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Effectiveness of N-Acetylcysteine on Zinc oxide Nanoparticles-Induced Cardiotoxicity in Adult Albino Rats

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Abstract

Background: Zinc Oxide nanoparticles (ZnO NPs) are broadly utilized in medications, foodstuffs, cosmetics plus toothpastes. Studies have shown that the heart is one of the target organs following oral exposure to ZnO NPs. N-acetylcysteine (NAC) is a free radical scavenger, used to combat damage in various tissues. This research was performed to define the mechanistic hypothesis of ZnO NPs induced cardiotoxicity and the possible protective role of NAC. **Methods**: The research was performed on 40 adult albino rats; divided into 5 groups each of 8 rats, group I as a negative control, group II (positive control) received distilled water, group III (NAC group) received (200 mg/kg) NAC dissolved in distilled water, group IV (ZnO NPs group)**:** received (422 mg/kg) ZnO NPs dissolved in distilled water, group V (NAC and ZnO NPs group): received NAC then ZnO NPs in the same doses. The treatments were given via oral gavage, once daily for 4 weeks. **Results**: There was a significant increase in mean values of cardiac enzymes and a significant decline in the total antioxidant capacity in ZnO NPs treated group as compared with the control group. DNA fragmentation was observed in heart tissues of ZnO NPs treated group. Histological examination of the heart of ZnO NPs treated group revealed degenerated myocardium, vacuolated cytoplasm, and congestion in myocardial blood vessels when compared with control group. **Conclusion:** Administration of NAC offered protection against cardiotoxic effects induced by ZnO NPs.

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Key words Zinc oxide nanoparticles, Oxidative stress, DNA damage, Cardiotoxicity, N-acetylcysteine

Introduction

The great advancement in technology supports the reduction of material size from micro to nano measure that is not only provides benefits to different scientific fields but also has possible risks to humans and environment. Nanotechnology is the field of studying particles at the nano scale (1–100 nanometers) measure (Gigault et al., 2021). A nanometer (nm) is defined as a one billionth of a meter (10^{-9} meter). Nanoparticles (NPs) have created a deep influence in their applications in the fields of biomedicine, commercial products and industrial practice. Zinc Oxide NPs (ZnO NPs) are frequently used in cosmetic products, food industries, drug delivery systems, drugs and synthetic metal valves used in open heart surgeries (Anjum et al., 2021). Nano-ZnO is utilized in multiple fields as an additive in industry, together with plastics, porcelains, crystals, elastics, lubricants, dyes, creams, glues, stains, foodstuffs, batteries and fire retardants, etc. The pathologic mechanisms introduced by ZnO NPs are inflammation- resultant effects. Inflammation is a dangerous effect if chronically provoked via the environmental stimuli (Li et al., 2020). Zinc Oxide NPs can affect many organs through the blood stream. Studies have revealed the accumulation of ZnO NPs in the hearts of laboratory rats. Blood borne ZnO NPs could disturb the cardiomyocytes directly, causing inflammation, necrosis and apoptosis (Wang et al., 2019). N-Acetylcysteine is an antioxidant; it acts as a cysteine supporter and preserves or even raises the intracellular levels of glutathione that guards cells from poisons such as free radicals. NAC is used to avoid oxidative stress-induced damage in several tissues (Ezerina et al., 2018). The aim of the current study was to detect the pathophysiology of ZnO NPs induced cardiotoxicity and to evaluate the protective role of NAC supplementation in albino rats.

Material and Methods

A- Chemicals

Zinc Oxide nanoparticles: nanopowder less than 110 nm particle size with surface area of 40-70 m^2/g and purity more than 99.6% trace metals basis. Molecular weight equals 81.38 g / mol. Its (CAS No) is 1314-13-2. It is a white odorless fine particle, dissolved in distilled water. It was industrially manufactured by Sigma -Aldrich chemical company, USA and obtained from Sigma, Cairo, Egypt.

N-Acetylcysteine: it was acquired from SEDICO Company, Cairo, Egypt in the form of effervescent instant sachets, 200 mg each.

Distilled water: it was obtained from SEDICO Company, Egypt.

B-Animals and experimental design

The study was conducted on 40 adult albino rats

(having a weight 170- 190 gm.), achieved from the animal housing of Zagazig faculty of Medicine. The rats were adapted for 2 weeks prior to the research. This study was permitted by the Institutional Animal Care and Use Committee (IACUC) and the experimental procedure was carried out according to the guidelines of the Laboratory Animals Resources Institute (1996).

C-Grouping of animals

The study involved 5 equal experimental groups, each contained 8 rats, Group I (Negative control group) received regular nutrition and tap water to record the basic parameters. Group II (Positive control group) received 1 ml distilled water. Group III (NAC treated group) received NAC (200 mg/kg) dissolved in distilled water according to (Sakthibalan et al., 2013). Group IV (ZnO NPs treated group) received ZnO NPs (422mg/kg) (1/20 of LD50) dissolved in distilled water because the lethal dose (LD50) of ZnO NPs in rats is (8437mg/kg BW) after oral administration according to (US Research Nanomaterials, 2016). Group V (NAC and ZnO NPs treated group) received NAC (200 mg/kg according to (Sakthibalan et al., 2013) at this dose NAC obtain antioxidant properties). One hour later, ZnO NPS was given (422 mg/kg) dissolved in distilled water. The treatments were given via oral gavage, once daily for 4 weeks.

