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REVIEW

PANAX GINSENG C.A. MEY. AS POTENTIAL RAW MATERIAL IN TREATMENT OF NEGATIVE EFFECTS OF ALCOHOL CONSUMPTION

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Abstract: An alcohol hangover is a complex set of adverse symptoms that occur after excessive consumption of alcoholic beverages. Hangovers are not solely caused by ethanol, but mainly by its toxic metabolites, such as acetaldehyde and acetic acid. Most of the negative symptoms occur when the concentration of alcohol in the blood decreases after drinking. Given that a large percentage of people consume alcohol and experience negative effects from its consumption, potential supplementation to help eliminate these adverse effects has been proposed. One promising ingredient is ginseng, which has been used in Eastern culture and traditional Chinese medicine for over 2,000 years. The aim of this study was to present the potential of *Panax ginseng* C.A. Mey. as an aid for the adverse effects of alcohol consumption and its protective effect on liver function. The literature analysis was based on data indexed in the medical databases PubMed, Scopus, and Medline since 2010, using keywords such as Panax ginseng, hangover, alcohol consumption, and metabolism, connected by the logical conjunction and. The analysis confirmed the effectiveness of *P. ginseng* in the treatment and prevention of hangovers. Preparations containing *P. ginseng* can support ethanol metabolism by inducing enzymes such as alcohol dehydrogenase, aldehyde dehydrogenase, and the cytochrome P450 isoform 2E1 system. An additional advantage of using *P. ginseng* may be its hepatoprotective effects.

Keywords: *Panax ginseng*, hangover, acetaldehyde, ethanol.

Natural products, such as traditional herbs, fruits, and vegetables, have garnered considerable interest as potential dietary supplements or medicinal products for preventing and treating issues stemming from excessive alcohol consumption. The scientific literature points to many plant species and isolated compounds from plants that can be used as potential remedies for the symptoms associated with alcohol consumption (1, 2).

One such plant is kudzu (*Pueraria montana* var. *lobata* (Willd.)), and compounds derived from dried roots, particularly puerarin, show promise in the treatment of alcohol use disorders (3). Other potential remedies for alcohol hangover symptoms include fructus evodiae from *Tetradium ruticarpum* (A. Juss.) T.G. Hartley, *Hovenia dulcis* Thunb., mango (*Mangifera indica* L.), and persimmon (*Diospyros kaki* Thunb.) (1, 4).

A plant such as thyme (*Thymus vulgaris* L.) was shown to have hepatoprotective effects (5) similar to silymarin (6), and dihydromyricetin, a flavonoid found in *Hovenia dulcis* (7), supported liver regeneration. *Hypericum perforatum* L. (8), *Salvia miltiorrhiza* Bunge (9), and *Scutellaria baicalensis* Georgi (10) also showed potential usefulness in reducing the effects of alcohol consumption. Ginger (*Zingiber officinale* Roscoe), ibogaine (*Tabernanthe iboga* H. Bn.), evening primrose (*Oenothera biennis* L.), prickly pear fruit (*Opuntia ficus indica* (L.) Mill.), purple passionflower (*Passiflora incarnata* L.), *Asparagus officinalis* L., *Oenanthe javanica* (Blume) DC., and *Opuntia ficus-indica* (L.) Mill.

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(pear cactus) were also mentioned as potentially effective in reducing the negative effects of alcohol consumption (2).

In turn, *Panax ginseng* C.A. Mey (Araliaceae) is a plant known for its potential health benefits and boasts a rich history of traditional use in various medicinal systems, which may encompass all of the abovementioned properties, including the ability to reduce the effects of alcohol consumption.

Aim of the Study and Data Search Strategy

Therefore, the aim of this work was to present the potential of *P. ginseng* C.A. Mey. as an aid in treating the negative effects after drinking alcohol and its protective effects on liver function, mainly related to the alcohol consumption. The analysis of the literature data was based on the world literature indexed in medical databases PubMed, Scopus, and Medline since 2010, using keywords such as: Panax ginseng, hangover, alcohol consumption, and metabolism. The starting point for the literature selection was the phrase alcohol and hangover. However, due to obtaining only three results in the PubMed database, the search was extended to include the phrase Panax ginseng and alcohol consumption, and papers with a reference to alcohol consumption in the title were selected. Additionally, phrases such as Panax ginseng and metabolism were included to find a relationship between alcohol metabolism and *P. ginseng*. Furthermore, the query Panax ginseng and liver injury were used to determine or exclude the regenerative effect of *P. ginseng* on liver damage.

History and Origin of *Panax ginseng* C.A. Mey.

The first mention of the healing effects of *Panax ginseng* C.A. Mey. (*Araliaceae*) dates back to about 5,000 years ago and it was associated with the geographical region of the Manchurian Mountains in China (11). *P. ginseng* is a herbaceous perennial cultivated in Northeast China, South Korea, North Korea, and Japan. This plant has occupied an essential place in traditional Chinese medicine for over 2,000 years and is defined as a remedy with revitalizing and energy-enhancing properties (11–13). In the past, the value of this raw material was evidenced by a high price comparable to the price of gold (14). The name "*Panax*" results from the wide medicinal use and is also related to Greek mythology, where the raw material was associated with the goddess Panakia (*Panákεia*), the daughter of the god of medicine—Asclepius. The name of the plant was additionally popularized by Carl Linnaeus, who described it as a "remedy for everything" which in Latin translates to panacea (11).

Species Classification of *P. ginseng* C.A. Mey.

