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Article:

Comparative Effects of Bulk and Nanoparticle Ginseng on Hepatorenal and Immune Function in Rats

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Abstract

The use of herbal medicine, particularly *Panax ginseng*, has gained substantial attention due to its therapeutic properties. This study investigates the impact of bulk ginseng (Gin) and ginseng nanoparticles (Gin NPs) on liver, kidney, and immune functions in male rats. Forty rats were divided into four groups: a control group receiving distilled water (1 ml), a Gin 50 group administered 50 mg / kg bulk ginseng, a Gin 100 group given 100 mg / kg bulk ginseng, and a Gin NPs 30 group receiving 30 mg / kg ginseng nanoparticles. Treatments were delivered orally each day for eight weeks. Biochemical assays for liver and kidney function, differential leukocyte counts, immunoglobulin G levels, and histological evaluations of liver and kidney tissues were conducted. No significant differences in liver or kidney enzyme levels, lymphocyte and eosinophil counts, or immunoglobulin G levels were observed between the treated groups and controls. However, the Gin NPs group displayed a significant decrease in monocyte count and an increase in neutrophil count, while no significant changes were observed in other treated groups compared to controls. Histological analysis revealed that hepatorenal architecture remained generally normal across treated groups, including structures such as the central vein, hepatic sinusoids, hepatocytes, renal medullary, cortical tubules, and proximal and distal convoluted tubules. Mild Kupffer cell proliferation, mononuclear cellular infiltration, dilated hepatic sinusoids, and intraglomerular congestion were noted in the Gin 50 and Gin 100 groups, while the Gin NPs 30 group exhibited mild glomerular vacuolation and an expanded Bowman's space. In conclusion, both bulk ginseng (50 and 100 mg / kg) and its nanoparticle form (30 mg / kg) support normal hepatorenal and immune functions, with Gin NPs demonstrating a slightly enhanced effect.

Keywords: Ginseng bulk., Nanoparticles., Liver., Kidney., Immunity.

Introduction

Throughout history, humans have turned to plants for their medicinal needs. This practice has been prevalent in ancient and contemporary societies, where plants play a crucial role in herbal medicines such as traditional Chinese medicine, and complementary and alternative medicine. In modern times, these herbs are commonly prepared and sold as botanical dietary supplements, which individuals consume to obtain vital nutrients and promote a healthy way of life [1]. Korean ginseng, also known as Panax ginseng Meyer is a well-known and ancient medicinal plant highly valued and widely used worldwide [2]. Ginseng or its active compound ginsenoside has been found to have positive effects in addressing a range of conditions including immune, endocrine, cardiovascular, and neurodegenerative diseases [3]. It has been utilized as a beneficial tonic and for treating different ailments, such as liver disorders. Ginsenosides, also known as ginseng saponins, are the main components of ginseng and are thought to be accountable for its numerous health advantages [4].

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Researchers have extensively examined extracts and bioactive substances derived from ginseng due to their potential to promote various health benefits. These include antioxidant, antitumor, antihyperglycemic, skin-protecting, anti-osteoporotic anticancer, anti-infective, and respiratory problem-relieving properties [5]. Numerous studies have shown that ginseng extract has a positive effect on the prevention and treatment of kidney disorders [6,7]. In addition, it has immunomodulatory activity [8]. At the nanoscale, the properties of substances and materials differ significantly from their larger forms. These variations are evident in areas such as chemical reactivity, color, strength, and electrical and thermal conductivity, as well as magnetic properties, which can display remarkable changes. Moreover, once insoluble substances can now dissolve at the nanoscale. Nano-sized particles also have exceptional mobility, allowing them to pass through biological membranes and reach cells, tissues, and organs that larger particles cannot. Their ability to move freely also enables them to bypass most water filters, paving the way for the creation of new materials with high surface reactivity and the capability to penetrate cell membranes, which was not achievable through conventional methods [9]. We are working on the whole plant of ginseng without performing any plant extraction. Most of the existing researches are focused on the extraction of ginsenosides and no research is available in support of the medicinal effects of ginseng bulk so, the main goal of the current study is to investigate the potential effect of ginseng bulk and nano ginseng bulk in hepatorenal function and immunity in normal adult male rat to realize the previous goal the liver and kidney enzymes assay, Differential leucocytic count, Immunoglobulin G measuring and histological examination of liver and kidney were carried out.

Material and methods

Approval and registration

The study's protocols were approved by the Ethical Research Committee of the Faculty of Veterinary Medicine at Sohag University, under approval number Soh.un.vet./ 00025. The handling of animals throughout the study adhered to the guidelines set forth by the Egypt National Institutes of Health for the Care and Use of Laboratory Animals, ensuring ethical standards were maintained.

Reagents

Ginseng was purchased in the form of Korean Red Ginseng (100 % natural Panax Ginseng Roots Powder) (IMTENAN Company, Assiut, Egypt) The ginseng nanoparticles (Gin NPs) used in the study were prepared by Nano Tech company (NanoTech, 6th October City, Egypt). The Gin nanoparticles (NPs) produced are a pale brown powder that readily disperses in water. Transmission electron microscopy (TEM) analysis revealed their average dimensions to be 60 ± 10 nm in length and 25 ± 5 nm in diameter, with a rod-like structure.

Animals

Forty mature male Wistar albino rats, weighing between 240 and 260 grams, were obtained from the Laboratory Animal House at the Faculty of Medicine, Sohag University. The animals were housed for one week to acclimatize to the laboratory environment in clean, pathogen-free metal cages at the animal house of the Physiology Department, Faculty of Veterinary Medicine, Sohag University. They were maintained under a 12-hour light/dark cycle at a temperature of 23 ± 2 °C, with humidity levels of 50 – 55 %. The rats had *ad libitum access* to standard rodent pellets and water. During the acclimatization period, they were handled daily for 5 minutes to familiarize them with human contact, helping to minimize any hypothalamus-pituitary-adrenal axis responses to handling during later experimental procedures [10].

