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Oxidants and Antioxidants levels in blood of mice that orally dosed with Silver – Copper (core-shell) Nanoparticles

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ABSTRACT
The current study included the preparation of the silver-copper nanoparticles Ag-Cu NPs in the form of a core-shell, and the hybrid compound from loading the commercial drug Albendazole on the nanoparticlesAg-Cu NPs /Alb , and diagnosing it with tests FTIR, AFM , XRD and SEM , then this compound was dosed orally to laboratory mice at concentrations of 400, 800 and 1200 mg/km for two days / one dose per day in order to know the effect of these compounds on the value of some oxidants and antioxidants compared with Albendazole and distilled water as control agents. The results showed that the oxidative value of MDA did not change compared to the control treatment except for the concentration of 800 mg / kg of Ag-Cu NPs , as well as ROS . The value of antioxidants did not change from the control treatment for both Catalase and Glutathione, except for the concentration of 400 mg / kg of the Ag-Cu NPs /Alb , whose value was increased compared to the control.
Keywards : Ag-Cu NPs , Ag-Cu NPs /Alb ,Core-Shell , Oxidants and Antioxidants

INTRODUCTION
Echinococcus is a parasite that causes zoonotic diseases (Zoonosis), the adult stages of it are found in the gastrointestinal tract of the final hosts, while the larval stages are found in the intermediate hosts and in the form of cysts known as Hydatid cysts , and this is one of the most common diseases that cause many health damages to many areas on Worldwide, *Echinococcus granulosus* which causes cystic Echinococcosis, is the most common but least harmful of *E. multilocularis* which causes alveolar Echinococcosis and *E. vogeli* that causes polycystic Echinococcosis (CFSPH, 2020).At the level of Iraq, the disease has a wide range among the difficult problems facing the health system (CDC, 2012). The central and southern regions of the country take the largest share of the casualties from the governorates of Basra, Nasiriyah and Samawah (Maktoof & Abu Tabeekh, 2015; Abdulhameed *et al*., 2019). This disease causes health, social and economic problems due to the availability of effective medicines and the absence of pathological symptoms on the affected person until he reaches advanced stages of disease, and it includes various body parts, especially the heart and brain, so controlling it is complex in terms of therapeutic and surgical So, researchers resorted to trying many methods to stop the disease and its spread (Kharebov, 1997) . Many studies have shown that nanoparticles such as copper Cu NPs , Ag NPs , chitosan NPs and many other minerals have an inhibitory ability as well as high toxicity against many parasites such as *Leishmania* , *Giardia* and *toxoplasma* as well as the larval stages of some types of insects (Elmi *et al.*, 2013) . Mahmoud*et al.* (2014) showed that Ag NPs are the best in terms of efficacy and are present in the environment and have anti-parasites as well as bacteria and viruses. That is why many scientists tended to recommend the use of nanoparticles as anti-parasites because of their good efficiency and the lack of harm caused by them, so it

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is possible to benefit from them as effective drugs against parasites and stop their spread and various diseases (Elmi *et al*., 2013) .

The antioxidant system consists of a group of enzymatic and non-enzymatic elements that work to inhibit the oxidants produced by the living body itself or from the surrounding environment, such as reactive oxygen species ROS, minerals, chemical pesticides and nanoparticles. As for glutathione and catalase are examples of antioxidants and others important in countering the oxidative stress caused by these toxic substances (Atli and Canli , 2008 ; Yilmaz *et al*., 2015).Therefore, the current research tended to find out the effect of nanoparticles of copper and silver metals and the hybrid compound on loading Albendazole on nanoparticles compared with the commercial drug Albendazole alone on the values of oxidants and antioxidants and the different concentrations used.

MATERIAL AND METHODS

Laboratory animals

In the current study, mice of Mus musculus of Balb / c strain were used, which were obtained from the Iraqi Center for Cancer Research and Medical Genetics / Al-Mustansiriya University. It was transferred to its designated place, where the conditions of the place were set from the temperature of 25+ 5 and ventilation and lighting (12 hours of light and 12 hours of darkness).It was provided with water and food (pallet) on a regular basis twice a day, and the floors of the cages were cleaned weekly, where they were covered with sawdust.

Preparation of NPs

The Ag-Cu NPs was prepared in a core-shell method of 2 ml (0.1 N) copper CuCl2 chloride which is the core , and 1 ml (0.1 N) of the shell was silver nitrate AgNo3 in the presence of 10 ml (0.1 N) of ascorbic acid (vitamin C), copper chloride added into a Ascorbic acid solution , then nitrates were added to the mixture with continuous shaking at room temperature for an hour, then the sediment formed was separated, washed with distilled water and left until dryness, then it was kept in an opaque glass tube that was kept at room temperature until use.(Nadagouda&Varma, 2007) . The concentrations used in the study were prepared (400, 800 and 1200) mg / kg and were dosed orally for two consecutive days, then blood was drawn directly from the heart separate serum and exam oxidants and antioxidants .

