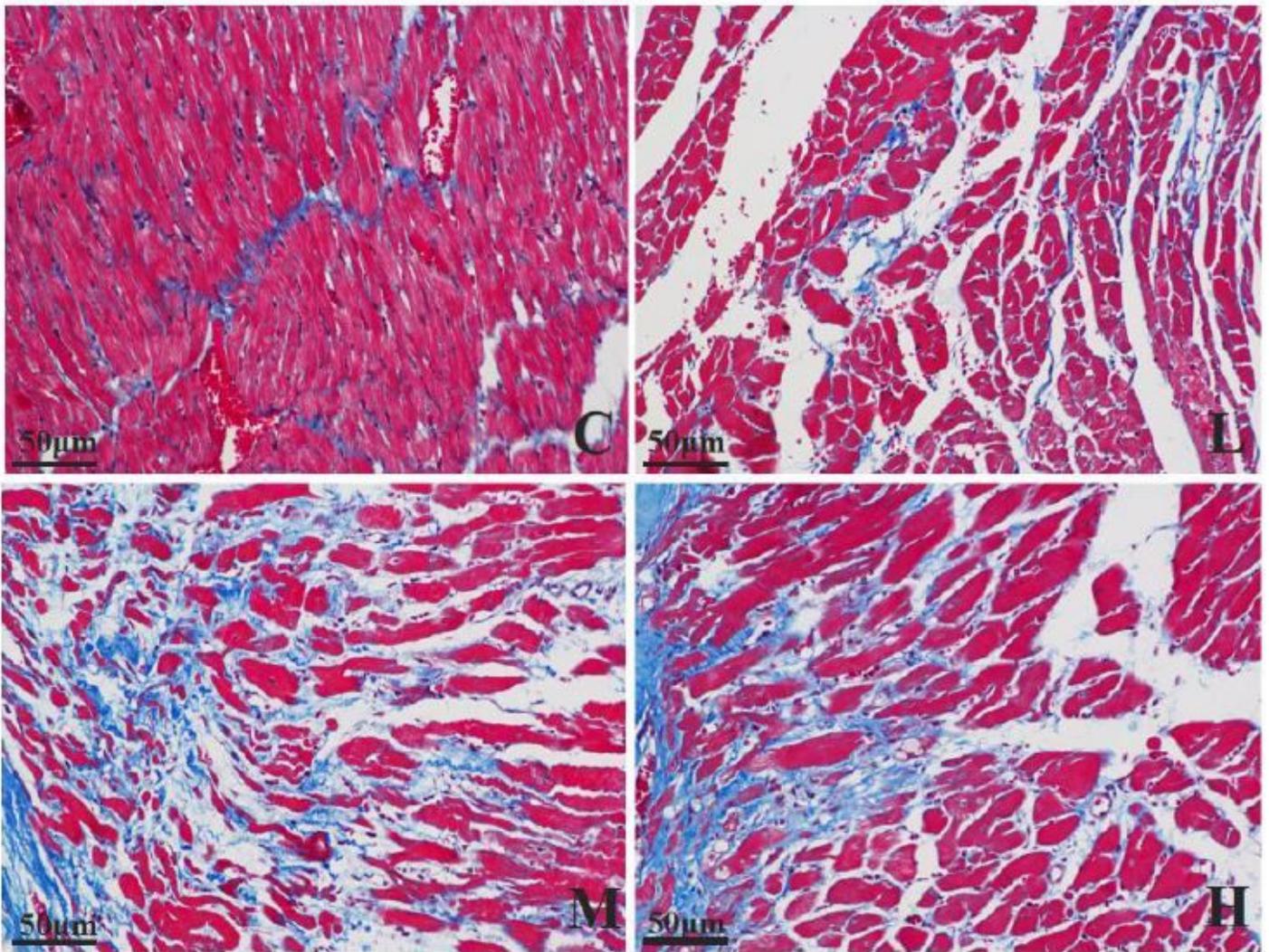
Figure 2

Comparison of NP levels in the heart between experimental 288 groups ( $n = 6, \bar{x} \pm s, **P < 0.01$ ).



**Figure 3**

Effect of NP dose on the myocardial tissue (HE staining,  $\times 400, n = 6$ ). C: control group, L: low NP dose, M: medium NP dose, H: high NP dose.