Experimental Design

Forty rats were randomly distributed into four groups (10 animals per group):

Group I (control): rats received distilled water (1 ml / day) .

Group II (Gin 50 group): rats were administered with Korean red ginseng roots powder bulk 50 mg/kg body weight (BW) dissolved in 1 ml distilled water / day [11,12].

Group III (Gin 100 group): rats were administered with Korean red ginseng roots powder bulk 100 mg / kg BW dissolved in 1 ml / day distilled water.

Group IV (Gin NPs 30 group): rats were gavage with Gin NPs powder bulk 30 mg / kg BW dissolved in 1 ml/ day distilled water.

All rats received distilled water and the drug solution orally via a drenching tube for a period of eight weeks. To ensure accurate dosing, the rats were weighed weekly for dose adjustments. The administration was carried out orally, beginning at 9:00 a.m. each day.

Samples collection

Blood samples collection

At the end of the experimental period, rats were anesthetized by diethyl ether; individual blood samples were collected from retro-orbital venous plexus from each group; one part of these blood samples was kept in test tubes without anticoagulant. Blood was left to be clotted and then centrifuged at 3000 rpm for 15 minutes. The sera were collected separately in Eppendorf tubes and kept at -80°C until liver and kidney function tests assay and immunoglobulin G determination. The other part of these blood samples was kept with anticoagulant

Ethylenediaminetetraacetic acid (EDTA) and was used to create smears, which were then stained with Giemsa stain to determine the differential leukocytic count.

Liver and kidney samples collection

At the end of the experimental period, rats were sedated with an intraperitoneal dose of sodium thiopental (50 mg / kg BW, intraperitoneally) then sacrificed and the Liver and kidneys were excised out and kept in neutral buffered paraformaldehyde 4% for histological examination.

Examination

liver functions test (liver enzymes assay)

The frozen serum was thawed for measuring serum liver enzymes: Alanine aminotransferase (ALT) Catalogue NO. (265001) and aspartate aminotransferase (AST) Catalogue NO. (261001) (Egyptian Company for Biotechnology (S.A. E), Obour city industrial area, block 20008 piece19A. Cairo. Egypt). The assay was performed by spectrum kits according to the manufacturer's instructions **[13],** using a microplate reader (Infinite 50, Mannedorf, Switzerland) at wavelength 340 nm).

Kidney functions test (Kidney enzymes assay)

The frozen serum was thawed for measuring kidney enzymes: Creatinine, Catalog No. (234001) and Urea / Blood urea nitrogen (BUN), Catalog No. (318 001) (Egyptian Company for Biotechnology (S. A. E), Obour city industrial area, block 20008 piece19A. Cairo. Egypt). The assay was performed by spectrum kits according to the manufacturer's instructions **[14,15]** respectively, using a microplate reader (Infinite 50, Mannedorf, Switzerland) at wavelength 492 nm/min).

Differential leucocytic count

A manual differential leukocyte count was performed on the previously prepared dried blood smears using the Battlement method to count 100 / 200 cells with the assistance of a microscope and a cell counter **[16].**

Immunoglobulin G (IgG) Detection

Immunoglobulin G (IgG) is measured by using Chemistry analyzer model Cobas 501 (F. Hoffmann-La Roche Ltd, Basel, Switzerland).

Histological examination of liver and kidneys

Liver and kidney separate specimens from the experimental groups were dissected out and quickly fixed in neutral buffered paraformaldehyde (PFA) 4 %, after that the organs samples were dehydrated in each ascending concentration of alcohol then cleared by xylene, processed through the conventional paraffin embedding technique **[17],** sectioned at 5 µm thick the sections were floated out in a warm water bath to lay on the slides and dried on oven 50-55 C and stained with Hematoxylin and Eosin (H & E) for standard histological examination using light microscope **[18].**

Statistical analysis

The collected data were statistically analyzed using GraphPad Prism 8 (GraphPad Software, San Diego, California, USA). Results were expressed as mean ± standard error of the mean (SEM). Differences between groups were assessed using a one-way analysis of variance (ANOVA), and Tukey's test was employed for multiple comparisons when a significant difference was observed. A p-value of less than 0.05 was considered statistically significant compared to the control group **[19].**

Results

liver function parameters

All treated groups showed a non-significant change in ALT and AST compared with the control group **Table 1.**

kidney function parameters

In all treated rats, urea (mg / dl) and creatinine (mg / dl) levels denoted a non-significant change compared with the corresponding control **Table 2.**

Differential leukocytic count parameter

The count of lymphocytes, monocytes, Neutrophils, and Eosinophils after administration of ginseng powder 50 and 100 mg / kg and ginseng NPs 30 mg / kg for 8 weeks were assessed. All treated rats showed a non-significant change in lymphocyte count compared with the control group. However, rats treated with ginseng NPs 30 mg / kg showed a significant decrease ($p \leq 0.05$) in lymphocytes compared with the Gin 50 group. Rats treated with Gin NPs 30 showed a significant decrease ($p \leq 0.05$) in monocyte count compared with the corresponding control. While all other treated groups showed no change in monocyte count compared with the control group. All treated groups showed a non-significant change in neutrophil count, except for the Gin NPs 30 group, which displayed a significant increase ($p \leq 0.05$) compared to the control. Rats treated with Gin 100 and Gin NPs 30 also showed a significant increase in neutrophil count ($p \leq 0.05$) compared to those treated with Gin 50. Furthermore, neutrophil count in the Gin NPs 30 group was significantly elevated ($p \leq 0.05$) compared to the Gin 100 group. In addition, all treated groups demonstrated a non-significant change in eosinophil count relative to the control group **Table 3.**

Immunoglobulin G (IgG) level

All treated groups showed a non-significant change in the level of IgG compared with the control groups **Table 4.**

Table (1): Liver function parameters in control and treated rats after administration with Gin (50 and 100) and Gin NPs 30 mg / kg BW for 60 days.

