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ORIGINAL ARTICLE

Effectiveness of Saffron against Hepatotoxicity Caused by Silver Nanoparticles in Vivo

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ABSTRACT

Adverse effects of silver nanoparticles (Ag-NPs) on health remain a concern. This research study was performed to appreciate the activity of saffron plant (SAF) upon Ag-NPs-induced hepatotoxicity. Eighteen male rats were consumed, separated into three groups of equal numbers. The animals of the group (CON) were not dosed with either treatment, while the animals of the group (Ag-NPs) were treated with Ag-NPs orally. In the latter group (Ag-NPs + SAF) intoxicated rats with Ag-NPs were provided with SAF. The experiment lasted seven days. The study found that dosing with Ag-NPs led to a considerable elevates in serum levels of biochemical parameters of liver function and hepatic oxidative stress, while significantly diminished glutathione activity. But the combined use of SAF extract improved the disturbed hepatic parameters. It was concluded that SAF could efficaciously mitigate Ag-NPs-induced liver toxicity in vivo. More investigations are needed to determine the exact mechanisms behind affront's ability to protect the liver.

Keywords: Silver nanoparticles, biochemical parameters, hepatotoxicity.

INTRODUCTION

Nanomaterials (1-100 nm) are widely produced and applied, which bring enormous benefits to humans [1,2]. Silver nanoparticles (Ag-NPs) can be considered as one of the most important nanomaterials for diversified use, especially in pharmaceuticals, medical devices and other industries. Also, Ag-NPs are the most consumer products with nanotechnology, as they have antimicrobial properties [3,4]. This increase in the employing and releasing of Ag-NPs into the environment around people raises risks and concerns about the harmfulness of Ag-NPs to human health [5].

Several studies have also confirmed the poisonous effects of Ag-NPs on different organisms and cell types, including the liver [6]. It has been shown that the systemic administration of Ag-NPs in experimental animals led to the penetration of these particles into many organs of the body and the liver was the main target, causing infiltration of inflammatory cells and necrosis of affected cells [7,8]. Even today, there are still people who resort to herbal medicine to improve their health, especially to be safe from the harmful side effects of manufactured medicines [9].

Saffron (SAF), the dry red stigma of Crocus sativus L., is a stem less autumnal herb of the Iridaceae family that is vastly grow in Iran, India, Greece and other regions [10]. In traditional medicine, SAF has been used in the remediation of many health disorders due to its anti-inflammatory and antioxidant susceptibility. It is likely that crocin, picrocrocin, and safranal are the biologically active compounds [11,12].

Therefore, this study aimed to estimation the activity of saffron against disturbances of biochemical indicators of liver function as well as oxidative stress of liver homogenates to prove the enhanced action of saffron on hepatotoxicity caused by silver nanoparticles in laboratory rats.

MATERIALS AND METHODS

Aqueous-dispersed silver nanoparticle product, a highly complex silver solution with very small nanoparticles, was obtained from the US Research Nanomaterials, Inc (USA). This product is intended for research purpose which has very good anti-bacterial and anti-yellowing properties. It is also characterized by the following: Purity = 99.99%, average particle size = 2 nm, PH = 7 ± 0.5, and without discoloration. As for the organic saffron supplement, vegetarian capsules were used for pure saffron extract (100% natural), completely free from harmful stimulants, caffeine and side effects, manufactured in the laboratory without the use of any artificial colors, flavors or chemical preservatives, made in the USA (GOLDEN SAFFRON).

Experiment design: Eighteen healthy adult albino male rats, their ages ranged between 4 to 8 months, and their weight ranged between 175 to 225 g. were gained from animal houses belonging to Iraqi universities. They were housed in plastic cages under appropriate laboratory conditions, temperature and lighting, with conventional ventilation. After they were accustomed to the laboratory environment for a week, those experimental animals were distributed into three groups of equal numbers (six in each) as exhibited in table (1).

Table 1: Experimental groups and doses

Groups	Seven-day treatments
CON	Rats without any treatment served as a control group.
Ag-NPs	Rats were intoxicated with Ag-NPs orally at a dose of 100 mg/kg [13].
Ag-NPs+ SAF	Intoxicated rats were supplied with saffron by gastric tube [14] .

