Research Article

Efficiency of *Cichorium Intybus* in Reducing Hepatotoxicity Induced by Zinc Oxide Nanoparticles

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Received date: 01-Mar-2022, Manuscript No. AMHSR-22-51517; **Editor assigned date:** 03-Mar-2022, Pre QC No. AMHSR-22-51517(PQ); **Reviewed date:** 18-Mar-2022, QC No. AMHSR-22-51517; **Revised:** 24-Mar-2022, Manuscript No: AMHSR-22-51517(R); **Published date:** 30-03-2022, **DOI:** 10.54608.annalsmedical.2022.93

Abstract

With the growing development of nanotechnology and the increase in exposure to nanoparticles, there is an urgent need for more studies to assess the toxicity caused by these particles to the body and to find ways to avoid their harmful effects. This experiment was designed to estimate the toxicity of Zinc Oxide Nanoparticles (ZnO-NPs) on rats hepatic function parameters, and then noting the beneficial effect of *Cichorium Intybus* (CI) on those disorders that may be caused by ZnO-NPs. 24 male rats were randomly divided into 4 groups, each group comprising 6. CON group without treatment, the ZnO-NPs group received ZnO-NPs, in the ZnO-NPs+CI group animals were co-administered with a combination of ZnO-NPs with CI, and finally the animals of the CI group were dosed only with CI extract. Levels of hepatic biochemical parameters including ALT, AST and ALP were measured to detect toxic changes in the liver. The study found that ZnO-NPs caused a significant increase in the activity of those serological parameters compared to the control. But it was seen that the combined treatment of CI led to a clearly reduce in the levels of hepatic parameters in the serum. Thus, we can consider *Cichorium Intybus* as a medicinal plant capable of reducing the ZnO-NPs hepatotoxicity in laboratory rats.

Keywords: Hepatotoxicity; Zinc oxide nanoparticles; Biochemical parameters

Introduction

Nano science is considered one of the driving up-to-date sciences that have a significant impact on various industrial sectors, as well as medicine. [1] It has been proven that the introduction of nanotechnology in the medical field is useful in the field of health care, [2] its efficiency has been noted in improving medical diagnosis as well as treating some diseases. [3,4] Zinc Oxide Nanoparticles (ZnO-NPs) are one of the most important metallic nanoparticles due to their biocompatibility properties that make them very desirable in medical applications. [5] They are powerful antimicrobial agents which allow them to be used in abundance in body lotions and ointments, as well as in hair and skin care formulations. [6,7] In addition to entering the domains of cosmetics to produce sunscreens to protect the human body from ultraviolet rays. [8,9] These particles have also been used as a dietary supplement for their efficacy in stimulating the body's anti-inflammatory response and for boosting the immune system. [10,11] This increased use of ZnO-NPs has generated the need to investigate the potential unintended toxic effects of them on human health, to avoid potential negative consequences. Taking into account the existence of previous studies that confirmed that metal nanoparticles may aggregate in various organ tissues of experimental animals, including the liver. [12,13] Since ancient times, herbs have occupied a prominent position in medicine for their curative and preventive properties, especially in developing countries due to the availability of appropriate agricultural conditions, in addition to being accepted by the body with minimal side effects. [14] *Cichorium Intybus L* (CI), a traditional perennial herb medicine, hails from the family asteraceae and is also known as chicory. [15] It has antimicrobial, immune-modulatory, gastro-protective and anti-hepatotoxic properties. Especially it is commonly used in Asia to improve liver function, where it prevents infection mediated by free radicals, which explains its liver protective effect. [16,17] Therefore, We designed our study to assess the effectiveness of *Cichorium Intybus* extract in diminution hepatotoxicity resulting from zinc oxide nanoparticles in male rats .

Materials and Methods

Chemicals

A white liquid dispersion of zinc oxide nanoparticles was applied to the following specifications: APS=30 nm-40 nm, molecular weigt= 81.37 g/mol, purity=99.9%, concentration=30.7%. Acquired from Nanoshell Corporation-LLC (UK). Whereas, *Cichorium Intybus* was obtained as a health care herb supplement (Liv.52) from The Himalaya Drug Company Ltd.

