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A network pharmacology approach to explore the potential role of *Panax ginseng* on exercise performance

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INTRODUCTION

The World Health Organization (WHO) defines health as the absence of disease and stable physical states as a state of complete mental and social perfection¹. However, it is difficult for modern people to maintain a healthy state physically and mentally due to irregular lifestyles, imbalance in nutritional intake, excessive drinking, and stress. Although health care focused on the purpose of treatment for the consequences of the disease in the past, the new approach to health care is comparatively balanced by finding ways to reduce or prevent chronic and lethargic conditions along with lifestyle changes². Lack of exercise can reduce the amount of physical activity and leading to weakened muscles, which can consequently lead to a decrease in exercise performance³. Some studies suggest that increasing physical activity or improving nutrition can increase life expectancy and improve health and lifestyle⁴⁻⁶.

G protein-coupled receptors (GPCRs) are a transmembrane receptor superfamily that transduce multiple signals of several hormones and neurotransmitters and are involved in cellular physiological responses ranging from regulating intracellular cyclic adenosine monophosphate (cAMP) concentrations to gene expression. In the intracellular signaling cascade through GPCR, various signaling cascades begin activation through a special protein, namely G protein (GTP-binding protein)⁷. Some studies have suggested that GPCR signaling is associated with potential drug targets in cardiovascular diseases. In particular, GPCRs play a crucial role in cardiovascular homeostasis by regulating blood pressure elevation and ventricular hypertrophy^{8,9}. Therefore, there may be a close relationship between exercise capacity improvement and the GPCR signaling system at the molecular level.

Panax ginseng C.A. Meyer (ginseng), also known as Korean ginseng, a representative agricultural product of Korea, has been known to be a mysterious medicine since ancient times, and is known to exhibit various physiological activities¹⁰. Characteristic effects include vitality recovery and metabolism promotion, immunity enhancement, prevention of infec-

[Purpose] As *Panax ginseng* C. A. Meyer (ginseng) exhibits various physiological activities and is associated with exercise, we investigated the potential active components of ginseng and related target genes through network pharmacological analysis. Additionally, we analyzed the association between ginseng-related genes, such as the G-protein-coupled receptors (GPCRs), and improved exercise capacity.

[Methods] Active compounds in ginseng and the related target genes were searched in the Traditional Chinese Medicine Database and Analysis Platform (TCMSP). Gene ontology functional analysis was performed to identify biological processes related to the collected genes, and a compound-target network was visualized using Cytoscape 3.7.2.

[Results] A total of 21 ginseng active compounds were detected, and 110 targets regulated by 17 active substances were identified. We found that the active compound protein was involved in the biological process of adrenergic receptor activity in 80%, G-protein-coupled neurotransmitter in 10%, and leucocyte adhesion to arteries in 10%. Additionally, the biological response centered on adrenergic receptor activity showed a close relationship with G protein through the beta-1 adrenergic receptor gene reactivity.

[Conclusion] According to bioavailability analysis, ginseng comprises 21 active compounds. Furthermore, we investigated the ginseng-stimulated gene activation using ontology analysis. GPCR, a gene upregulated by ginseng, is positively correlated to exercise. Therefore, if a study on this factor is conducted, it will provide useful basic data for improving exercise performance and health.

[Key words] *Panax ginseng* C. A. Meyer, exercise, GPCR, beta-1 adrenergic receptor, traditional Chinese medicine database and analysis platform, exercise nutrition

tious diseases, concentration enhancement, and antioxidant action¹¹. Additionally, in our previous study, carbohydrate and fat metabolism increased in the gastrocnemius of mice treated with ginseng for two weeks and energy metabolism was increased¹². Some studies have shown that walking after taking red ginseng increases immune globulin and antibodies that increase white blood cell immunity, which is also associated with improved exercise performance¹³. Numerous studies have shown that *P. ginseng* contains physiologically active ingredients such as ginseng saponin, polyacetylene, antioxidant phenolic compounds, gomisin, and acid peptides¹⁴. Although ginseng contains various ingredients, there has been no research on its active ingredients and the target genes associated with improved exercise performance. In our study, we aimed to elucidate the potential active ingredients of ginseng and the related target genes using network pharmacological analysis and present basic biological data. Furthermore, the purpose of this study was to analyze the association between GPCRs and the regulatory role of ginseng in improving athletic performance.

