

Original Research Article

Metabolic and anti-obesity effects of *Panax ginseng* root extract in mice

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Abstract

Purpose: To determine the anti-obesity effect of *Panax ginseng* root extract and isolates.

Methods: Thirty Swiss albino mice, randomly divided into three groups of ten mice each, were used. Group 1 (E1) received sterilized crude aqueous ginseng extract (50 mg/kg/day), while Group 2 (E2) mice received sterilized saponin isolate (20 mg/kg/day) intravenously, for 30 days. Control group did not receive any treatment. Metabolic and obesity parameters evaluated include animal weight, insulin and leptin levels, which were determined using enzyme-linked immunosorbent assay (ELISA).

Results: After the 30-day monitoring period, there was a distinct trend in weight gain across groups. The control animals showed a linear upward increase, starting at 25 g and reaching 35 g at the end of the study ($p < 0.05$). On the other hand, groups 1 and 2 showed a significant decrease from 25 g to 19 g ($p < 0.05$). The E1 group showed a non-significant decline in the concentrations of insulin and leptin after treatment ($p > 0.05$). However, in the E2 group, both insulin and leptin levels decreased significantly ($p < 0.05$), revealing a relationship between increased metabolic activity and weight loss.

Conclusion: This study offers preliminary report that intravenous administration of crude aqueous ginseng extract leads directly to reduction in body weight and decreased circulating insulin and leptin levels in mice.

Keywords: Obesity, *Panax ginseng*, Crude ginseng extract, Saponins extract, Insulin, Leptin

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INTRODUCTION

Obesity is used to describe excess body fat that accumulates to the point at which it becomes damaging to the health of organs such as the heart, liver and kidneys [1]. Obesity has been linked to an increased risk of several illnesses, including type 2 diabetes. Although several factors are associated with obesity, such as diet, lifestyle, genetics, gut flora and microbiome, eating calorie-rich meals is believed to be the primary cause [1]. Several medications, including Lorcaserin, Orlistat, Phentermine, and

Topiramate, are available to treat obesity in addition to dieting and exercise. Regrettably, side effects such as fatigue, dizziness, and paresthesia, and rebound weight gain upon drug cessation are frequently associated with challenges in drug treatment for obesity [2]. Studies have reported that rats and mice are suitable models for exploring diet-induced obesity [3]. Maintaining energy balance depends on adipocytes, which also mediate a variety of processes related to vascular disorders, hunger management, and immunological responses [4]. Adipocyte control is essential for disease

prevention and health maintenance [4]. Alternative and complementary medicines, which have been utilized for a long time, are today gaining a lot of attention and generating interest all over the world.

Panax ginseng (Fam. Araliaceae) is commonly known as the ivy or *ginseng* family [5]. It is a perennial plant in the genus *Panax*, which is widely used in traditional medicine for its medicinal properties. Currently, studies have suggested that *Panax ginseng* leaf extract may have anti-obesity properties [6]. The primary ingredient in *ginseng* that gives it its diverse properties is ginsenosides. The two categories of dammarane-type ginsenosides are proto*Panaxadiol* (PPD) and proto*Panaxatriol* (PPT) kinds [7]. The quantity of hydroxyl groups that can be attached to sugar moieties through a dehydration reaction determines which groups are used. The gut microbiota has the ability to break down ginsenosides into a deglycosylated form. The degraded versions of PPD and PPT types, cK and Rh1 (or F1), are the only ginsenosides that may typically be absorbed into the bloodstream following oral ingestion [8]. The body mass index (BMI) is a commonly used parameter to assess an individual's body fat percentage. It is calculated as the proportion of weight in kilograms to height in meters squared (kg/m^2). In many groups, there is a correlation between the BMI and the risk of morbidity and mortality [9]. Numerous studies have demonstrated that *ginseng* decreases fat storage and adipocyte size in mice and rats given a high-fiber diet (HFD) [10,11]. Ginsenosides actually cause fat cells to activate their AMPK pathway. Ginsenosides suppress the production of triglycerides (TAGs) in cells and raise the amount of adenosine monophosphate-activated kinase (AMPK). Studies using the HFD model have shown that *ginseng* inhibits differentiation of fatty cells in the adipose tissue of rats and mice and has an anti-obesity effect [6]. In contrast, studies using diabetic mice have demonstrated that *ginseng* treatment increases PPAR γ expression, adipogenesis, and has effects similar to those of insulin [12]. Lipoprotein lipase (LPL) facilitates the removal of blood fats by releasing free fatty acids from circulating TAG-rich lipoprotein [9]. Additionally, ginsenosides raise insulin-induced LPL expression, although PPT-type ginsenosides produced inconsistent results. While *ginseng* therapy increases LPL expression in diabetic animals, it decreases it in HFD-fed mice [12]. It has been demonstrated that ginsenosides increase cells' absorption of glucose [13]. This study aims to assess the effectiveness of crude aqueous *ginseng* extract and saponin isolates for enhancing metabolic parameters and