Group	Alanine aminotransferase (ALT) (U/l)	Aspartate aminotransferase (AST) (U/l)
Control	5.55 ± 0.34	14.65 ± 1.14
Gin 50	5.02± 0.43	13.38± 0.75
Gin 100	4.95±0.42	16.05± 1.04
Gin NPs 30	5.45± 0.49	14.90± 1.45

n = 10, values are expressed in mean ± S.E.M.

Table (2): kidney function parameters in control and Gin (50 and 100) and Gin NPs 30 mg /kg BW treated rats for 60 days.

Group	Urea (mg/dl)	Creatinine (mg/dl)
Control	57.96± 1.93	0.82± 0.11
Gin 50	53.27± 2.86	0.86± 0.08
Gin 100	59.38± 2.58	0.75± 0.05
Gin NPs 30	58.71± 3.75	0.89± 0.11

n = 10, values are expressed in mean ± S.E.M.

Table (3): Differential leukocytic count parameter in control and Gin (50 and 100) and Gin NPs 30 mg /kg BW treated rats for 60 days.

Group	Lymphocyte	Monocyte	Neutrophils	Eosinophils
Control	55.20±0.99	10±0.52	35.20±0.42	0.00±0.00
Gin 50	57.70±0.84	9.30±0.80	33±0.75	0.00±0.00
Gin 100	54.60±0.96	8±0.37	37.20±1.12β	0.20±0.13
Gin NPs 30	51.80±1.09β	7.30±0.42*	40.70±0.79*βΔ	0.10±0.10

n = 10, values are expressed in mean ± S.E.M. * $p \leq 0.05$ compared with control, β $p \leq 0.05$ compared with Gin 50 and Δ $p \leq 0.05$ compared with Gin 100.

Table (4): levels of immunoglobulin G (IgG) (mg/dl) in control and Gin (50 and 100) and Gin NPs 30 mg/kg BW treated rats for 60 days.

Group	Immunoglobulin G (mg/dl)
Control	200.40±18.80
Gin 50	206.40±18.13
Gin 100	211.20±22.27
Gin NPs 30	199.50±27.92

n = 10, values are expressed in mean ± S.E.M. Immunoglobulin G (IgG) (mg/dl)

Histological assessment of liver and kidney.

The liver tissue section from the control group displayed normal histological architecture, including a central vein with normal structure, hepatocytes arranged in cords, normal intervening sinusoids, and a typical portal triad comprising a normal portal vein, hepatic artery, and bile duct **(Figure 1A, B).** In the Gin 50-treated group, the liver section also showed a normal central vein, hepatic sinusoids, and hepatocytes, with a mild Kupffer cell reaction along the hepatic sinusoids, and a normal portal triad consisting of the portal vein, hepatic artery, and bile duct, along with mild Kupffer cell proliferation and minimal mononuclear cellular infiltration **(Figure 1C, D).** The Gin 100-treated group showed a dilated and congested central vein, slightly dilated hepatic sinusoids, and normal hepatocytes, as well as a congested portal triad and a mild Kupffer cell reaction **(Figure 1E, F).** In the Gin NPs 30-treated group, liver sections demonstrated hepatocytes arranged in cords with mildly dilated sinusoids, a normal portal triad with a regular portal vein, and evidence of mononuclear cellular infiltration **(Figure 1G, H).**The kidney tissue section from the control group displayed a normal renal cortical structure, including a glomerulus of typical size and structure with a capillary tuft, normal Bowman's space, and intact proximal and distal convoluted tubules. The cortico-medullary junction exhibited normal arcuate arteries and veins, along with well-structured renal medullary tubules **(Figure 2A, B).** In the Gin 50-treated group, the renal cortex showed mild intraglomerular congestion and normal renal cortical tubules, while the renal medulla displayed typical renal tubules with mild interstitial nephritis, indicated by intratubular inflammatory cellular infiltration **(Figure 2C, D).** The Gin 100-treated group exhibited a normal glomerular size and structure, as

well as normal proximal and distal convoluted tubules in the cortex. The renal medulla showed normal renal tubules with mild intratubular congestion **(Figure 2E, F).** In the Gin NPs 30-treated group, the kidney tissue displayed mild glomerular vacuolation, widened Bowman's space, renal tubules with vacuolated tubular lumens, and intact renal medullary tubules and blood vessels **(Figure 2G, H).**

