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Evaluate the Role of Ginseng Roots against the Toxic Effect of Ibuprofen on Lipid Profiles, Liver Enzymes and Oxidative Stress Status in Male Albino Rats

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Abstract: Introduction & aim: The therapeutic qualities of ginseng (Panax ginseng) have attracted a lot of interest. So, this investigation was aimed to study the effect of alcoholic Ginseng extract against Ibuprofen induced reproductive dysfunction in male rat.

Materials & methods: From August 24 to September 26, 2024, this study was carried out in the Veterinary Medicine College's animal house at Tikrit University. From the animal house of the Veterinary Medicine College at Tikrit University, fifty (70) adult, seemingly healthy Albino male rats were acquired.

Results: A significant ($P \leq 0.05$) differences were found in the concentration of cholesterol, triglyceride, LDL, HDL, where the highest concentration was in the fourth group, which administrated Ibuprofen for 30 days compared to the control group, while the treated groups revealed non-significant ($P \leq 0.05$) variations from the untreated group. In the ginseng group, the cholesterol levels revealed significant (P≤0.05) reduced from the untreated group. for Liver enzymes, AST, ALT and ALP activity in Ibuprofen (30 days) group revealed significant (P≤0.05) variations from the untreated group. also, in the treated groups and ginseng group revealed significant (P≤0.05) variations from the untreated group. for oxidative stress, MDA levels in Ibuprofen (30 days) group revealed significant (P≤0.05) variations from the untreated group. while, in the treated groups and ginseng group showed significant (P≤0.05) reduced compared to the control group. The SOD levels in Ibuprofen (30 days) group showed non- significant (P≤0.05) differences compared to the control group. also, in the treated groups and ginseng group showed non-significant (P≤0.05) differences compared to the control group.

Conclusions: Its concluded that the alcoholic extract of ginseng roots shows a protective and therapeutic effect liver enzymes and its act as antioxidant regents.

Keywords: Panax ginseng, Ibuprofen, Lipid profile, MDA, liver enzymes.

Introduction

Russia and East Asia are home to Panax ginseng, a member of the Araliaceae family (1). For thousands of years, East Asian nations have utilized ginseng, known as the "king of all herbs," as a traditional medicine to heal various ailments. It has grown to be one of the most widely used herbs globally during the past three decades (2). In many nations, it is utilized in pharmaceuticals, food and health supplements, and agricultural products. Ginsenosides are triterpene saponins that are the characteristic bioactive components of ginseng. However, ginsenosides are not the only component that contributes to ginseng's medicinal benefits. Gintonin was recently discovered to be the active component (3). Despite the fact that all other parts of the plant contain active substances, the root is used medicinally. Red and white ginseng are the two distinct varieties of

Panax ginseng (4,5). The red and white variants have somewhat different amounts of ginsenoside chemicals. The amount of ginsenoside is also affected by growing time; roots from plants older than five years have a higher potency than roots from plants that are only one to two years old (5). Ginsenosides/saponins, nonsaponins, and miscellaneous are the three primary categories of chemical constituents in this genus; these can be further divided into subcategories (6,7). Worldwide, nonsteroidal anti-inflammatory medicines (NSAIDs) are among the most commonly recommended drugs for managing inflammation and reducing pain related to various illnesses (8). A significant number of patients utilize these drugs; globally, 5–10% of NSAID prescriptions are written each year. Although the effectiveness of NSAIDs is widely acknowledged, prolonged use of these drugs is linked to kidney damage and gastrointestinal side effects (9). One of the non-steroidal anti-inflammatory medicines (NSADS) with both analgesic and antipyretic properties is ibuprofen, a propionic acid (8,9). Ibuprofen's potential for toxicity arises from its suppression of the cyclooxygenase pathway and the ensuing impact on numerous organ systems and cellular functions. Even at therapeutic dosages, ibuprofen is linked to a slightly increased risk of adverse gastrointestinal and renal events; prostaglandins and thromboxanes aid in maintaining the stomach mucosal barrier and renal blood flow. The most frequent NSAID implicated in overdose cases is ibuprofen; ibuprofen consumption alone accounts for 29% of overdoses. When ibuprofen is taken with additional analgesics, patients may also overdose (10). Reye syndrome is brought on by NSAIDs' damage to hepatocyte mitochondria (11). Moreover, nothing is known about the mechanism underlying NSAID-induced liver injury. It is important to take into account the potential for elevated rates of drug-induced liver damage and Reye syndrome due to the growing usage of ibuprofen in children (12). Therefore, the present study aimed to evaluate the role of ginseng roots against the toxic effect of ibuprofen on lipid profiles, liver enzymes and oxidative stress status in male albino rats.

