Review Article ISSN: 2836-3647

American Journal of Pathology & Research

Systematic Review of PubMed Studies Prior to 31 December 2025 on Potential Health Benefits of Panax Ginseng

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Received: 04 Jun 2026; **Accepted:** 10 Jul 2026; **Published:** 20 Jul 2026

Citation: Esther Suet Fong Quek, Maurice Han Tong Ling. Systematic Review of PubMed Studies Prior to 31 December 2025 on Potential Health Benefits of Panax ginseng. American J Pathol Res. 2026; 5(7): 1-10.

ABSTRACT

Panax ginseng C.A. Meyer (Asian ginseng) has long been used in traditional East Asian medicine. It is increasingly incorporated into global herbal supplement and functional food markets, and potentially modulating pathways involved in metabolic regulation, oxidative stress and inflammation. However, this may not translate into consistent clinical efficacy, especially when studies differ in extract type, dose, duration and participant characteristics. As such, this systematic review aims to critically evaluate current evidence on the biological effects and potential health benefits of Panax ginseng. A PubMed search was performed to identify studies up to 31 December 2025. Of the 215 articles identified, 37 were included. The evidence clusters into three main themes: (1) metabolic and physiological regulation, (2) cellular and molecular protective mechanisms, and (3) immune function and host defence. Preclinical studies support the modulation of signalling pathways relevant to metabolic homeostasis, oxidative stress, inflammation and host defence; including AMPK and PI3K/Akt, Nrf2/HO-1, and TLR4/NF-κB/NLRP3-related mechanisms, with metabolomic and microbiomic-related findings suggesting gut microbial biotransformation may contribute to interindividual differences in systemic response. Clinical trials report potentially beneficial effects on glycaemic control, vascular function, stress-related outcomes and selected aspects of cognition; however, the clinical evidence remains difficult to generalise because many studies are small, use heterogeneous preparations, and rely on short-term or surrogate endpoints. Although Panax ginseng appears to be generally well tolerated, a translational gap remains between mechanistic preclinical findings and variable human outcomes, despite its biological plausibility and potential as a complementary intervention.

Keywords

Panax ginseng, Asian ginseng, Ginsenosides, Systematic review, Metabolic regulation, Oxidative stress, Inflammation, Immune function.

Introduction

Panax ginseng C.A. Meyer, commonly referred to as Asian or Korean ginseng, is a perennial medicinal plant native to East Asia and widely used in traditional medicine. Its root contains a chemically diverse mixture of constituents, including ginsenosides, polysaccharides, oligopeptides and phenolic compounds, which have been investigated for potential effects on metabolism, vascular function, neurocognition, inflammation and host defence [1]. Hence, interest in *Panax ginseng* has expanded beyond traditional use into the contemporary supplement, functional food and complementary health sectors. Moreover, cardiovascular disease remains a leading cause of mortality worldwide, while the prevalence of type 2 diabetes continues to rise substantially. Neurodegenerative conditions and stress-related disorders also represent major and growing public health challenges [2].

As these conditions are multifactorial and often require long-term management, there is continuing interest in adjunctive nutritional and botanical interventions that may influence multiple factors

relevant to disease risk and symptom burden. Studies have explored the mechanisms through which *Panax ginseng* may act. Reported effects include modulation of pathways involved in metabolic regulation, oxidative stress and inflammation, such as AMPK, PI3K/Akt, Nrf2/HO-1 and NF-κB/NLRP3 signalling [3-5]. These findings provide important mechanistic context and support biological plausibility. However, mechanistic promise does not automatically translate into consistent clinical efficacy, particularly when studies differ in extract type, dose, duration and participant characteristics. Hence, this systematic review aims to critically evaluate and synthesise the current evidence on the biological effects and potential health benefits of *Panax ginseng*.

Methods

Search Strategy

A systematic literature search was conducted using PubMed for studies up to 31 December 2025 investigating the health effects of *Panax ginseng*. The search string, ("panax ginseng" OR "asian ginseng") AND ((health AND benefi*) OR adapto*), was systematically structured to capture core pharmacological categories and common medical terminology associated with the herb; resulting in the following search URL: https://pubmed.ncbi.nlm.nih.gov/?term=("panax+ginseng"+OR+"asian+ginseng")+AND+((health+AND+benefi*)+OR+adapto*)&filter=dates.1000/1/1-2025/12/31

Inclusion / Exclusion Criteria

The following exclusion criteria were applied in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework [6]: (A) Articles not written in English. (B) Articles without free full-text availability. (C) Secondary literature, including systematic reviews, literature reviews, and meta-analyses. (D) Articles not focusing on ginseng. (E) Articles that did not explicitly investigate the health benefits of ginseng. (F) Articles not reporting primary data from human or animal studies.