By the end of the research, the blood samples were collected then rats were sacrificed after ether anesthesia. Parts of the hearts were homogenized for DNA damage assay via gel electrophoresis, while the other parts were processed for histological examination.

D-Methods

Biochemical study

Blood collection

Blood samples were taken from rats using micro-capillary glass tubing from the retro-orbital plexus. A tube has a capillary opening of 0.7 mm; inserted in the orbit of the eye at an anterior approach, rotated to drill through the conjunctiva so that the blood could freely shoot in this capillary tube (Johnson, 2007).

Cardiac enzymes:

Serum Troponin I (pg/mL):

It was assessed according to the method of Wang and Chatham, (2004)

Calculation:

1) Define the mean absorbance value (Optical Density 440) for all reference values (controls and samples).
2) Create a standard curve via plotting the mean absorbance found for each reference standard against its concentration in ng/ml on a graph paper, with absorbance on the vertical (y) plane besides concentration on the horizontal (x) plane.
3) By using the mean absorbance value for each sample, outline an equivalent concentration of troponin I (pg/ml) from the standard curve.

Creatine Kinase (CK-MB) (U/L):

It was assessed according to the method of Oliver, (1995).

Calculation:

An international unit (U/L) is well-defined as the amount of enzymes which catalyzes the conversion of 1 micromole of substance per minute in distinct conditions:

U/L= (Δ Abs./min×1.024×1000) / (6.23×0.026) = Δ Abs. /min× 6592

Δ Abs. /min= Average absorbance change per minute 1.024= Total reaction time 1000= Conversion of U/ml to U/L 6.23= Millimolar absorptivity of NADH 0.026= Sample volume in ml.

Total antioxidant capacity (TAC) (mM/L):

It was assessed according to the method of (Koracevic and Koracevic, 2001).

Calculation:

Total Antioxidants concentrations:

$$mM/L = A_B - A_{SA} \times 3.33$$

Detection of DNA fragmentation:

DNA laddering*:*

It is a qualitative investigation of DNA fragmentation that was defined according to Wlodek et al., (1991). Nuclear morphology variations, distinctive of apoptosis, seem inside the cell plus characteristic biological events, the endonuclease-mediated cleavage of nuclear DNA. In fact, formation of DNA fragments of oligonucleosomal size (170-220 bp length) is a mark of apoptosis in numerous cell types (Singh et al., 2014). In the apoptotic cells, specific DNA cleavage becomes apparent in electrophoresis analysis as a typical ladder form due to multiple DNA fragments. However, while this method is simple and usually capable of offering worthy results, it is only a qualitative analysis (Arora et al., 2012).

Calculation:

It is a qualitative investigation of DNA fragmentation through agarose gel electrophoresis, the DNA ladders were visualized and photographed under UV Trans- illuminator.

Histopathological study:

At the phase of sacrifice, the hearts were removed through thoracic incisions. Tissues were perfused with a phosphate buffered saline (PBS) that contain 0.15 mg /mL heparin in order to remove any red blood cells or clots, the hearts were immediately excised, dried and dissected out. Then, heart tissues were washed with ice-cold normal saline, blotted with a part of filter paper to be examined by light microscope.

Methods used for histopathological examination of the heart:

Heart tissue specimens were fixed in 12% neutral buffered formalin, embedded in paraffin then divided at a width of 6 mm (Kiernan, 2001). These sections were submitted to Haematoxylin and Eosin (H&E) staining: as a routine method for studying the general histological architecture of the hearts.

E-Statistical analysis

Data analysis of the results was conducted by using IBM SPSS Statistics software (version 25, USA). Numerical results from the tests were expressed as mean ± standard deviation (mean±SD). For the statistical analysis, one-way analysis of variance (ANOVA) was used. *P* value (probability of chance) <0.05 was considered significant.

Results

There was no statistically significant difference between negative, positive control and NAC groups as regard the studied biochemical and histological parameters (Table1). Thus, the negative control group was used for comparison with the other groups.

I-Biochemical results

There was a high significant difference in troponin I and CK-MB between control group, ZnO NPs group and (NAC+ZnO NPs) group (P<0.001) as shown in (Table 2). There was a high significant increase in troponin I and Ck-MB level in ZnO NPs treated when compared with control group (p<0.001). Co-administration of NAC showed a significant decrease in troponin I and CK-MB mean values when compared with those of ZnO NPs group (p<0.001) (Table 2) (Figures 1,2). There was a high significant difference in TAC level between negative control group, ZnO NPs group and (NAC+ZnO NPs) treated group (P<0.001) as shown in (Table 2). In ZnO NPs group, there was a high significant decrease in TAC mean values when compared with negative control group (P<0.001). Co-administration of NAC, revealed a high significant increase in TAC mean values when compared with those of ZnO NPs group (P<0.001) (Figure 3).