**Figure 4**

Myocardial fibrosis induced by different doses of NP (Masson staining,  $\times 400$ ,  $n = 6$ ). C: control group, L: low NP dose, M: medium NP dose, H: high NP dose.

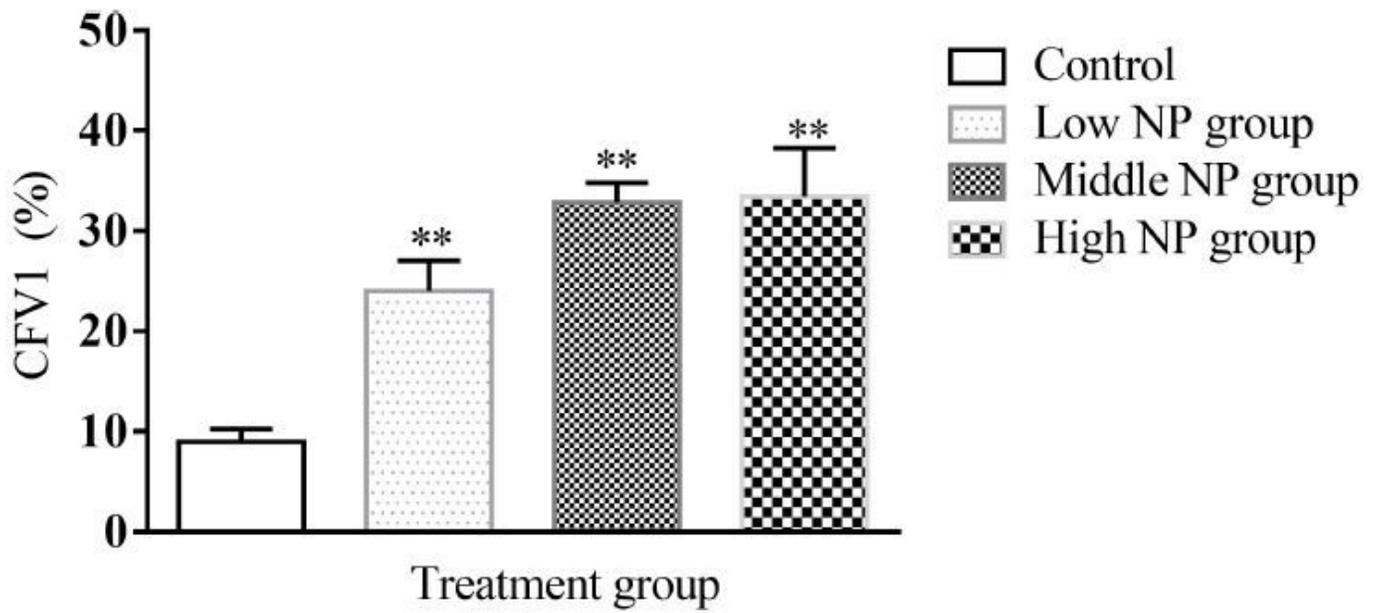
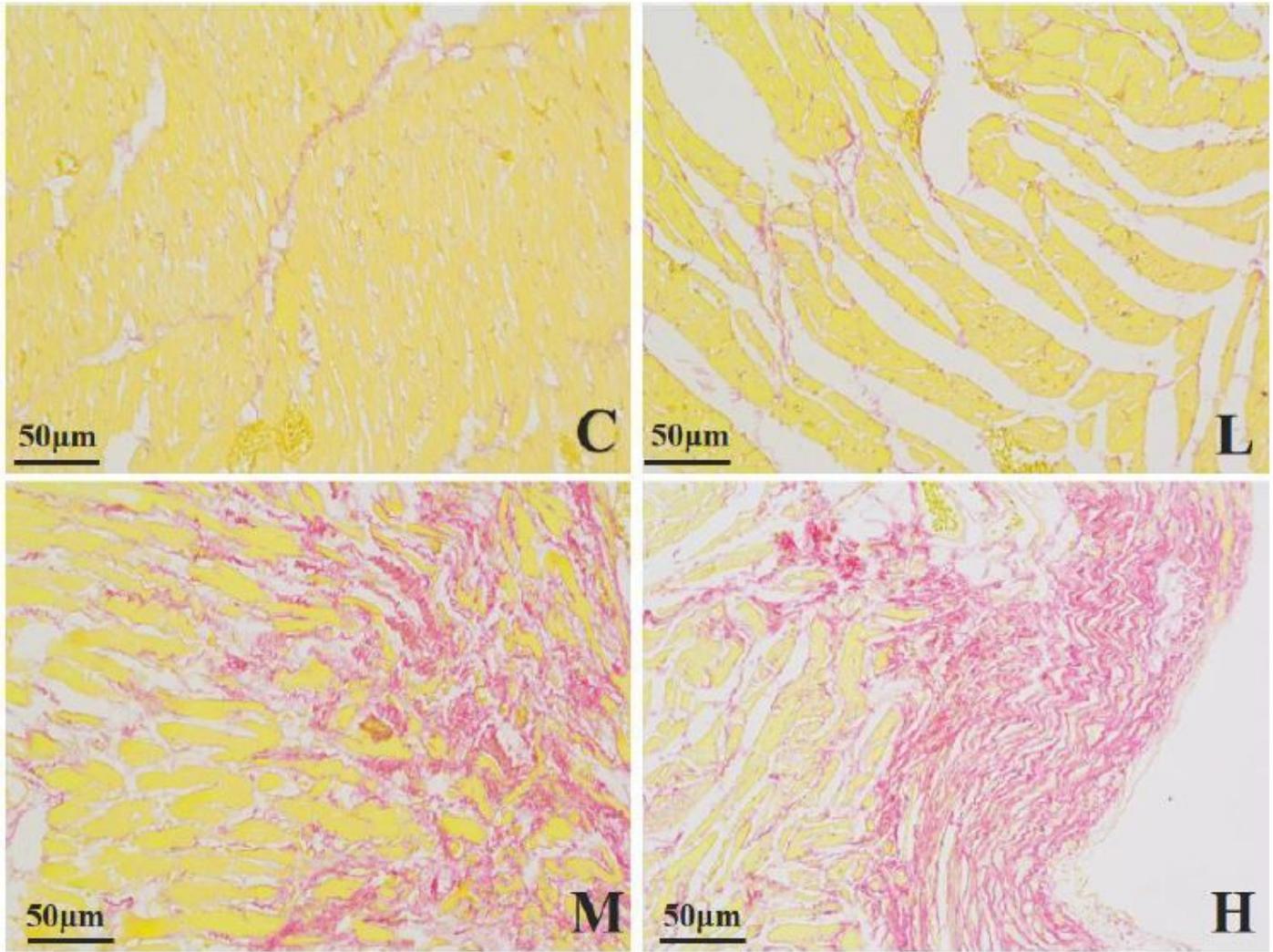