METHODS

Identification of the active ingredients of ginseng

The active ingredients of ginseng were screened using the Traditional Chinese Medicine Database and Analysis Platform (TCMSP, <https://tcmsp-e.com/>), a unique pharmacology system for drug discovery¹⁵. The drug ability of the bioactive substances was analyzed based on the pharmacokinetics (absorption, distribution, metabolism, and excretion) properties of the drug, including oral bioavailability (OB), Caco-2 permeability (Caco-2), intestinal epithelial permeability, and drug-likeness (DL). As recommended by TCMSP, the main active compounds with $OB \geq 30\%$, $Caco-2 \geq -0.4$, and $DL \geq 0.18$, were selected as candidate compounds for further analysis.

Target protein collection and related biometabolic analysis

The targets of the key active ingredients in ginseng were obtained directly from the TCMSP, enabling assessment of biological functions through relevant targets¹⁵. The protein names of all target genes were converted into their corresponding gene symbols in the UniProt database. Gene Ontology (GO) analysis was performed to identify the biological processes related to the collected genes using Cytoscape visualization software 3.7.2 (<https://cytoscape.org/>). The *P*-value was set to >0.01 and calculated using the Benjamini–Hochberg method.

Target network analysis of ginseng bioactive substances

To understand the molecular mechanisms between various active ingredients and target genes fully, compound-target networks were constructed using Cytoscape visualization software 3.7.2¹⁶. The selected candidate compounds and targets were input into the software, and the network

was carried out. The relationships between various active ingredients of ginseng and their target genes, biological metabolic processes related to exercise metabolism were selected, and a network (Process-Target network, PT network) was constructed.

Statistics

GO analysis and enriched compound-target-pathway network analysis were performed using Cytoscape 3.7.2. Based on the genes with Benjamini–Hochberg FDR-corrected *P*-values < 0.1 , the collected data identified significantly enriched pathways for the active compounds. To construct the compound-target network, all node degrees of the enriched network were used to visualize the interaction networks.

RESULTS

Identification of active compounds of ginseng and their target genes using TCMSP

To identify and analyze the major active compounds in ginseng, the TCMSP and analysis platform were utilized. Based on the drug pharmacokinetics, DL values of 0.18 or more and OB values of 30% or more were analyzed by excluding Caco-2 values of -0.4 or more. A total of 21 active compounds in ginseng (Table 1) were detected, namely diop, stigmasterol, beta-sitosterol, inermin, kaempferol, chrysanthemaxanthin, aposiopolamine, celabenzine, deoxyharringtonine, dianthramine, arachidonate, frucinone

Table 1. Active compounds of *Panax ginseng*.

	Molecule name	OB (%)	Caco-2	DL
1	Diop	43.59	0.79	0.39
2	Stigmasterol	43.83	1.44	0.76
3	beta-sitosterol	36.91	1.32	0.75
4	Inermin	65.83	0.91	0.54
5	kaempferol	41.88	0.26	0.24
6	Chrysanthemaxanthin	38.72	0.51	0.58
7	Aposiopolamine	66.65	0.66	0.22
8	Celabenzine	101.88	0.77	0.49
9	Deoxyharringtonine	39.27	0.19	0.81
10	Dianthramine	40.45	-0.23	0.2
11	arachidonate	45.57	1.27	0.2
12	Frutinone A	65.9	0.89	0.34
13	Ginsenoside-Rh4	31.11	0.5	0.78
14	Girinimbin	61.22	1.72	0.31
15	Gomisin B	31.99	0.6	0.83
16	malkangunin	57.71	0.22	0.63
17	Panaxadiol	33.09	0.82	0.79
18	suchilactone	57.52	0.82	0.56
19	Alexandrin	36.91	1.3	0.75
20	ginsenoside Rg5	39.56	0.88	0.79
21	Fumarine	59.26	0.56	0.83

* OB, oral bioavailability; Caco-2, Caco-2 permeability; DL, drug-likeness.

A, Ginsenoside-Rh4, girinimbin, gomisin B, malkangunin, panaxadiol, suchilactone, alexandrin, ginsenoside Rg5, and fumarine.

Next, the compound-target gene network using Cytoscape visualization software 3.7.2 was analyzed to identify the target gene by 21 active compounds. As shown in Figure 1, the results of the 17 compound-gene networks were identified as eight highly redundant genes. By analyzing the number of genes regulated by 17 active substances in ginseng, 110 targets, excluding duplicates, were identified (Table 2). Eight active ginseng substances (ADRA1B, GABRA1, ADRB2, PIK3CG, HSP90, CHRNA7, NCOA2, and CHRM3) showed low correlations in the compound network. Subsequent experiments attempted to explore the molecular mechanisms affecting physical activity by analyzing the active substance network of ginseng via 110 genes.