II-DNA damage results

There was a statistical significant difference in DNA damage assay between the studied groups (P<0.001). In control groups (I, II) and group III (NAC group), DNA was normal. While in groups IV (ZnO NPs group) & group V (ZnO NPs &NAC group), DNA was fragmented (Table 3)**.** DNA fragmentation (DNA laddering): was evaluated by agarose gel electrophoresis of DNA isolated from adult albino rat heart. Generally, DNA moves as one band on gel, and scattering of this band means damage of DNA. By comparison to control, DNA damage was classified into mild, moderate and severe. Gel electrophoresis of DNA isolated from heart tissues of group I (negative control group) showed normal DNA bands (Figure 4). Administration of ZnO NPs 422mg/kg BW once daily for 4 weeks resulted in fragmentation or severe shearing of DNA extracted from heart tissue (Figure 5). Co-administration of 200 mg/kg BW NAC resulted in regression of DNA fragmentation in 75% of the rats in group V while no improvement was seen in the remaining 25% of rats as shown in (Figure 6)

III- Histological results

Macroscopic examination of the heart of all the studied groups revealed normal appearance with no significant changes and normal cut sections. Light microscopic examination of hearts of control group revealed typical myocardial tissues in the form of branching and anastomosing cardiac muscle fibers, normal connective tissue in between cardiac fibers with acidophilic cytoplasm and centrally located nuclei**.** Microscopic examination of the cardiac tissues of ZnO NPs group revealed karyolysis, disorganized and degenerated myocardium with vacuolated cytoplasm**.** Also, congestion in the myocardial blood vessels and thrombus formation were seen**.** However, co-administration of NAC caused significant improvement of all histopathological alterations compared with cardiac tissues from rats treated with ZnO NPs (Figure 7)

Table (1): One-way ANOVA statistical analysis for comparison between mean values of troponin I, CK-MB and TAC among control groups (I and II) and (NAC group):

Group / Parameter	Group I (N=8)	Group II (N=8)	Group III (N=8)	F	P value
Troponin I Mean ± SD Range	27.25 ± 8.78 16.8 – 37.7	27.35 ± 8.79 16.9 – 37.8	27.45 ± 7.62 17 – 38.3	0.01	0.99 NS
CK-MB: Mean ± SD Range	14.88 ± 2.42 12 – 18	14.25 ± 3.01 10 – 19	11.88 ± 1.96 8 – 15	3.21	> 0.05 NS
TAC: Mean ± SD Range	1.24 ± 0.26 0.9 – 1.5	1.46 ± 0.21 1.2 – 1.8	1.55 ± 0.33 1 – 2	2.80	0.08 NS

NS: Non–significant (P>0.05), N: Number of rats in each group, SD: Standard Deviation, CK-MB: Creatine kinase-MB, TAC: Total antioxidant capacity, ANOVA test: Analysis of variance test

Table (2): One-way ANOVA statistical analysis for comparison between mean values of troponin I, CK-MB and TAC in group I (control group), group IV (ZnO NPs) and group V (NAC& ZnO NPs):

Group / Parameter	Group I (N=8)	Group IV (N=8)	Group V (N=8)	F	P value
Troponin I:					
Mean ± SD	27.25 ± 8.78	85.48 ± 26.83	27.30 ± 8.74	38.79	<0.001**
Range	16.8 – 37.7	37.11 – 145.43	12.24 – 39.19		
CK-MB:					
Mean ± SD	14.88 ± 2.42	45.5 ± 4.44	19 ± 1.31	243.1	<0.001**
Range	12 – 18	39 – 50	17 – 21		
TAC:					
Mean ± SD	1.24 ± 0.26	0.08 ± 0.02	1.03 ± 0.34	49.36	<0.001**
Range	0.9 – 1.5	0.02 – 0.13	0.69 – 1.6		

= Highly significant (P<0.001), N: Number of rats in each group, SD: Standard Deviation, CK-MB: Creatine kinase-MB, TAC: Total antioxidant capacity, ANOVA test: Analysis of variance test

Table (3): Chi square test for comparison between DNA fragmentations in the different studied groups:

Variable	Group I (N=8)	Group II (N=8)	Group III (N=8)	Group IV (N=8)	Group V (N=8)	χ^2	P value
DNA fragmentation:							
Normal	8 (100%)	8 (100%)	8 (100%)	0 (0%)	0 (0%)		
Mild	0 (0%)	0 (0%)	0 (0%)	0 (0%)	6 (75%)	64	<0.001**
Sever	0 (0%)	0 (0%)	0 (0%)	8 (100%)	2 (25%)		

: highly significant (p<0.001), N: Number of rats in each group, X^2: Chi square test

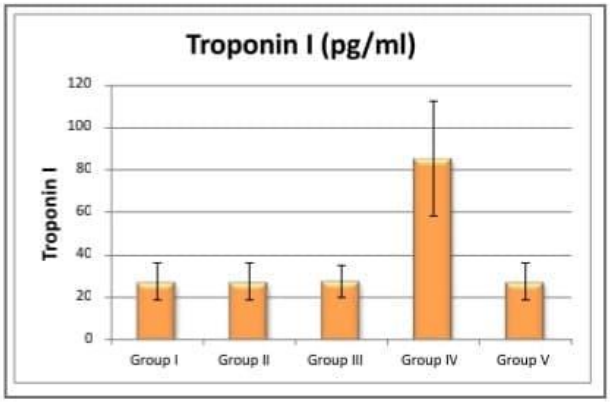

Figure (1): Bar chart showing comparative magnitude of mean values of troponin I in between the study groups