Diversity in Composition, Dosing, and Processing of Ginseng Preparations

The 37 included studies exhibit considerable diversity in experimental design; encompassing human randomised controlled trials (RCTs) of 15–108 participants and intervention durations spanning 2 to 24 weeks [7-11], preclinical *in vivo* rodent models of 6 to 20 animals per group and spanning single dose to 8 weeks [4,12-15] and deep mechanistic *in vitro cell* culture analyses spanning 18 to 72 hours [3,5,16,17].

The included studies utilised a diverse array of *Panax* species and preparation types. *Panax ginseng* C.A. Meyer (Korean or Asian ginseng) predominated in both preclinical and clinical contexts.

Results

215 studies were identified from PubMed search; of which, 37 were included (Figure 1).

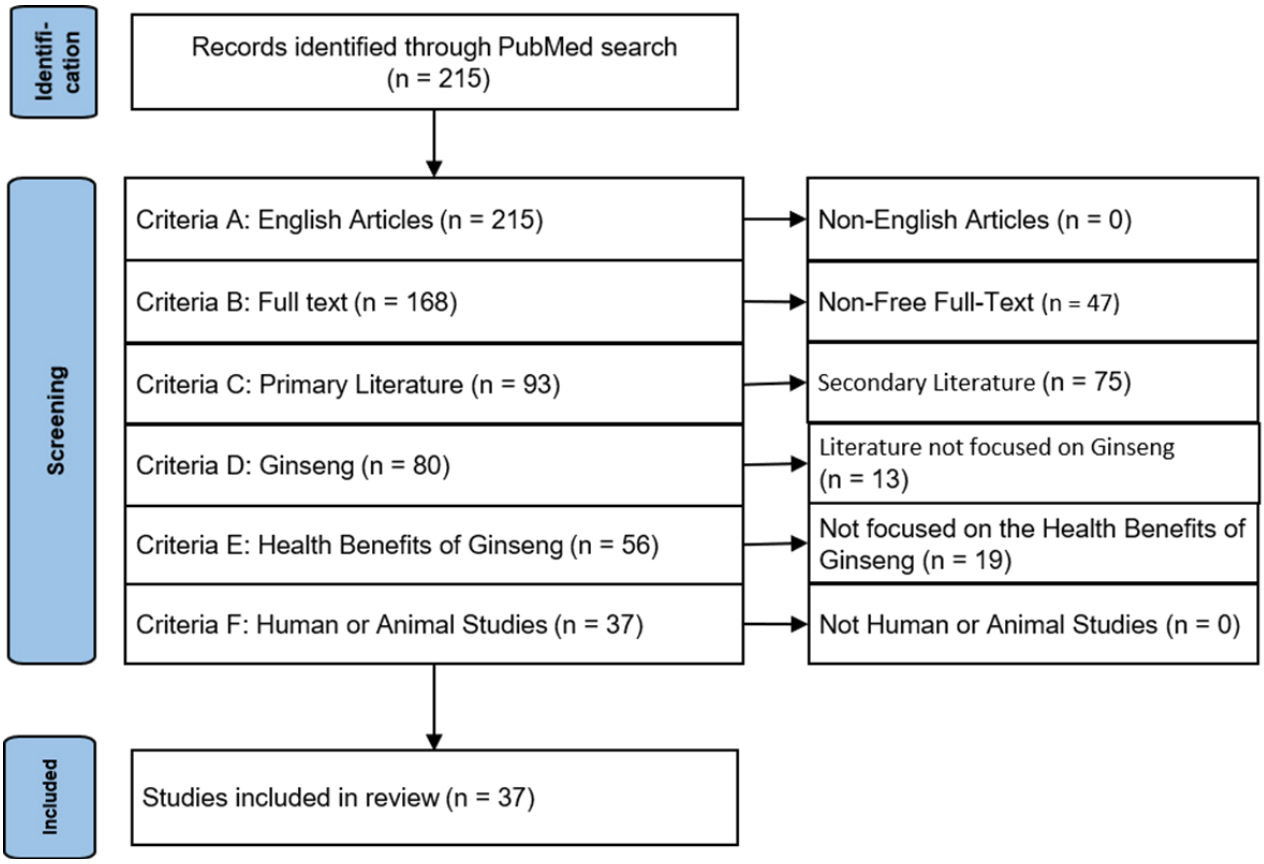

Figure 1: Flow of screening through the 6 exclusion criteria using PRISMA [6]

Additionally, *Panax quinquefolius* (American ginseng) and *Panax notoginseng* were reported in selected studies focusing on metabolic and immunological endpoints [8,10,18]. Preparation forms ranged from raw or white root powders to steamed red ginseng and purified, ginsenoside-enriched extracts.

