



Original Article

Multifaceted Benefits of Ginseng and Its Extracts: A Brief Review of Immunomodulation, Quality of Life Improvement, and Antitumor Potential



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Abstract

Ginseng, a traditional Chinese medicinal herb, has been used for centuries to enhance vitality and overall well-being. This review synthesizes multiple studies to summarize the latest discoveries on the immunoregulatory effects of ginseng, its role in improving patients' quality of life, and new evidence of its antitumor properties. It concludes that ginseng and its extracts can improve patients' quality of life and may have the potential to target tumor cells. Meanwhile, ginseng extracts significantly improve sub-health status, with an 85% improvement rate observed in young adults after 30 days of intervention. This review provides valuable new evidence for ongoing research on ginseng and its extracts.

Introduction

Ginseng (*Panax ginseng* C.A. Meyer) has been revered for its restorative and tonic effects in traditional medicine. For centuries, ginseng has been prescribed to replenish original Qi and resolve deficiency syndrome, which manifests clinically as fatigue and immune vulnerability, especially in tumor patients. Recent research has elucidated the mechanisms behind these traditional uses, revealing the potential of ginseng to impact immune function, alleviate symptoms of sub-health, and combat cancer. This review explores the current body of literature on these topics, focusing on the scientific evidence supporting the multifaceted benefits of ginseng and its extracts.

Immunomodulatory effects of ginseng

Ginseng has been shown to possess immunomodulatory properties, which are crucial for maintaining homeostasis and combating disease. Recent research findings indicate that the active compo-

nents of ginseng, known as ginsenosides, can influence the functions of immune cells, including regulating the production of cytokines and enhancing the activity of natural killer (NK) cells.¹ Similarly, flavonoids and phenolic substances, which are also types of polysaccharide compounds, have anti-fatigue effects, enhance the body's immunity, and promote hematopoietic function.² A study by Mahara *et al.*³ highlighted factors associated with sub-optimal health status among adolescents in China, suggesting that ginseng could play a role in immunomodulation to improve health outcomes. Furthermore, the effects of ginsenoside Rg3 on tyrosine hydroxylase and related mechanisms in fatigue rats indicate its potential in modulating stress responses, which are closely tied to immune function.^{4–6}

Immunomodulatory mechanisms

Cytokine network regulation

Ginsenoside Rg1 and Rb1 can significantly inhibit the excessive secretion of pro-inflammatory factors, such as tumor necrosis factor- α and interleukin-6, while promoting the production of the anti-inflammatory factor interleukin-10. This bidirectional regulatory effect is crucial for maintaining immune homeostasis.¹ Studies have shown that in inflammatory models induced by lipopolysaccharide, ginsenosides can normalize cytokine levels by up to 40–60%.

NK cell activation pathway

By activating the TLR4/MyD88 signaling pathway, ginsenosides can increase the expression of activation receptors on NK cells (such as NKG2D), thereby enhancing their killing activity by two

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to three times. A comprehensive review of the literature indicates that ginsenosides can stimulate lymphocyte proliferation, enhance NK cell activity, and modulate antibody production, thus bolstering the immune response.¹

The role of the coordinated immune substances

Apart from saponins, the polysaccharide components in ginseng (such as arabinogalactan) can activate complement receptor 3 on the surface of macrophages, enhancing phagocytic function and promoting the proliferation of hematopoietic stem cells. Animal experiments have shown that ginseng polysaccharides enable the white blood cell count of irradiated mice to recover to normal levels five to seven days earlier than usual. Further studies have demonstrated that ginsenosides, polysaccharides, proteins, volatile oils, and other constituents can serve as quality indicators for regulating the immune function of ginseng.^{7,8}

Immunomodulatory effects in the clinical context

The immunomodulatory effects of ginseng are particularly relevant in cancer treatment, where the immune system's ability to recognize and eliminate tumor cells is critical. The main active component involved is ginsenoside CK.^{9,10} A study by Baek *et al.*¹¹ applied metabolomics to investigate the effects of ginseng on Spleen-Qi deficiency syndrome, revealing its potential to modulate immune function in patients treated with ginseng. These findings suggest that ginseng may enhance the body's natural defenses against disease, support overall health, and potentially improve treatment outcomes for conditions such as cancer.