Materials and Methods

Ibuprofen

Was obtained from General Company for the Manufacture of Pharmaceuticals and Medical Appliances Samarra Iraq.

Panax ginseng roots extraction

The roots of Panax ginseng were purchased from the Baghdad, Iraq, market. To get rid of any contaminants, properly wash the ginseng roots in distilled water. After that, thoroughly dry the roots in the shade for five to seven days at room temperature until they are entirely dry. cleaned the dried roots to get rid of any dirt or debris that could have remained. Using a grinder, grind the cleaned roots into a fine powder. 200 milliliters of 99% ethanol were added to a round-bottom flask that contained 20 grams of powdered ginseng roots. To improve extraction efficiency, the mixture was left to stand for 24 to 72 hours while being shaken periodically. Use a filter sieve to separate particles and contaminants from the solution when the soaking time is over. To eliminate the alcohol and concentrate the flavonoids, use a rotary evaporator to concentrate the filtrate at a low temperature of about 40–50°C. After that, the extract was applied to nylon bags and allowed to dry at room temperature.

Animals

From August 24 to September 26, 2024, this study was carried out in the Veterinary Medicine College's animal house at Tikrit University. Fifty (70) adult male Albino rats that appeared to be in good health were acquired from the Veterinary Medicine College's animal house at Tikrit University. Animals ranged in weight from 190 to 250 g, with an average of 225 g, and ranged in age from 8 to 10 weeks. The animals were kept in ordinary plastic cages that were 46 by 28 by 13 cm. they were kept under suitable environmental conditions of 20-25 C°.

General Experimental Design

The animals that used in current study were divided into 7 groups, and each group contain 10 rats, as following:

- G1: control group received normal saline (orally) for 30 days.
- G2: rats received dimethyl sulfoxide (DMSO) (orally) daily for 30 days.
- G3: rats received Ibuprofen (120mg/kg) (orally) daily for 10 days.
- G4: rats received Ibuprofen (120mg/kg) daily for 30 days.
- G5: rats received ginseng extract (20mg/kg) (orally) daily for 30 days.
- G6: rats received Ibuprofen (120mg/kg) for 10 days and followed by ginseng extract (20mg/kg) daily for 20 days.
- G7: rats received Ibuprofen (120mg/kg) and ginseng extract (20mg/kg) daily for 30 days.

Measurements

- Total cholesterol (TC): Total cholesterol Kit (Biolabo, France) assays TC concentration in serum, plasma using spectrophotometer technique.
- Triglyceride (TG): Triglyceride Kit (Biolabo, France) assays TG concentration in serum, plasma using spectrophotometer technique.
- High-Density Lipoprotein (HDL): HDL Kit (Biolabo, France) assays HDL concentration in serum, plasma using spectrophotometer technique.
- Low High-Density Lipoprotein (LDL): LDL Kit (Biolabo, France) assays LDL concentration in serum, plasma using spectrophotometer technique.
- Aspartate transaminase (AST): AST Kit (Biolabo, France) assays AST activity in serum, plasma using spectrophotometer technique.
- Alanine aminotransferase (ALT): ALT Kit (Biolabo, France) assays ALT activity in serum, plasma using spectrophotometer technique.
- Alkaline phosphatase (ALP): ALP Kit (Biolabo, France) assays ALP activity in serum, plasma using spectrophotometer technique.
- Malondialdehyde (MDA): ELISA Kit (SUNLONG, China) uses the Sandwich-ELISA ELISA technique to measure the amount of MDA in serum and plasma.
- Superoxide dismutase (SOD): Sandwich-ELISA, an ELISA technique, is used by the ELISA Kit (SUNLONG, China) to measure the amount of SOD in serum and plasma.