Standardised ginseng powders were utilised across several clinical and preclinical contexts, though preparation descriptions and dosing regimens vary considerably. In clinical settings, daily dosages differed significantly; for example, Yang et al. [9] administered 2,700 mg of Korean red ginseng daily while Yeo et al. [7] used up to 4,500 mg per day in capsule form, noting that the specific preparation type was not explicitly detailed beyond ginsenoside content. Conversely, Shishtar et al. [8] evaluated an acute dose-escalation of white ginseng spanning 1,000 mg, 3,000 mg, and 6,000 mg. Some studies such as Wang et al. [19] report dosing based on specific isolated ginsenosides evaluated groups receiving varying levels of ginsenoside Rd, though precise dose quantities were not clearly stated. Overall, dosing regimens for standardised powders vary widely across the literature, with treatment durations typically ranging between 3 and 8 weeks.

Whole root powders, including dried and ground *Panax* roots, were used in preclinical and clinical studies. Notably, Dormal et al. [11] administered 200 mg/day of hydroponically grown red *Panax* ginseng root powder to moderately stressed adults, showing cognitive benefits. Additional studies, such as Shishtar et al. [8], used whole root powders encapsulated for metabolic syndrome and diabetes, though detailed preparation data were limited.

Aqueous and ethanolic extracts were the most prevalent interventions in preclinical *in vivo* studies, with dosages in rodent models typically ranging from 20 mg/kg to 1,000 mg/kg per day. Within this broader spectrum, studies focusing specifically on standardised extracts applied doses of 150 to 400 mg/kg/day over intervention periods spanning 1 to 10 weeks [9,20,21]. Specialised fractions have also been extensively characterised. Ginseng oligopeptides (GOPs), which are small peptides isolated from ginseng extracts, were investigated in animal models at doses ranging from 62.5 to 500 mg/kg [22,23]. Furthermore, advanced processing techniques, such as ultrasound-assisted extraction and chromatography utilised by Zhang et al. [24], have enabled the isolation of purified polysaccharides from red ginseng. These polysaccharides demonstrated significant cardioprotective effects in cellular and *ex vivo* models at concentrations as low as 50 µg/mL [25].

In clinical settings, reported daily doses generally ranged between 500 mg and 2,000 mg in studies examining cardiovascular or metabolic outcomes [13,25,26]. For example, one study of red ginseng extract reported improvements in selected cardiovascular measures at 2,000 mg/day over 12 weeks [13], whereas other standardised extract regimens used lower daily doses. Given the variation in formulation, population, and study design, these dose ranges should be interpreted cautiously rather than as directly comparable therapeutic equivalents.

Fermented ginseng extracts have been developed in an effort to modify ginsenoside composition and potentially improve bioavailability [22]. Preclinical studies such as Zhang et al. [12] suggest that fermentation can increase the conversion of larger parent ginsenosides into smaller metabolites that may be more readily absorbed, with associated improvements in selected metabolic outcomes in animal models. However, the extent to which these processing methods translate into more consistent systemic exposure in humans remains uncertain and is likely to depend on both the preparation itself and individual differences in gut microbiota-related metabolism.

Processing Effects on Bioactivity

Processing appears to be an important determinant of the bioactivity of *Panax ginseng*, because thermal and enzymatic treatments can alter the relative abundance and chemical form of its ginsenosides. Repeated steaming and drying, used to produce red ginseng, are reported to convert some major polar ginsenosides into less polar derivatives, including Rg3, Rh2 and Compound K, thereby changing the overall phytochemical profile of the preparation [13,24]. These compositional changes may influence membrane permeability, intestinal absorption and downstream biological effects, although the magnitude of this advantage is likely to depend on the specific preparation and study model rather than reflecting a uniform increase in efficacy across all outcomes. Similarly, fermentation and other biotransformation techniques are designed to generate metabolites that are more readily absorbed, potentially reducing dependence on individual gut microbiota composition for activation of parent ginsenosides [24,27]. Taken together, the available evidence suggests that processing does not simply preserve ginseng but may substantially modify its pharmacological characteristics, which has important implications for comparing studies and for interpreting variability in clinical response.

Thematic Synthesis of Health Benefits

The 37 included studies were categorised into three themes

Table 1: Thematic classification studies on the potential health benefits of ginseng across the 37 evaluated studies.

Theme	Subtheme	Number of Studies
1. Metabolic and Physiological Regulation	1.1. Anti-diabetic & Metabolic Regulation	7 studies [3,8,12,18,19,28,29]
	1.2. Cardiovascular & Antihypertensive Effects	5 studies [10,13-15,24]
	1.3. Adaptogenic & Anti-stress Effects	6 studies [11,25,30-33]
2. Cellular and Molecular Protection	2.1. Antioxidant & Anti-inflammatory Effects	9 studies [34-42]
	2.2. Neuroprotection & Cognitive Enhancement	6 studies [7,11,20,43-45]
3. Immune Function and Host Defence	3.1. Immunomodulation	2 studies [46,47]
	3.2. Anti-infective	1 study [47]

(Table 1), namely, (a) metabolic and physiological regulation, (b) cardiovascular and molecular protection, and (c) immune function and host defence.