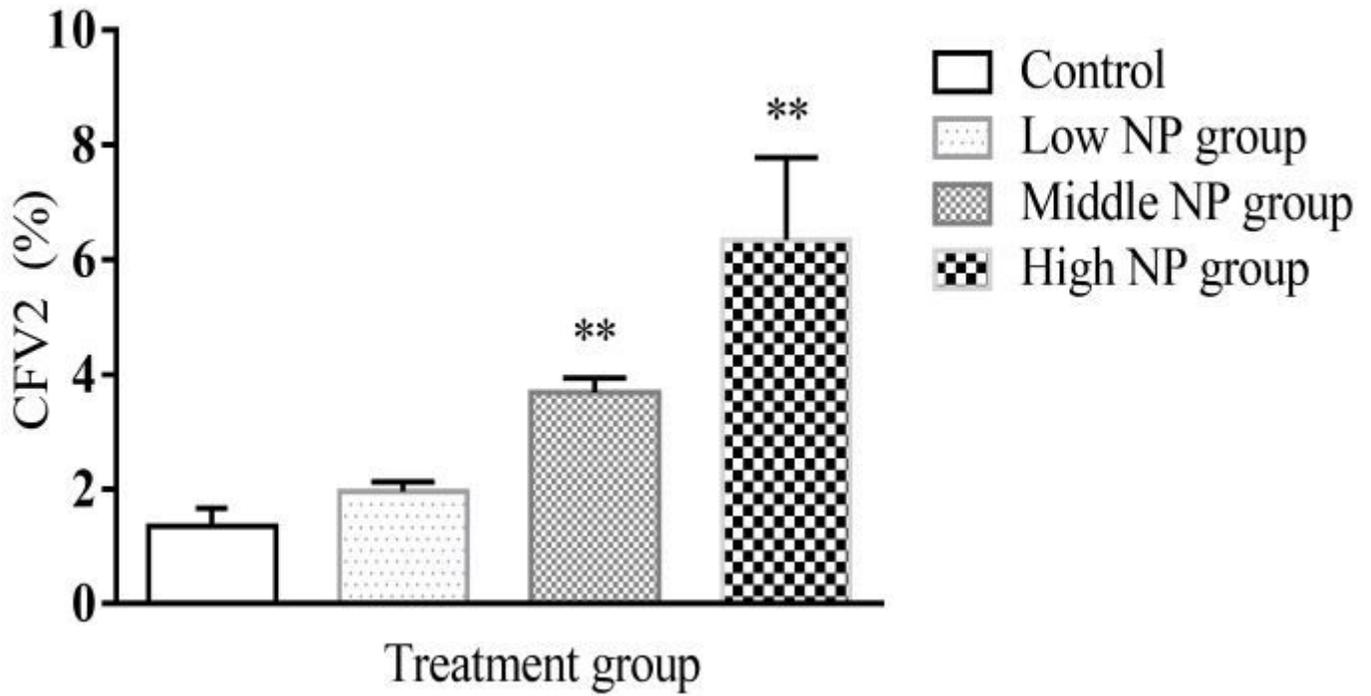
Figure 5

Comparison of myocardial CVF between groups exposed to different NP doses (n = 6,  $\bar{x} \pm s$ , \*\*P < 0.01).



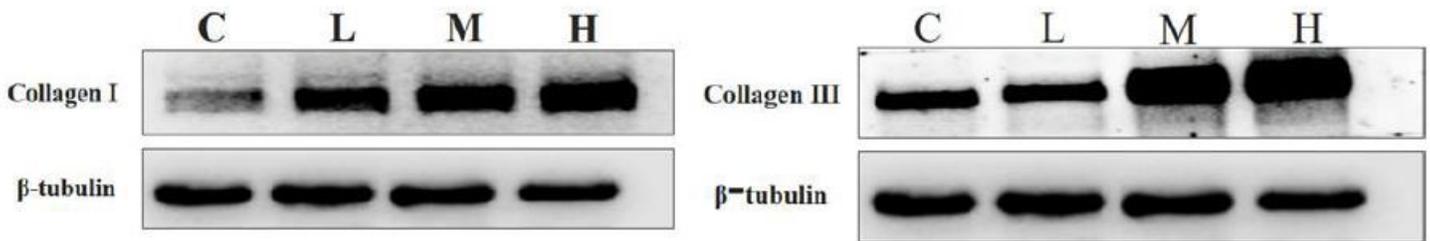
**Figure 6**

Myocardial fibrosis induced by different NP doses (Sirius staining,  $\times 400$ ,  $n = 6$ ). C: control group, L: low NP dose, M: medium NP dose, H: high NP dose.



**Figure 7**

Comparison of myocardial CVF2 between groups 380 exposed to different NP doses (n = 6,  $\bar{x} \pm s$ , \*\*P < 0.01).



**Figure 8**

Expressions of collagen I and collagen III in the myocardial tissues exposed to different NP doses. C: control group, L: low NP dose, M: medium NP dose, H: high NP dose.