After 24 hours of completion of the last dose, the experimental animals were dissected after being anesthetized. Blood was collected from the cardiac perforation of each animal and stored in tubes (without anti-coagulants) for quantification of serum biomarkers of liver function. This research experiment was done in accordance with the ethical controls for the use of animals applicable in scientific research accredited in Iraqi universities.

Biochemical indicators of liver function: In respect of estimate liver function, the biochemical parameters of serum alkaline phosphatase (ALP) alanine transaminase (ALT), and aspartate transaminase (AST), were estimated using commercial diagnostic kits and following manufacturing protocols.

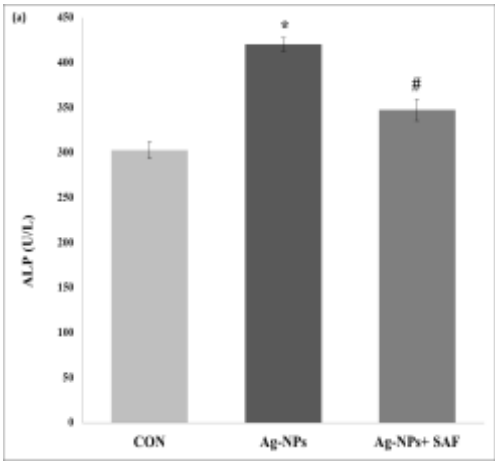
Oxidative stress assays: After the livers of all animals were extracted and stocked at (-20)°C, liver homogenates were tested for oxidative stress analysis. Malondialdehyde (MDA) which is the end-product marker of lipid peroxidation as well as glutathione (GSH) contents were determined by spectrophotometry according to previously adopted protocols [15].

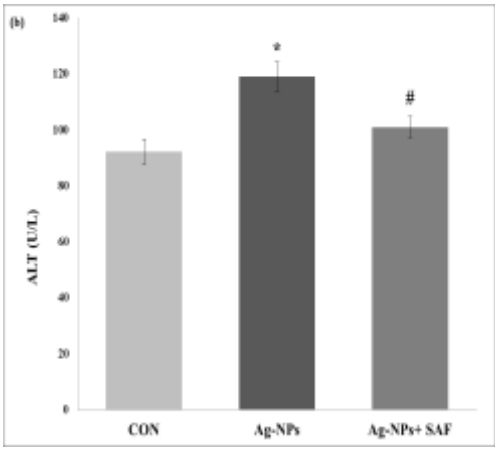
Data Statistics: The data were statistically analyzed by applying the statistical SPSS (version 25), with the data presented in a scale of mean and standard deviation. Using ANOVA to analyze the variance, the significance of the variance between the three groups was evaluated, followed by Duncan's multiple range tests. Probability levels for values less than 0.05 were considered significant.