Quality of life improvement

The impact of ginseng on quality of life has been a significant focus of recent research. A study by Mu *et al.*¹² demonstrated that ginseng extract, specifically the Renshen Yuanqi (RSYQ) Drink, improved sub-health status in young adults, with 85% of participants showing significant improvements in their sub-health scores after a 30-day intervention. The aspects of sub-health that saw the most significant improvements included feelings of sadness and depression, fatigue, and cognitive function, all of which are integral to an individual's overall quality of life. These findings are supported by earlier research that not only showed ginseng's ability to relieve chronic fatigue and protect cerebral function, thereby maintaining body homeostasis,^{13–15} but also reported its whitening and anti-aging benefits.^{16,17} We can be confident that the numerous benefits of ginseng improve patients' physical condition in multiple ways and enhance their quality of life.

Clinical studies and observational research

Clinical studies and observational research have been instrumental in elucidating the benefits of ginseng. A study conducted by the School of Traditional Chinese Medicine at Capital Medical University, as detailed in a progress report, focused on the effects of RSYQ Drink on tumor patients. The study, part of a larger collaboration between Capital Medical University and China Medico Corporation, aims to assess the efficacy of ginseng products in improving the sub-health status of high-pressure individuals and tumor patients. Preliminary results indicate that ginseng may help alleviate symptoms of sub-health in tumor patients, with potential implications for improving their quality of life.

While the benefits of ginseng are well documented, its safety and efficacy must be thoroughly assessed. High doses of ginseng have been associated with adverse effects, including nervous sys-

tem disturbances and interactions with certain medications.^{18,19} For instance, ginseng may have certain adverse effects on the action of the beta-blocker metoprolol.^{20,21} Therefore, it is crucial to establish safe dosage ranges for ginseng supplementation, especially in the context of long-term use. The study by Mu *et al.*¹² reported mild adverse effects, such as constipation and headache, which resolved after discontinuation of the supplement. In particular, cancer patients may be taking anticoagulant drugs such as aspirin and warfarin. The combined effect of these drugs with ginseng may increase the risk of bleeding. Additionally, ginsenosides (such as Rk1 and Rg5) may inhibit liver drug-metabolizing enzymes like CYP3A4, thereby increasing toxicity. For targeted therapies such as epidermal growth factor receptor (EGFR) inhibitors and poly ADP-ribose polymerase (PARP) inhibitors, ginseng may have antagonistic effects. As a traditional Chinese medicine (TCM), the simultaneous use of ginseng with aconite and *Saussurea involucreata* can cause extremely strong toxicity. These findings underscore the need for ongoing monitoring and research to ensure the safe integration of ginseng into healthcare practices.

Quality of life improvement in patient populations

The improvement in quality of life associated with ginseng use is particularly significant for patient populations experiencing fatigue and cognitive decline, such as those undergoing cancer treatment. The study by Mu *et al.*¹² highlighted the positive impact of ginseng extract on sub-health conditions, which are common in high-pressure groups like college students and young professionals. This may be due to ginsenosides, the main active substances in ginseng, having an antidepressant effect.^{21–23} The aspects of sub-health that saw the most significant improvements included feelings of sadness and depression, fatigue, and cognitive function. These findings are supported by earlier research that showed ginseng's ability to relieve chronic fatigue and protect cerebral function, thereby maintaining body homeostasis.

Antitumor potential

The antineoplastic effects of ginseng and its extracts are an exciting area of research. While the direct cytotoxic effects of ginseng on tumor cells are not yet fully established, there is evidence to suggest that certain ginsenosides may inhibit tumor growth and metastasis.^{24–27} For instance, ginseng has shown neuroprotective effects against cancer-related complications. A study by Li *et al.*¹⁴ demonstrated that ginsenoside compound K reduced neuronal damage and improved synaptic dysfunction by targeting A β , suggesting a potential role in neuroprotection against cancer-related cognitive impairment. Additionally, ginsenoside Rg3 improves cancer-related fatigue by activating AMPK and enhances patients' quality of life.^{28–30}