Preparation of commercial drug

The commercial drug Albendazole was purchased from one of the commercial pharmacies and is in the form of 200 mg tablets from the manufacture Julphar of the U.A.E. company, and the approved dosage is 400 mg / kg, and it was used as a control treatment.

Loading the commercial drug on NPs

Albendazole was loaded onto the Ag-Cu NPs, taking an equal volume of 250 mg of the two compounds and adding to them 250 mL of distilled water and mixed well and left on the magnetic stirrer device for 12 hours. Distilled, then dried and grinded, then kept in a glass tube until use .

Diagnosis of NPs

FTIR, AFM and XRD tests were used to ensure the formation of the Ag-Cu NPs and Ag-Cu NPs /Alb and the safety of their preparation method , the validity of the tests used to form a core-shell was confirmed by SEM examination .These tests were carried out in each of the Al-Fadil foundation - Babel / Hilla / Iraq and the test SIM done in Iran.

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Oxidant and antioxidant Tests

After the blood was drawn from the heart, it was placed in gel tubes and then the serum was separated from the blood by a 2000 rpm centrifuge for 5 minutes. The checks took place at Al-Fadhil foundation - Babel / Hilla / Iraq .

RESULTS& DISCUSSION

Group of oxidants and antioxidants include a system of antioxidants that contain many enzymes that stimulate many reactions that inhibit free radicals and (ROS). These enzymes include Superoxide dismutase (SOD), Catalase, Glutathione and Vitamins (C, A, E), these antioxidants prevent the oxidation of molecules necessary in the metabolism process and important for chemical reactions including loss of an electron or increased oxidation state, for the liver and kidneys, defense systems of antioxidants that protect the organism from the oxidative stress generated by free radicals and ROS of minerals (Jorgensen , 2010) .

The results showed as in the figure (1) that the ROS did not change when comparing Albendazole with control, as well as when comparing the Ag-Cu NPs and Ag-Cu NPs /Alb with the control and with all the concentrations used, and the values of the two compounds did not differ when compared with Albendazole and without any significant differences. As for MDA, there was a decrease in its value when treating with Albendazole compared to control with significant differences. As for the Ag-Cu NPs, the significant differences appeared with a concentration of 800 mg / kg, where the value of MDA decreased compared to the control, while its value did not change with the remaining concentrations, Ag-Cu NPs /Alb did not differ from control and did not show any significant differences.But if we compare the two compounds with Albendazole, we will find that a significant difference appeared with the concentration of 400 mg / kg of the Ag-Cu NPs , as the value of MDA increased with it, while the three concentrations of the Ag-Cu NPs /Alb all showed an increase in the value of MDA with the emergence of clear significant differences.

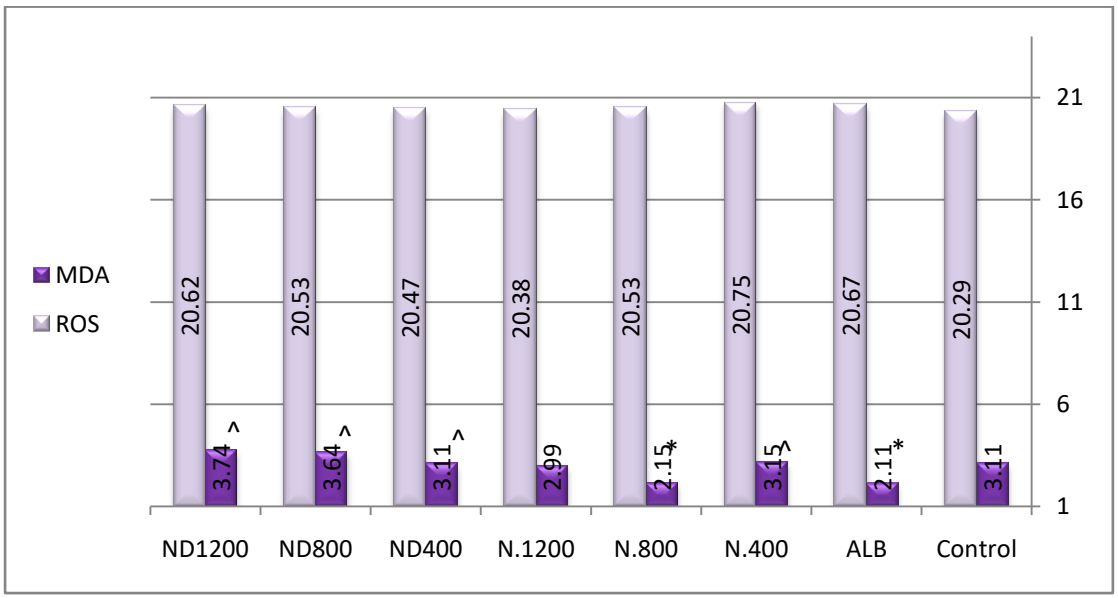

Figure (1) : Value of Oxidants in compare with ALB and control

*significant differences with control ^significant differences with ALB

Figure (2) shows that the antioxidants in the current study did not change their value, for example the value of catalase did not change from the control for