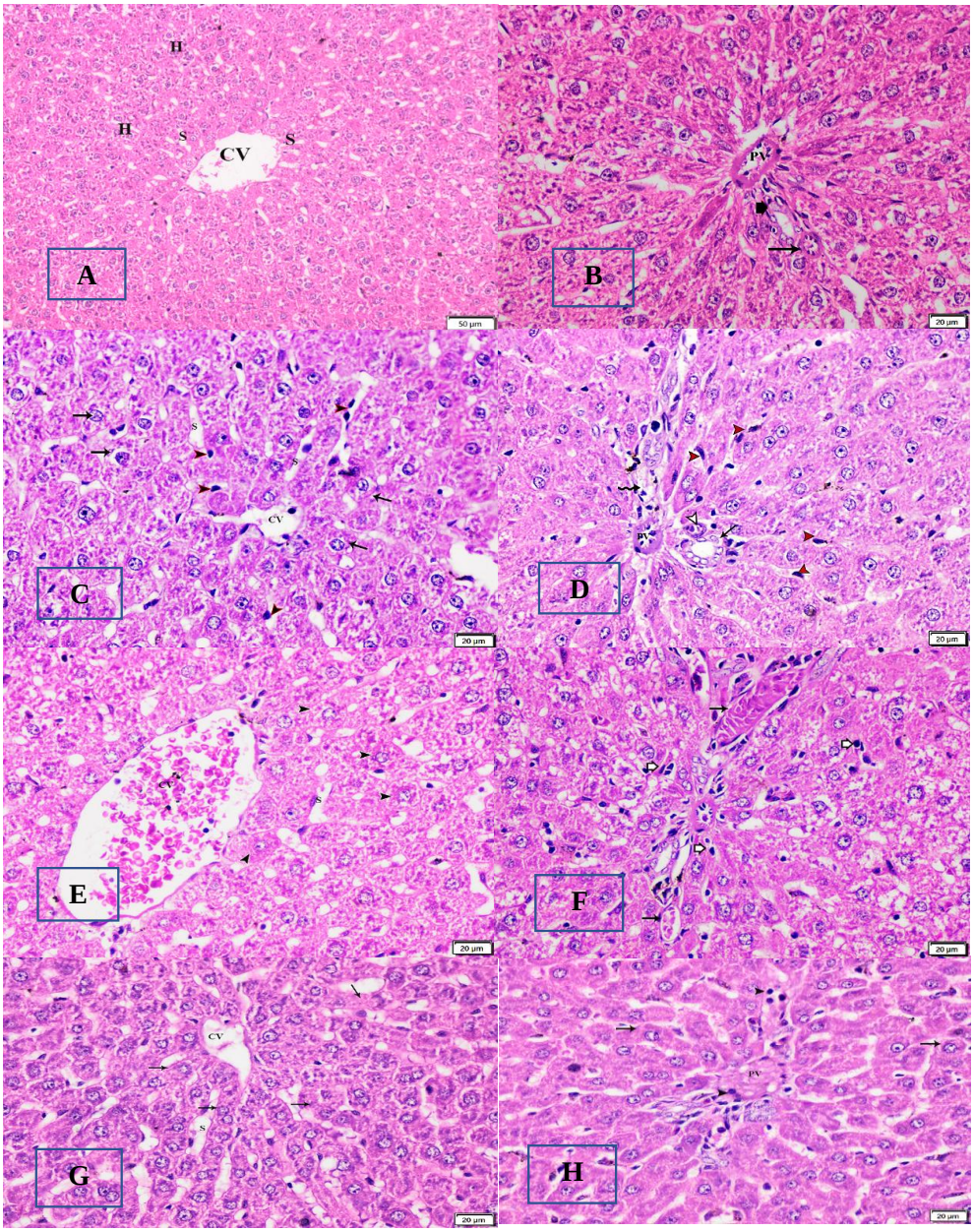

Figure (1): Photomicrograph of liver in control and treated rats. control group showing normal histological architectures: normal central vein (CV), normal hepatocytes (H) arranged in cords, with in-between normal sinusoids (S) (A). normal portal tirade: normal portal vein (PV), normal hepatic artery (thin arrow) and normal bile duct (arrowhead) (B). Liver tissue section from the Gin 50- treated group showing: normal central vein, normal hepatic sinusoids, normal hepatocytes (arrows), mild Kupffer cell (arrowheads) reaction arranged in the sides of hepatic sinusoids (C). Showing normal portal tirade: normal portal vein, normal hepatic artery (white arrowhead) and normal bile duct (thin arrow). Mild Kupffer cell proliferation (red arrowheads), mild mononuclear cellular infiltration (zigzag arrow) (D). Liver of rats administrated the Gin 100 mg / kg BW showing: dilated and congested central vein, mild dilated hepatic sinusoids, normal hepatocytes (arrowheads) (E). Showing portal tirade with congested blood vessels (thin arrows), mild Kupffer cell reaction (white arrowheads) (F). Liver of rats from the Gin NPs 30 mg / kg BW- treated group showing normal hepatocytes (arrows) arranged in cords, with in-between mild dilated sinusoids (G) and showing: normal hepatocytes (arrows), normal portal triad with normal portal vein (PV), mononuclear cellular infiltration (arrowheads) (H).