Antitumor potential and mechanisms

While the direct cytotoxic effects of ginseng on tumor cells are not yet fully established, evidence suggests that certain ginsenosides may inhibit tumor growth and metastasis. Multiple studies have shown that the PI3K/AKT pathway is influenced by various ginsenoside factors. Ginsenoside Rg1 and Rb1 regulate macrophage polarization, maintaining the balance between M1 and M2 phenotypes to enhance PI3K/AKT signaling. Ginsenoside Rg3 and Re regulate T cell activation and maintain the dynamic balance between Th1 and Th2. Ginsenoside Rh2 upregulates NKG2D and perforin through the PI3K/AKT/ERK pathway, thereby enhancing NK cell cytotoxicity. A study by Song *et al.*²⁴ demonstrated that

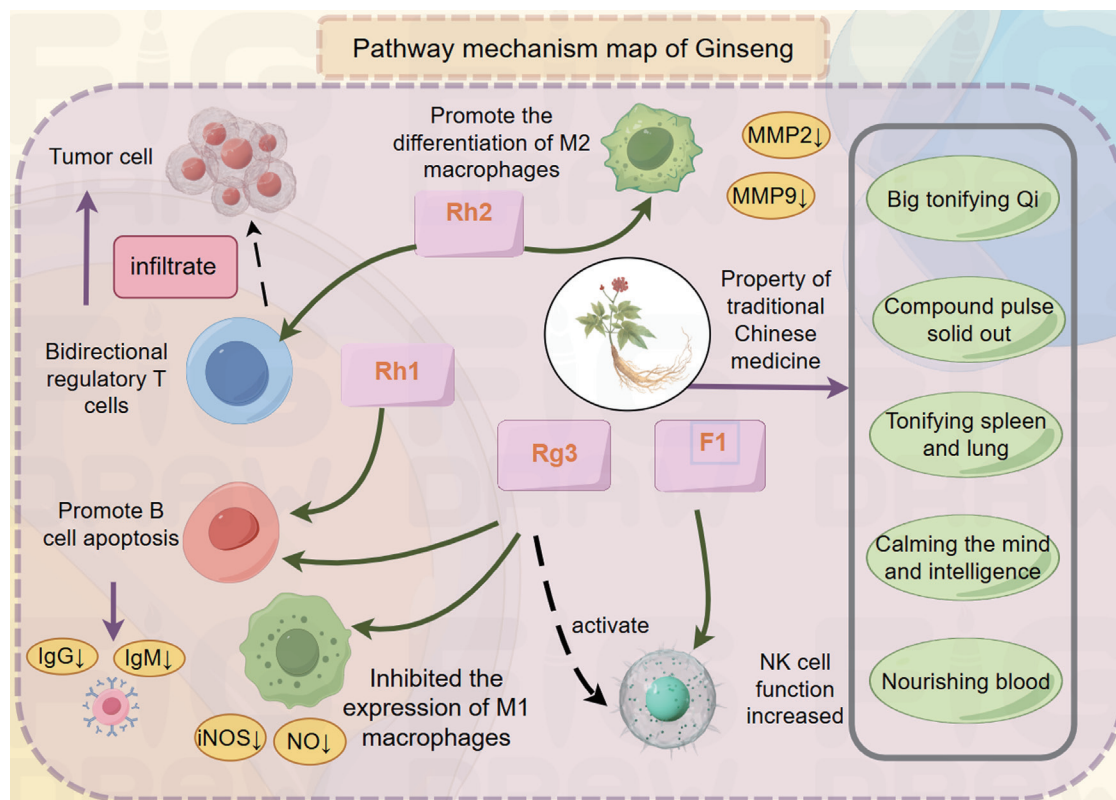


Fig. 1. The proposed immunomodulatory and antitumor mechanisms associated with ginseng and its bioactive constituents. Created with Figdraw. The downward arrow indicates a decrease in content. The solid arrow represents "direct action", with a clear path of influence; the dashed arrow indicates "indirect action", which involves going through a roundabout route and achieving the effect through other factors. IgG, immunoglobulin G; iNOS, inducible nitric oxide synthase; MMP, matrix metalloproteinase; NK, natural killer; NO, nitric oxide; Rg, ginsenoside-Rg; Rh, ginsenoside Rh.