GO functional enrichment analysis and constructing the network of compound-target

To discover the biological process of the target, we first performed GO functional enrichment analysis of the identified differentially expressed proteins of the target genes, which includes a biological process related to a gene for an individual gene, a molecular function of a gene, and a cellular component of an individual gene for gene function

research. GO enrichment analysis identified 932 core targets involved in biological processes, molecular functions, and cellular composition. In terms of biological processes, we found that proteins in the active compounds were significantly enriched within the GO categories linked cellular response to chemical stimulus, and response to organic substance, adenylate cyclase-modulating G-protein coupled receptor signaling pathway, G-protein coupled receptor signaling pathway, vascular process in circulatory system, blood circulation, positive regulation of intracellular signal transduction, response to nitrogen compounds, phospholipase C-activating G-protein coupled receptor signaling pathway, and response to oxygen-containing compounds. The *P*-values of enrichment analysis were calculated, and values < 0.01 were considered significantly enriched. These expression categories showed adrenergic receptor activity in 80%, G protein-coupled neurotransmitter in 10%, and leucocyte adhesion to arterial in 10% (Figure 2).

Next, we analyzed the relationship between related ontology and gene expression using Cytoscape. The top 10 enrichment results of biological processes based on *P*-values are shown in Table 3, including G protein-coupled neurotransmitter receptor activity (GO:0099528), adrenergic receptor activity (GO:0004935), and positive regulation of leukocyte adhesion to arterial endothelial