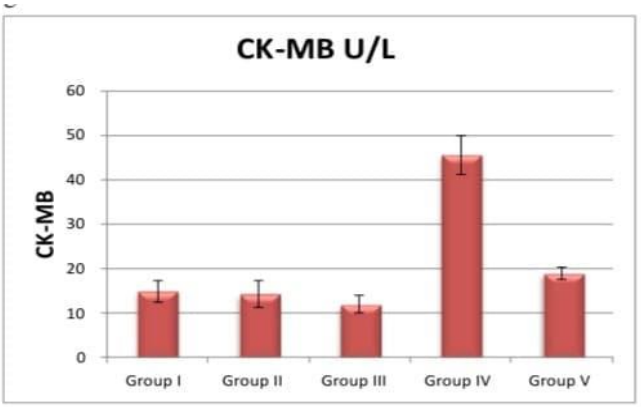

Figure (2): Bar chart showing comparative magnitude of mean values of serum CK-MB in between the study groups

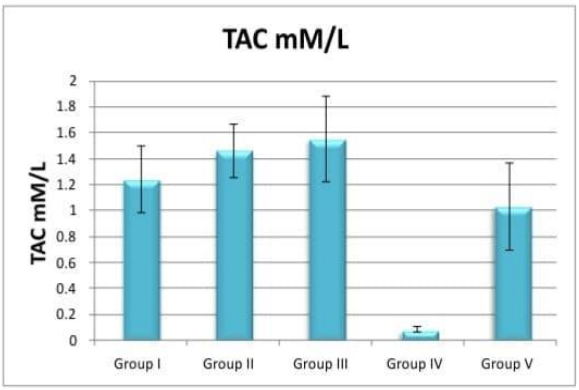

Figure (3): Bar chart showing comparative magnitude of mean values of serum TAC in between the study groups

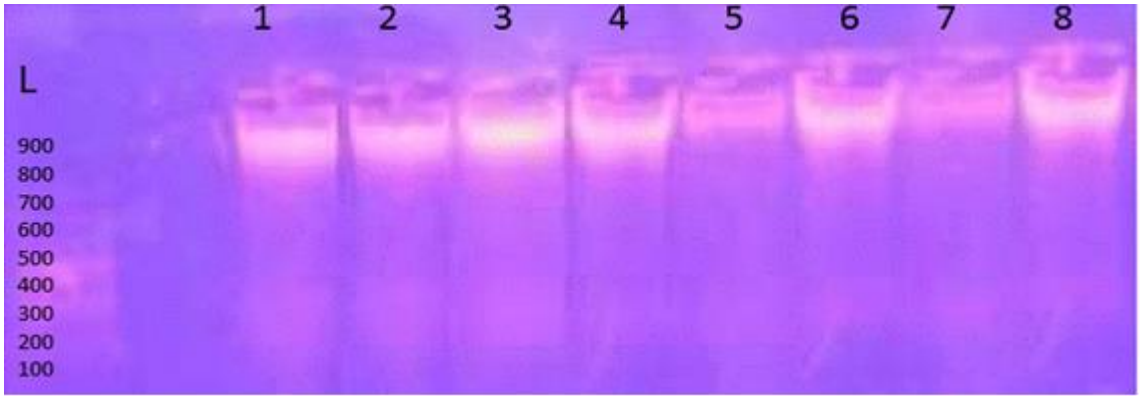

Figure (4): Agarose gel electrophoresis of DNA isolated from heart tissues of control group. (L): DNA ladder assay showed normal DNA bands.

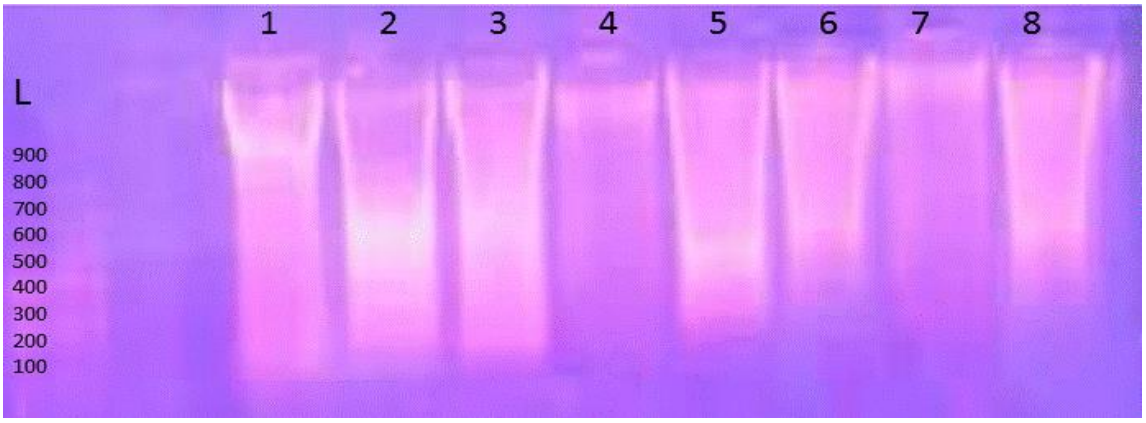

Figure (5): Agarose gel electrophoresis of DNA isolated from heart tissues of ZnO NPs group DNA ladder assay showed advanced fragmentation