ginsenoside Rh2 inhibits tumor growth and metastasis in prostate cancer by suppressing the PI3K/AKT pathway. Research by Wang *et al.* indicates that ginsenoside Rb1 regulates cuproptosis through CTR1 ubiquitination, thereby improving hypoxia-reoxygenation injury in H9c2 cells.^{31–33} These findings suggest that ginsenosides may target specific signaling pathways in cancer cells, offering a potential therapeutic strategy for cancer treatment.^{34,35}

Safety considerations and adverse effects

Despite the promising effects of ginseng, safety must remain a paramount concern. High doses of ginseng have been associated with adverse effects, including nervous system disturbances and interactions with certain medications.^{18,19} For example, ginseng may alter the effects of the beta-blocker metoprolol.^{20,36} Using small doses of ginseng can maximize medicinal value while minimizing adverse effects and adverse reactions.³⁷ These findings underscore the need for ongoing monitoring and research to ensure the safe integration of ginseng into healthcare practices.^{38,39}

The illustrated pathway map delineates the proposed immunomodulatory and antitumor mechanisms associated with ginseng and its bioactive constituents (Fig. 1). Ginseng demonstrates bidirectional regulatory effects on T cells and promotes apoptosis in B cells. Furthermore, specific ginsenosides, including Rh1, Rg3, and F1, are implicated in activating and promoting the differentiation of M2 macrophages. The compound F1 is also associated with enhanced NK cell function. Ginseng components, potentially including F1, may influence the activity of matrix metalloprotein-

ases such as MMP9, indicated via MMP21.

Concurrently, ginseng exerts inhibitory effects on the expression of M1 macrophages, potentially acting through mechanisms involving gM1, nitric oxide synthase, and NO1. These immunomodulatory actions occur alongside ginseng's fundamental properties in TCM, characterized as "Big tonifying Qi", which encompasses effects such as "Compound pulse solid out", "Tonifying spleen and lung", "Calming the mind and intelligence", and "Nourishing blood". Collectively, this map integrates these immunological mechanisms with the foundational TCM therapeutic principles attributed to ginseng.

Typical cases and future directions

In 2023, we conducted preliminary research investigating the effects of RSYQ Drink, composed of high-quality ginseng extract, on sub-health status in young college students. Building upon these findings, we aim to expand our research to a larger population. Given ginseng's traditional use in replenishing Qi and addressing deficiency patterns in TCM, we hypothesize that it may improve sub-health conditions in tumor patients, who are mostly considered to suffer from deficiency syndrome during treatment.

To test this, we refined our study protocol and initiated patient recruitment at the Traditional Chinese Medicine Outpatient Department of Capital Medical University. Prior to study initiation, the research team provided comprehensive explanations of the study objectives and participation procedures to potential partici-

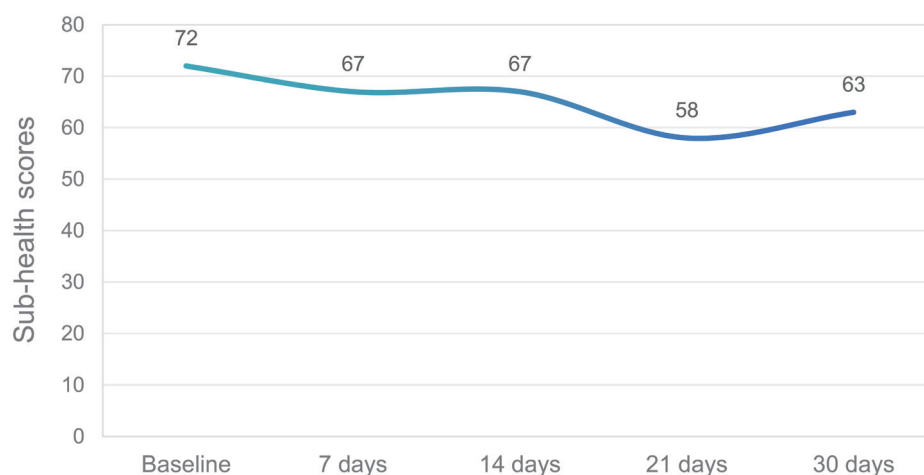


Fig. 2. Change of sub-health scores at different time points after Renshen Yuanqi (RSYQ) Drink administration in a female patient.