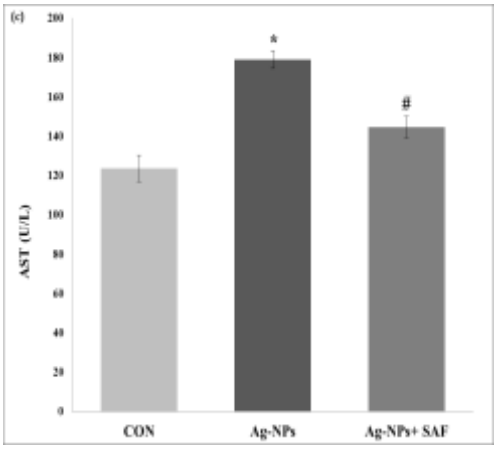
RESULTS

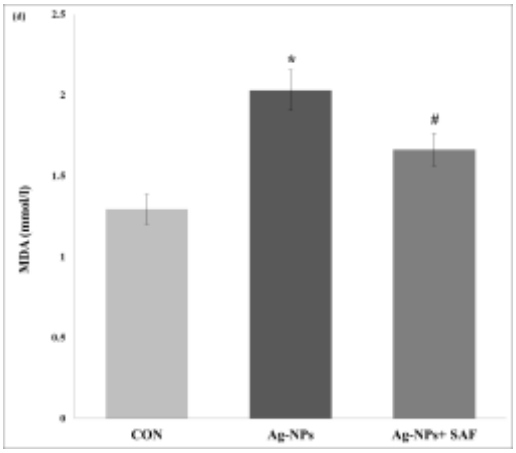
According to the results obtained from this experiment, rats dosed with Ag-NPs significantly increased the serum levels of the following hepatic enzymes: ALP (420.11±7.54), ALT (119.06±5.17) and AST (178.80±4.45) compared to CON rats (302.73±9.27, 92.21±4.45, and 123.68±6.71 respectively). However, saffron extract clearly reduced the serum levels of these three parameters in the Ag-NPs + SAF animals compared to the Ag-NPs animals (347.35±11.79, 101.04±3.78, and 144.52±5.44 sequentially). In a

similar context, when evaluating the effect of SAF on the oxidative stress induced by Ag-NPs in liver tissues, it was demonstrated that Ag-NPs caused an obvious augmentation in the concentration of MDA metabolites in the Ag-NPs animals (2.03±0.12) when compared to CON (1.29±0.09) group. Whereas, co-administration with SAF significantly reduced the concentration of hepatic MDA metabolites in Ag-NPs + SAF rats (1.66 ± 0.1) when compared to those poisoned with Ag-NPs. In contrast, Ag-NPs caused a significant reduction in GSH activity (0.40±.03) when compared to CON group (0.54±0.01). Animals supplemented with SAF revealed a significant improvement in GSH activity (0.47±0.02) as displayed in figure (1).









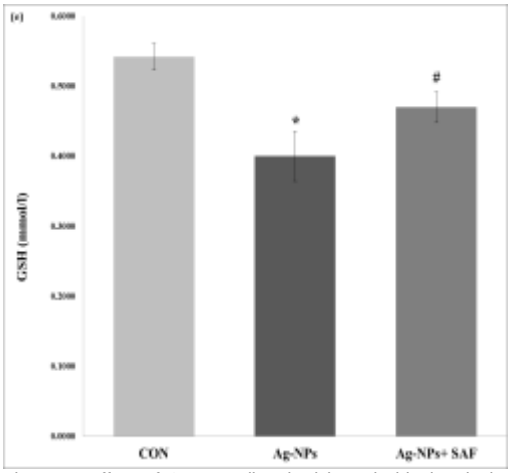


Figure 1: Effect of SAF on disturbed hepatic biochemical parameters and oxidative indices: (a) ALP, (b) ALT, (c) AST, (d) MDA, and (e) GSH in experiment rats. Values for 6 samples are presented as mean ± SD, the symbol (*) was set to show the statistical difference compared to CON group, while (#) to denote a significant difference compared to Ag-NPs group.

DISCUSSION

Depending on the final results of this study, it was shown that Ag-NPs clearly caused hepatotoxicity through disruption of liver function as well as generation of oxidative stress in liver homogenates. Since the liver is a major target of chemicals [16] as well as secondary to nanoparticle toxicity [17]. The Ag-NPs significantly increased the serum levels of biochemical indicators of liver function, which indicated that hepatic function was impaired as a result of hepatocyte necrosis and extravasation of these enzymes into the serum [18]. Besides, oxidative stress and lipid peroxidase have a negative effect on hepatocytes [19]. Similar previous studies confirmed the harmful effects and oxidative damage of metallic nanoparticles, including silver, on the liver at certain concentrations [20-22]. Co-administration with saffron reset hepatic enzyme levels by altering the permeability and integrity of hepatocyte membranes. It is worth noting that medicinal plants are able to normalize the levels of these enzymes in some diseases [23]. Additionally, the flavonoids present in saffron have demonstrated potent liver-protective activities and it has been speculated on its main active contents [24].This was in agreement with the findings of Okdah and Ibrahim in their previous study (2014), as their results indicated that saffron extract improves the hepatotoxicity of sodium valproate by ameliorative the liver function enzymes with inhibiting oxidative stress and enhancing the antioxidant defense system in laboratory rats [25].In another study

conducted by Harchegani and colleagues (2019) they found that treatment with alcoholic extract of saffron stigma reduced the hepatotoxicity of vincristine in rats, by inhibiting the action of hepatic enzymes and suppressing the level of MDA values in hepatotoxic rats, likely due to its antioxidant properties [26].