encouraging weight loss in male Swiss albino mice over a period of thirty days. In order to clarify the endocrine consequences linked to *ginseng* supplementation, this study will also examine the regulation of insulin and leptin levels.

EXPERIMENTAL

Materials

Pure pharmaceutical-grade, dried *Panax ginseng* roots (Viet Loyal, Vietnam), diethyl ether (Roche, Germany), ethanol 70 % (AL-Hikmah, Jordan), n-butanol (Loba Chemie, India), distilled water (Pioneer, Iraq), normal saline 9 % (Pioneer, Iraq), and sodium hydroxide (P. Shale FZE, United Arab Emirates) were all used. An ELISA kit from Sunlong Biotech in China was used for the hormonal (leptin and insulin) analysis.

Preparation of crude *ginseng* extract

Dried *Panax ginseng* roots (100 g) were ground into a fine powder. The powdered *ginseng* was then suspended in 1,000 mL of distilled water and heated at 60 – 70 °C for two to three hours while being continuously stirred. To remove insoluble components, the mixture was filtered using Whatman filter paper once it had cooled to room temperature. To guarantee microbiological safety, the filtrate was further sterilized by being passed through a sterile syringe filter with a pore size of 0.22 μm . After filtering, sterile saline was added to the resulting solution to bring its osmolality down to physiological values (~300 mOsm/L). After that, diluted sodium hydroxide was used as needed to bring the pH down to about 7.4. Before being administered intravenously to animals, the extract was diluted to facilitate administration of a dosage of 12.5 mg/kg. This dilution ensures that the final injection solution has a dosage appropriate for mice [14]. The usual range for intravenous (IV) dosages is 50 – 150 mg/kg body weight. A dose of 50 mg/kg was chosen because studies on the weight-reducing potential of *ginseng* frequently utilize doses on the lower end of this spectrum (50 to 100 mg/kg) to evaluate the benefits without producing toxicity [15]. The finished extract solution was used within two weeks, and the produced extract was kept at -20 °C for long-term storage. Intravenous (IV) route in this study was intentionally selected as a pharmacological approach to ensure controlled systemic exposure and to avoid the variability related to gastrointestinal absorption, metabolism, and gut microbiota transformation of ginsenosides, which are known to significantly affect their bioavailability after oral administration.