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Albendazole and for the Ag-Cu NPs and Ag-Cu NPs /Alb and for all the concentrations used, and there were no significant differences, as is the case with glutathione and for all concentrations except for the concentration of 400 mg / Kg of the Ag-Cu NPs /Alb , with which the glutathione value increased, whether the comparison was with control or with Albendazole, and the significant differences appeared with both cases.

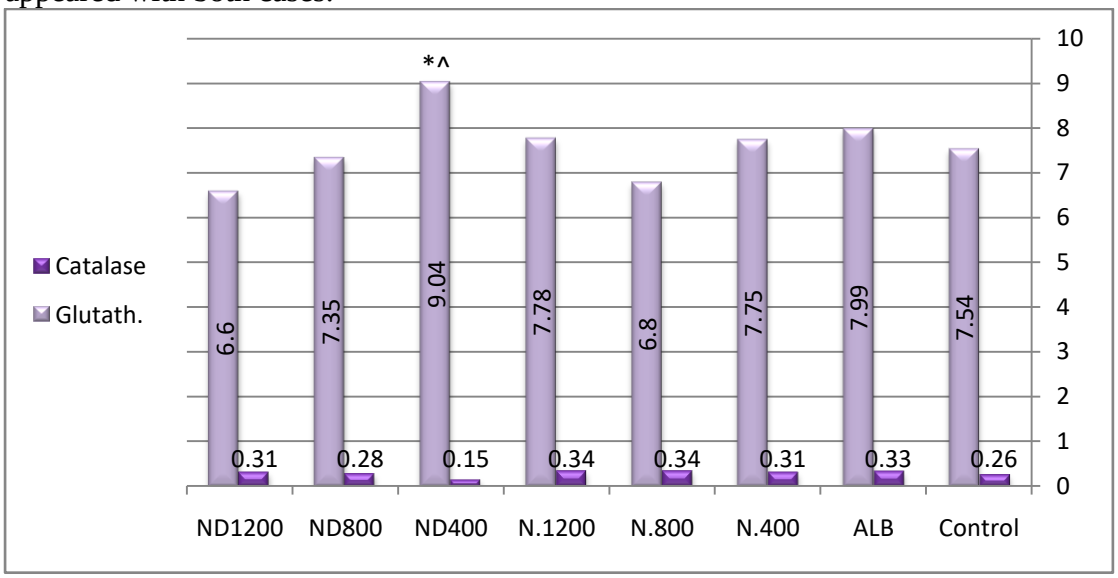

Figure (2) : Value of Antioxidants in compare with ALB and contro

*****significant differences with control^ significant differences with ALB

Shrivastava*et al.* (2013) considered nanoparticles to be one of the means inducing toxic manifestations in vivo due to their ability to penetrate the cytoplasm and the nucleus. In his study on rat serum, Canli and Canli (2017) stated that levels of oxidants increased overall and significantly, while antioxidants did not increase, and this was not consistent with the current study and its findings, as oxidants and antioxidants did not increase compared to the control.Syama *et al.* (2013) saw that there was a direct decrease between concentration, cell vitality and antioxidant value when different concentrations of Zn NPs were used in rat livers. Shrivastava *et al.* (2013) also studied the effect of nanoparticles of titanium oxide NPs TiO2, ZnO NPs and Al2O3 NPs on the oxidative stress in red blood cells, liver and brain of male mice after oral administration for 21 days, and found that there was an increase in the production of ROS and anti-enzyme. Antioxidants and this disagreed with the current results. Many studies in recent years have indicated an increase in ROS after exposure of rats to nanoparticles of titanium dioxide, zinc oxide, aluminum oxide and CuO (Sha *et al*., 2011; Yu *et al*., 2014; Hu *et al*., 2015; Lei *et al.*, 2015).

CONCLUSION

The present study concluded that Ag-Cu NPs and Ag-Cu NPs /Alb did not affect the value of the oxidants and antioxidants under study compared to the control treatment , except for the concentration of 400 mg / kg of the Ag-Cu NPs /Alb that increased the value of glutathione , while Albendazole decreased the MDA value compared to the control .

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