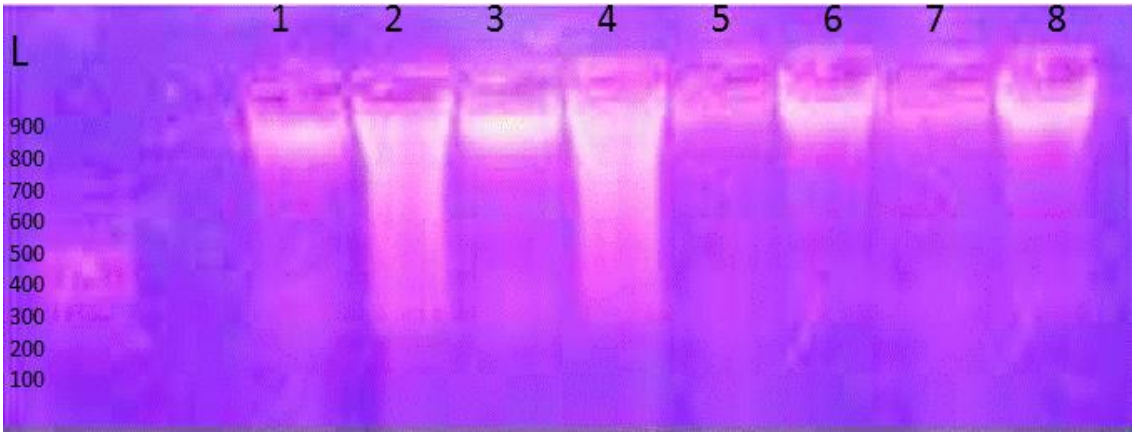

Figure (6): Agarose gel electrophoresis of DNA isolated from heart tissues of (NAC+ZnO NPs) group (L): DNA ladder showed mild DNA fragmentation in only 6 rats while severe shearing in the 2th and 4th rats