Extraction of saponins from *ginseng*

To achieve effective recovery of bioactive components, the Soxhlet apparatus was used to extract saponins from *ginseng*. First, a mechanical grinder was used to grind the *ginseng* roots into a fine powder. To get rid of lipophilic contaminants, the powdered material (100 g) was processed by defatting with 1000 mL diethyl ether, corresponding to 1:10 w/v solid-to-solvent ratio, for four hours [16]. The dried *ginseng* powder was inserted into a cellulose thimble and put in the Soxhlet extractor after defatting. Ethanol (70 % v/v) was chosen as the extraction solvent for saponins. A continuous cycle of evaporation, condensation, and percolation was started by heating the solvent in the round-bottom flask. The procedure continued for eight hours, until the target compounds were exhausted and the solvent in the siphon tube became clear. A rotary evaporator was used to collect and concentrate the ethanol extract under low pressure in order to eliminate superfluous solvent and produce an extract that is high in saponins. The extract was dissolved in distilled water and then subjected to liquid-liquid partitioning with n-butanol in order to further purify it. The saponin-enriched aqueous phase was separated and concentrated. The resultant concentrated extract was dried at 40 °C in a vacuum oven until it reached a consistent weight. The dried saponin extract was kept at room temperature in an airtight container. To guarantee isotonicity and biocompatibility, the dried extract was reconstituted in sterile normal saline (0.9 % NaCl) for intravenous administration. After that, a 0.22 µm membrane filter was used to sterilize the mixture in order to get rid of particles and microbiological contaminants. Before being used, the final sterile saponin solution was kept in sterile, airtight vials at 4°C. The IV dose was carefully regulated based on body weight (10 to 50 mg/kg) to prevent toxicity, and the solution was vortexed before administration to guarantee homogeneity. In particular, because it has been linked to advantageous metabolic effects like enhanced fat metabolism, increased energy expenditure, and improved insulin sensitivity, which aid weight loss, a dose of about 20 to 30 mg/kg is frequently used in preclinical research to examine weight reduction effects [17]. In our investigation, we will employ a dose of 20 mg/kg.

Animals

Thirty male Swiss albino mice weighing between 25 and 30 g and aged between 7 and 8 weeks were employed in this investigation. The Center for Drug Control and Research of the Iraqi

Ministry of Health provided the mice. All animal care and protocols were carried out strictly in accordance with the AVMA 2020 recommendations [18] and the animal ethics rules established by Al-Bayan University's College of Pharmacy. The animals were housed at the Al-Bayan University animal care facility, which provided 40 % humidity, 12-hour light/dark cycles, and temperatures between 18 and 22 °C. Before the experiments, the animals were allowed a seven-day acclimatization period. They had unrestricted access to standard rodent food and water, and the facility was maintained with a well-ventilated environment, ensuring 100 % fresh air circulation.

Ethical consideration

The Research Ethical Committee of Al-Bayan University College of Pharmacy approved this study (approval no. ALBCOP/2024/651) in December 2024 in accordance with the American Veterinary Association's (AVMA) rules [18].

Study design

To assess each extract's effects on Swiss albino mice over a 30-day duration, three different groups of ten Swiss albino mice each were randomly selected: Control Group (Control): Mice in this group received no extract, only standard diet and care. Group 1 (E1): Mice in this group were administered the crude aqueous *ginseng* extract (50 mg/kg) once a day for 30 days. Group 2 (E2): Mice in this group received saponin extract at a daily dose of 20 mg/kg for 30 days.

Determination of the dose of crude aqueous *ginseng* extract

A target dose of 50 mg/kg body weight was selected. This dosage was selected to represent a range that is both biologically active and non-toxic, which is consistent with earlier findings of *ginseng*'s metabolic activity, especially in terms of lowering body weight, enhancing lipid metabolism, and modifying endocrine parameters like insulin and leptin levels [19].

A 12.5 mg/mL of crude aqueous *ginseng* extract solution was prepared by sterile filtering, osmolality correction (300 mOsm/L), and pH modification (to 7.4) for dosing and animal safety reasons. The dose was adjusted for each mouse individually according to the weight of the animal, to maintain the applied volumes under a safety limit recommended for IV administration in mice (100 – 200 µL) [20]. For a target dose of 50 mg/kg in a 30 g mouse, for example, to accumulate this in the body, it required 120 µL

of the 12.5 mg/mL solution. Nevertheless, 100 μ L was administered to a 25 g mouse.