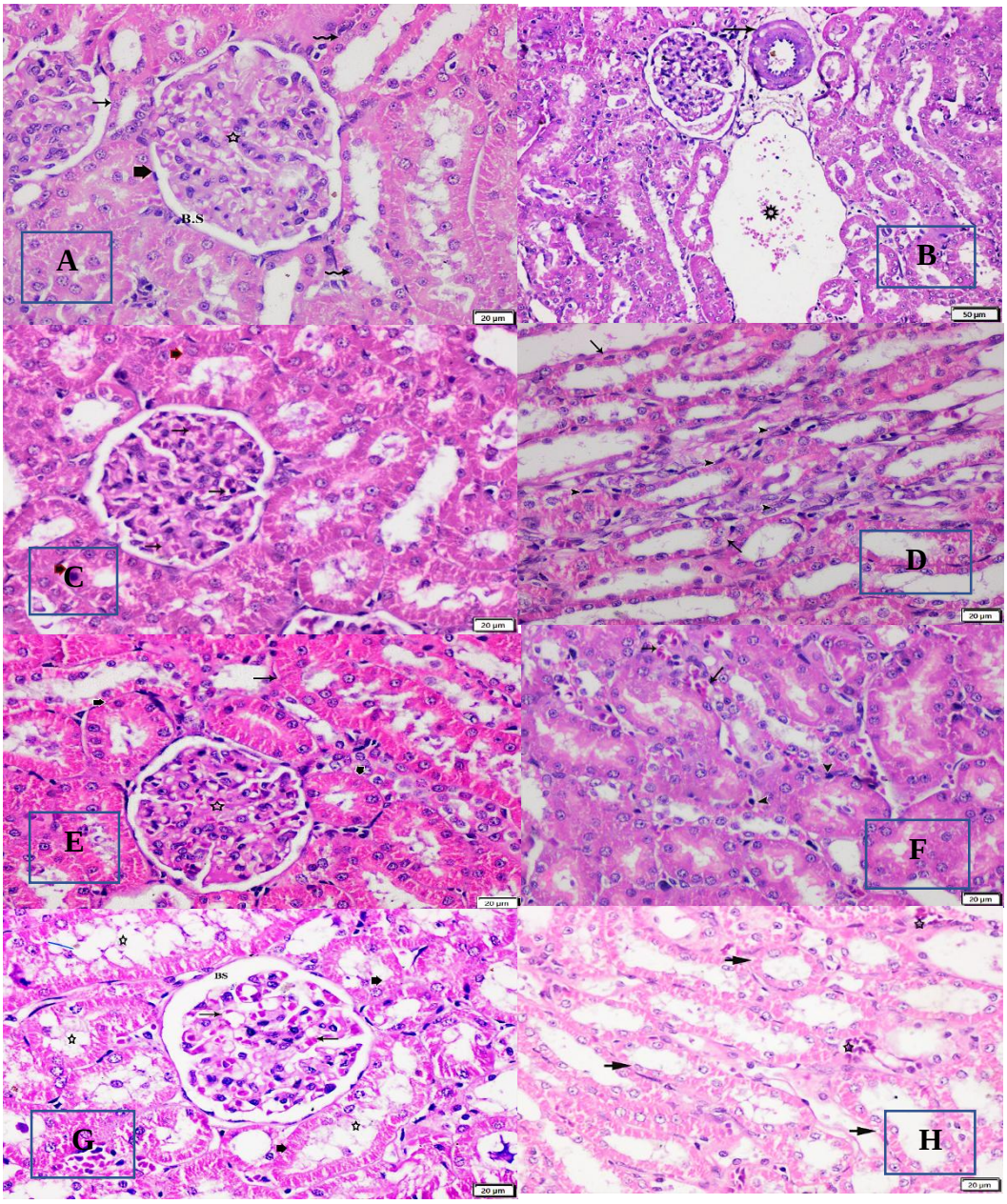

Figure (2): Photomicrograph of kidney in control and treated rats. control group showing normal renal cortical histological structure: normal glomerulus size and structure (arrowheads) contain tuft of capillaries (stars), normal Bowmans's space (BS), normal proximal convoluted tubules (thin arrows), and distal convoluted tubules (zigzag arrows) (A). showing normal cortico-medullary junction contain: normal arcuate artery (arrow) and arcuate vein (star). normal renal medullary tubules (B). Kidney tissue section from the Gin 50- treated group showing: renal cortex: mild intraglomerular congestion (arrows), normal renal cortical tubules (red arrowheads) (C). Showing renal medulla: normal renal tubules (arrow), mild (interstitial nephritis) intertubular inflammatory cellular infiltration (arrowheads) (D). Kidney of rats administrated the Gin 100 mg / kg BW showing: renal cortex: normal glomerular size and structure (star), normal proximal convoluted tubule (arrowheads), and distal convoluted tubule (arrow) (E). renal medulla: normal renal tubules (arrowheads), mild intertubular congestion (arrows) (F). Kidney of rats from the Gin NPs 30 mg / kg BW treated group showing mild vacuolation in glomerulus (arrows), wide Bowman's space (BS), more or less renal tubules (arrowheads) with vacuolated tubular lumen (stars) (G) and showing: normal renal medullary tubules (arrows), normal blood vessels (stars) (H).

