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Article

Study protective role *Camellia sinensis L.* (black tea) and silver, Zn oxide nanoparticles on antioxidant-oxidant enzymes and biochemical level against paracetamol overdose in adult male rats

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ABSTRACT

This study aims to measure the preventive effect of the silver, Zn oxide nanoparticles, and *Camellia sinensis* L. (black tea) on liver toxicity caused by the paracetamol drug. The Nanomaterials, with a practical size range of 33–40nm, black tea was extracted by Soxhlet apparatus using methanol alcohol at a concentration (80%); design in this study, 60 adult male rats weighing between 195 and 330 g and aged 11 to 14 weeks were used. They were kept in a relatively regulated setting with a temperature of 25C^{o} at the University of Karbala's animal facility. They received food. There were eight rat group divisions. G1: just received saline solution (0,85%) as the control. G2: 250 milligrams of black tea and 250 milligrams of paracetamol per kilogram of body weight. G3: 400 milligrams of *C. sinensis* L. and 250 milligrams of paracetamol per kilogram of body weight. G4: injection of 0.3 milligrams of zinc nanoparticles and 250 milligrams of paracetamol per kilogram of body weight. G5: injection of 0.5 milligrams of zinc nanoparticles and 250 milligrams of paracetamol per kilogram of body weight. G6: injection of 0.3 milligrams of silver nanoparticles and 250 milligrams of paracetamol per kilogram of body G7: injection of 0.5 milligrams of silver nanoparticles and 250 milligrams of paracetamol per kilogram of body, G8: 250 milligrams of paracetamol per kilogram of body administered intravenously, the blood bled for 30 days after receiving all dosages orally once daily for 21 days. When rats were given injections of 0.5 mg of nanoparticles and when injections of 250 mg of a black tee., it was discovered that the concentration of Malondialdehyde MDA, Lipid Peroxidation LPO, Triacylglycerid, cholesterol levels, and glucose decreased significantly. In contrast, Glutathione peroxidase GPX and protein levels are increased considerably. This was due to the injections' preventive and antioxidant action against the oxidative stress brought on by the paracetamol height dose.

Keywords: silver nanoparticles, Zn oxide nanoparticles, *Camellia sinensis* L., paracetamol.

INTRODUCTION

Metallic nanoparticles are used in a wide range of nanoscience and nanotechnology fields. These nanoparticles may take the place of regularly used drugs in certain applications[1]. Emerging materials called gold nanoparticles have different optical and electrical properties from traditional materials and have a promising future in the medical industry[2]. Silver particles attracted people because of their unique properties compared to silver of a smaller size, the large (Bulk). Due to its wide applications, the scientific and industrial community has paid specific attention to the topic of these minutes. As silver nanoparticles represent more than 23% of

the nano products available in the current market[3], silver nanocomposites impact fungi, bacteria, and viruses. Due to their small size (less than 5 nanometers), silver particles tend to migrate to the surface. This migration is facilitated by the nanoparticles' increased surface area and increased synthesis of reactive oxygen, resulting in free radicals forming[4] zinc oxide nanoparticles. One of the most crucial microelements requires vital activities. It enters the body through food and water, is primarily absorbed in the small intestine, and then travels to the blood plasma[5], which significantly impacts apoptosis. Zinc overload results in necrosis or apoptosis, which is cell death[6]; ZnO nanoparticles are among the most common nanoparticles used in ointments, lotions, and other products that protect skin from UV burns and cancer[7]; ZnO nanoparticles impartment role in Dermatology, endocrinology, radioisotope diagnostics, and the treatment of immune deficiency diseases, ZnO nanoparticles are essential for biological processes such cell growth and division, immunological response, teratogenesis, and osteogenesis. According to the percentage of tea sold overseas globally, there are three main types: 78% black, 20% green, and 2% oolong. Theaflavin, 3-gallate a flavin, 3-gallate flavin, and 3-gallate a flavin are the primary flavins in black tea. Black tea's astringent flavor and copper color result from the orange-red flavins component[8].