According to the previous pilot data and the recommendation of tail vein injection, both pharmacological effects and animal welfare were considered when using this particular concentration and dosage. When planning, the oral or intraperitoneal routes were discarded in favor of the intravenous injection (IV) based on bioavailability considerations, as well as for bypassing the first pass metabolism, allowing direct systemic contact with bioactive crude extract. During the 30-day treatment period, this dose regimen allowed both extracts to exert their biological effects without overstepping toxicity limits or injection-associated problems.

Dose determination for saponin extract

Based on prior research that demonstrated advantageous metabolic effects at this dose, such as enhanced insulin sensitivity, lipid mobilization, and energy homeostasis, without causing systemic toxicity, the IV dose of 20 mg/kg body weight for the purified saponin extract derived from *Panax ginseng* was chosen [10]. A moderate dose of 20 mg/kg was deemed both pharmacologically active and safe since ginsenosides, the main bioactive saponins in *ginseng*, show strong effects at lower concentrations than crude extracts [6].

The reconstituted solution was made at a concentration of 5 mg/mL to enable exact volume-based administration depending on each animal's body weight for safe and accurate dosage. A 25 g mouse was given 100 μ L based on this concentration, whereas a 30 g mouse needed 120 μ L to reach the 20 mg/kg dose. This method ensured that all injected volumes were kept within the 200 μ L intravenous administration threshold, which was set for murine models [21].

Clinical observations and animal care

Throughout 30-day treatment, the mice's general state of health and behavior were closely observed. Regular checks were carried out to identify signs of fatigue, unusual activities, changes in fur, and loss or gain of appetite. Body weight was measured at intervals of 15 days, and any abnormal physical signs or toxicity signs were recorded. To detect metabolic variations, insulin and leptin concentrations were tested at baseline and at the end of the experiment in addition to these clinical evaluations.

Serum sample collection

On days 1, 15, and 30 of treatment, 1.0 ml of blood was withdrawn from the jugular veins of the mice and transferred to gel tubes. Blood samples were allowed to coagulate for 15 minutes at room temperature. Serum was separated by centrifugation for 10 minutes at 3000 rpm following clotting. Serum was kept at -20 °C and used to quantify the levels of the hormones (insulin and leptin) [22].

Determination of insulin and leptin levels

Enzyme-linked immunosorbent assay (ELISA) kits were used while adhering to the manufacturer's instructions. Quantitative measurement of insulin and leptin levels in mouse serum was carried out. For precise hormone quantification, these kits make use of the Sandwich-ELISA technique. Antibodies specific to insulin and leptin are pre-coated on the strip plate of the kit. After adding to the wells, standards or serum samples attach to the particular antibodies. Each well is then filled with an insulin or leptin-specific horseradish peroxidase (HRP)-conjugated antibody, which is subsequently incubated. Each well is filled with a tetramethylbenzidine (TMB) substrate solution after any unbound components have been removed. When the stop solution is added, the reaction will cause a color shift, first going blue and then yellow. Spectrophotometric measurements of the absorbance (A) are made at a wavelength of 450 nm. By comparing the sample absorbance to standard, it is possible to determine the levels of insulin and leptin because the absorbance values are directly proportional to the concentrations of the hormones [23].

Statistical analysis

Mean $\pm$ standard deviation (SD) was used to express all data. One-way analysis of variance (ANOVA) was used for statistical assessments between groups, and Tukey's Honestly Significant Difference (HSD) post-hoc test was used to evaluate pairwise differences. By correcting for type I error across several comparisons, this method made it possible to identify group-level differences. The magnitude of treatment effects was determined by calculating effect sizes (η^2), which were interpreted using standard thresholds (small: 0.01, medium: 0.06, large: 0.14). For every comparison, 95 % confidence intervals (CIs) were given to illustrate the correctness of the predicted means and effect sizes. Statistical power ($1-\beta$) was also calculated to guarantee an adequate sensitivity for identifying significant changes, and a threshold of ≥ 0.80 was deemed

appropriate. Each analysis was conducted using Statistical Packages for the Social Sciences (SPSS; version 22), and the significance level was determined using $p < 0.05$.