Discussion

There are no available studies concerning the effect of ginseng bulk and its nanoparticles on different physiological processes. All the available literature was conducted on ginseng extract and its nanoparticles. So, the present study is aimed to examine the potential effect of ginseng bulk and nano ginseng bulk on hepatorenal function and immunity in normal adult male rats. The result of the present study showed a non-significant change in ALT and AST levels in Gin 50, Gin 100, and Gin NPs 30 compared with their control. This means that these given doses have no harmful effect on the liver. There are many results of the previous studies performed by using ginseng extract on liver function and support our results that obtained by using ginseng bulk. For example, the study showed suppression in liver carcinogenesis after oral administration of red ginseng extracts at a 1% concentration in the diet of mice **[20].** Another recent research **[21]** showed improvement in liver function tests, reduction in tumor marker levels, and lowered viral titers in HCV patients in mature rats after administration of Panax ginseng extract. In addition to the study that reported the protective effects of ginseng extracts on liver cells in laboratory studies as well as clinical models of liver injury induced by different toxins **[4].** Nanotechnology is regarded as a cutting-edge modern technology across scientific domains. Recently, various phytochemicals and substances from ginseng have been employed to create nanoparticles, which have been evaluated for their medical uses such as fighting cancer, obesity, inflammation, microbes, and in biosensor applications. Chinese ginseng (Panax. notoginseng), American ginseng (Panax. quinquefolius), and Korean ginseng (Panax. ginseng) are the primary Panax species utilized for producing nanoparticles **[22].** Nanoparticles red ginseng boost inflammatory factors to eliminate cancer cells or impede tumor advancement, while reducing chemokine levels that support tumor growth, effectively restraining Hepatocellular carcinoma (HCC) progression and inducing metabolic changes, and controls the modification of essential metabolites to impede HCC advancement **[23].** The results of the present study also showed non-significant change in Urea and Creatinine levels in Gin50, Gin100, and Gin NPs 30 treated rats compared with control rats. There are some previous studies obtained by using ginseng extract on Urea and Creatinine levels and like our results obtained by using ginseng bulk. For example, the study **[24]** showed that ginseng, can potentially enhance the quality of life in rats with streptozotocin-induced diabetic nephropathy by reducing serum creatinine and urea nitrogen levels. Another study **[25]** found that administration of ginseng extract to white rats at doses of 0.8, 1.6, and 2.4 g / kg B.W. for 28 days did not show any harmful impact on kidney function. Ginseng extract administration also, improved renal function in diabetic rats by reducing serum urea, uric acid, and creatinine levels **[26].** There is no, available literature that detects the effect of nano-ginseng extract or nano-ginseng bulk on kidney function. The obtained data showed a non-significant increase in lymphocyte, monocyte, neutrophils, and eosinophils levels in the Gin50 and Gin100 groups compared with their control. These results indicate that giving ginseng bulk with these doses for rats causes slight improvement in immunity through these effects on differential leucocytic count (DLC) as improves the production of antibodies through lymphocytes and phagocytosis through neutrophils and monocytes. There are many previous studies obtained by using ginseng extract on DLC and in line with our results obtained by using ginseng bulk. For example, the study **[27]** reported a non-significant effect on total white blood cell counts, concentrations of neutrophils, monocytes, or various lymphocyte subtypes, lymphocyte proliferation, or neutrophil oxidative burst after ginseng administration. In addition, the study **[28]** reported a significant increase in lymphocyte proliferation and neutrophil count in the bloodstream ($P < 0.01$) after ginseng extract administration. The results of the current study showed a non-significant increase in lymphocytes, and eosinophils, a significant increase in neutrophils, and a significant decrease in monocyte levels in Gin NPs 30 compared with their control. A recent study **[29]** reported that ginseng extract nanoparticles increased the CD8+ T/regulatory T cells ratio in the tumor microenvironment in vivo and promoted the proliferation of CD8+ T lymphocytes in vitro. The results of this study demonstrated a non-significant increase in IgG levels in the Gin 50, Gin 100, and Gin NPs 30 groups compared to the control. These findings suggest that administration of bulk ginseng or its nanoparticles at the given doses may stimulate immune function, as evidenced by increased IgG production. IgG is a key antibody produced by the immune system, often indicating a mid-to-late-stage infection or previous exposure. Testing both IgM and IgG can aid in the early diagnosis of infectious diseases and provide insights into the infection stage**[30]**. These results are consistent with previous studies using ginseng extract to enhance IgG levels and align well with our findings obtained from bulk ginseng. **[31]** which reported that Pre-treating mice with ginseng before oral immunization of Salmonella for two weeks resulted in increased production of serum IgG1, IgG2, and secretory IgA against Salmonella. The study demonstrated that after 8 weeks of saponin administration, there was a significant increase in IgG levels. This suggests that Rb1 and Re can enhance long-term immune defense, leading to improved immunity over an extended period **[32].**

Additionally, the study [33] reported that oral administration of red ginseng for 3 months has immunomodulatory effects, as it can increase IgG levels. Also, another study [34] reported that Intranasal administration of ginseng extract with influenza virus A/PR8 led to notable increases in IgA and total IgG levels in blood in mice. There is no available previous literature conducting in the use of ginseng extract nanoparticles or ginseng bulk nanoparticles on IgG production. In the present study, the histological examination of the liver tissue section from Gin 50 showed a normal central vein, normal hepatic sinusoids, normal hepatocytes, and mild Kupffer cell reaction arranged in the sides of hepatic sinusoids. The portal triad is normal, with Mild Kupffer cell proliferation and mild mononuclear cellular infiltration. The liver section from Gin100 showed a dilated and congested central vein, mild dilated hepatic sinusoids, and normal hepatocytes. congested blood vessels and mild Kupffer cell reaction in the portal triad. the histological findings of the liver tissue in Gin NPs 30 showed that normal hepatocytes arranged in cords, with in-between mild dilated sinusoids and normal portal triad with mononuclear cellular infiltration compared with the control group. There are many results of the previous studies obtained by using ginseng extract in histological findings of the liver and online with our results obtained by using ginseng bulk. The study [35] reported that Korean red ginseng (KRG) accelerated liver regeneration and improved liver injury in dogs following partial hepatectomy. Also, the study [36] reported that administering Panax ginseng at a dose of 200 mg / kg BW daily has been shown to improve liver damage caused by a mixture of Lambda-cyhalothrin (LCT) and acetamiprid pesticides in rats, leading to the restoration of normal liver structure. There is no literature found that examines the effect of nano-ginseng extract or nano-ginseng bulk on liver histology. The current study's histological examination of kidney tissue revealed mild intraglomerular congestion, normal renal cortical tubules, and normal renal medullary tubules in the Gin 50 group, along with mild interstitial nephritis marked by intratubular inflammatory cell infiltration. In the Gin 100 group, the renal cortex showed normal glomeruli, proximal and distal convoluted tubules. In the Gin NPs 30 group, kidney tissue displayed mild glomerular vacuolation, an expanded Bowman's space, and vacuolated renal tubules, while the renal medullary tubules and blood vessels appeared normal. These findings align with previous studies that used ginseng extract, supporting similar histological effects observed with bulk ginseng administration. One study [37] found that ginseng may reduce cell damage caused by toxic substances by stabilizing cell membranes, offering protection against toxic agents and induced tissue injury. Another study [25] reported that ginseng extract administration at a dose of 0.8 g / kg BW showed no histological abnormalities. However, hydropic degeneration and inflammation were observed in the extract groups given doses of 1.6 and 2.4 g / kg BW. There is no literature found that examines the effect of nano-ginseng extract or nano-ginseng bulk on kidney function. These results indicate that using ginseng bulk or its nano at the given doses has slight effect on kidneys of normal rats.