pants. Following informed consent, patients completed the Sub-health State Assessment Scale (see Supplementary File 1), which incorporates items derived from the EORTC QLQ-C30 (version 3) and EORTC QLQ-HCC18 instruments. Baseline health status was recorded during initial participation, with subsequent data aggregation and analysis.

RSYQ has demonstrated great efficacy in improving sub-health conditions among tumor patients. For instance, a 62-year-old female patient strictly adhered to the prescribed daily regimen of RSYQ. Sub-health status was assessed using a standardized evaluation scale at baseline and follow-up intervals (days 7, 14, 21, and 30). As illustrated in Figure 2, her sub-health score decreased by nine points after 30 days of treatment compared to baseline, indicating marked improvement.

From this medical case of RSYQ Drink, the future of ginseng research holds promise, with a focus on optimizing assessment scales for sub-health status and expanding trials to include more participants.^{40,41} The potential for the development of ginseng tonics is optimistic. Statistical analysis was not applied due to the single-case design; future studies will incorporate t-tests and error bars. Further research should aim to elucidate the mechanisms underlying ginseng's immunomodulatory effects, its impact on quality of life, and its direct antitumor potential.

Conclusions

Ginseng and its extracts show potential for immunomodulation, quality-of-life enhancement, and antitumor applications. Ginseng offers significant advantages for maintaining human health, especially among the elderly population, where its application is more widespread.⁴² While preliminary findings indicate the multifaceted therapeutic value of ginseng products, clinical validation remains limited. Future research should focus on large-scale, randomized controlled trials to establish the efficacy and safety of ginseng in various patient populations. Additionally, exploring the synergistic effects of ginseng with conventional treatments could unveil new paradigms in integrative medicine. Ginseng's journey from a traditional remedy to a scientifically validated therapeutic agent is ongoing, and its full potential is yet to be realized.

The content presented in this article still has certain limitations. The relevant clinical trials mentioned have not undergone large-scale controlled trials yet. The small sample size may lead to

limitations in the conclusions drawn. Some conclusions, although verified in animal experiments, remain to be confirmed in clinical settings. Overall, this article provides new evidence for research on ginseng and its related components.

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Conflict of interest

Dr. Jiangning Peng and Dr. Lin Tang are employees of China Medico Corporation. Dr. Ling Yao is an employee of Shenzhen Tsumura Medicine Co., LTD. The other authors have no conflicts of interest to declare.

Author contributions

Conceptualization (HYM), formal analysis (JNP, LY), supervision (LT), and writing – review and editing (HYM, TQW). All authors have approved the final version and publication of the manuscript.

References

- [1] Yao W, Guan Y. Ginsenosides in cancer: A focus on the regulation of cell metabolism. *Biomed Pharmacother* 2022;156:113756. doi:10.1016/j.biopha.2022.113756, PMID:36228372.
- [2] Liu SJ, Zhang X, Sun X, Hou Y, Jia M. Research Progress on the Immunomodulatory Effects of Polysaccharides from the Panax genus of the genus Panax. *Ginseng Research* 2023;35(5):52–55. doi:10.19403/j.cnki.1671-1521.2023.05.014.
- [3] Mahara G, Liang J, Zhang Z, Ge Q, Zhang J. Associated Factors of Suboptimal Health Status Among Adolescents in China: A Cross-Sectional Study. *J Multidiscip Healthc* 2021;14:1063–1071. doi:10.2147/JMDH.S302826, PMID:33994792.