RESULTS

Weight outcomes

The following changes in the groups' body weights happened over the one-month observation duration: The mean weight of the control group (Control) increased steadily from 25 – 30 g on day 1 to about 28 – 32 g on day fifteen and about 31 – 35 g on day thirty. Whereas some of the mice in Group 1 (E1) kept their body weight, others lost a considerable amount of weight, with an average final weight of 22 – 25 g on day thirty, ranging from 25 – 30 g on day 1 to 25 – 28 g on day fifteen. On the other hand, the body weight of Group 2 (E2) decreased significantly, from 25 – 30 g on day 1 to 23 – 27 g on day fifteen, with an average ultimate reduction of about 19 – 22 g by day thirty (Table 1).

Hormone levels

Pre- and post-treatment hormonal assays revealed unique patterns, as shown in Figure 1 and Figure 2. Control group remained stable in levels of serum insulin and leptin during the study. The E1 group showed a slight decline, after treatment, in the concentrations of insulin and leptin. However, in E2 group, both insulin

and leptin levels decreased significantly ($p < 0.05$), indicating a clear association between increased metabolic activity and weight loss.

The integrated statistical summary for all significant measurements of outcome, including mean values, ANOVA, post-hoc Tukey HSD results, effect sizes, confidence intervals, and power estimates, is shown in Table 2.

DISCUSSION

This study shows significant preclinical evidence that, in a mouse model, intravenous injection of crude aqueous *ginseng* extract significantly reduces body weight as well as circulating blood amounts of leptin and insulin ($p < 0.05$). The metabolic effects were pronounced in Group E2, which was the saponin extract group. These results provide credibility to *ginseng*'s potential as a treatment for obesity and associated metabolic problems, particularly when its systemic distribution is altered to minimize the drawbacks of oral administration.

Table 1: Weight (g) changes in mice administered *ginseng* root aqueous extract and saponin isolate

Group	Day 1	Day 15	Day 30
Control	27.5±1.8	30.0±1.5	33.0±1.6
1	27.5 ± 1.6	26.5 ± 1.5	24.0 ± 1.8
2	27.5 ± 1.7	25.0 ± 1.4	20.5 ± 1.5