Theme 1.1. Metabolic and Physiological Regulation: Anti-diabetic & Metabolic Regulation

Panax ginseng has been investigated in a range of models relevant to glucose regulation, insulin sensitivity, and lipid metabolism. Several mechanistic studies suggest that ginsenosides may influence energy homeostasis through AMP-activated protein kinase (AMPK) and PI3K/Akt signalling. For example, Park et al. [3] reported that 20(S)-ginsenoside Rg3 enhanced glucose-stimulated insulin secretion in pancreatic β-cells and increased phosphorylation of AMPK and acetyl-CoA carboxylase in C2C12 myotubes, indicating a possible dual effect on insulin release and peripheral metabolic regulation. These findings support biological plausibility, although they derive from controlled cell-based systems and therefore cannot on their own establish clinical efficacy.

Animal studies also suggest that specific ginsenosides may affect hepatic glucose production, adipocyte signalling, and body-weight regulation. In streptozotocin-induced diabetic rats, Wang et al. [19] found that ginsenoside Rd was associated with reduced expression of gluconeogenic enzymes and activation of Akt-related pathways, alongside alterations in gut microbiota composition. Zhang et al. [12] similarly reported that ginsenoside Re reduced insulin resistance in high-fat diet models and 3T3-L1 adipocytes, while Li et al. [18] observed improvements in body weight, adipocyte hypertrophy and glucose tolerance in obese mice treated with ginsenoside Rb1. Although these findings are mechanistically informative, they remain preclinical and involve different models, doses and outcome measures, which makes direct comparison difficult.

Human evidence in this domain is more limited. In an acute double-blind, multiple-crossover trial, Shishtar et al. [8] reported that Korean white ginseng reduced postprandial glycaemic excursions and improved vascular augmentation indices in participants with well-controlled type 2 diabetes, without inducing hypoglycaemia. These results suggest short-term metabolic effects, but the study does not establish whether such benefits are sustained over longer periods or across more diverse patient populations. In addition, Banz et al. [28] reported that dietary ginseng altered the diabetic phenotype and expression of metabolic genes in Zucker diabetic fatty rats, further supporting biological relevance but not providing direct human confirmation. Overall, the evidence in this subtheme indicates potential metabolic benefit, but it remains weighted towards preclinical data and short-term outcomes rather than long-term clinical endpoints.

Theme 1.2. Metabolic and Physiological Regulation: Cardiovascular & Antihypertensive Effects

Evidence relating to cardiovascular and antihypertensive effects of *Panax ginseng* is drawn primarily from preclinical models, with more limited support from human studies. In spontaneously hypertensive rats, Lee et al. [14] reported that a hypotensive component-enriched fraction of red ginseng containing ginsenoside Rg3 and arginine-fructose was associated with reductions in systolic and diastolic blood pressure over an 8-week intervention, alongside increased angiotensin-converting enzyme inhibition and plasma nitric oxide levels. Park et al. [13] similarly found that Rg3-enriched *Panax ginseng* improved indices of endothelium-dependent vasodilation, suggesting a possible effect on vascular responsiveness. These findings support a plausible vascular mechanism, although both studies were conducted in controlled preclinical settings and therefore cannot be assumed to translate directly into routine clinical benefit.

Evidence for cardioprotection in severe cardiac injury is also largely preclinical. In murine models of doxorubicin-induced cardiomyopathy, Yoshikawa et al. [15,26] reported that red ginseng administration was associated with preservation of left ventricular ejection fraction, reduced cardiomyocyte injury, and improved survival, with proposed involvement of antioxidant pathways including Nrf2/HO-1. Zhang et al. [24] further described the cardiac protective effects of a pectin-like polysaccharide isolated from red ginseng in experimental models. Together, these studies suggest that *Panax ginseng* and its fractions may influence vascular and myocardial function through multiple mechanisms. However, the evidence remains dominated by animal studies, and there is currently insufficient human data to determine the magnitude, durability, or clinical relevance of these effects in cardiovascular disease management.

Theme 1.3. Metabolic and Physiological Regulation: Adaptogenic & Anti-stress Effects

Evidence relevant to adaptogenic and anti-stress effects includes early experimental stress models, more recent animal studies, and a small number of human trials. In foundational rodent studies using cold-hypoxia-restraint conditions, Ramachandran et al. [30] and Kumar et al. [31] reported that ginseng administration was associated with preservation of body temperature, increased thermogenic response, and prolonged endurance or survival under severe physiological stress. More recently, Zhang et al. [25] described improvements in body temperature rhythm and reductions in inflammatory markers in propylthiouracil-induced hypothermic rats receiving ginseng extract. These findings suggest that *Panax ginseng* may influence stress adaptation and physiological homeostasis in animal models, although the specific stress paradigms and outcome measures differ substantially across studies.