- [4] Xu Y, Zhang P, Wang C, Shan Y, Wang D, Qian F, *et al*. Effect of ginsenoside Rg3 on tyrosine hydroxylase and related mechanisms in the forced swimming-induced fatigue rats. *J Ethnopharmacol* 2013;150(1):138–147. doi:10.1016/j.jep.2013.08.016, PMID:23994341.
- [5] He X. Study on the Effect of Ginsenoside Rg3 on in Vitro Immune Enhancement in Patients with Esophageal Cancer Undergoing Radiotherapy. *Int Immunopharmacol* 2022;22(18):98–111. doi:10.13638/j.issn.1671-4040.2022.18.001.
- [6] Zuany-Amorim C, Hastewell J, Walker C. Toll-like receptors as potential therapeutic targets for multiple diseases. *Nat Rev Drug Discov* 2002;1(10):797–807. doi:10.1038/nrd914, PMID:12360257.
- [7] Xu H, Ran J, Wang D, Zhang W, Bai XY. Research Progress on Ren Shen (Ginseng Radix et Rhizoma) Regulating Immune System Diseases and Quality Marker Prediction Analysis. *Chinese Archives of Traditional Chinese Medicine* 2025;43(5):129–138. doi:10.13193/j.issn.1673-7717.2025.05.026.
- [8] Wang K, Han C, Li J, Qiu J, Sunarso J, Liu S. The Mechanism of Piezocatalysis: Energy Band Theory or Screening Charge Effect? *Angew Chem Int Ed Engl* 2022;61(6):e202110429. doi:10.1002/anie.202110429, PMID:34612568.
- [9] Hotchkiss RD. The identification of nucleic acids as genetic determinants. *Ann N Y Acad Sci* 1979;325:320–342. doi:10.1111/j.1749-6632.1979.tb14143.x, PMID:378075.
- [10] Stein RJ, Gerarde HW. Cytologic Demonstration of Nucleic Acids in Tissue Culture. *Science* 1950;111(2880):256–257. doi:10.1126/science.111.2880.256, PMID:17795467.
- [11] Baek JH, Heo JY, Fava M, Mischoulon D, Choi KW, Na EJ, *et al*. Effect of Korean Red Ginseng in individuals exposed to high stress levels: a 6-week, double-blind, randomized, placebo-controlled trial. *J Ginseng Res* 2019;43(3):402–407. doi:10.1016/j.jgr.2018.03.001, PMID:31308812.
- [12] Mu H, Gao Y, Wang J. Ginseng Extract Improves the Subhealth Status in Young Population: An Observational Study. *Future Integr Med* 2023;2(2):113–115. doi:10.14218/FIM.2023.00004.
- [13] Lu G, Liu Z, Wang X, Wang C. Recent Advances in Panax ginseng C.A. Meyer as a Herb for Anti-Fatigue: An Effects and Mechanisms Review. *Foods* 2021;10(5):1030. doi:10.3390/foods10051030, PMID:34068545.
- [14] Li N, Pang Q, Zhang Y, Lin J, Li H, Li Z, *et al*. Ginsenoside compound K reduces neuronal damage and improves neuronal synaptic dysfunction by targeting Aβ. *Front Pharmacol* 2023;14:1103012. doi:10.3389/fphar.2023.1103012, PMID:36873999.
- [15] Chen L, Geng N, Chen T, Xiao Q, Zhang H, Huo H, *et al*. Ginsenoside Rb1 Improves Post-Cardiac Arrest Myocardial Stunning and Cerebral Outcomes by Regulating the Keap1/Nrf2 Pathway. *Int J Mol Sci* 2023;24(5):5059. doi:10.3390/ijms24055059, PMID:36902487.
- [16] Lee SB, Cho HI, Jin YW, Lee EK, Ahn JY, Lee SM. Wild ginseng cambial meristematic cells ameliorate hepatic steatosis and mitochondrial dysfunction in high-fat diet-fed mice. *J Pharm Pharmacol* 2016;68(1):119–127. doi:10.1111/jphp.12487, PMID:26806698.
- [17] Solano F. Photoprotection and Skin Pigmentation: Melanin-Related Molecules and Some Other New Agents Obtained from Natural Sources. *Molecules* 2020;25(7):1537. doi:10.3390/molecules25071537, PMID:32230973.