CONCLUSIONS

This experiment examined the liver damage caused by silver nanoparticles exposing to a rat model, and evaluated the role of saffron in mitigating hepatotoxic damage, by improving both biochemical markers of liver function and oxidative stress in liver tissue. Thus, saffron can be considered effective against hepatotoxicity caused by exposure to silver nanoparticles.

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Conflict of interest: None.

REFERENCES

1- Karpagam T, Balamuralikrishnan B, Varalakshmi B, Anand AV, Sugunabai J. An Insight on Emerging Nanomaterials for the Delivery of Various Nutraceutical Applications for the Betterment of Heath. In Emerging Nanomaterials for Advanced Technologies 2022 (pp. 1-27). Springer, Cham.
2- Mahmoud JH, Ghareeb OA, Mahmood YH. The Role of Garlic Oil in Improving Disturbances in Blood Parameters Caused by Zinc Oxide Nanoparticles. J. Med. Chem. Sci. 2022;5(1):76-81.
3- Dawadi S, Katuwal S, Gupta A, Lamichhane U, Thapa R, Jaisi S, Lamichhane G, Bhattarai DP, Parajuli N. Current research on silver nanoparticles: Synthesis, characterization, and applications. Journal of Nanomaterials. 2021 Feb 8;2021.
4- Ghareeb OA, Sulaiman RR, Ibrahim SH. Impact of Silver Nanoparticles on Hematological Profiles and Hepatorenal Functions in Photosensitivity: In Vivo. Annals of the Romanian Society for Cell Biology. 2021; 25(4):7448 – 7459.
5- Bobyk L, Tarantini A, Beal D, Veronesi G, Kieffer I, Motellier S, Valsami-Jones E, Lynch I, Jouneau PH, Pernet-Gallay K, Aude-Garcia C. Toxicity and chemical transformation of silver nanoparticles in A549 lung cells: dose-rate-dependent genotoxic impact. Environmental Science: Nano. 2021;8(3):806-21.
6- Al-Doaiss A, Jarrar Q, Moshawih S. Hepatic histopathological and ultrastructural alterations induced by 10 nm silver nanoparticles. IET nanobiotechnology. 2020 Jul 21;14(5):405-11.
7- Recordati C, De Maglie M, Bianchessi S, Argentiere S, Cella C, Mattiello S, Cubadda F, Aureli F, D'Amato M, Raggi A, Lenardi C. Tissue distribution and acute toxicity of silver after single intravenous administration in mice: nano-specific and size-dependent effects. Particle and fibre toxicology. 2015 Dec;13(1):1-7.
8- Zhang J, Liu S, Han J, Wang Z, Zhang S. On the developmental toxicity of silver nanoparticles. Materials & Design. 2021 May 1;203:109611.
9- Al-Haidari KA, Faiq TN, Ghareeb OA. Preventive Value of Black Seed in People at Risk of Infection with COVID–19. Pakistan Journal of Medical and Health Sciences. 2021 Jan 1; 15(1):384-387.
10- Cardone L, Castronuovo D, Perniola M, Cicco N, Candido V. Saffron (Crocus sativus L.), the king of spices: An overview. Scientia Horticulturae. 2020 Oct 15;272:109560.
11- Cerdá-Bernad D, Valero-Cases E, Pastor JJ, Frutos MJ. Saffron bioactives crocin, crocetin and safranal: Effect on oxidative stress and mechanisms of action. Critical Reviews in Food Science and Nutrition. 2020 Dec 16:1-8.
12- Roshanravan N, Ghaffari S. The therapeutic potential of Crocus sativus Linn.: A comprehensive narrative review of clinical trials. Phytotherapy Research. 2022 Jan;36(1):98-111.