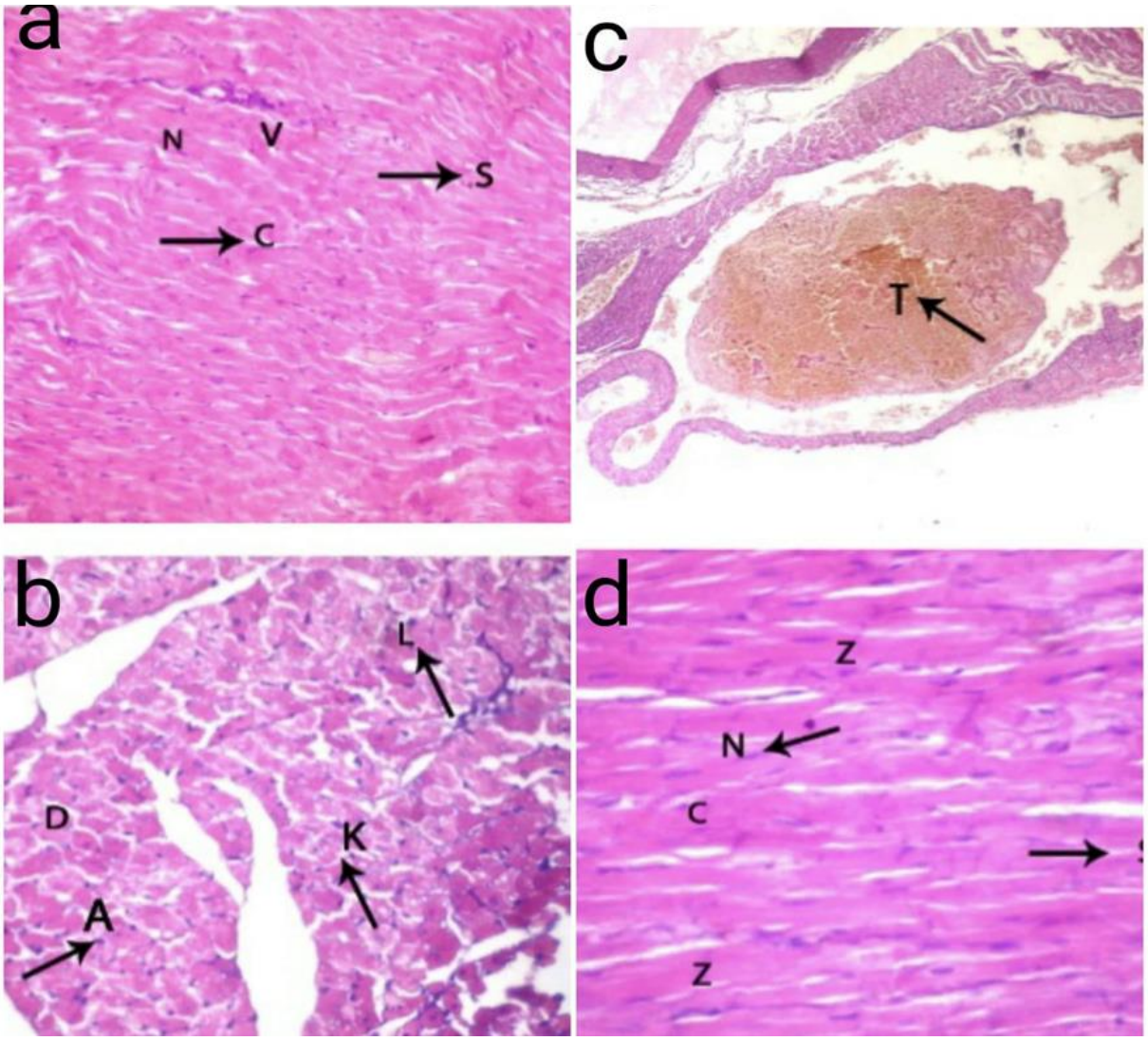

Figure (7) a: Photomicrograph of a section from myocardium of control rat showing normal myocardial tissue; anastomosing cardiac fibers with acidophilic cytoplasm (C), central bright nuclei (N) and striations (S). Connective tissue (V) between cardiac fibers is normal (H&E x 200) b: Photomicrograph of a section from myocardium of a rat treated with 422mg/kg/day ZnO NPs for 4 weeks, showing disarray of cardiac fibers with karyolysis (K). Necrotized degenerated myocardium (D). Some apoptotic nuclei (A), vacuolated cytoplasm (L), increased connective tissue space between cardiomyocytes and absent Z disc (H&E x 400) c: Photomicrograph of a section from myocardium of a rat treated with ZnO NPs. This panoramic view of heart shows severe congestion and mostly thrombus formation (T) (H&E x 400) d: Photomicrograph of a section from myocardium of a rat treated with NAC + ZnO NPs showing nearly normal myocardial tissue with vesicular nuclei (N), normal Z junction and normal cardiomyocytes' striations (S), normal connective tissue space (V) (H&E x 400)

Discussion

In the present study, there was a significant increase in cardiac troponin I mean values in ZnO NPs treated group as compared to control groups and (ZnO NPs &NAC) group. This could be explained by the study of Manke et al., (2015) who proved that the systemic dissemination of local oxidative stresses and pro-inflammatory mediators, triggered by ZnO NPs, results in alteration of the cardiac autonomic functions, impairing the coronary blood flow. These results were in agreement with Faddah et al., (2013) who recorded that ZnO NPs caused significant increase in cardiac troponin I in albino rats. Also, Nemenqani, (2015) observed an increase in the level of cardiac troponin I in rats treated by ZnO NPs through oral exposure. Moreover, Milivojević et al. (2015) studied the dose-dependent effects of ZnO NPs on isolated heart models, following repeated oral exposure. On the contrary, Li et al., (2012) reported no obvious cardiotoxic adverse effects caused by orally administered ZnO NPs in 14 days single-dose acute toxicity study in albino rats. Regarding CK-MB, there was a significant increase in CK-MB mean values in ZnO NPs group as compared to control group and (ZnO NPs &NAC) group. These results were in agreement with studies of Kermanshahi et al. (2015) who reported an increase in CK-MB level with high absorption rate of ZnO NPs in the heart tissue after repeated oral administration for 28 days in adult rats.

On the contrary, Asri-Rezaei et al. (2016) in a comparative study regarding ZnO NPs dose showed that oral intake of ZnO NPs at dose 3mg/kg for 56 days reduced CK-MB activity in the serum of diabetic rats induced by streptozotocin (an antibiotic and anticancer agent). The endothelium is a sensitive target of NPs, exposure to ZnO NPs show endothelial dysfunction and endothelial progenitor cells (EPC) depletion (Haberzettl et al., 2012). EPC dysfunction is not only a sign of cardiovascular risk, but also signifies a pathological indicator of the development of atherosclerosis. Although the usage of ZnO NPs in the diagnosis and management of diseases such as atherosclerosis is being considered, it should be noted that ZnO NPs of certain types and particle sizes can disturb the body's homeostasis and can cause diseases such as atherosclerosis (Benetti et al., 2014). Co-administration of NAC with ZnO NPs caused significant decrease in cardiac enzymes mean values as compared to ZnO NPs group. The result of the study is in agreement with Lin et al. (2009) who demonstrated the protective role of the antioxidant NAC on ZnO NPs- induced cytotoxicity, associated with oxidative stress and free Zn^{2+} ions in human lung epithelial cells. Also, Sakthibalan et al. (2013) used NAC as a part of a protective combination, together with vitamin C and enalapril, against the toxic myocardial damage and cardiomyopathy induced by doxorubicin via oxidative stress, where it was effective in the recovery of cardiotoxicity, restoration of cardiac markers which may be caused by its potent antioxidant properties. Concerning TAC, there was a significant depletion in the level of plasma TAC in ZnO NPs group as compared to control group and (ZnO NPs& NAC) group. The results of the study were in accordance with Nagarajan et al. (2022) who observed glutathione peroxidase (GPx) and catalase (CAT) depletion associated with an increase in lipid peroxidation levels when exposed to ZnO NPs which indicates an oxidative stress. On the contrary, Singh et al. (2014) studied the antioxidant activity of synthesized ZnO NPs through a biological route using Pseudomonas aeruginosa rhamnolipids (RLs) with a particle size ranging from 30 to 85 nm, defined as "stable RL@ZnO NPs", there inhibitory effect on superoxide anion free radicals, β-carotene oxidation and lipid peroxidation were also observed in the biological system. Also, Sharma et al. (2013) proved that the major mechanism of ZnO NPs induced cardiovascular toxicity results from free radicals overproduction that compromise the mitochondrial bioenergetics. Xu et al. (2012) explained another mechanism of ZnO NPs- induced cardiotoxicity which is the creation of the Charnoly body (CB), which is a multilameller pleomorphic structure, created by condensation of degenerated mitochondrial membranes. These deleterious bodies induce oxidative stress and can be inhibited by antioxidants as glutathione. Moreover, co-administration of NAC with ZnO NPs caused significant rise in TAC mean values compared to ZnO NPs group. The result of the study was coincided with Baky et al. (2013) who studied the cardioprotective role of vitamin E which is an antioxidant, prevents the propagation of oxidative stress after subsequent oral administration of ZnO NPs and ameliorates ZnO NPs cardiotoxicity.