- [18] Ran X, Dou D, Chen H, Ren G. The correlations of adverse effect and tonifying effect of ginseng medicines. *J Ethnopharmacol* 2022;291:115113. doi:10.1016/j.jep.2022.115113, PMID:35202711.
- [19] Williams CT. Herbal Supplements: Precautions and Safe Use. *Nurs Clin North Am* 2021;56(1):1–21. doi:10.1016/j.cnur.2020.10.001, PMID:33549278.
- [20] Triposkiadis F, Xanthopoulos A, Parissis J, Butler J, Farmakis D. Pathogenesis of chronic heart failure: cardiovascular aging, risk factors, comorbidities, and disease modifiers. *Heart Fail Rev* 2022;27(1):337–344. doi:10.1007/s10741-020-09987-z, PMID:32524327.
- [21] Shi ZY, Zeng JZ, Wong AST. Chemical Structures and Pharmacological Profiles of Ginseng Saponins. *Molecules* 2019;24(13):2443. doi:10.3390/molecules24132443, PMID:31277214.
- [22] Xie J, Zhu F, Zhao Y, Wang Y, Matsubisa MG, Chabalala H, *et al*. Ginsenosides for depression treatment: From benchside to bedside. *Journal of Traditional Chinese Medical Sciences* 2025;12:210–220. doi:10.1016/j.jtcm.2025.03.007.
- [23] Dang H, Chen Y, Liu X, Wang Q, Wang L, Jia W, *et al*. Antidepressant effects of ginseng total saponins in the forced swimming test and chronic mild stress models of depression. *Prog Neuropsychopharmacol Biol Psychiatry* 2009;33(8):1417–1424. doi:10.1016/j.pnpbp.2009.07.020, PMID:19632285.
- [24] Song C, Yuan Y, Zhou J, He Z, Hu Y, Xie Y, *et al*. Network Pharmacology-Based Prediction and Verification of Ginsenoside Rh2-Induced Apoptosis of A549 Cells via the PI3K/Akt Pathway. *Front Pharmacol* 2022;13:878937. doi:10.3389/fphar.2022.878937, PMID:35600856.
- [25] Xiaodan S, Ying C. Role of ginsenoside Rh2 in tumor therapy and tumor microenvironment immunomodulation. *Biomed Pharmacother* 2022;156:113912. doi:10.1016/j.biopha.2022.113912, PMID:36288668.
- [26] Zhou G, Wang CZ, Mohammadi S, Sawadogo WR, Ma Q, Yuan CS. Pharmacological Effects of Ginseng: Multiple Constituents and Multiple Actions on Humans. *Am J Chin Med* 2023;51(5):1085–1104. doi:10.1142/S0192415X23500507, PMID:37385964.
- [27] Dai TY, Lan JJ, Gao RL, Zhao YN, Yu XL, Liang SX, *et al*. Panaxdiol saponins component promotes hematopoiesis by regulating GATA transcription factors of intracellular signaling pathway in mouse bone marrow. *Ann Transl Med* 2022;10(2):38. doi:10.21037/atm-21-4800, PMID:35282082.
- [28] Calabrese MF, Rajamohan F, Harris MS, Caspers NL, Magyar R, Withka JM, *et al*. Structural basis for AMPK activation: natural and synthetic ligands regulate kinase activity from opposite poles by different molecular mechanisms. *Structure* 2014;22(8):1161–1172. doi:10.1016/j.str.2014.06.009, PMID:25066137.
- [29] Asby DJ, Cuda F, Beyaert M, Houghton FD, Cagampang FR, Tavassoli A. AMPK Activation via Modulation of De Novo Purine Biosynthesis with an Inhibitor of ATIC Homodimerization. *Chem Biol* 2015;22(7):838–848. doi:10.1016/j.chembiol.2015.06.008, PMID:26144885.
- [30] Pradelli LA, Bénétteau M, Chauvin C, Jacquin MA, Marchetti S, Muñoz-Pinedo C, *et al*. Glycolysis inhibition sensitizes tumor cells to death receptors-induced apoptosis by AMP kinase activation leading to Mcl-1 block in translation. *Oncogene* 2010;29(11):1641–1652. doi:10.1038/nc.2009.448, PMID:19966861.