Conclusion

We concluded that ginseng bulk whole particles with doses of (50 and 100) mg / kg BW and ginseng bulk nanoparticles with doses of 30 mg / kg BW have no harmful effect and are recommended to maintain and improve normal hepatorenal and immunity functions.

Conflict of interests

The authors declare that they have no conflict of interest related.

References

1. **Husain I, Dale OR, Martin K, Gurley BJ, Adams SJ, Avula B, Chittiboyina AG, Khan IA & Khan SI.** Screening of medicinal plants for possible herb-drug interactions through modulating nuclear receptors, drug-metabolizing enzymes and transporters. Journal of ethnopharmacology. 2022; 301: 115822.

2. **Park JD, Rhee DK & Lee YH.** Biological activities and chemistry of saponins from Panax ginseng C. A. Meyer. Phytochemistry Reviews. 2005; 4 (2–3): 159-175.

3. **Shin HS, Yu M, Kim M, Choi HS & Kang DH.** Reno protective effect of red ginseng in gentamicin-induced acute kidney injury. Laboratory Investigation. 2014; 94 (10): 1147-1160.

4. **Huu Tung N, Uto T, Morinaga O, Kim YH & Shoyama Y.** Pharmacological effects of ginseng on liver functions and diseases: A minireview. In Evidence-based Complementary and Alternative Medicine. 2012; 2012 (1): 173297.

5. **Riaz M, Rahman NU, Zia-Ul-Haq M, Jaffar HZE & Manea R. Ginseng:** A dietary supplement as immune-modulator in various diseases. In Trends in Food Science and Technology 2019; 83 (12-30).

6. **Sen S, Chen S, Feng B, Wu Y, Lui E & Chakrabarti S.** Preventive effects of North American ginseng (Panax quinquefolium) on diabetic nephropathy. Phytomedicine. 2012; 19 (6): 494-505.

7. **Kang KS, Ham J, Kim YJ, Park JH, Cho EJ& Yamabe N.** Heat-processed Panax ginseng and diabetic

renal damage: active components and action mechanism. Journal of ginseng research. 2013; 37 (4): 379.

8. **Lakshmi T, Anitha R& Geetha RV.** Panax ginseng–a universal panacea in the herbal medicine with diverse pharmacological spectrum–a review. Asian journal of pharmaceutical and clinical research. 2011; 4 (1): 14-18.

9. **Park SK, Kim YK, Youn HS& Lee MY.** Application of nanotechnology to Korean black-red ginseng: solubility Enhancement by particle size reduction. Molecular & cellular toxicology. 2008; 4 (1): 52-60.

10. **Basuony M, Tousson E, Massoud A, Saad S, Maha & Rizk Z.** Preventive/Ameliorative Effects of Ginseng Aqueous Extract on Cisplatin-induced Hepatic and Renal Injuries Chemoreceptors View Project Hepatic ameliorative role of vitamin B17 against Ehrlich ascites carcinoma-induced liver toxicity View project Preventive/Ameliorative Effects of Ginseng Aqueous Extract on Cisplatin-induced Hepatic and Renal Injuries. Asian Oncology Research Journal. 2020; 3 (1): 54687.

11. **Hassan H, Mabrouk EA, Atef N, Ahmed H& Abo Zakaib Ali F.** Pilot study to know the best doses of ginseng bulk and its nanoparticles in normal testicular function of rats. International Journal of Comprehensive Veterinary Research. 2024a; 2 (1): 10-20.

12. **Hassan H, Mabrouk EA, Atef N, Ahmed H& Ali FA.** Effect of ginseng bulk and its nanoparticles in testicular functions of normal rats. Journal of Advanced Veterinary Research. 2024b; 14 (4): 670-677.

13. **Breuer J.** Report on the symposium" Drug effects in Clinical Chemistry Methods". In European journal of clinical chemistry and clinical biochemistry. journal of the Forum of European Clinical Chemistry Societies. 1996; 34 (4): 385-386.

14. **Wu AH.** Tietz Clinical Guide to Laboratory Tests-E-Book: Tietz Clinical Guide to Laboratory Tests-E-Book. Elsevier Health Sciences. 2006.

15. **Bowers LD& Wong ET.** Kinetic serum creatinine assays. II. A critical evaluation and review. Clinical chemistry. 1980; 26 (5): 555-561.

16. **Bajimaya MM, Mahotra NB, Shrestha L, Pradhan S, Malla N, Kandel S, Chaudhary S& Gurung S.** Manual differential count and automated differential leukocyte count in normal individuals: a comparative study. Journal of Physiological Society of Nepal. 2021; 2 (1): 21–24.

17. **Bancroft J& Gamble M.** Theory and practice of histological techniques, 5th Edition. London Edinburgh New York Philadelphia, St. Louis Sydney, Toronto, 2002; 53: 5143-5147.