Statistical analysis

The Data of sexual hormones were analyzed by using a program called Minitab (statistical program). The difference between the experimental group's means was analyzed by ANOVA.

Ethics and institutional animal care and use committee (IACUC):

The research methodology and protocols were reviewed and approved by the scientific committee of veterinary medicine, university of Tikrit, Salah Alden-Iraq (TU.VET.30) in compliance with animal welfare ethical measures prior to any experiments being conducted.

Results & Discussion

Lipid profile

Table (4-1) showed the levels of lipid profile in male rats and in all study groups. significant ($P \leq 0.05$) differences were found in the concentration of cholesterol, where the highest concentration was in the fourth group, which administrated Ibuprofen for 30 days (89.00 ±9.46) compared to the control group (81.95 ±8.26), while the treated groups revealed differences that were not significant (P≤0.05) as when compared with the untreated group. In the ginseng group (73.26 ±5.75), the cholesterol levels showed significant (P≤0.05) reduced compared to the control group. The triglyceride levels in Ibuprofen (30 days) group (127.40 ± 9.90) revealed differences that were significant (P≤0.05) as when compared with the untreated group (100.38 ± 8.78). while, in the treated groups and ginseng group (81.81±7.78) showed significant (P≤0.05) reduced compared to the control group. The HDL levels in Ibuprofen (30 days) group (57.64±4.11) showed non-significant (P≤0.05) differences compared to the control group (57.72 ±1.8). while, in the treated groups and ginseng group (86.56±5.81) revealed differences that were significant (P≤0.05) as when compared with the untreated group. The LDL levels in Ibuprofen (30 days) group (37.39 ±5.07) showed significant (P≤0.05) elevated compared to the control group (8.60 ±1.64). while, in the treated groups show significant (P≤0.05) elevated compared to the control group but less that Ibuprofen groups. The ginseng group (5.8 ±5.41) revealed differences that were not significant (P≤0.05) as when compared with the untreated group.

Table (1): the concentrations of lipid profile in studied groups

Groups	Cholesterol (mg/dL)	Triglycerides (mg/dL)	HDL (mg/dL)	LDL (mg/dL)
G1	81.95 ±8.26 b	100.38±8.78 b	57.72 ±1.8 b	8.60 ±1.64 c
G2	79.92±4.11 bc	83.29±7.33 c	58.91 ±4.54 b	11.6 ±1.2 c
G3	79.23±8.16 bc	98.72±6.11 b	51.04 ±2.9 b	8.43±2.30 c
G4	89.00 ±9.46 a	127.4±9.90 a	57.64±4.11 b	37.39 ±5.07 a
G5	73.26 ±5.75 c	81.81±7.78 c	86.56±5.81 a	5.8 ±5.41c
G6	76.06±6.7 bc	76.57±9.96 c	97.45±4.13 a	25.39±3.36 b
G7	82.04±7.0 b	80.01±8.35 c	98.09±8.49 a	26.29±4.52 b
P- value	0.05 *	0.01**	0.01**	0.01**

If the letters are the same, the differences are not significant (P≤0.05). In this case, distinct letters indicate significant (P≤0.05) differences.