In addition to their antioxidant characteristics, tea polyphenols are recognized for their antibacterial action[9]. Reactive oxygen species (ROS), which include a range of chemicals produced from molecular oxygen, such as O_2-, H_2O_2, and OH-, can harm cells and tissues. Antioxidants can lessen or prevent this damage. Antioxidants are divided into many types. Super Enzymatic Antioxidants are made up of enzyme oxidation as well as other enzymes that cause CAT, catalase, and SOD, oxide dismutase, to transform into non-interacting molecules[10]. Non-enzymatic antioxidants A, C, E, and Menia are the second type. Vitamins Antioxidants Non-enzymatic albumin, glutathione, zinc, copper, and other antigens are crucial in preventing the harm caused by free radicals in the body. The study attempts to pinpoint the significant alterations in the non-enzymatic antioxidant levels in the serum of infected women. Compared to women with toxic diseases, breast cancer[11] Paracetamol, which has a vital role in treating oxidative damage in the body, is used to treat moderate fever and pain. Aspirin and ibuprofen's gastrointestinal adverse effects are absent when taken in large dosages, making it a suitable overdose medication[12]. However, acute overdoses of paracetamol, whether accidental or planned, are relatively common and can be exceedingly dangerous. Adults may suffer severe hepatocellular necrosis if they consume 10–15 grams of paracetamol, and 20–25 grams are lethal[13].

MATERIALS AND METHODS

1- Practicable size (33–40nm) silver and Zinc oxide nanoparticles were acquired from Nanomaterials.
2- After being cleaned and foreign things removed, the black tea leaf was purchased at a nearby market in Karbala. Three times with tap water and once with (DW) distilled water were used to wash the leaves. Electrical grinding was performed on each dry component. The powdered components were kept in polypropylene tubes and the refrigerator at 40C0 until use[14-15].
3- Soxhlet apparatus (100g of powdered (black tea) *Camellia sinensis* L. leaf, 100ml of methanol alcohol solvent (80%) in a 500ml flask for extraction through 24 hours and then separation alcohol from the extract by using rotary evaporation[16,17, 18, 19, 20].

Experiment Design

Design In this study, 60 adult male rats weighing between 195 and 330 g and aged 11 to 14 weeks were used.

They were kept in a relatively regulated setting with a temperature of 25C° at the University of Karbala's animal facility. They received food. There were eight rat group divisions. G1: just received saline solution (0,85%) as the control. G2: 250 milligrams of black tea and 250 milligrams of paracetamol per kilogram of body weight. G3: 400 milligrams of *C. sinensis* L. and 250 milligrams of paracetamol per kilogram of body weight. G4: injection of 0.3 milligrams of zinc nanoparticles and 250 milligrams of paracetamol per kilogram of body weight. G5: injection of 0.5 milligrams of zinc nanoparticles and 250 milligrams of paracetamol per kilogram of body weight. G6: injection of 0.3 milligrams of silver nanoparticles and 250 milligrams of paracetamol per kilogram of body G7: injection of 0.5 milligrams of silver nanoparticles and 250 milligrams of paracetamol per kilogram of body, G8: 250 milligrams of paracetamol per kilogram of body administered intravenously, The blood bled for 30 days after receiving all dosages orally once daily for 21 days.

Biochemical analysis

The cardiac puncture method was used to take blood, which was then spun for 10 minutes at 3000 rpm to separate the blood serum. Blood was drawn after 30 days, and the serum was kept at 40 °C for enzyme assays. Serum total protein concentration[21] Utilizing an analysis kit from the Biomaghreb company, triacylglycerides, total cholesterol, and glucose[22] were also determined [23].

Oxidative and antioxidant assay

Malondialdehyde (MDA), Glutathione peroxidase (GPX), and Lipid Peroxidation (LPO) analysis by using a kit from chin Bioassay Technology Laboratory (BT LAB)

Statistical Analysis

Mean was used to express the data. A one-way analysis of variances was used to assess the statistical significance of differences between the control group and the other groups (ANOVA). The SPSS for Windows version was used for statistical analysis, and P values of 0.05 or less were considered significant (SPSS, Inc., Chicago, Illinois).