Evidence for effects on physical fatigue and psychological stress in humans remains limited but suggestive. In mice, Hsiao et al. [32] reported that a combined formulation of *Panax ginseng* and *Antrodia camphorata* increased exhaustive swimming time and reduced several biochemical markers associated with fatigue. However, because this was a mixed formulation, the effects cannot be attributed solely to ginseng. In human participants, Dormal et al. [11] reported reductions in perceived stress and improvements in selected measures of emotional and cognitive processing following

supplementation with hydroponically grown red *Panax ginseng* root powder. Yang et al. [9] also reported reductions in urinary bisphenol A and malondialdehyde concentrations, alongside improvements in gynaecological complaints and quality of life in young women receiving Korean red ginseng. Taken together, these studies suggest that *Panax ginseng* may influence fatigue-related and stress-related outcomes, but the evidence base remains relatively small and heterogeneous, with variation in formulations, populations, and outcome measures limiting broader inference.

Theme 2.1. Cellular and Molecular Protection: Antioxidant & Anti-inflammatory Effects

Reduction of oxidative stress and inflammation appears to be central to many of the reported biological effects of *Panax ginseng*. Several studies suggest that individual ginsenosides and non-saponin fractions may modulate inflammatory signalling pathways such as nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), which plays a central role in regulating immune response and inflammation. In an *in vivo* model of lipopolysaccharide-induced acute lung injury, Cheng and Li [4] reported that ginsenoside Rg3 was associated with reduced NF-κB p65 phosphorylation, lower cyclooxygenase-2 expression, and decreased neutrophil infiltration into lung tissue. Shi et al. [5] further reported that ginsenoside Rg3 inhibited NLRP3 inflammasome activation by disrupting NEK7–NLRP3 interaction and downstream caspase-1 activation. Together, these findings suggest a plausible anti-inflammatory mechanism, although they derive from preclinical models and therefore should not be interpreted as direct evidence of clinical efficacy.

Protective effects have also been described for ginseng oligopeptides and other isolated fractions in tissue-specific injury models. Xu et al. [23] reported that ginseng oligopeptides reduced dextran-induced paw oedema and granuloma formation in rats, suggesting anti-inflammatory activity in vivo. He et al. [22] found that similar oligopeptide fractions were associated with preservation of intestinal barrier integrity in irradiated mice, including reductions in circulating endotoxin and diamine oxidase levels. In a separate model of alcoholic liver disease, Pan et al. [16] reported that ginsenoside Rc enhanced SIRT6-related signalling and attenuated oxidative stress and lipid accumulation. While these studies collectively support the view that *Panax ginseng* contains multiple bioactive fractions capable of influencing inflammatory and oxidative pathways, the evidence remains heterogeneous and predominantly preclinical, with different fractions, tissues and outcome measures examined across studies.

Theme 2.2. Cellular and Molecular Protection: Antioxidant: Neuroprotection & Cognitive Enhancement

Evidence relevant to neuroprotection and cognitive enhancement includes both preclinical injury models and a smaller number of human studies. In a rat model of transient focal cerebral ischaemia, He et al. [43] reported that 20(R)-ginsenoside Rg3 was associated with reduced infarct volume and improved behavioural outcomes, alongside lower expression of calpain I and caspase-3 mRNA in the hippocampal CA1 region. These findings suggest a possible anti-apoptotic mechanism in acute neuronal injury, although they remain specific to an experimental model of ischaemia and do not directly establish benefit in human neurological disease.

Additional preclinical studies suggest that different ginseng-derived fractions may influence neuroinflammation, oxidative stress and synaptic integrity. Wang et al. [45] found that ginsenoside Re attenuated cognitive impairment in mice exposed to chronic restraint stress, with associated changes in brain-derived neurotrophic factor (BDNF), Nrf2 signalling and synaptic protein expression. Xu et al. [44] similarly reported that water-soluble ginseng oligosaccharides reduced scopolamine-induced learning and memory impairment in mice and were associated with lower astroglial activation and reduced hippocampal pro-inflammatory cytokine expression. Aryal et al. [20] further observed that ginseng attenuated loss of calretinin in the mouse hippocampus after chronic radiofrequency exposure, suggesting a possible effect on calcium-related neuronal homeostasis. While these studies support biological plausibility, they involve distinct models of neurological stress or injury and therefore cannot be assumed to reflect a single or consistent neuroprotective effect across conditions.