- [31] Wang LY, Gu XY, Cui Y, Liu ST, Wang Y, Zhang JQ, *et al*. Mechanism of ginsenoside Rb1 in ameliorating hypoxia/reoxygenation injury in H9c2 cardiomyocytes through CTR1 ubiquitination-mediated regulation of cuproptosis. *China Journal of Chinese Materia Medica* 2025. doi:10.19540/j.cnki.cjcm.20250529.401.
- [32] Gunata M, Parlakpinar H. A review of myocardial ischaemia/reperfusion injury: Pathophysiology, experimental models, biomarkers, genetics and pharmacological treatment. *Cell Biochem Funct* 2021;39(2):190–217. doi:10.1002/cbf.3587, PMID:32892450.
- [33] Nasiri R, Arefnezhad R, Baniasad K, Hosseini SA, Jeshari AS, Miri M, *et al*. Baicalin and baicalein against myocardial ischemia-reperfusion injury: A review of the current documents. *Tissue Cell* 2025;93:102772. doi:10.1016/j.tice.2025.102772, PMID:39923649.
- [34] Ye R, Li N, Han J, Kong X, Cao R, Rao Z, *et al*. Neuroprotective effects of ginsenoside Rd against oxygen-glucose deprivation in cultured hippocampal neurons. *Neurosci Res* 2009;64(3):306–310. doi:10.1016/j.neures.2009.03.016, PMID:19447300.
- [35] Ye R, Han J, Kong X, Zhao L, Cao R, Rao Z, *et al*. Protective effects of ginsenoside Rd on PC12 cells against hydrogen peroxide. *Biol Pharm Bull* 2008;31(10):1923–1927. doi:10.1248/bpb.31.1923, PMID:18827356.
- [36] Kelly H, Goldberg RM. Systemic therapy for metastatic colorectal cancer: current options, current evidence. *J Clin Oncol* 2005;23(20):4553–4560. doi:10.1200/JCO.2005.17.749, PMID:16002847.
- [37] Barnett AH, Mithal A, Manassie J, Jones R, Rattunde H, Woerle HJ, *et al*. Efficacy and safety of empagliflozin added to existing antidiabetes treatment in patients with type 2 diabetes and chronic kidney disease: a randomised, double-blind, placebo-controlled trial. *Lancet Diabetes Endocrinol* 2014;2(5):369–384. doi:10.1016/S2213-8587(13)70208-0, PMID:24795251.
- [38] Zhang MM, Hu LM, Zhou Q, Wang SH, Wu SC. Therapeutic effect and mechanism of ginsenoside Ro on SH-SY5Y cell injury induced by oxygen-glucose deprivation/reoxygenation. *Chin J Neuroimmunol & Neurol* 2025;32(1):35–41. doi:10.3969/j.issn.1006-2963.2025.01.006.
- [39] Douglas-Escobar M, Weiss MD. Hypoxic-ischemic encephalopa-

- thy: a review for the clinician. *JAMA Pediatr* 2015;169(4):397–403. doi:10.1001/jamapediatrics.2014.3269, PMID:25685948.
- [40] Xue YL, Xu J, Liu GH, Huang C, Feng YF, Xu MY, *et al*. Evaluation of sub-health status of Chinese urban residents using the Sub-health Measurement Scale Version 1. *Chinese General Practice* 2021;24(7):834–84. doi:10.12114/j.issn.1007-9572.2020.00.530.
- [41] Ginsburg LR, Tregunno D, Norton PG, Mitchell JI, Howley H. ‘Not another safety culture survey’: using the Canadian patient safety climate survey (Can-PSCS) to measure provider perceptions of PSC across health settings. *BMJ Qual Saf* 2014;23(2):162–170. doi:10.1136/bmjqs-2013-002220, PMID:24122954.
- [42] Latocha KM, Løppenthin KB, Østergaard M, Jennum PJ, Christensen R, Hetland M, *et al*. Cognitive behavioural therapy for insomnia in patients with rheumatoid arthritis: protocol for the randomised, single-blinded, parallel-group Sleep-RA trial. *Trials* 2020;21(1):440. doi:10.1186/s13063-020-04282-6, PMID:32471477.