Also, we found a significant increase in fragmented DNA in the form of laddered (sheared) DNA fragments in ZnO NPs group compared to control groups and (ZnO NPs& NAC) group; established qualitatively by gel electrophoresis of DNA extracted from hearts of ZnO NPs group and these results were in agreement with Baky et al. (2013) who proved that ZnO NPs lead to cardiotoxic DNA destruction and apoptotic alterations. Similarly, the results were coincided with Alarifi et al. (2013) who studied ZnO NPs induced apoptosis, evidenced qualitatively by the creation of laddered (sheared) DNA on agarose gel. Zinc Oxide NPs cause a variety of DNA damage including, chromosomal fragmentation and induction of gene mutations (Al Gurabi et al., 2015). Generation of free radicals and oxidative stress following ZnO NPs toxicity triggers various cellular events including apoptosis. ZnO NPs were found to induce apoptosis due to their minor size, they are able to reach the nucleus (Alarifi et al., 2013). In (ZnO NPs & NAC) group, there was regression of DNA fragmentation. As a result, co-administration of NAC with ZnO NPs caused moderate improvement in DNA fragmentation compared to their corresponding in ZnO NPs treated group. Thiol suppliers such as NAC could be used to down regulate apoptosis in different cell models. Additionally, NAC has been shown to be an antigenotoxic agent by its antioxidant properties as it can decrease cytogenetical damage and mutagenic agents' effects (Mamashli et al., 2022)

In the histopathological examination, ZnO NPs induced several alterations in ZnO NPs group as compared to control group and (ZnO NPs &NAC) group, evidenced by disorganization and degeneration of the myocardium, congestion in myocardial blood vessels with thrombus formation. These results were supported by Nemenqani, (2015) who observed severe myocardial necrosis with subendocardial loss of heart muscles in ZnO NPs administered rats in a two weeks study using a dose 1 g/kg BW once daily via oral route. Moreover, Chuang et al., (2014) observed the presence of focal fibrosis in the heart tissues 8 days following exposure while, lymphocytic inflammatory infiltration, degeneration in addition to necrosis of the myocardium were detected 4 weeks after high dose inhalational contact to ZnO NPs. This can be explained by the capability of Zinc Oxide NPs to corrode, degrade and release ions. Corrosion causes the spread of ions that may interact with metabolic sequences along the Krebs cycle. If the cycle is stopped, there is no ATP creation thus, the whole energetic level of the cells is diminished and there is no energy adequate for the cells to survive (Mytych and Wnuk, 2013). The histopathological studies of (ZnO NPs & NAC) treated group showed the same histological results of the myocardium as that detected in the control group. As a result, co-administration of NAC with ZnO NPs caused significant preservation of the myocardium compared to their

correspondings in ZnO NPs treated group. These results were in accordance with Nemenqani, (2015) who revealed the protective nature of antioxidants against ZnO NPs induced- necrotic damage of the heart tissues in a two weeks study via oral administration in adult albino rats. NAC may prevent pro-inflammatory cytokines TNF-α and IL-1β creation and NF-κB triggering, to diminish the number of inflammatory cells and impair chemotaxis of polymorphonuclear leukocytes. NAC could deliver a cardiac protection in animals via its antioxidant and anti-inflammatory effects. These cardioprotective effects might be beneficial in the management of myocardial ischemia that would not occur if patients are prophylactically treated by NAC (Khan et al., 2021)

Conclusion

The mechanistic hypothesis of ZnO NPs induced cardiotoxicity is oxidative stress, and DNA damage. Co-administration of NAC could protect against these hazardous effects.

Recommendations

1. Periodic estimation of Total antioxidant capacity (TAC) as an early marker of oxidative stress in people who are occupationally exposed to ZnO NPs.
2. N-acetylcysteine and diet rich with antioxidants can be used as supplement to occupationally exposed workers.
3. Novel alternative safe food colors additives should be explored carefully.