Human evidence in this area is comparatively limited. In a double-blind randomised controlled trial, Yeo et al. [7] reported that Korean red ginseng improved selected aspects of cognitive performance and motor function in healthy young men without major psychiatric adverse effects. Dormal et al. [11] also reported improvements in emotional processing and cognitive measures in moderately stressed adults receiving hydroponically grown red *Panax ginseng* root powder. However, these studies were short in duration and involved relatively small samples, which limits conclusions about long-term cognitive benefit or applicability to patients with established neurodegenerative disease. Overall, the evidence suggests that *Panax ginseng* may influence neurocognitive outcomes, but current support remains stronger for mechanistic plausibility than for clinically established efficacy.

Theme 3. Immune Function and Host Defence

Evidence relating to immunomodulation and anti-infectious properties is comparatively limited and is drawn primarily from preclinical studies. Anh et al. [46] investigated Ginsan, a purified ginseng polysaccharide fraction, in murine infection models and reported increased macrophage activity, enhanced bacterial clearance, and reduced expression of selected Toll-like receptor signalling components and pro-inflammatory cytokines. These findings suggest that certain polysaccharide fractions may influence innate immune responses while moderating excessive inflammatory signalling. However, the evidence is derived from acute animal models of severe infection, and its relevance to broader human immune function remains uncertain.

Additional studies suggest that immunological effects may also be linked to longer-term interactions with metabolism and the gut microbiota. Sun et al. [27] reported that chronic administration of ginseng extract in rats altered gut microbial composition, including increased relative abundance of *Bifidobacterium* and *Lactobacillus*, alongside changes in selected immune-related

markers. These observations raise the possibility that part of ginseng's immune effect may be mediated indirectly through host–microbiota interactions rather than through acute immune stimulation alone. Human evidence in this domain remains sparse. In a placebo-controlled trial involving patients with moderate chronic obstructive pulmonary disease (COPD), Shergis et al. [10] found that ginseng was generally well tolerated; however, the study was not sufficient to establish clear anti-infective efficacy or broader clinical benefit in host defence. Overall, the available evidence suggests that *Panax ginseng* may influence immune and inflammatory processes, but current support remains limited, heterogeneous, and weighted towards preclinical models.

Discussion

Main Clinical Findings

The clinical evidence reviewed in this review suggests that *Panax ginseng* may confer beneficial effects across metabolic, cardiovascular, cognitive and stress-related outcomes; however, the strength of that evidence varies considerably by domain and remains constrained by substantial methodological heterogeneity. In metabolic health, the most consistent human finding is a short-term improvement in postprandial glycaemic control, as shown in the acute multiple-crossover trial by Shishtar et al. [8]. While these results are encouraging, they derive from a relatively small cohort and primarily reflect acute physiological responses rather than durable changes in long-term diabetic control. Similarly, cardiovascular studies suggest that selected ginseng preparations, particularly those enriched in rare ginsenosides such as Rg3, may improve endothelial function and vascular responsiveness; however, evidence for consistent reductions in blood pressure or broader cardiovascular risk remains limited and is not yet sufficient to support firm clinical recommendations [13,14].

The evidence for cognitive and stress-related outcomes is also promising but should be interpreted cautiously. Trials in healthy or moderately stressed adults report improvements in selected cognitive domains, subjective stress indices and aspects of emotional processing [7,11]. Nevertheless, these findings are based on relatively short interventions, modest sample sizes and differing preparation types, which limit generalisability. More broadly, the current clinical literature is marked by considerable variation in botanical source, preparation, dose, duration and outcome selection. Many studies rely on surrogate biomarkers or short-term functional outcomes rather than hard clinical endpoints, making it difficult to determine the true magnitude, durability and clinical relevance of benefit. Taken together, the evidence supports *Panax ginseng* as a promising complementary intervention, but not yet as a standardised therapeutic option supported by sufficiently robust and uniform clinical data.

The Emerging Role of Gut Microbiota

Previous reviews of *Panax ginseng* have often focused on individual outcome domains, such as fatigue, respiratory symptoms, or specific cardiometabolic endpoints, which have been useful for evaluating targeted questions but have tended to fragment the broader evidence base [48,49]. In comparison, the present review brings together mechanistic, preclinical and clinical findings across several physiological systems, allowing a more integrated assessment of where the evidence is consistent and where major translational gaps remain. This broader synthesis suggests that one reason for the disparity between strong preclinical findings and more variable human outcomes may lie not only in differences in dose, formulation and study design, but also in variation in microbiota-mediated biotransformation.

Therefore, the current review extends earlier literature in two main ways. First, it places pathway-level findings, such as AMPK, PI3K/Akt, Nrf2/HO-1 and NF-κB/NLRP3 signalling, alongside human outcome data rather than treating these as separate bodies of evidence. Second, it considers the gut microbiota as an important pharmacokinetic and pharmacodynamic context for interpreting heterogeneity in response. Experimental and metabolomic studies suggest that the conversion of poorly absorbed parent ginsenosides into more bioavailable metabolites, including Compound K, may influence systemic exposure and therapeutic effect [27]. However, this should not be interpreted as a complete explanation for all clinical inconsistencies. Variability in extract standardisation, participant characteristics, intervention duration, and endpoint selection is also likely to contribute substantially. Table 2 summarises this comparison by aligning robust preclinical mechanisms with the more variable clinical evidence across major health domains and situating these discrepancies within the context of microbiome-related biotransformation.

