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Potential Effect of *Aloe Vera* against Oxidative Stress Induced by Iron Oxide Nanoparticles

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ABSTRACT— Iron oxide nanoparticles (IO-NPs) are involved in many medical fields, besides these nanoparticles can cause cytotoxicity and oxidative stress so it is requisite to estimate the safety of NPs in vivo. Purpose of the present experiment is to investigation the beneficial action of *Aloe vera* (AV) in reducing oxidative stress caused by exposure to IO-NPs in an animal model. Twenty-four rats were used and divided into three equal groups. Rats that were without any doses were included in the CON group, while IO-NPs rats were administered orally iron oxide nanoparticles, and IO-NPs + AV rats were co-administered of *Aloe vera* with iron oxide nanoparticles. The experiment was continued for 14 uninterrupted days, after which animals were sacrificed and the serum was obtained for oxidative stress analyzes. The results showed a significantly higher MDA accompanied by lower levels of GSH and CAT for rats receiving IO-NPs when they were compared to control group, but the combined dose with AV significantly improved those toxic changes. We concluded that AV extract can reduce intoxication of IO-NPs on serum oxidative stress indicators.

KEYWORDS: oxidative stress, iron oxide nanoparticles, toxicity.

1. INTRODUCTION

The implementation of nanotechnology in the medical fields has led to the development of health care remarkably [1], [2]. Employment of magnetic nanoparticles is an important orientation in medical diagnosis and treatment [3]. Magnetic iron oxide nanoparticles (IO-NPs) are utilized in a broad extent of biomedical applications such as drug delivery, bio-imaging, gene therapy, oncology, and even as an iron supplement for anemic patients [4], [5]. After these particles enter the body, the innate immunity begins to distinguish, collect and bring out these foreign particles to the body's major elimination pathways [6]. Several in vivo experimental studies concluded that iron oxide nanoparticles have toxic effects on vital organs of the body [7- 9]. Therefore, more is needed to know the safety of these foreign particles on body cells and their potential toxicity [10]. Herbal medicine has been popular since ancient times until today [11]. *Aloe vera* (AV) is among those medicinal herbs used by many Asian countries and Mediterranean regions to treat various diseases [12]. Because it contains many potential active ingredients such as vitamins, minerals, etc., this makes it biologically active as well as anti-inflammatory, anti-oxidant, and anti-microbial properties [13], [14]. In this study, oxidative stress parameters were analyzed to assess the clinical pathotoxicity of laboratory rats exposed to iron oxide nanoparticles and to clarify the possibility preventative significance of Aloe vera extract through its effect on reducing toxicity and improving oxidative stress.

2. MATERIALS AND METHODS

2.1 Chemicals

Dispersion of alpha iron oxide (γ- Fe2O3) nanoparticles suspension (15 wt. %) with the following specifications: APS = 10 nm, color = orange-red, molar mass = 159.69 g/mol, purity = 99.9%, and making method =laser synthesized, obtained from US Research Nanomaterials, Inc. (USA). As for *Aloe vera* extract, it was purchased from the manufacturer, La Grande Pvt Ltd, located in New Delhi, in the form of aloe vera capsules specialized in promoting healthy digestion and improving immunity.

2.2 Laboratory rats and doses of treatments

Twenty-four healthy male albino rats, aged 3–4 months and weighing 190–225 g, were obtained from the animal laboratory centers of Iraqi universities for this experimental study. All rats were placed in their own cages under typical environmental conditions in terms of temperature and humidity, with considerateness a twelve-hour light cycle, as well as easy access to food and water. Rats were acclimatized for seven days prior to the experiment, then they were divided into three groups, eight in each group. They were dosed continuously for 14 days as illustrative in table (1). On the 15th day of the stydy, the anesthetized rats were scarified and blood was obtained through cardiac puncture, collected in tubes without anticoagulant. Blood tubes were centrifuged to collect serum for assess the parameters of oxidative stress.

Table 1: Dosing treatments for experimental groups.