Originally, the name of the Asian species was *Panax schin-seng*. It was systematized by the botanist C.A. Meyer, who gave the current name *Panax ginseng* C.A. Mey. (14). Both the *Ginseng radix root* (14) and *Ginseng folium leaf* (15) are used in medicine. The fresh raw material is relatively easily oxidized at room temperature. Therefore, to inhibit this process, it is subjected to thermal treatment and drying. Depending on the method of processing the raw material, we distinguish red and white ginseng. Sun-dried ginseng immediately after harvesting is called white, while red ginseng is steamed and then dried (16). Red ginseng shows more beneficial biological effects while showing fewer side effects compared to fresh and white ginseng. Heat treatment significantly affects the phytochemical composition, increasing the content of ginsenosides in red ginseng.

Ginseng Root as Pharmacopoeial Raw Material

Ginseng root is a pharmacopoeial raw material according to the FP XII (17). The content of ginsenosides must not be less than 0.40% of the combined sum of ginsenosides Rg1 ($C_{42}H_{72}O_{14}$) and Rb1($C_{54}H_{92}O_{23}$) in the dried plant material.

The Pharmacopoeia of the People's Republic of China (PPRC) contains two separate monographs that detail the requirements and handling of ginseng root. The first concerns the unprocessed raw material, *Ginseng Radix et Rhizoma*, Renshen PPRC 2015: "Ginseng is the dried root of *Panax ginseng* C. A. Mey. (Fam. Araliaceae). The drug derived from the cultivated form is known as *Yuanshenv* (garden ginseng), and the drug derived from the wild origin is known as *Linxia Shanshen* (Zihai). The drug is collected in autumn and washed clean, and its assay must contain not less than 0.27% of the total amount of ginsenoside Rg1 ($C_{42}H_{72}O_{14}$) and ginsenoside Re ($C_{48}H_{82}O_{18}$), and not less than 0.18% of ginsenoside Rb1($C_{54}H_{92}O_{23}$), following the method for the crude drug" (15).

The second monograph describes the method of stabilization mentioned above and includes the description, *Ginseng radix et rhizoma rubra*, Red ginseng, Hongshen: "Red Ginseng is the steamed and dried root of the cultivar of *Panax ginseng* C.A. Mey. (Fam. *Araliaceae*). The drug is collected in autumn, washed clean, steamed, and dried, and its

assay must contain not less than 0.25% of the total amount of ginsenoside Rg1 ($C_{42}H_{72}O_{14}$), ginsenoside Re ($C_{48}H_{82}O_{18}$), and not less than 0.20% of ginsenoside Rb1($C_{54}H_{92}O_{23}$), calculated with reference to the dried drug" (15). According to PPRC (15), the dosage of both substances is 3-9 g in the form of a separate decoction. "Administration and dosage: 3-9 g. Decocted separately and added into decoction; or ground into powder for oral administration. 2 g per time, twice a day."

P. ginseng Root Phytochemistry

The main compounds isolated from *P. ginseng* root are triterpene saponins, called ginsenosides (18). Ginsenosides are glycosides whose main aglycones are derivatives of the dammarane type—including protopanaxadiol and protopanaxatriol—as well as the oleanane type—such as oleanolic acid—and the ocotillol type (14, 19). The sugar part of ginsenosides consists of one or more sugar chains, made of hexoses (glucose, galactose), 6-deoxyhexoses (furanose, rhamnose), pentoses (arabinose, xylose), or uronic acids (glucuronic acid) (14, 20). The percentage of ginsenosides varies depending on how the root is processed. Thermal treatment increases the content of ginsenosides in red ginseng due to the inactivation of enzymes present in the raw material (16).

In addition, *P. ginseng* root contains polyacetylenes, fatty acids, essential oils, and phenolic compounds including flavonoids, vitamins, and minerals (13, 18). Polyacetylenes in *P. ginseng* root include diacetylene alcohol and triacetylene alcohol (13). Fatty acids are an important component because they have a wide range of healing properties and are synthetic precursors of important biological substances, including hormones. *P. ginseng* mainly contains unsaturated fatty acids, and the largest percentage is