Results are mean ± standard deviation

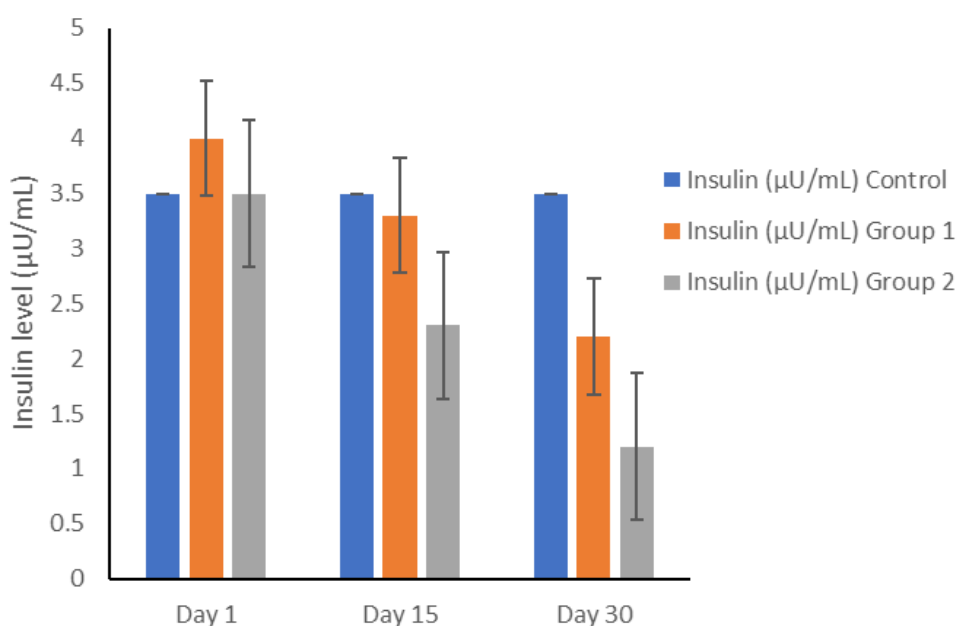


Figure 1: Insulin levels in *ginseng* and saponin-treated mice from days 1 to 30

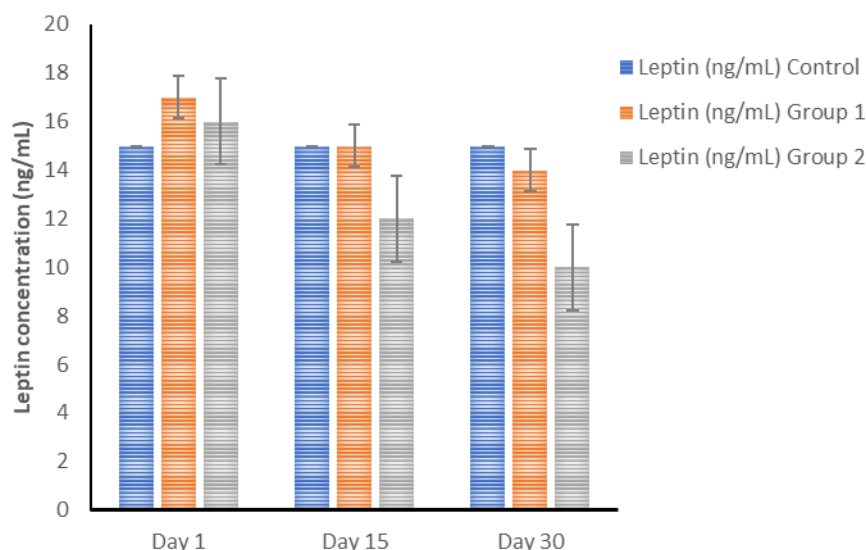


Figure 2: Leptin concentration in *ginseng* and saponin-treated mice from days 1 to 30

Table 2: Body weight, insulin, and leptin descriptive summary

Measure	Group	ANOVA (<i>p</i> -value)	Effect size (η^2)	95% CI (Days 1-30)	Post-hoc (Tukey HSD)	Power (1- β)
Weight (g)	Control	0.031	0.42	2.1, 6.2	C vs E2: $p < 0.01$	>0.8
	1	0.044	0.39	-4.1, -1.6	E1 vs E2: $p < 0.05$	>0.8
	2	0.005	0.51	-7.3, -4.2	C vs E2: $p < 0.01$	>0.8
Insulin (μ U/mL)	Control	1.000	0.00	0.0, 0.0	NS	<0.5
	1	0.021	0.47	-1.9, -0.6	E1 vs E2: $p < 0.01$	>0.8
	2	0.008	0.55	-2.5, -1.4	C vs E2: $p < 0.01$	>0.8
Leptin (ng/mL)	Control	1.000	0.00	0.0, 0.0	NS	<0.5
	1	0.068	0.33	-3.6, -1.0	NS	0.6
	2	0.022	0.44	-6.5, -4.2	C vs E2: $p < 0.01$	>0.8

Note: NS = not significant, CI = confidence interval

Several models have shown that *ginseng* has anti-obesity and anti-diabetic properties, mainly when taken orally. Mice given ginsenoside Rb1 showed decreased food intake and increased glucose tolerance, according to Attele *et al* [24]. Adults with obesity and diabetes who take standardized *ginseng* supplements have shown insignificant increases in insulin sensitivity, according to previous studies [25]. Nevertheless, inadequate bioavailability and unequal preprocessing have also been implicated for inconsistent results in health care settings. The systemic availability of active ginsenosides was enhanced by intravenous delivery, which possibly increased the metabolic actions observed in this study.