Our physiological study's findings, which are displayed in Table (4-2), showed that the positive groups (G2, G3, and G4) had higher average levels of (TC), (Tg), and (LDL) (P<0.05) and lower average levels of (HDL) (P<0.05) than the negative control group (G1). Following ginseng treatment, the current study's findings indicated that the G6 and G7 groups' rates of HDL and Tc, Tg, and LDL increased (P<0.05) and decreased (P<0.05) in comparison to the G3 and G4 groups. The current study's findings are consistent with previous research (13,14). According to studies, ginseng lowers the high blood serum lipid levels by promoting acetyl-CoA carboxylase and AMP-Activated Protein Kinase phosphorylation. It also promotes lipolysis by activating AMPK. Ginseng's saponins increase the secretion of cholesterol through the formation of bile acids, which lowers blood cholesterol levels (15). Because it regulates the genes that form lipogenesis, including acetyl transferase 2,3-hydroxyl-3-methylglutrayl-coA and sterol regulatory element-binding protein, the administration of aqueous and alcoholic ginseng extract results in a decrease in the average of total cholesterol, triglycerides, and low-density lipoproteins (16). In their investigation on male and female rats, Ayaz and Alnahdi (17) found that giving ginseng extract at a dose of 150 mg/kg for two weeks improved the lipid profiles in the serum of rats given ethanol by raising HDL and lowering TC, TG, and LDL levels. Ginseng's saponins lower blood fat levels via regulating LDL receptors and increasing the release of cholesterol into bile acids (18). A reduction in intestinal and hepatic lipoprotein production as well as blood cholesterol levels has been seen in another investigation using mice given the alcoholic extract of North American ginseng at 4 and 32 weeks of age. The mice were shielded from fatty liver by ginseng treatment. Additionally, ginseng decreased the expression of genes that regulate the lipoproteins' release of fatty acids and triglycerides. Ginseng, however, promoted lipolysis (19). Ginseng may have preventive effects on dyslipidemia due to increased phosphorylation of acetyl-CoA carboxylase and AMP-activated protein kinase (AMPK). Additionally, there was an increase in the expression of several genes linked to lipolysis and fatty acid absorption, including CD36 and peroxisome proliferator-activated receptor-α. According to these findings, ginseng reduced hyperlipidemia via inducing lipolysis via AMPK activation (20).

Liver enzymes

Table (2) showed the activity of liver enzymes in male rats and in all study groups. AST activity in Ibuprofen (30 days) group (96.63± 8.08) showed significant (P≤0.05) elevated compared to the control group (47.40±8.46). while, in the treated groups and ginseng group (58.53±6.19) revealed differences that were significant (P≤0.05) as when compared with the untreated group. The ALT activity in Ibuprofen (30 days) group (92.83±6.90) showed significant (P≤0.05) elevated compared to the control group (67.0 ± 8.98). while, in the treated groups and ginseng group (55.69±6.22) revealed differences that were significant (P≤0.05) as when compared with the untreated group.

The ALP activity in Ibuprofen (30 days) group (86.75±8.23) showed significant (P≤0.05) elevated compared to the control group (56.67±5.99). while, in the treated groups and ginseng group (52.77±8.23) revealed differences that were significant (P≤0.05) as when compared with the untreated group.

Table (2): the activity of liver enzymes in studied groups

Groups	AST (IU/L)	ALT (IU/L)	ALP (IU/L)
G1	47.40±8.46 c	67.0 ± 8.98 b	56.67 ± 5.99 b
G2	71.72 ± 8.08b	58.98 ± 7.34 c	46.98±7.72 b
G3	77.12±7.24 b	73.98 ± 8.32 b	74.44±6.12 a
G4	96.63± 8.08 a	92.83± 6.90 a	86.75 ± 8.23 a
G5	58.53±6.19 c	55.69± 6.22 c	52.77± 8. 23 b
G6	42.70±9.12 c	57.66 ±4.4 c	41.49±7.01 b
G7	90.52 ±8.89 a	86.63±5.38 a	64.58±6.18 c
P- value	0.05 *	0.05 *	0.01**