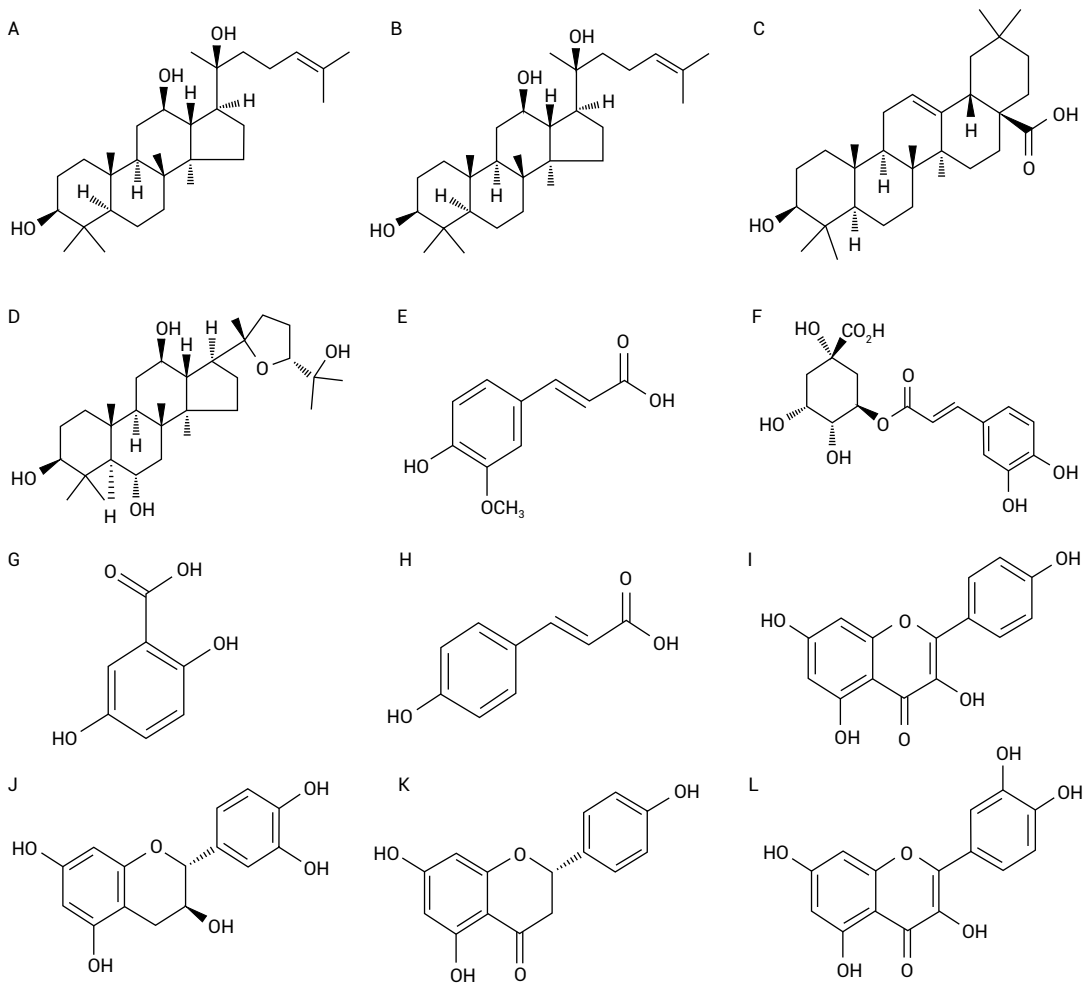

Figure 1. Chemical structure of selected active compounds present in *Panax ginseng* C.A. Mey.: (20S)-protopanaxadiol (A), 20(R)-protopanaxatriol (B), oleanolic acid (C), 20(S),24(R)-ocotillol (D), ferulic acid (E), chlorogenic acid (F), gentisic acid (G), p-coumaric acid (H), kaempferol (I), (-)-catechin (J), naringenin (K), quercetin (L).

linoleic acid (21). After thermal treatment, the content of linoleic acid increases to 62–65% (19, 21). Other unsaturated fatty acids presented in *P. ginseng* root are oleic acid and linolenic acid. The root also contains saturated acids such as pentadecanoic acid, palmitic acid, stearic acid (19, 21). The volatile essential oil found in *P. ginseng* root contains mainly sesquiterpenoids as well as *n*-hexadecanoic acid and falcarinol (13).

P. ginseng root also contains protein amino acids such as glutamic acid, aspartic acid, arginine, glycine, leucine, alanine, proline, lysine, serine, threonine, tyrosine, isoleucine, phenylalanine, and tryptophan. An important role is played by phenolic compounds, among which we distinguish phenolic acids, such as ferulic acid, chlorogenic acid, gentisic acid, and *p*- and *m*-coumaric acid (22). Among the flavonoids, the following can be distinguished: kaempferol, catechin, epicatechin, naringenin, myricetin, and quercetin (23). Vitamins present in *P. ginseng* root include vitamins B_1, B_2, B_3, B_5, and B_{12}, as well as choline; while minerals include trace amounts of elements such as zinc, copper, calcium, iron, magnesium, potassium, sodium, and phosphorus (11). The chemical structures of selected active compounds present in *P. ginseng* are depicted in Figure 1.

Pharmacological Activity of *P. ginseng*

The pharmacological activity of *P. ginseng* is attributed to its phytochemical composition, which correlates with its medicinal properties. *P. ginseng* contains ginsenosides that exhibit anticancer (24–26), antidiabetic (27–29), anti-inflammatory, antifatigue (30, 31), and anti-stress (18, 32) effects. The anti-fatigue and anti-stress properties are particularly significant from a marketing perspective, which is why *P. ginseng* is referred to as an adaptogenic plant. Phenolic compounds including flavonoids are associated with antioxidant (33), anti-inflammatory (34–36), and anticancer (18, 37, 38) effects. Furthermore, *P. ginseng* has been shown to strengthen the immune system (39), improve cognitive functions (40, 41), and enhance sexual function (42). The current research is also exploring the hepatoprotective effect of *P. ginseng* and its potential in the treatment of hangovers (43).

Additionally, it is worth mentioning the Traditional Chinese Medicine indications found in the Pharmacopoeia (15): "Actions and indications to tonify the original qi greatly, resume pulse, secure collapse, tonify spleen, replenish kidney, engender fluid, nourish the blood, tranquilize the mind, and replenish wisdom."