The gut microbiota may therefore represent one important factor influencing the clinical variability observed with *Panax ginseng*. Because several parent ginsenosides have relatively low oral bioavailability and depend on intestinal metabolism for conversion into more absorbable metabolites, differences in microbial composition may affect systemic exposure and downstream physiological response. This possibility is supported by recent work using faecal microbiota transplantation, in which Lin et al. [50] reported that microbiota from ginseng-supplemented aged mice transferred some neuroprotective, anti-ageing and immunomodulatory effects to antibiotic-treated recipient mice, alongside shifts in microbial composition and metabolite profiles. Although these findings are still preclinical, they suggest that the microbiome may act as an important mediator of response rather than merely a background variable, and they further highlight the need to consider host–microbiota interactions when interpreting inconsistent clinical outcomes.

Strengths and Limitations of this Review

A key strength of this review is its integrative scope. By bringing together mechanistic *in vitro* studies, preclinical animal models and human clinical trials, the dissertation is able to examine *Panax ginseng* across different levels of evidence rather than focusing on a single experimental context. This allows pathway-level findings to be considered alongside physiological and clinical outcomes, which is useful for assessing where biological plausibility is well supported and where translation into human benefit remains

Table 2: Comparison of preclinical mechanistic evidence and clinical variability across major health domains, with consideration of microbiota-related influences on bioavailability and response.

Health Domain	Robust Preclinical Mechanistic Findings	Variable Clinical Findings	Translational Discrepancies & Microbiota Influence
Metabolic Control [8,12,19]	Activation of PI3K/Akt and AMPK; reduced expression of selected gluconeogenic pathways.	Short-term improvements in glycaemic measures have been reported, but effects on longer-term markers remain variable.	Some parent ginsenosides have low oral bioavailability, and microbiota-mediated deglycosylation may contribute to variability in systemic exposure.
Cardiovascular Health [13,14,24]	Changes in eNOS-related signalling, ACE inhibition and markers of cardiomyocyte protection have been reported.	Improvements in endothelial function have been reported, but effects on systemic blood pressure remain inconsistent.	Differences in preparation and processing may influence exposure to less polar ginsenosides and contribute to variability between studies.
Neuroprotection [11,43,44]	Reduced expression of selected apoptotic markers and attenuation of scopolamine-related cognitive impairment have been reported.	Improvements in subjective stress and selected cognitive measures have been reported, but longer-term cognitive outcomes remain uncertain.	Low oral bioavailability and limited brain penetrance of some parent ginsenosides may contribute to inconsistent neurocognitive findings.

uncertain. A further strength lies in the effort to distinguish between different ginsenosides and non-saponin fractions, such as Rg3, Re, Rd, Rb1, Ginseng and ginseng oligopeptides, thereby avoiding the treatment of ginseng as a single uniform intervention. This review also benefits from its attempt to situate the evidence within a wider translational context. Consideration of preparation type, processing method and microbiota-mediated biotransformation helps explain why findings may differ across studies, particularly when extracts vary in composition and bioavailability. In addition, the inclusion of market and product-format context provides some insight into why standardisation has become increasingly relevant in both research and commercial practice. Taken together, these features strengthen the dissertation by supporting a more nuanced interpretation of heterogeneity rather than presenting the literature as internally uniform.

A major limitation of the current evidence base is the limited comparability between ginseng interventions used across studies. The phytochemical composition of a ginseng preparation may vary according to factors such as geographic origin, harvest age, cultivation conditions, and post-harvest processing, including drying, steaming, and fermentation. As a result, studies often evaluate preparations that differ substantially in composition, which makes direct comparison difficult and limits the interpretability of pooled quantitative conclusions. In addition, many clinical studies are limited by relatively small sample sizes and short intervention periods. Trials lasting only a few weeks are unlikely to capture sustained changes in long-term clinical outcomes such as HbA1c, atherosclerotic progression, or neurodegenerative decline. Consequently, much of the current human evidence relies on short-term physiological measures or surrogate biomarkers, which are informative but do not always indicate durable clinical benefit. This review is also subject to methodological limitations. Restricting inclusion to English-language, free full-text articles indexed in PubMed may have introduced publication and language bias, potentially excluding relevant studies published in regional databases or behind paywalls. In addition, the search window ended on 31 December 2025, which means that newer evidence published subsequently was not captured. These constraints should be considered when interpreting the completeness of the review, although they do not negate the broader patterns identified in the included literature.