Declaration of conflicting interests

The authors report no declarations of interest.

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فَاعلية الأستيل سيستايين على السُمية القلبية المُحْدَثة بجُزيئات أكسيد الزنك النانوية في الجرذان البيضاء البالغة

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الملخص العربى

مقدمة البحث: تستخدم جزيئات أكسيد الزنك النانوية في العديد من التطبيقات، وتضاف إلى بعض المواد الغذائية ومستحضرات التجميل و بعض الصناعات الدوائية. ويعد القلب من أهم الأعضاء المستهدفة عند التعرض الفمى لهذه الجزيئات بسبب الإجهاد التأكسدى. إن الأستيل سيستايين من مضادات الأكسدة الهامة ولذلك فيستخدم لمكافحة الأضرارالناجمة عن الاجهاد التأكسدى في الأنسجة المختلفة. **الهدف من البحث** : أجريت هذه الدراسة لفحص التأثيرالسام لجُزيئات أكسيد الزنك النانوية على القلب ودراسة فاعلية الأستيل سيستايين ضد هذا التأثيرالسام فى الجرذان البيضاء البالغة.**طريقة البحث:** تم إجراء البحث على عدد ٤٠ من الجرذان البيضاء البالغة مقسمة إلى خمس مجموعات متساوية (٨ فى كل مجموعة) كما يلى المجموعة الأولى: تم اعطاءها الطعام والشراب فقط لقياس المعايير الأساسية. المجموعة الثانية: تم اعطاءها المادة المذيبة وهى الماء المقطربجرعة (١ملليلتر/ ١٠٠ جرام من وزن الجرذ). المجموعة الثالثة (مجموعة الأستيل سيستايين): تم اعطاءها الأستيل سيستايين (٢٠٠ مجم /كجم) مذابا فى الماءالمقطر.المجموعة الرابعة (مجموعة أكسيد الزنك النانوى): تم إعطاءها أكسيد الزنك النانوى (٤٢٢مجم / كجم) مذابا فى الماء المقطر. المجموعة الخامسة (مجموعة أكسيد الزنك النانوى والأستيل سيستايين): تم إعطاءها الأستيل سيستايين (٢٠٠مجم/كجم) ثم أكسيد الزنك النانوى (٤٢٢ مجم /كجم) وقد تم اعطاء هذه المواد يوميا عن طريق الفم بواسطة التغذية الأنبوبية لمدة أربعة اسابيع. **النتائج:** اظهرت الدراسة ارتفاعا ملحوظا في مستوي إنزيمات القلب فى مجموعة أكسيد الزنك النانوى مقارنة بالمجموعة الضابطة ،وتحسناً فى مستوي إنزيمات القلب لمجموعة (أكسيد الزنك النانوى والاسيتيل سيستايين) مقارنة بمجموعة أكسيد الزنك النانوى . وأوضح قياس القدرة الكلية لمضادات الأكسدة وجود انخفاضا لدى مجموعة أكسيد الزنك النانوى مقارنة بالمجموعة الضابطة وتحسناً ملحوظاً فى مجموعة (أكسيد الزنك النانوى والاسيتيل سيستايين) مقارنة بمجموعة أكسيد الزنك النانوى. وأظهرالترحيل الكهربائى للحمض النووى لأنسجة القلب لمجموعة أكسيد الزنك النانوى عن وجود تجزئة فى الحمض النووى بينما أسفرت عن تحسنا ملحوظا لدى مجموعة (أكسيد الزنك النانوى والاسيتيل سيستايين) مقارنة بمجموعة أكسيد الزنك النانوى. وأوضح الفحص المجهرى باستخدام صبغة الهيماتوكسلين والايوسين لعضلة القلب لمجموعة أكسيد الزنك النانوى عن وجود تحلل وفوضى بالخلايا العضلية واحتقان وتحلط بالأوعية الدموية بينما أسفرالفحص عن تحسن جميع التغيرات الهستوباثولوجية لدى مجموعة (أكسيد الزنك النانوى والاسيتيل سيستايين) حيث كانت الشرائح قرب وضعها الطبيعي مقارنة مع مجموعة أكسيد الزنك النانوى. **الخلاصة:** إن التعرض لجزيئات اكسيد الزنك النانوية أدى الى إرتفاع مستوى إنزيمات القلب وإنخفاض مستوى القدرة الكلية لمضادات الأكسدة ,كما أدي الي حدوث تغييرات هستوباثولوجية في عضلة القلب مع وجود آثار سمية على المستوى الجزيئى حيث أنه سبب تدميرا في الحمض النووي في خلايا القلب. واظهرت الدراسة أن إعطاء الاسيتيل سيستايين قد وفر قدراً من الحماية ضد الآثار السمية الناتجة عن أكسيد الزنك النانوى، وأدى إلى تحسن فى مستوى انزيمات القلب والقدرة الكلية لمضادات الأكسدة ، كما أدى إلى تحسن فى التغيرات الباثولوجية للقلب وانخفاض فى معدلات التدمير الجزيئى في الحمض النووي.

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