According to our research, ibuprofen administration for 15 to 30 days significantly raised the serum levels of liver function indicators like ALT, AST, and ALP, which were signs of hepatotoxicity, as compared to the control group. Serum enzyme concentrations in the Ibuprofen-using groups rose in the current study; this could be due to hepatotoxicity (21,22). The increase in these enzymes in the blood is a sign of ibuprofen toxicity and potential hepatocellular damage that may be caused by changes in liver function. These results support the findings of the earlier study by Garba et al. (23), which found that rats administered with 100 mg/kg of ibuprofen had significantly higher plasma ALT and AST activity. In their study, Aprioku et al. (24) found that ibuprofen increased serum levels of alkaline phosphatase (ALP) and alanine transaminase (ALT), indicating cellular damage to the liver. According to Kim et al. (25), giving rats a high-fat diet for eight weeks could lower their hepatic MDA levels as well as their ALT, AST, TC, TG, and LDL-C levels. Additionally, ginseng enhanced the hepatic SOD, CAT, and GSH-Px activities as well as the HDL-C level brought on by a high-fat diet. These findings showed that ginseng enhanced antioxidant activity, changed lipid profiles, and inhibited lipid peroxidation.

Oxidative stress

Table (3) showed the levels of some oxidative stress in male rats and in all study groups. MDA levels in Ibuprofen (30 days) group (25671 ± 1524) showed significant (P≤0.05) reduced compared to the control group (31266 ± 2524). while, in the treated groups and ginseng group (25665±1948) showed significant (P≤0.05) reduced compared to the control group. The SOD levels in Ibuprofen (30 days) group (15.113 ±0.742) revealed differences that were non-significant

(P≤0.05) as when compared with the untreated group (17.043 ±1.403). while, in the treated groups and ginseng group (15.630 ± 2.559) revealed differences that were non-significant (P≤0.05) as when compared with the untreated group.

Table (3): the oxidative stress in studied groups

Groups	MDA (µmol / L)	SOD (IU/L)
G1	31266 ± 2524 a	17.043 ±1.403 a
G2	27494 ±1249 b	16.970 ±1.544 a
G3	27538 ±1015 b	16.306 ±1.253 a
G4	25671 ± 1524 c	15.113 ±0.742 a
G5	25665 ± 1948 c	15.630 ± 2.559 a
G6	26052 ±1402 bc	15.180 ±1.982 a
G7	25586 ± 2324 c	14.136 ± 2.539 a
P- value	0.05 *	0.05 *

Same letters mean there are non-significant (P≤0.05) differences. Where, different letters mean there are significant (P≤0.05) differences.

According to the results of this study, mice treated with the NSAID Ibuprofen had an antioxidant effect when compared to the stress control group. It has been shown that ibuprofen prevents animals from experiencing oxidative stress brought on by chemicals. Ibuprofen's preventive action against ROS has likely been ascribed to its capacity to first suppress inflammation and then oxidation. Ibuprofen's nonspecific suppression of cyclooxygenase-2 is thought to be the cause of its anti-inflammatory and antioxidant properties (26). Ginseng reduced biomarkers of oxidative stress in this study by reducing oxidative stress biomarkers, that found in the study of Sun et al., (27) who referred that the administration of ginseng leads to reduced biomarkers of oxidative stress and free radical. Faghani et al., (29) referred that the ginseng treatment showed a reduction in tissue MDA levels and an increase in SOD compared to the nicotine group. The numerous active components in the plant extract are what give ginseng its health advantages. Numerous active components, including as ginsenosides, ginseng peptides, ginseng polysaccharides, and others, have been found in ginseng, according to recent studies. Among them, ginsenosides are significant active components in ginseng's physiological action, which affects the immunological, cardiovascular, and neurological systems and makes ginseng a significant antioxidant (29). In rats given alloxan, ginseng lowers free radicals, improves the action of antioxidants, and protects oxidative damage (30).

Conclusions

Its concluded that the alcoholic extract of ginseng roots shows a protective and therapeutic effect liver enzymes and its act as antioxidant regents.

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