Rats and experimental design

Twenty-four healthy adult males aged 16-24 weeks, weighing 175-225 grams were used in the present experiment. They were placed in cages made of polypropylene with access to their standard food and water. Laboratory conditions were standard in terms of temperature (25°C ± 2°C), humidity (60%-70%), and light/dark cycles (12 hours). They were acclimated one week before the start of the experiment. Then the animals were

How to Cite this Article: Alsaleh K, et al. Efficiency of *Cichorium Intybus* in Reducing Hepatotoxicity Induced by Zinc Oxide Nanoparticles. Ann Med Health Sci Res. 2022;12:93-96.

randomly divided into four groups comprising six animals in each one [Table 1]. One day after the end of the experiment, the rats were dissected under light anesthesia with chloroform. Blood samples were obtained by piercing the heart and placed in tubes prepared for serum biochemical procedures.

Bio-chemical analysis

Using special biochemical diagnostic kits and an automated machine, serum markers for liver function (ALT, AST, and ALP) were analyzed.

Data analysis

The mean standard deviation was used to express the study data, and for the statistical evaluation among the experiment groups. One-way analysis of variance (ANOVA) was used, followed by comparisons using Duncan's test. Statistics were conducted using the program SPSS version 25. A difference was considered significant when a P-value less than 0.05.

Table 1: Experimental design.

Groups	Treatments
CON	Healthy control rats.
ZNO-NPs	Rats intoxicated with zinc oxide nanoparticles 50 mg/kg orally, and lasts 28 days.
ZNO-NPs+CI	Intoxicated rats received C. intybus (200 mg/kg) orally, and lasts 28 days.
CI	Rats administrated only C. intybus (200 mg/kg) via oral rout,and lasts 28 days.

Results and Discussion

The final data showed a statistically significant increase at P>0.05 in the levels of biomarkers of liver function (ALT, AST, and ALP) of rats poisoned with Zn-ONPs. (145.06 ± 5.17; 169.81 ± 6.45; 368.32 ± 7.55, respectively) compared to the control group rats (91.42 ± 4.44; 105.88 ± 5.71; 265.54 ± 6.28, respectively). Whereas, co-administration of *Cichorium Intybus* in Zn-ONPs exposed rats returned all values close to the control group level. No significant changes in liver function parameters were demonstrated between the CON and the CI groups [Figure 1].

After the nanoparticles enter the blood circulation, they can transference and reach the various parts of the body, including the liver, which can be considered the target tissue for toxic substances. It has a key role in the metabolism of chemicals and drugs and is quick to respond to oxidative stress. [18-20] ZnO-NP is one of the more metallic nanoparticles that accumulate in the liver than the rest of the organs, as confirmed by the results of this study where doses of metal oxide nanoparticles had negative effects on the parameters of liver function, which were in agreement with the studies we evaluated previously. [21,22] Liver function tests are indicators of a variety of specific liver disorders, such as necrosis. These tests are particularly useful in detecting hepatotoxicity that occurs in animals after administration of drugs or chemicals. Generally, most toxicology studies involve a liver profile because chemicals taken must first pass through the liver after intestinal absorption. [23] A significant increase in enzyme levels indicates liver injury, indicating damage or destruction of liver cells. The levels of