Groups	Administrations with dosage
CON	Untreated rats were employed as control.
IO-NPs	Rats were poisoned with iron oxide nanoparticles at 100 mg/kg orally [15].
IO-NPs+AV	Iron oxide nanoparticles -treated rats were co-administered with *Aloe vera* extract at a dose of 300 mg/kg [16] orally over the course of the experiment.

2.3 Assessment of serum oxidative stress

The lipid peroxidation (MDA) in serum of experimental rats was assessed by spectrophotometric method which was previously described by [17] low (GSH) glutathione level by method modified by Jollow and colleagues [18] as for catalase (CAT) activity, it was performed as explained by [19].

2.4 Statistical analysis

All data were analyzed by means of Graph Pad Prism 9 software and results were presented as means ± standard deviation. To determine the variation within the study groups, ANOVA test was applied, followed by Duncan's multiple range test with the adoption of a P value less than 0.05 statistically significant.

3. RESULTS

The results indicated that rats exposed to iron oxide nanoparticles stimulated lipid peroxidation, where an obvious elevated level of MDA (2.16±0.52) was found compared with the control group (0.89±0.22). But when it was accompanied by *Aloe vera* treatment, the level of MDA (1.26±0.32) reduced clearly. Also, in the animals poisoned with iron oxide nanoparticles, a considerable decrease in the activity of both GSH (0.56±0.05) and CAT (0.70±0.09) was observed compared to the healthy control group (0.82±0.07 and 1.14±0.18 respectively). Supplementing the rats with *Aloe vera* confirmed the important amelioration in the levels of both these enzymes. The effects of iron oxide nanoparticles and *Aloe vera* on serum oxidative biomarkers are illustrated in figures (1-3).

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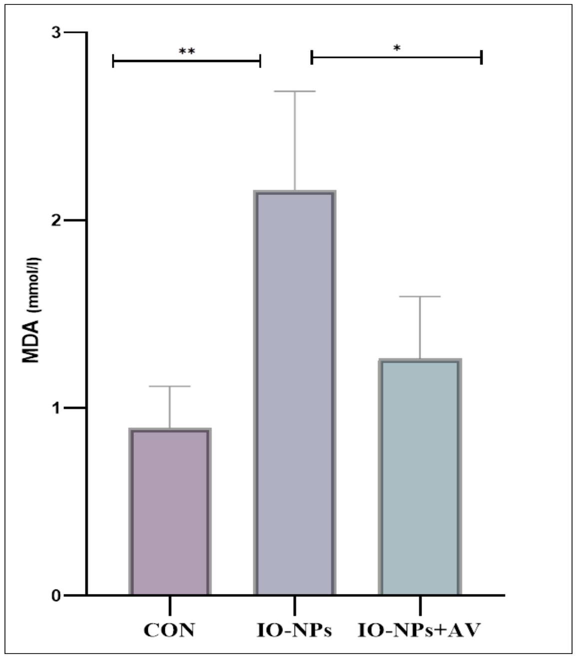

Figure1: Influence of IO-NPs and AV on MDA level in the serum of rats. Values are represented as mean ± SD. Superscripts*,** represent statistically important differences between groups.

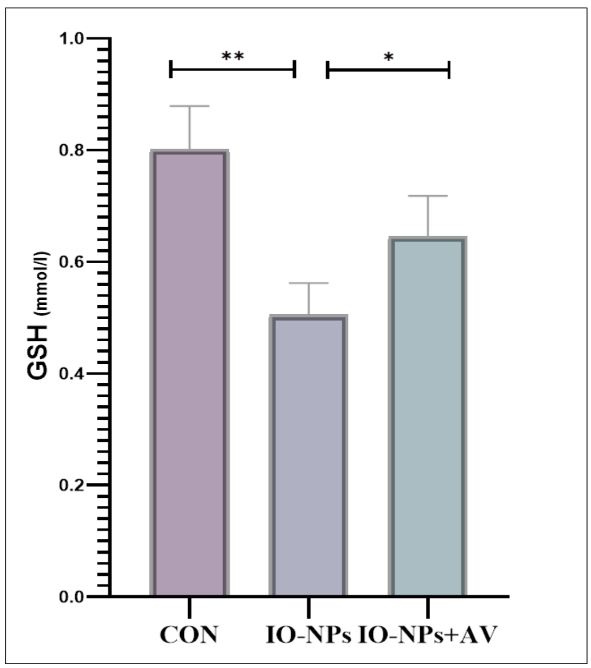

Figure 2: Influence of IO-NPs and AV on GSH level in the serum of rats. Values are represented as mean ± SD. Superscripts *,** represent statistically important differences between groups.