Searching for a Hangover Cure

In survey research, Mackus et al. (44) suggest that 69.9% of participants expressed their willingness to purchase a hangover cure if it were available, while 8.1% answered negatively, stating that they would not buy such a product. Additionally, 22.1% of respondents were unsure or did not have a clear opinion. Surprisingly, only 13.4% indicated that using such a remedy would lead to increased alcohol consumption. The majority of participants (71.6%) claimed that it would not influence their alcohol intake, and 15.1% were uncertain. Consequently, this review aimed solely to highlight the potential benefits of *P. ginseng* in alleviating hangover symptoms. However, it is crucial to emphasize that alcohol consumption should not be encouraged or promoted. The availability of a hangover cure should not be seen as a justification for or encouragement of unhealthy alcohol consumption.

Hangover

Definition of Hangover

A hangover is a collection of adverse physical and mental symptoms that occur after episodic excessive alcohol consumption. It is commonly referred to as an alcoholic hangover. The symptoms of alcohol intoxication manifest when the concentration of ethanol in the blood serum is close to zero (45).

Hangover Symptoms

The most commonly reported hangover symptoms include drowsiness, difficulty concentrating, excessive excitability, dizziness, memory impairment, dry mouth, profuse sweating, and gastrointestinal complaints such as diarrhea, nausea, vomiting, and abdominal pain (46). However, due to individual differences among respondents, research on the course of hangover and its treatment does not provide consistent results. Significant variations include sex, as the severity of hangover symptoms differs between women and men (47); age, with older individuals experiencing less severe hangovers (48); genetic factors, as individuals with a mutation in the aldehyde dehydrogenase (ALDH) gene experience more severe hangover symptoms (49); and nutrition and adequate hydration may also play a role (50). A hangover may result from dehydration, an immune system response to ethanol (involving pro-inflammatory cytokines), and the toxic effects of alcohol and its metabolites on the liver (51).

Alcohol Metabolism

Orally ingested ethanol is absorbed from the gastrointestinal tract into the bloodstream and

transported to the liver. Alcohol metabolism in the liver involves the conversion of ethanol to acetaldehyde by alcohol dehydrogenase (ADH), followed by the conversion of acetaldehyde to acetic acid by ALDH. The resulting acetic acid is transported via the bloodstream to peripheral tissues, where it is converted to acetyl coenzyme A (CoA), a key metabolite of the Krebs cycle (50). However, with frequent and long-term consumption of large amounts of alcohol, the ADH and ALDH pathway becomes insufficient. The microsomal alcohol oxidation system (MEOS) is then responsible for the oxidation of ethanol to acetaldehyde, which is based on the action of the CYP2E1 isoenzyme, belonging to the cytochrome P450 system, and the catalase system.

The use of MEOS in alcohol metabolism generates free radicals, including the superoxide radical and hydrogen peroxide, as well as reactive oxygen species (ROS), which contribute to increased oxidative stress in hepatocytes, leading to liver damage and severe hangover symptoms (50, 52). Additionally, the use of the MEOS system in ethanol metabolism may result in the depletion of the glutathione pool, which is important in the elimination of pharmaceuticals and environmental factors through coupling reactions in the metabolism stage (53). The non-oxidative pathway results in the formation of metabolites such as ethyl glucuronide, ethyl sulfate, fatty acid ethyl ester, and phosphatidyl ethanol, which are markers of chronic ethanol consumption (54–56).

Body's Immune Response to Ethanol

The body's immune response to ethanol can also contribute to the development of hangover symptoms. Following alcohol consumption, there is an increase in the levels of pro-inflammatory cytokines, such as interleukin-6 (IL-6), interleukin-1β (IL-1β), and tumor necrosis factor (TNF-α), as well as a high level of C-reactive protein (CRP). This increase in pro-inflammatory cytokines indicates an inflammatory response to ethanol and alcohol-induced oxidative stress (57, 58). These immune changes are important because the overproduction of pro-inflammatory cytokines can negatively affect the hippocampus and result in central nervous system symptoms during a hangover, such as drowsiness, loss of concentration, and memory impairment (49).

Given the large percentage of people who consume alcohol and experience negative hangover symptoms, it is important to consider supplementation that may help eliminate ethanol and its harmful metabolites more quickly, and therefore reduce the adverse effects of alcohol consumption (59).

***P. ginseng* in Preventing Severe Hangover Symptoms**

P. ginseng has documented health-promoting properties, but its effects on the treatment of hangovers are not the subject of many studies. The available literature data (43, 49, 60–63) suggest a beneficial effect of *P. ginseng* in treating the negative effects after drinking alcohol. Roberts' literature review (63) evaluated a total of 21 studies and found that, when compared to placebo, the individual studies demonstrated a statistically significant reduction in the mean percentage of overall hangover symptom scores for several substances. These substances included clove extract (42.5% vs. 19.0%, $p < 0.001$), tolfenamic acid (84.0% vs. 50.0%, $p < 0.001$), pyritinol (34.1% vs. 16.2%, $p < 0.01$), *Hovenia dulcis* fruit extract ($p = 0.029$), L-cysteine ($p = 0.043$), red ginseng root (21.1% vs. 14.0%, $p < 0.05$), and Korean pear juice (41.5% vs. 33.3%, $p < 0.05$). However, it is important to note that the available evidence of efficacy is of very low quality.

Study of the Influence of *P. ginseng* Sprouts on Liver Marker Activity

Je J. et al. (2021) (43) conducted a study using a mouse model and divided the research area into three groups. Unfermented (SG) and fermented (FSG) ginseng sprouts were administered orally one hour before intraperitoneal injection of ethanol (EtOH) at a dose of 1.5 g/kg. Ginseng was administered at the following doses: 10 mL/kg SG + 1.5 g/kg EtOH; 2.5 mL/kg FSG + 1.5 g/kg EtOH; 10 mL/kg FSG + 1.5 g/kg EtOH; and placebo water + 1.5 g/kg EtOH. The mice were sacrificed after six hours, and blood was drawn to measure plasma alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels. The results showed that FSG reduced ALT and AST activity in plasma compared to the control group ($p < 0.05$) and the water + ethanol group ($p < 0.05$) (43).