Research Gaps and Potential Future Directions

Several important research gaps remain in the literature on *Panax ginseng*, particularly in relation to standardisation, translational relevance, and the sources of interindividual variability in response. Firstly, extract standardisation and participant stratification. One of the most persistent limitations across the current literature is poor comparability between interventions. Future clinical trials would benefit from using chemically characterised and consistently reported preparations, including clearer information on ginsenoside composition and processing method [51]. In addition, parallel microbiome and metabolomic profiling may help explain why some participants appear to respond more strongly than others. Such approaches could improve the interpretation of heterogeneity, although their practical value for routine stratification still requires further validation. Secondly, advanced *in vitro* modelling. Traditional 2D cell culture models remain useful for isolating specific mechanisms, but they provide limited insight into multi-organ interactions, metabolism, and tissue-specific pharmacokinetics. Emerging organoid and organ-on-a-chip systems may offer a more physiologically relevant platform for studying ginseng pharmacology. A recent review suggests that these technologies are increasingly being used in drug screening, development, and personalised medicine contexts [52]. Their application to ginseng research could help narrow part of the gap between simplified mechanistic assays and human biology, although direct evidence in this specific area remains limited. Lastly, larger and longer-term clinical trials. The existing human literature is dominated by relatively short interventions and modest sample sizes, which limit inference about sustained clinical benefit. Future studies should therefore prioritise adequately powered, multicentre trials with longer follow-up and more clearly defined primary endpoints. In cardio-metabolic and neurocognitive research in particular, greater emphasis on clinically meaningful outcomes, rather than short-term surrogate biomarkers alone, would strengthen the evidence base and improve the relevance of findings for practice.

Addressing these gaps will require more methodologically consistent and biologically informed study designs rather than simply increasing the number of trials. In particular, future work should aim to clarify which preparations are being used, how their composition relates to observed effects, and why clinically relevant responses appear to vary across populations.

Implications for Practice

From a practice perspective, the current evidence suggests that *Panax ginseng* may have value as a complementary intervention in selected contexts, particularly where fatigue, perceived stress, mild metabolic dysregulation, or vascular function are relevant concerns. However, the evidence base does not yet justify broad or standardised clinical recommendations. The likely effects of *Panax ginseng* appear to depend on multiple factors, including the specific preparation used, ginsenoside composition, dose, treatment duration, and individual differences in metabolism and gut microbiota activity. As a result, clinicians and nutrition practitioners should be cautious about extrapolating findings from one formulation or population to another.

In practical terms, this means that any consideration of *Panax ginseng* use should be individualised and accompanied by attention to concurrent medication use, cardiovascular risk profile, glycaemic control, and factors that may influence intestinal biotransformation, such as recent antibiotic exposure. Although ginseng is generally well tolerated in clinical studies, with adverse effects usually mild and transient, possible herb–drug interactions remain an important consideration, particularly in relation to anticoagulant or intensive glucose-lowering therapies [53-56]. At present, the most appropriate position is to regard *Panax ginseng* as a potentially useful adjunct rather than a replacement for established therapy, and one that requires careful product selection and ongoing evaluation in both clinical practice and future research.

Conclusion

This systematic review synthesised 37 primary studies investigating the biological effects and potential health benefits of *Panax ginseng* across metabolic, cardiovascular, neurocognitive, anti-inflammatory and immunomodulatory domains. Collectively, the evidence indicates that *Panax ginseng* has a broad range of biologically plausible actions mediated through multiple pathways, including AMPK, PI3K/Akt, Nrf2/HO-1 and NF-κB/NLRP3 signalling. Preclinical studies provide substantial support for these mechanisms and consistently demonstrate metabolic regulation, antioxidant activity, anti-inflammatory effects, neuroprotection and modulation of host defence.

However, the clinical evidence remains less definitive. Human trials suggest potentially beneficial effects on postprandial glucose control, endothelial function, stress-related outcomes and selected aspects of cognition, but the literature is characterised by small sample sizes, short intervention periods, heterogeneous preparations and frequent reliance on surrogate endpoints. A central conclusion of this review is that variation in preparation method and microbiota-mediated biotransformation appears to be a major source of interindividual variability and may partly explain the gap between strong mechanistic findings and inconsistent clinical outcomes. Overall, *Panax ginseng* should be regarded as a promising but not yet fully standardised complementary intervention. Future research should prioritise larger, methodologically rigorous clinical trials using chemically characterised preparations and integrated microbiome or metabolomic profiling in order to clarify which formulations, doses and patient groups are most likely to benefit.

Supplementary Materials

Supplementary materials can be downloaded from https://bit.ly/Ginseng_SR.

Acknowledgements

The authors wish to thank the institute, Management Development Institute of Singapore, for its support towards this work. The cost of publication fees was borne by the authors.

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