RESULTS

The extract of *C. sinensis L*. consists of several active components produced naturally and accumulated in plants. The secondary metabolic screen study was carried out to identify the active components of C. sinensis L. Table (1) in the current study, protean level in group G8 significantly decreased to 2.99 mg/dl Compared to the control group (6.45 mg/dl), G2, G3, G4, G5, and G7 all demonstrated a significant increase (5.34, 5.44, 5.87, 5.99, 6.27, and 6.56 mg/dl, respectively) Compared to G8 (2.99 mg/dl). While glucose level group G8 showed a significant increase (0.294 mg/dl) compared to the control group's of 0.175 mg/dl, G2, G3, G4, G5, G6, and G7, all displayed a significant decrease (0.167, 0.156, 0.148, 0.125, 0.111, and 0.104 mg/dl) respectively compared with G8 (0.294 mg/dl). Total cholesterol level in group G8 (164.22 mg/dl) showed a significant increase Compared to the control group (145.34 mg/dl). While the G2, G3, G4, G5, and G6 all exhibited a significant decrease (142.34, 122.59, 111.54, 94.43, 89.74, and 78.28 mg/dl, respectively

Compared to G8 (164.22 mg/dl), Triacylglycerid levels in group G8 (101.53 mg/dl) were significantly higher than those in the control group 72.39 mg/dl. While G2, G3, G4, G5, G6, and G7 all exhibited a significant decrease from G8 101.53 mg/dl mg/dl to 88.64, 79.64, 73.38, 67.80, 59.56, and 55.34 mg/dl, respectively. In table (2). When compared to the control, the MDA level of group G8 rats exhibited a significant rise (0.756 mol/L) and displayed a substantial increase; G2, G3, G4, G5, and G6 all showed a significant decline (0.667, 0.653, 0.637, 0.629, 0.601, and 0.586 mol/L, respectively)., Compared to the control level of 6.56 mol, the LPO level of group G8 exhibited a considerable rise (7.99 mol/L). G2, G3, G4, G5, and G6 significantly declined (6.98, 6.85, 6.65, 6.56, 6.43, and 6.32 mol/ L, respectively). Compared to the control group's GPX level of 66.35 mol/L, group G8's level was significantly lower (30.56 mol/L). G2, G3, G4, G5, and G7 significantly rose (58.91, 56.81, 53.72, 52.86, 50.64, and 49.84 mol/ L, respectively). Compared with G8, 30.56 mol/ L.

Groups	Protean	Glucose	Total cholesterol	Triacylglycerid
G 1	6.45	0.175	145.34	**72.39**
G2	5.34	0.167	142.34	**88.64**
G3	5.44	0.156	122.59	**79.83**
G4	5.87	0.148	111.54	**73.38**
G 5	5.99	0.125	94.43	**67.80**
G6	6.27	0.111	89.74	**59.56**
G7	6.56	0.104	78.28	**55.34**
G8	2.99	0.294	164.22	**101.53**
LSD	0.37	0.96	0.47	**0.94**

Table 1. Effect of silver and zinc nanoparticles on glucose, protein, Total cholesterol, and Triacylglycerid Concentration mol/L.

Groups	MDA	LPO	GPX
G 1	0.605	6.56	**66.35**
G2	0.667	6.98	**58.91**
G3	0.653	6.85	**56.81**
G4	0.637	6.65	**53.72**
G 5	0.629	6.56	**52.86**

G6	0.601	6.43	**50.64**
G7	0.586	6.32	**49.84**
G8	0.756	7.99	**30.56**
L.S.D	0.86	0.36	**0.65**

Table 2. Shows the effect of silver and zinc nanoparticles on MDA, LPO, and GPX Concentrations mol/L, in male Rats.