Study of the Effects of *P. ginseng* Sprouts on Plasma Ethanol and Acetaldehyde Concentrations

In the same study (43), vehicle, SG, and FSG sprouts were orally administered one hour prior to intraperitoneal injection of ethanol (1.5 g/kg) or (4.5 g/kg). Mice were sacrificed one hour, three hours, and six hours after sample administration, and blood ethanol and acetaldehyde levels were measured ($p < 0.05$ vs. control, $p < 0.05$ vs. water + ethanol).

The administration of SG and FSG reduced the ethanol and acetaldehyde concentrations in the blood of mice injected with ethanol (43).

Examination of the Activity of Alcohol Dehydrogenase and Aldehyde Dehydrogenase Expression after Administration of *P. ginseng* Sprouts

In the same study (43), vehicle, SG, and FSG sprouts were orally administered one hour prior to intraperitoneal injection of ethanol (1.5 g/kg). Mice were sacrificed one hour, three hours, and six hours after sample administration. The study used PCR to determine the level of dehydrogenase mRNA expression ($p < 0.05$ compared to control, $p < 0.05$ compared to water + ethanol). The results showed that SG and FSG increased the activity and expression of alcohol and aldehyde dehydrogenase genes, with an approximately 30-fold increase in the activity and expression of dehydrogenases after the administration of the samples containing the ginseng extracts compared to the placebo sample (43).

Study of the Antioxidant Activity of *P. ginseng* Sprouts using DPPH, Hydroxyl Radicals and ABTS

The antioxidant activity of SG and FSG extracts was determined using various methods *in vitro*, including 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), and hydroxyl radicals. First, the free radical levels were determined using DPPH in the presence of SG or FSG extract by monitoring the discoloration of the DPPH solution, which reflects the antioxidant activity of the extracts. Subsequently, the levels of ABTS radicals were monitored spectroscopically in the presence of SG or FSG extracts by converting ABTS to a colorless product after reaction with the antioxidants contained in the extracts. Finally, the scavenging activity of hydroxyl free radicals was determined. The results showed that FSG had a strong antioxidant effect, which was enhanced during the fermentation process (43).

Effect of Red *P. ginseng* Extract on Ethanol Concentration in Exhaled Air

The study by Lee MH, et al. (2014) (60) investigated the effect of a red ginseng drink on the content of ethanol in exhaled air. The study was conducted on 25 men in a randomized crossover design. The subjects were given 100 mL of whiskey (40% alcohol) and 100 mL of either water or 100 mL of a red ginseng drink with a concentration of 0.321 mg mL^{-1}. The study found that the concentration of ethanol in exhaled air decreased after 30 and 60 minutes (60, 63).

Active Substances Present in *P. ginseng* and Their Effect on Antioxidant Properties

The active substances present in *P. ginseng* that are responsible for its antioxidant effect include ginsenosides, polyphenols including flavonoids, and various other phytochemical compounds. These compounds have been shown to possess strong antioxidant properties, which help in neutralizing free radicals and reducing oxidative stress in the body. The presence of ginsenosides and the antioxidant properties of ginseng have been studied extensively. Gas chromatography coupled with a mass detector (GC/MS) analysis of *P. ginseng* berries devoid of ginsenosides in the process of steaming and drying has revealed the presence of linoleic acid (34.66%), methyl linoleate (34.10%), and palmitic acid (30.00%) (61), which have been found to have antioxidant properties by reducing the amount of free radicals.

Ethanol metabolism generates large amounts of ROS through cytochrome 2E1, which can be cytotoxic and cause oxidative damage to hepatocytes, leading to hangover symptoms (49). Antioxidant substances can eliminate ROS, protecting liver cells and minimizing the adverse effects of a hangover. It is suggested that ginsenosides are not responsible for the anti-hangover effect, and the component responsible for the main effect may be linoleic acid (61). Furthermore, the study by Choi et al. (62) indicated that during the fermentation process of *P. ginseng* berries, there is an increase in the concentration of chlorogenic acid and 3,4-dihydroxybenzoic acid, both of which possess antioxidant properties. Additionally, the content of ginsenosides, specifically Rh1 and Rg2, also increases. These ginsenosides have the potential to act as antioxidants. Through the process of fermentation, ginsenosides Rg3 and Rh2 undergo conversion, resulting in the formation of substances that exhibit a protective effect against oxidative damage induced by alcohol.

Reduction of the Negative Symptoms of a Hangover and the Long-Term Effects of Alcohol Exposure

A study was conducted on 25 men who were given 100 mL of a 40% alcoholic beverage (whiskey). In addition, they were given 100 mL of either a red ginseng root drink or plain water. The study found that symptoms of central nervous system

distress during alcohol intoxication—such as fatigue, difficulty concentrating, headache, dizziness, memory loss, and drowsiness—improved after the administration of *P. ginseng*-based preparations. Furthermore, gastrointestinal symptoms—such as vomiting, nausea, loss of appetite, abdominal pain, and diarrhea—also improved with *P. ginseng*-based preparations. The participants reported an overall improvement in their well-being and a reduction in feelings of thirst. However, symptoms such as palpitations, tremors, depression, anxiety, and increased sweating did not improve with *P. ginseng*-based preparations (49, 60).