18. **Mayada RF, Taghred MS& Haytham AA.** Boldenone-induced apoptotic, structural, and functional alterations in the liver of rabbits. World Rabbit Science. 2015; 23 (1): 39-46.

19. **Brown AM.** A new software for carrying out one-way ANOVA post hoc tests. Computer methods and programs in biomedicine. 2005; 79 (1): 89-95.

20. **Nishino H, Tokuda H, Ii T, Takemura M, Kuchide M, Kanazawa M& Okuyama T.** Cancer chemoprevention by ginseng in mouse liver and other organs. Journal of Korean Medical Science. 2001; 16 (l): S66-S69.

21. **Abdel-Wahhab MA, Gamil K, El-Kady AA, El-Nekeety AA& Naguib KM.** Therapeutic effects of Korean red ginseng extract in Egyptian patients with chronic liver diseases. Journal of Ginseng Research. 2011; 35 (1): 69-79.

22. **Balusamy SR, Perumalsamy H, Huq MA, Yoon TH, Mijakovic I, Thangavelu L, Yang D C& Rahimi S. A** comprehensive and systemic review of ginseng-based nanomaterials: Synthesis, targeted delivery, and biomedical applications. In Medicinal Research Reviews. 2023; 43 (5): 1374-1410.

23. **Ren Z, Chen X, Hong L, Zhao X, Cui G, Li A, Liu Y, Zhou L, Sun R, Shen S, Li J, Lou J, Zhou H, Wang J, Xu G, Yu Z, Song Y& Chen X. Nanoparticle** Conjugation of Ginsenoside Rg3 Inhibits Hepatocellular Carcinoma Development and Metastasis. Small. 2020; 16 (2): 1905233.

24. **Jin D, Zhang Y, Zhang Y, Duan L, Zhou R, Duan Y, Sun Y, Lian F& Tong X.** Panax Ginseng C.A. Mey. as Medicine: The Potential Use of Panax Ginseng C.A. Mey. as a Remedy for Kidney Protection from a Pharmacological Perspective. In Frontiers in Pharmacology. 2021; 12: 734151.

25. **Emelda A, Santi I, Besse SCD, Aderafni A& Yuliana D.** Nephrotoxicity effect of Ginseng Bugis (Talinum paniculatum (Jacq) Gaertn) leaves ethanolic extract on creatinine, urea, and kidney histopathological features. International Food Research Journal. 2024; 31 (2): 417-422.

26. **Sawiress FAR.** Effect of Ginseng Extract Supplementation on Renal Functions in Diabetic Rats. Journal of Agricultural Science. 2011; 3 (2).

27. **Biondo PD, Robbins SJ, Walsh JD, McCargar LJ, Harber VJ& Field CJ.** A randomized controlled

crossover trial of the effect of ginseng consumption on the immune response to moderate exercise in healthy sedentary men. Applied Physiology, Nutrition and Metabolism. 2008; 33 (5): 966-975.

28. **Nguyen NH& Nguyen CT.** Pharmacological effects of ginseng on infectious diseases. Inflammopharmacology. 2019; 27 (5): 871-883.

29. **Han X, Wei Q, Lv Y, Weng L, Huang H, Wei Q, Li M, Mao Y, Hua D, Cai X, Cao M& Cao P.** Ginseng-derived nanoparticles potentiate immune checkpoint antibody efficacy by reprogramming the cold tumor microenvironment. Molecular Therapy. 2022; 30 (1): 327-340.

30. **Hu F, Shang X, Chen M& Zhang C**. Joint Detection of Serum IgM/IgG Antibody Is an Important Key to Clinical Diagnosis of SARS-CoV-2 Infection. Canadian Journal of Infectious Diseases and Medical Microbiology. 2020. 2020 (1): 1020843.

31. **Na HS, Lim YJ, Yun YS, Kweon MN& Lee HC.** Ginsan Enhances Humoral Antibody Response to Orally Delivered Antigen. Immune Network. 2010; 10 (1): 5.

32. **Shi M, Ma J, Jin S, Wang T, Sui Y& Chen L.** Effects of saponins Rb1 and Re in American ginseng combined intervention on immune system of aging model. Frontiers in Molecular Biosciences. 2024; 11: 1392868.

33. **Lee BJ, So HJ, Kim JW& Lew JH.** The Comparative Study of IgG, IgM, and IgA in Laboratory Animal Administrated Red-ginseng, Using Immunoglobulin Productivity Assay. The Journal of Internal Korean Medicine, 2007; 28 (4): 886-895.

34. **Kang S& Min H.** Ginseng, the “immunity boost”: The effects of panax ginseng on immune system. In Journal of Ginseng Research. 2012; 36 (4): 354-368.

35. **Kwon YS, Jang KH& Jang IH.** The effects of Korean red ginseng (ginseng radix rubra) on liver regeneration after partial hepatectomy in dogs. Journal of Veterinary Science. 2003; 4 (1): 83-92.

36. **Abdul-Hamid M, Mohamed HM, Abd El-Twab SM & Zaied K.** Histological, ultrastructural, and biochemical study on the possible role of Panax ginseng in ameliorating liver injury induced by Lambda cyhalotherin. Beni-Suef University Journal of Basic and Applied Sciences. 2020; 9 (1).

37. **Morsy FA, El Din AAG, Farrag ARH, Badawi MA & Shaffie NM. Ochratoxin A toxic effect on rat kidneys** and the potential protective effect of ginseng: Histopathologic, histochemical, and image analysis morphometric studies. Macedonian Journal of Medical Sciences. 2012; 5 (1): 40-48.