DISCUSSION

The current study aimed to examine silver and zinc nanoparticles' antioxidant and defense mechanisms on liver enzymes against methotrexate-induced toxicity and ROS. A table with the results is shown (1,2), which shows that the G8 group (250 milligrams of paracetamol per kilogram of body administered intravenously) had significantly increased glucose, total cholesterol, triacylglyceride, MDA, and LPO concentrations than the G1 control group. As a result, taking paracetamol with drinking water causes oxidative stress and an increase in ROS by raising MDA and LPO levels in the liver tissue and lowering GPX and protein levels. These outcomes were in line with prior research. Because ROS can harm cells by oxidizing the lipids in cell membranes, deactivating the protein sulfhydryl enzyme[24], and disrupting DNA synthesis [25] Due to the conjugation of glutathione with NAPQI to produce mercapturic acid, paracetamol causes hepatic glutathione depletion and eventually liver damage from overdoses[26]. Paracetamol significantly increased serum GPT and total protein when compared to the results[27]. The resulting ROS may cause cellular damage through the peroxidation of membrane lipids, inactivation of the sulfhydryl enzyme, protein cross-linking, and DNA synthesis [28]. As a result of GSH conjugating with NAPQI to produce mercapturic acid, high doses of paracetamol deplete the liver's GSH, which in turn raises lipid peroxidation by absorbing hydrogen from a polyunsaturated fatty acid and finally damages the liver[29]. The enzyme serum glutamic pyruvic transaminase (sGPT) is produced when the liver or heart is damaged. It is released into the bloodstream and is frequently found in heart and liver cells. Therefore, the blood levels of sGPT increase when the heart or liver is damaged. Some medications, including paracetamol and aspirin sodium diclofenac, can also raise sGPT levels. Paracetamol lowers levels of uric acid and total protein.

In contrast, it is pointed out that increasing levels of the GPT, GOT enzyme, and glucose[30] increase the risk of paracetamol poisoning. It is well known that the toxicity of paracetamol causes levels of the GPT, GOT enzyme, and glucose to rise and that taking a paracetamol dose lowers uric acid and total protein. Poisons like paracetamol also cause levels of the GPT, GOT enzyme, and glucose to rise[31].

The experiment's results demonstrated that 250 milligrams of black tea increased the activity of antioxidant enzymes and effectively scavenged free radicals because of their ability to scavenge ROS electrons. An antioxidant effect at intracellular or extracellular levels inhibits the xanthine oxide enzyme activity, changing the product xanthine oxide to xanthine dehydrogenase[32]. The reasons for the significant rise in GSH levels in response to active compounds may include increased resistance or activation of the enzyme glutamyl cysteine synthesis[33]. This substance or glutathione synthesis might cause glutamyl trance peptidase to become active[34]. When this extract and a mutagen overlap, the phenol from C. sinensis leaves inhibits the enzymatic effectiveness of the harmful action of methotrexate[35]. The processes by which phenolic compounds exert their antioxidant action include neutralizing lipid free radicals and inhibiting hydrogen peroxide's decomposition into free

radicals [36]. Due to tea's unique capacity for auto-oxidation and the consequent rise in reactive oxygen species, catechins in tea have both pro-oxidant and antioxidant properties[37] and work as a hydrogen donor [38]. The apparent chemical and structural similarity of tea catechins to some traditional anti-folic drugs, such as trimethoprim and methotrexate, further supports this observation [39]. Earlier studies have found various antioxidants, including parsley extract [40].

Injection of 0.5 milligrams of zinc oxide and silver nanoparticles increased the activity of antioxidant enzymes and effectively scavenged free radicals, increasing antioxidant enzyme levels and protecting cell membranes from oxidative stress damage, according to the investigation—a decrease in MDA, LPO, protean, and GPX amounts. Nanoparticles can boost antioxidant activity and reduce ROS levels[41]. These outcomes were in line with prior research that showed the stability, antioxidant properties, non-toxicity, and approval of gold nanoparticles for additional in-vitro and in-vivo studies [42]. In line with the study, In male rats, liver damage and the quantity of serum proteins are reduced by nanoparticles[43], whereas the male reproductive systems of mice are preserved[44]. The outcomes Cell membranes can be shielded from oxidative stress damage by ZnO nanoparticles, which can also boost levels of antioxidant enzymes and lower MDA levels. ZnO nanoparticles can increase antioxidant activity while lowering ROS levels[45,46].

CONCLUSIONS

The study investigated the effects of paracetamol, black tea, zinc oxide and silver nanoparticles on liver enzymes against methotrexate-induced toxicity and ROS. The results showed that paracetamol caused oxidative stress and increased ROS by raising MDA and LPO levels in the liver tissue and lowering GPX and protein levels. Black tea increased the activity of antioxidant enzymes and effectively scavenged free radicals. Zinc oxide and silver nanoparticles increased the activity of antioxidant enzymes and protected cell membranes from oxidative stress damage.

Based on the results of this study, it is concluded that paracetamol, black tea, zinc oxide and silver nanoparticles can all be used to protect the liver from oxidative stress and methotrexate-induced toxicity.

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