13- Patlolla AK, Hackett D, Tchounwou PB. Silver nanoparticle-induced oxidative stress-dependent toxicity in Sprague-Dawley rats. Molecular and cellular biochemistry. 2015 Jan;399(1):257-68.
14- Riaz H, Saleem N, Ahmad M, Mehmood Y, Raza SA, Khan S, Anwar R, Kamran SH. Hepatoprotective effect of Crocus sativus on amiodarone-induced liver toxicity. Br. J. Pharm. Res. 2016 Jan 1;12(4):1-1.
15- Albrahim T, Alonazi MA. Role of beetroot (Beta vulgaris) juice on chronic nanotoxicity of silver nanoparticle-induced hepatotoxicity in male rats. International Journal of Nanomedicine. 2020;15:3471.
16- Heindel JJ, Blumberg B, Cave M, Machtinger R, Mantovani A, Mendez MA, Nadal A, Palanza P, Panzica G, Sargis R, Vandenberg LN. Metabolism disrupting chemicals and metabolic disorders. Reproductive toxicology. 2017 Mar 1;68:3-3.
17- Ghareeb OA, Mahmoud JH, Qader HS. Efficacy of Ganoderma lucidum in Reducing Liver Dysfunction Induced by Copper Oxide Nanoparticles. Journal of Research in Medical and Dental Science. 2021;9 (12):14-17.
18- Dong V, Nanchal R, Karvellas CJ. Pathophysiology of acute liver failure. Nutrition in Clinical Practice. 2020 Feb;35(1):24-9.
19- Eftekhari A, Ahmadian E, Azarmi Y, Parvizpur A, Fard JK, Eghbal MA. The effects of cimetidine, N-acetylcysteine, and taurine on thioridazine metabolic activation and induction of oxidative stress in isolated rat hepatocytes. Pharmaceutical Chemistry Journal. 2018 Feb;51(11):965-9.
20- Yousof SM, Erfan H, Hosny MM, Shehata SA, El-Sayed K. Subacute toxic effects of silver nanoparticles oral administration and withdrawal on the structure and function of adult Albino Rats' hepatic tissue. Saudi Journal of Biological Sciences. 2022 May 1;29(5):3890-8.
21- Parang Z, Moghadamnia D. Effects of silver nanoparticles on the functional tests of liver and its histological changes in adult male rats. Nanomedicine Research Journal. 2018 Sep 1;3(3):146-53.
22- Ramadhan SA, Ghareeb OA. Toxicity of AgNPs upon Liver Function and Positive Role of Tinospora Cordifolia: In Vivo. Pak. J. Med. Health Sci. 2021 Jun;15(6): 2164-2166.
23- Azab AE, Albasha MO. Hepatoprotective effect of some medicinal plants and herbs against hepatic disorders induced by hepatotoxic agents. J Biotechnol Bioeng. 2018;2(1):8-23.
24- Milajerdi A, Jazayeri S, Bitarafan V, Hashemzadeh N, Shirzadi E, Derakhshan Z, Mahmoodi M, Rayati A, Djazayeri A, Akhondzadeh S. The effect of saffron (Crocus sativus L.) hydro-alcoholic extract on liver and renal functions in type 2 diabetic patients: A double-blinded randomized and placebo control trial. Journal of Nutrition & Intermediary Metabolism. 2017 Sep 1;9:6-11.
25- Okdah Y, Ibrahim S. Effect of aqueous saffron extract (Crocus sativus L.) on sodium valporate-induced histological and histochemical alterations in liver of albino rats. Int. J. Adv. Res. 2014;2(7):735-45.
26- Harchegani AB, Abolfazl KH, Mahdiyeh Mirnam NI, Kaboutaraki HB, Shirvani H, Shahriary A. The hepatoprotective and antioxidative effect of saffron stigma alcoholic extract against vincristine sulfate induced toxicity in rats. Interdisciplinary toxicology. 2019 Dec;12(4):186.