Additionally, ginseng can also alleviate the symptoms of alcohol abuse. Alcohol consumption has been known to impair psychomotor and cognitive functions, particularly affecting the hippocampus, which plays a crucial role in these processes. Ginsenoside Rg1—a key active ingredient found in *P. ginseng* C.A. Mey., a traditional tonic medicine—has been utilized for the treatment of cognitive deficits (64).

In the study conducted by Huang et al. (65), male ICR (CD-1) mice were subjected to consecutive intragastric administration of 20% (w/v) alcohol for 21 days. Following this, behavioral tests were conducted to assess the psychomotor and cognitive deficits induced by repeated alcohol exposure. The results of the study indicated that Rg1, when administered at an optimal dose of 6 mg/kg, exhibited potential to mitigate the effects of repeated alcohol consumption.

Hepatoprotective Properties of *P. ginseng*

Ethyl Alcohol Hepatotoxicity

Ethanol (ethyl alcohol) can be toxic to the liver. Since the liver is the primary organ responsible for ethanol metabolism, it is particularly susceptible to the harmful effects of alcohol. Therefore, the negative impact on this organ should be considered when consuming alcohol. Alcohol-induced liver diseases include alcoholic fatty liver disease, alcoholic hepatitis, cirrhosis, and liver cancer (66–68). To prevent these conditions, it is recommended to take preventive measures such as hepatoprotective measures and the reduction of hangover symptoms (62, 69).

Mechanism of Liver Damage

The by-products of ethyl alcohol metabolism and its metabolites can cause liver damage through several mechanisms. Acetaldehyde, the basic metabolic product, is the most harmful to the liver (70). Acetaldehyde can bind to DNA, leading to numerous mutations that may contribute to the initiation of carcinogenic processes. Moreover, acetaldehyde can combine with albumins, inducing oxidative stress. Protein adducts of acetaldehyde may also increase lipid accumulation, leading to inflammation and liver fibrosis (71).

Excessive alcohol consumption disrupts the intestinal barrier, leading to the release of lipopolysaccharides (LPS) into the circulation. Acetaldehyde and LPS activate macrophages present in the liver, leading to the release of ROS and cytokines. The level of pro-inflammatory cytokines increases, including TNF-α, IL-1β, and IL-6, which induce the destruction of hepatocytes with the participation of neutrophils. Additionally, this process is favored by an increased amount of ROS (72, 73).

Effect of *Panax ginseng* on Liver Function

The effects of ginseng extracts on supporting the regeneration of liver cells have been demonstrated not only in relation to alcohol (62) but also with other substances such as cyclophosphamide, acetaminophen, and D-galactosamine (62, 74–77). *P. ginseng* owes its hepatoprotective properties to the presence of ginsenosides (74, 75). An important compound in the protection of the liver is 20(R)-ginsenoside Rg3 (20(R)-Rg3), as its administration inhibits the depletion of glutathione (GSH) and overexpression of cytochrome P450 (CYP2E1) (76). *In vitro* studies have also shown positive effects of ginsenoside Rg1, which reduces the concentration of cytokines associated with inflammation, including TNF-α, IL-1β, and IL-6. Additionally, ginsenoside Rg1 increases the liver's detoxification capacity by activating the Nrf2 signaling pathway (nuclear factor erythroid 2-related factor 2) (78).

In the aforementioned studies, *P. ginseng* showed a hepatoprotective effect, as evidenced by the reduction of the concentration of liver damage markers. The liver markers include AST, ALT, and ALP (alkaline phosphatase), whose concentrations also increase as a result of the toxic effects of alcohol (79). The publications cited above (except ((62)) do not relate directly to alcohol-induced liver damage but show the hepatoprotective potential of preparations based on *P. ginseng.* The role of plant material derived from *P. ginseng* in the context of alcoholic liver damage has also been the subject of several studies.

The purpose of the Liu et al. study (80) was to examine the effects and underlying mechanisms of ginseng oligopeptides (GOPs) on alcohol-induced liver damage in rats caused by binge drinking. They

revealed that treatment with GOPs significantly improved levels of serum ALT and AST, plasma lipopolysaccharide (LPS), inflammatory cytokines, and oxidative stress markers that were affected by alcohol consumption. The results suggest that GOPs possess a significant protective effect against liver injury induced by binge drinking. The underlying mechanism may involve partial inhibition of the lipopolysaccharide-TLR4-NF-κB p65 signaling pathway in the liver.

Choi et al. (62) conducted a study that demonstrated the protective effect of ginseng berry kombucha in ethanol-induced liver damage. The study indicated that the kombucha formulation, when administered collectively, regulated the Nrf2/Keap1 pathway, thereby exerting a protective effect.

According to Han et al. (81), the administration of Korean red ginseng extract to mice resulted in the inhibition of CYP2E1 induction caused by chronic alcohol consumption and prevented fat accumulation in the liver. The authors suggested that the components of ginsenosides inhibit alcoholic steatosis and liver injury, indicating that *P. ginseng* may possess the potential to be used in the treatment of alcoholic liver disease. Lee et al. (82), in their study, obtained similar results to the aforementioned findings and further suggested that Korean red ginseng may have the potential to alleviate the effects of alcoholic fatty liver disease. These reports were also confirmed by Fan et al. (83).

Therefore, determining the optimal dosage and duration of ginseng supplementation for liver regeneration requires further investigation.