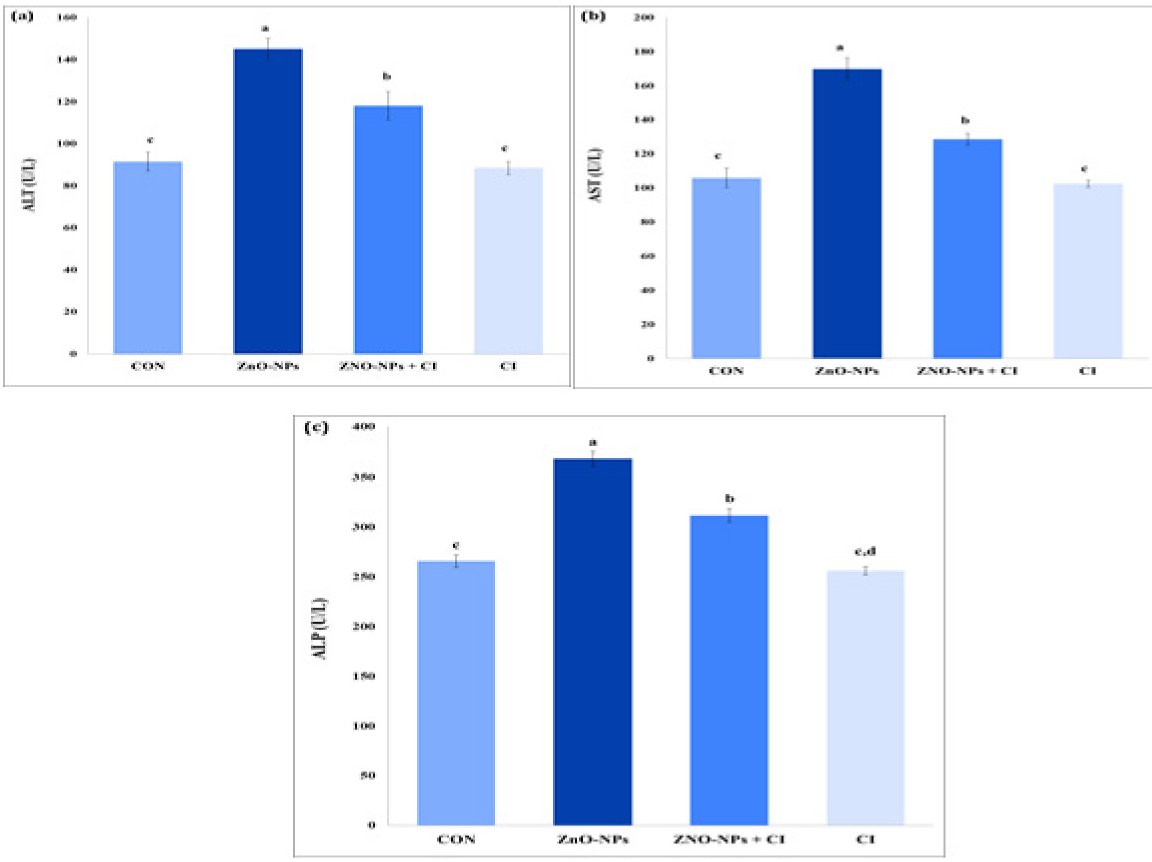

Figure 1: Results of zinc oxide NPs administration and co-administration with cichorium intybus on the hepatic parameters as follows: a) ALT b) AST, and c) ALP. Mean ± SD was used to represent the data; lowercase letters denote significant intra-column variances. ANOVA was conducted, and Duncan was post hoc.

these hepatic enzymes rise as a result of leakage of the cell content and abnormal functions of the liver cell membrane.[24] Due to the physicochemical properties of nanoparticles, they disrupt the stability and proper functioning of the liver.[25] Yao et al. reported that oxidative stress and inflammation are mechanisms that cause hepatocyte toxicity from exposure to metal NPs, which ends with different types of cell death outcomes.[26] *Cichorium Intybus* consists of phytochemicals like sesquiterpene lactones, inulin, proteins, flavonoids, alkaloids, steroids, terpenoids, oils volatile compounds, coumarins, caffeic acid derivatives, vitamins, and polyenes. In addition, it has many pharmacological effects, including liver-protective, anti-oxidant, anti-cancer, anti-inflammatory, anti-microbial, wound healing, and others. The results of our study came in line with a previous study conducted by Sadeghi and colleagues to examine the preventative capability of *C Intybus* on hepatocytes, when they evaluated the effect of CI extract on hepatic enzyme levels in the damaged liver, and concluded that the levels of the enzyme were clearly decreased. Another previous study demonstrated a relationship of CI supplementation with indicators of oxidative stress, as after CI intake they observed that malondialdehyde decreased in contrast to significantly increased levels of total antioxidant capacity. In addition, many experiments conducted on laboratory animals demonstrated a relationship between the CI and the improvement of serum antioxidant status.

Conclusions

In this experiment, we found that zinc oxide nanoparticles have a toxic effect on the biochemical functional indicators of the liver. *C Intybus* extract dosed to rats improved levels of liver enzymes. However, more studies are needed to prove that CI can protect the liver from possible damage or complications of hepatotoxicity with nanoparticles.

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