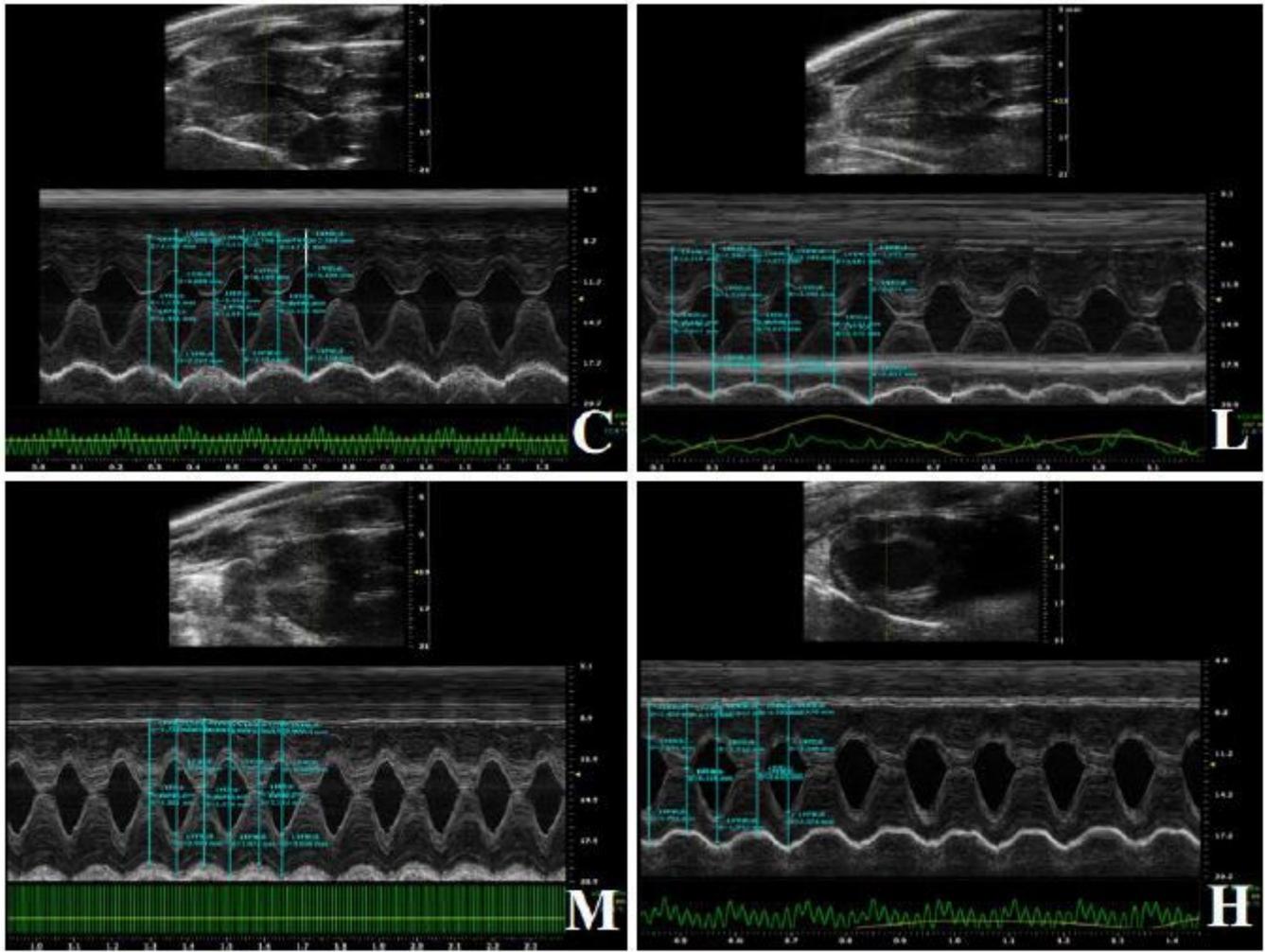
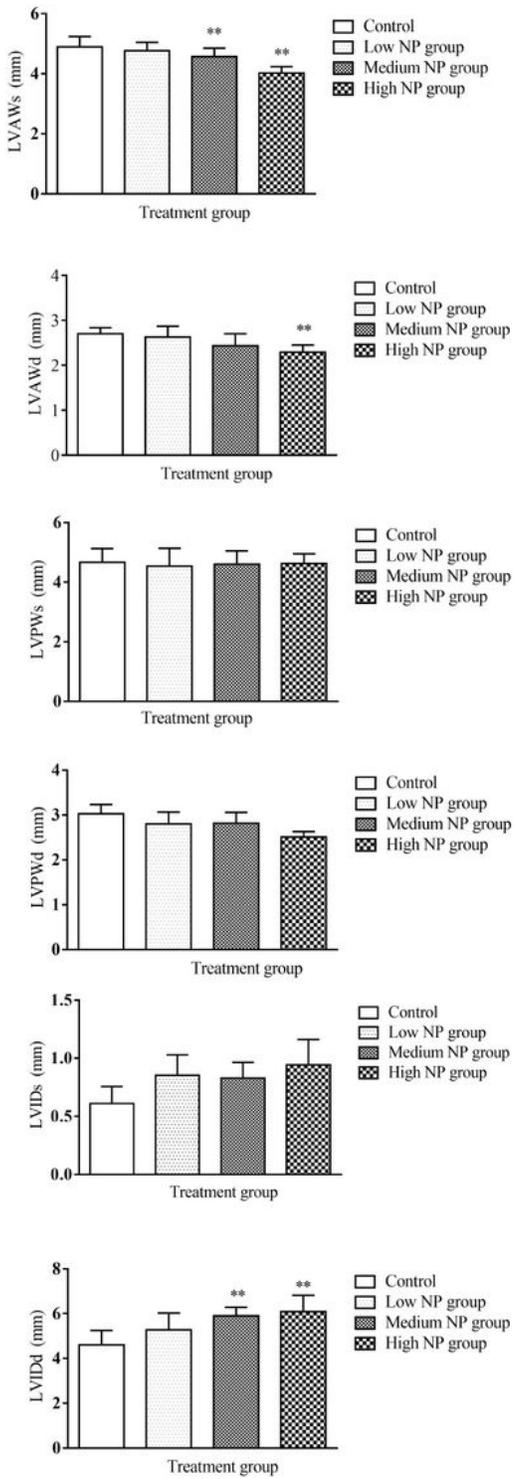