CONCLUSIONS

The available data suggest that *P. ginseng* (especially fermented and unfermented sprouts, extracts of red ginseng root and berries) relieves most symptoms of an alcoholic hangover and supports liver regeneration. Additionally, it may be beneficial in mitigating the effects of alcohol-induced liver damage. Preparations based on *P. ginseng* have an inducing effect on alcohol and aldehyde dehydrogenases, which correlates positively with reduced ethanol concentrations in the blood. A decrease in ethanol concentrations in exhaled air was also observed and a hepatoprotective effect has also been noticed. *P. ginseng* can play a significant role in reducing hangover symptoms and liver regeneration, thanks to its rich content of ginsenosides, flavonoids, phenolic acids, and unsaturated fatty acids.

However, the number of available studies on the reduction of hangover symptoms with *P. ginseng* is insufficient to draw clear conclusions, so more research is needed to prove the mechanism of its preventive action accurately.

While there may be potential benefits of *P. ginseng* in alleviating hangover symptoms, it is crucial to prioritize responsible drinking habits and avoid excessive alcohol consumption.

Conflicts of Interests

The authors declare no conflicts of interests.

REFERENCES

1. Wang F., Li Y., Zhang Y.J., Zhou Y., et al.: Molecules 21, 64 (2016).
2. Tomczyk M., Zovko-Koncić M., Chrostek L.: Nat. Prod. Commun. 7, 273 (2012).
3. Wang S., Zhang S., Wang S., et al.: Biomed. Pharmacother. 131, 110734 (2020).
4. Yu X., Wu D.Z., Yuan J.Y., et al.: Am. J. Chin. Med. 34, 1027 (2006).
5. Shati A.A., Elsaid F.G.: Food Chem. Toxicol. 47, 1945 (2009).
6. El-Newary S.A., Shaffie N.M., Omer E.A.: Asian Pac. J. Trop. Med. 10, 361 (2017).
7. Chen J., Wang X., Xia T., et al. Biomed. Pharmacother. 142, 111927 (2021).
8. Perfumi M., Mattioli L., Cucculelli M., Massi M.: J Psychopharmacol. 19, 448 (2005).
9. Nagappan A., Kim J.H., Jung D.Y., Jung M.H.: Int. J. Mol. Sci. 21, 265 (2019).
10. Dong Q., Chu F., Wu C., et al.: Mol. Med. Rep. 13, 3052 (2016).
11. Potenza M.A., Montagnani M., Santacroce L., et al.: J. Ginseng Res. 47, 359 (2023).
12. Todorova V., Ivanov K., Delattre C., et al.: Nutrients 13, 2861 (2021).
13. Liu H., Lu X., Hu Y., Fan X.: Pharmacol. Res. 161, 105263 (2020).
14. Wolski T., Ludwiczuk A., Baj T., et al.: Post. Fitoter. 9, 96 (2008).
15. Pharmacopoeia of the People's Republic of China: Vol. 1, pp. 216-219, English Edition, China Medical Science Press 2015.
16. Lee S.M., Bae B.S., Park H.W., et al.: J. Ginseng Res. 39, 384 (2015).
17. Pharmacopoea Polonica Editio XII. Volume 2. pp. 1674-1676. Urząd Rejestracji Produktów Leczniczych, Wyrobów Medycznych i Produktów Biobójczych, Warsaw 2020.