The significant reduction in serum insulin concentrations, especially in the saponin extract group, could be caused by ginsenoside-induced overexpression of GLUT4 transporters in the muscles and adipose tissues, as previously reported by Xiong *et al* and Zhou *et al* [17,22]. Reduced obesity and enhanced leptin signaling both result in leptin resistance, a characteristic of

metabolic syndrome. Lee *et al* and Wu *et al* have reported leptin regulation after *ginseng* therapy in diet-induced obese mice [6,23].

Crude *ginseng* root extract and saponins treatments also resulted in a significant decrease ($p < 0.01$) in insulin levels in both Groups, revealing a strong hormonal regulation, whereas leptin decline in this investigation was better in the E2 group. From a therapeutic standpoint, these results indicated that *ginseng* might make an effective remedy for managing obesity, especially in people with insulin resistance and hyperleptinemia. *Ginseng* supplies an all-natural substitute with complex mechanisms while conventional pharmacology increasingly targets metabolic hormones, as evidenced by the emergence of GLP-1 receptor agonists. *Ginseng*-based combined therapies may potentially improve efficacy and lessen the negative effects of synthetic drugs. But subsequent applications must be guided by safety issues. An extensive pharmacokinetic and toxicology study is required for the very rare intravenous use of herbal mixes. Nevertheless, recent studies on *ginseng*

nanoparticles [7,26] show parenteral phytomedicines are rising in popularity, indicating that this delivery method could soon be clinically viable. New findings that *ginseng* affects inflammation, neuroendocrine signaling, and gut microbiota are increasing the possibility of treatment options with *ginseng* [27].

Since isolated ginsenosides like Rb1, Rg3, and molecule K have been demonstrated to have obesity-preventing activities through modulation of PPAR γ , AMPK signaling, and inhibition of pancreatic lipase functioning, the intermediate dose strikes a balance between therapeutic efficacy and security [17]. By avoiding intestinal degradation and first-pass metabolism, which is essential for less well-absorbed phytochemicals like ginsenosides, IV delivery further increases systemic absorption. The chosen 20 mg/kg IV dose of saponins was pharmacologically confirmed before administration to the group. An assessment of the endocrine and gastrointestinal effects of the extracts over the duration of the 30-day study has been established.

Limitation of this study

Although intravenous administration was used in this study to ensure controlled systemic exposure and bypass variability associated with oral absorption and metabolism, this route is not clinically applicable for long-term obesity management. Herbal therapies are typically administered orally, and future studies should evaluate the efficacy of *ginseng* using clinically relevant oral formulations. This approach is commonly used in early-stage pharmacological studies to investigate direct systemic effects before developing clinically applicable formulations.

CONCLUSION

Intravenous injection of crude aqueous *ginseng* and saponin extracts exerts substantial anti-obesity effects by decreasing body weight, insulin, and leptin levels. These changes directly affect metabolic regulation. The concurrent regulation of insulin and leptin implies that *ginseng* has systemic metabolic effects besides weight loss. These results establish *ginseng* as a potentially beneficial supplementary therapy in obesity, insulin resistance, and related metabolic disorders. Further investigations should emphasize establishing molecular processes involved in the action of *ginseng*, mainly insulin signaling, adipogenesis, and neuroendocrine regulation. For it to translate properly into clinical practice, thorough pharmacokinetic profiling should be performed to address safety

assessment, especially since intravenous delivery was considered. Future studies should also concentrate on microbiome and cytokines in light of growing evidence that *ginseng* is responsible for the regulation of gut microbiome and inflammation by *ginseng*.

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