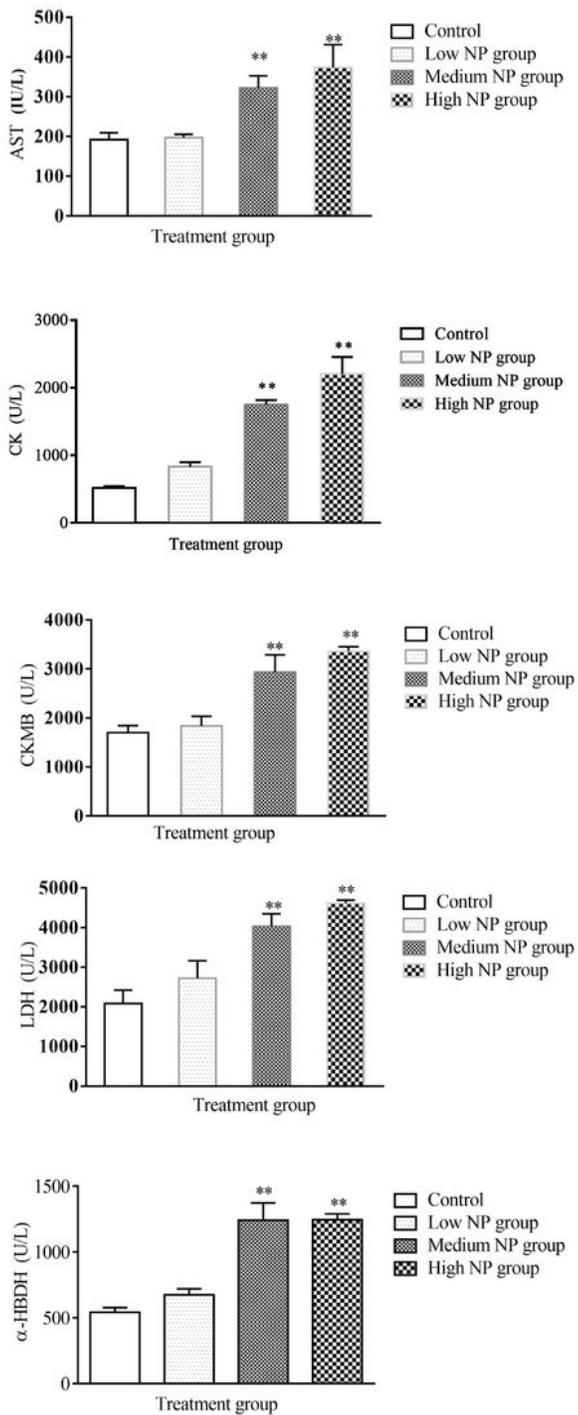
Figure 9

Comparison of collagen I, collagen III between groups 461 exposed to different NP doses ( $n = 6$ ,  $\bar{x} \pm s$ ,  $**P < 0.01$ ).



**Figure 10**

Comparison of changes of wall thickness and inner diameter of the left ventricle in rats exposed to different NP doses between groups (n = 6,  $\bar{x} \pm s$ , \*\*P < 0.01).



**Figure 11**

Comparison of serum myocardial enzyme levels between groups exposed to different NP doses (n = 6,  $\bar{x} \pm s$ , \*\*P < 0.01).

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