18. Zhang H., Abid S., Ahn J.C., et al.: Molecules 25, 2635 (2020).
19. Liu L., Xu F.R., Wang Y.Z.: J. Ethnopharmacol. 263, 112792 (2020).
20. Zhao B., Lv C., Lu J.: Int. J. Biol. Macromol. 133, 324 (2019).
21. Zhang X.J., Huang L.L., Cai X.J., et al.: Chem. Cent. 7, 12 (2013).
22. Chung I.M., Lim J.J., Ahn M.S., et al.: J. Ginseng Res. 40, 68 (2016).
23. Kim J.S.: Prev. Nutr. Food Sci. 21, 263 (2016).
24. Li X., Chu S., Lin M., et al.: Eur. J. Med. Chem. 203, 112627 (2020).
25. Wang C.Z., Anderson S., DU W., et al.: Chin. J. Nat. Med. 14, 7 (2016).
26. Zhang N., Fu J.N., Chou T.C.: Am. J. Cancer Res. 6, 97 (2016).
27. Liu Y., Zhang H., Dai X., et al.: Phytomedicine 92, 153717 (2021).
28. Bai L., Gao J., Wei F., et al.: Front. Pharmacol. 9, 423 (2018).
29. Zhou P., Xie W., He S., et al.: Cells 8, 204 (2019).
30. Yu Y., Nie J., Zhao B., et al.: J. Ethnopharmacol. 301, 115831 (2023).
31. Zhang G., Lu B.F., Wang E., et al.: Pharm. Biol. 61, 316 (2023).
32. Yang W.Z., Hu Y., Wu W.Y., et al.: Phytochemistry 106, 7 (2014).
33. Dyshlyuk L.S., Fotina N.V., Milentyeva I.S., et al.: Braz. J. Biol. 84, e256944 (2022).
34. Zhang M., Zhao J., Deng J., et al.: Food Funct. 10, 4124 (2019).
35. Im D.S.: Biomolecules 10, 444 (2020).
36. de Oliveira Zanuso B., de Oliveira dos Santos A.R., Miola V.F.B., et al.: Exp. Gerontol. 161, 111731 (2022).
37. Wang C.Z., Anderson S., Du W., et al.: Chin. J. Nat. Med. 14, 7 (2016).
38. Li X., Chu S., Lin M., et al.: Eur. J. Med. Chem. 203, 112627 (2020).
39. You L., Cha S., Kim M.Y., Cho J.Y.: J. Ginseng Res. 46, 711 (2022).
40. Carmichael O.T., Pillai S., Shankapal P., et al. J. Nutr. Health Aging. 22, 837 (2018).
41. Deng G., Wu C., Lin J., et al.: Zhong Yao Cai. 39, 1377 (2016).
42. Choi K.T.: Acta Pharmacol. Sin. 29, 1109 (2008).
43. Je J., Kim H., Park E.J., et al.: Am. J. Chin. Med. 49, 131 (2021).
44. Mackus M., Lantman M. van S., van de Loo A.J.A.E., et al.: Drug Sci, Policy Law. 3, 205032451774103 (2017).
45. van Schrojenstein Lantman M., van de Loo A.J.A.E., Mackus M., Verster J.C.: Curr. Drug Abuse Rev. 9, 148 (2016).
46. Verster J.C.: Alcohol Alcohol. 43, 124 (2008).
47. Van Lawick van Pabst A.E., Devenney L.E., Verster J.C.: J. Clin. Med. 8, 1308 (2019).
48. Verster J.C., Severeijns N.R., Sips A.S.M., et al.: Alcohol Alcohol. 56, 589 (2021).
49. Jayawardena R., Thejani T., Ranasinghe P., et al.: Hum. Psychopharmacol. 32, e2600 (2017).
50. Cederbaum A.I.: Clin. Liver Dis. 16, 667 (2012).
51. Wiese J.G., Shlipak M.G., Browner W.S.: Ann. Intern. Med. 132, 897 (2000).
52. Jiang Y., Zhang T., Kusumanchi P., et al.: Biomedicines 8, 50 (2020).
53. Bradford B.U., Rusyn I.: Alcohol 35, 13 (2005).
54. Heier C., Xie H., Zimmermann R.: IUBMB Life 68, 916 (2016).
55. Maenhout T.M., De Buyzere M.L., Delanghe J.R.: Clin. Chim. Acta 415, 322 (2013).
56. Laposata E.A., Lange L.G.: Science 231, 497 (1986).
57. van de Loo A.J.A.E., Mackus M., Kwon O., et al.: J. Clin. Med. 9, 2081 (2020).
58. van de Loo A.J.A.E., Raasveld S.J., Hogewoning A., et al.: Healthcare. 9, 395 (2021).
59. Mackus M., van de Loo A.J.A.E., Garssen J., et al.: Int. J. Environ. Res. Public Health. 17, 4324 (2020).
60. Lee M.H., Kwak J.H., Jeon G., et al.: Food Funct. 5, 528 (2014).
61. Ik Lee D., Tae Kim S., Hoon Lee D., et al.: J. Food Sci. 79, C1323 (2014).
62. Choi E.J., Kim H., Hong K.B., et al.: Antioxidants 12, 774 (2023).
63. Roberts E., Smith R., Hotopf M., Drummond C.: Addiction 117, 2157 (2022).
64. Lai Y., Tan Q., Xv S., et al.: Front. Pharmacol. 12, 616409 (2021).
65. Huang L., Peng Z., Lu C., et al.: Chin. Med. 15, 1 (2020).
66. Rocco A., Compare D., Angrisani D., et al.: World J. Gastroenterol. 20, 14652 (2014).
67. Schwartz J.M., Reinus J.F.: Clin. Liver Dis. 16, 659 (2012).
68. Zakhari S., Li T.K.: Hepatology 46, 2032 (2007).
69. Hyun J., Han J., Lee C., et al.: Int. J. Mol. Sci. 22, 5717 (2021).
70. Setshedi M., Wands J.R., de la Monte S.M.: Oxid. Med. Cell Longev. 3, 178 (2010).
71. Holstege A., Bedossa P., Poynard T., et al.: Hepatology 19, 367 (1994).

72. Ramaiah S.K., Jaeschke H.: Toxicol. Pathol. 35, 757 (2007).
73. Shen Z., Ajmo J.M., Rogers C.Q., et al.: Am. J. Physiol. Gastrointest. Liver Physiol. 296, G1047 (2009).
74. Abdelfattah-Hassan A., Shalaby S.I., Khater S.I., et al.: Complement Ther. Med. 46, 95 (2019).
75. Nam Y., Ko S.K., Sohn U.D.: J. Ginseng Res. 43, 606 (2019).
76. Zhou Y.D., Hou J.G., Liu W., et al.: Int. Immunopharmacol. 59, 21 (2018).
77. Jo Y.H., Lee H., Oh M.H., et al.: Nutr. Res. Pract. 14, 334 (2020).
78. Ning C., Gao X., Wang C., et al.: Environ. Toxicol. 33, 1050 (2018).
79. Li S., Zhang Y., Yang P., et al.: Molecules 26, 5456 (2021).
80. Liu R., Chen Q.H., Ren J.W., et al.: Nutrients 10, 1665 (2018).
81. Han J.Y., Lee S., Yang J.H., et al.: J. Ginseng Res. 39, 105 (2015).
82. Lee H.J., Ok H.M., Kwon O.: Molecules 20, 11604 (2015).
83. Fan J., Wang Y., You Y., et al. Food Funct. 10, 5566 (2019).