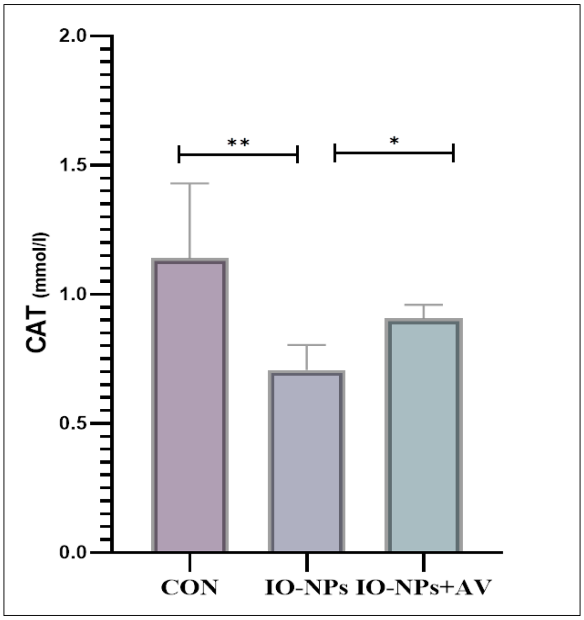

Figure 3: Influence of IO-NPs and AV on CAT level in the serum of rats. Values are represented as mean ± SD. Superscripts *,** represent statistically important differences between groups.

4. DISCUSSION

It is known that nanoparticles have a large surface in relation to their size, which enables them to penetrate into different cells of the body after entering the body and in various ways, including the mouth, and may generate toxicity [20- 23]. The characteristic small size of nanoparticles allows them to move clearly as well as to pass cellular physiological barriers and generate oxidative stress that causes significant damage to cells or tissues [24], [25]. Once the nanoparticles reach the blood, they will be in contact with proteins found in plasma and immune cells. The adsorption of nanoparticles occurs throughout diverse paths such as hemolysis ending in the encouragement of oxidative stress and the depression of cellular antioxidants [26], [27]. The current study found that exposure to IO-NPs increased oxidative stress and this is in consistent with a previous study by Gaharwar and colleagues who found that IO-NPs absorbed into lymphocytes stimulated cytotoxicity by oxidative stress with a marked raise in lipid peroxidation levels versus diminution of antioxidant enzymes [28]. Kazemipour and colleagues also found that dextran-coated IO-NPs of 100 mg/kg induced oxidative damage in hepatic tissue, whereby IO-NPs caused a considerable lowering in hepatic GSH and CAT activities with a marked growing in hepatic MDA level [29]. In this experimental study, we found that the co-administration of *Aloe vera* with nanoparticles greatly improved the oxidation parameters. This can be considered as an indication that the AV plant has acceptable antioxidant properties. Moreover, this may be evidence that these plant products can be used in the treatment of many health disorders. It contains a large amount of biologically active compounds such as anthraquinone, amino acids, vitamins, enzymes, hormones, inorganic compound and others [30- 33]. In a previous study conducted by Rahoui and his companions on obese rats, the administration of aloe vera gel reduced the accumulation of adipose tissue through its protective role against the metabolic changes associated with obesity and its antioxidant effects [34]. In another study by Baradaran and colleagues in male rats, they concluded that AV significantly protected kidney cells and reduced the severity of tubular damage caused by gentamicin by containing phenols and flavonoids as antioxidant compounds [35].

5. CONCLUSIONS

Dosing laboratory rats with iron oxide nanoparticles orally at 100 mg/kg for 14 consecutive days had a detrimental effect on serum oxidative stress, but the combined administration of aloe vera mitigated this toxicity, so there is a need for other experiments dealing with other parts of the body and more indicators.

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