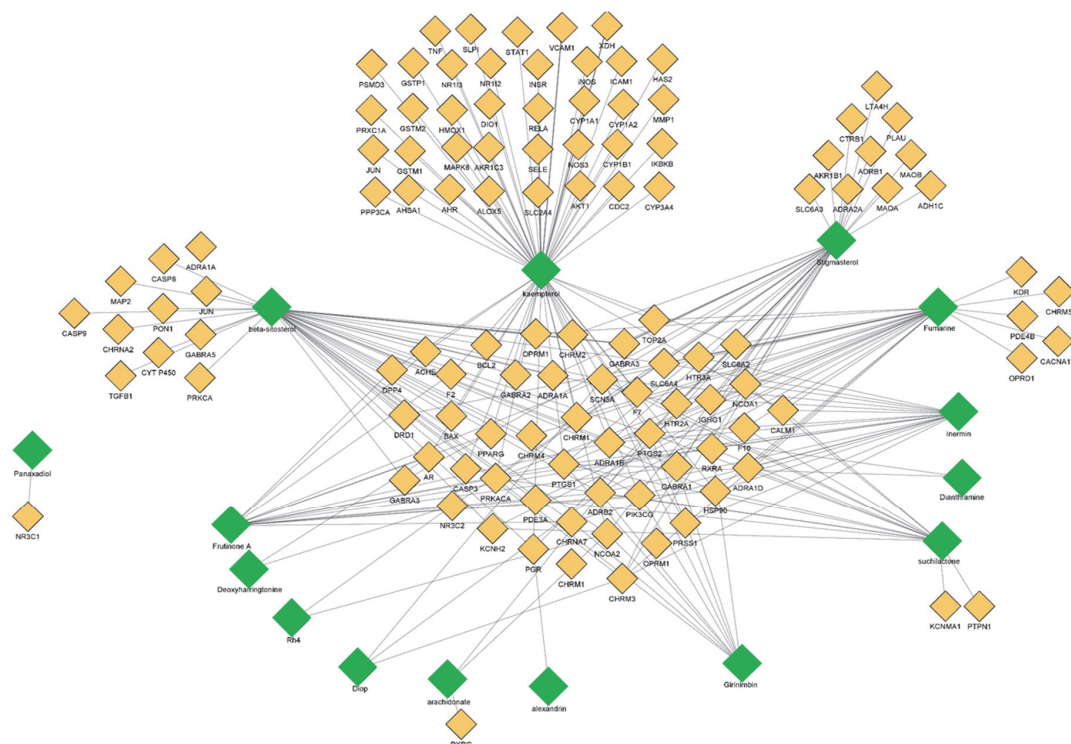


Figure 1. Gene network targeted by representative compounds of *Panax ginseng*. These active compounds are presented in light green text (Deoxyharringtonine, beta-sitosterol, Rh4, Dipo, arachidonate, alexandrin, Inermin, Girinimbin, suchilactone, Dianthramine, Panaxadiol, Fumarine, Sitigmasterol, Kampeferol, and fruinson A). The bold text in the different colored boxes indicates the target gene. The information of target genes is determined in Table 2. Top 8 targets of the representative compound-target networks of *Panax ginseng* are as follows (the bold font in yellow box): ADRB2: Beta-2 adrenergic receptor; ADRA1B: Alpha-1B adrenergic receptor; GABRA1: Gamma-aminobutyric acid receptor subunit alpha-1; PIK3CG: Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit, gamma isoform; CHRNA7: Neuronal acetylcholine receptor protein, alpha-7 cha; NCOA2: Nuclear receptor coactivator 2; CHRM3: Muscarinic acetylcholine receptor M3.

Table 2. Potential target genes by active compounds of *Panax ginseng*.

Molecule name	Gene symbol
Diop	ADRB2, CHRM3, SCN5A
Stigmasterol	ADH1C, ADRA1A, ADRA1B, ADRA2A, ADRB1, ADRB2, AKR1B1, CHRM1, CHRM2, CHRM3, CHRNA7, CTRB1, GABRA1, GABRA3, HTR2A, IGHG1, LTA4H, MAOA, MAOB, NCOA1, NCOA2, NR3C2, PGR, PLAU, PRKACA, PTGS1, PTGS2, RXRA, SCN5A, SLC6A2, SLC6A3
beta-sitosterol	ADRA1A, ADRA1B, ADRB2, BAX, BCL2, CASP3, CASP8, CASP9, CHRM1, CHRM2, CHRM3, CHRM4, CHRNA2, CHRNA7, CYT P450, DRD1, GABRA1, GABRA2, GABRA3, GABRA5, Hsp90, HTR2A, JUN, KCNH2, MAP2, NCOA2, OPRM1, PDE3A, PGR, PIK3CG, PON1, PRKACA, PRKCA, PTGS1, PTGS2, SCN5A, SLC6A4, TGFB1
Inermin	ADRA1B, ADRA1D, ADRB2, CALM1, CHRM3, CHRNA7, Hsp90, HTR3A, IGHG1, NCOA1, PIK3CG, PRKACA, PRSS1, PTGS1, PTGS2, RXRA, SCN5A, SLC6A4
kaempferol	ACHE, ADRB2, AR, CHRNA7, DPP4, F2, GABRA1, GABRA2, GSTM1, GSTM2, GSTP1, HAS2, HMOX1, Hsp90, ICAM1, IKBKB, iNOS, INSR, JUN, MAPK8, MMP1, NCOA2, NOS3, NR1I2, NR1I3, PGR, PIK3CG, PPARG, PPP3CA, PRKACA, PRSS1, PRXC1A, PSM3, PTGS1, PTGS2, RELA, SELE, SLC2A4, SLC6A2, SLPI, STAT1, TNF, TOP2A, VCAM1, XDH
Chrysanthemaxanthin	-
Aposiopolamine	-
Celabenzine	-
Deoxyharringtonine	AR, NR3C2
Dianthramine	Hsp90, PTGS1, PTGS2
arachidonate	NCOA2, PTGS1, PTGS2, RXRG
Frutinine A	ACHE, ADRB2, AR, CHRNA7, DPP4, F2, GABRA1, Hsp90
Ginsenoside-Rh4	PDE3A, PIK3CG, PPARG, PRKACA, PTGS1, PTGS2, XRA, SCN5A
Girinimbin	NCOA2, NR3C2
Gomisin B	ADRB2, CHRNA7, GABRA1, NCOA2, PIK3CG, PRKACA, PTGS1, PTGS2, RXRA, SCN5A
malkangunin	-
Panaxadiol	NR3C1
suchilactone	ADRA1D, ADRB2, CALM1, F10, F7, Hsp90, KCNH2, KCNMA1, NCOA1, PDE3A, PRKACA, PTGS1, PTGS2, PTPN1, RXRA, SCN5A
Alexandrin	PGR
ginsenoside Rg5	-
Fumarine	ADRA1B, ADRA1D, ADRB2, CACNA1S, CALM1, CHRM1, CHRM3, CHRM4, CHRM5, DRD1, F10, F7, Hsp90, HTR2A, HTR3A, KCNH2, KDR, OPRD1, OPRM1, PDE3A, PDE4B, PRKACA, PTGS1, PTGS2, SCN5A, SLC6A2, SLC6A4, TOP2A

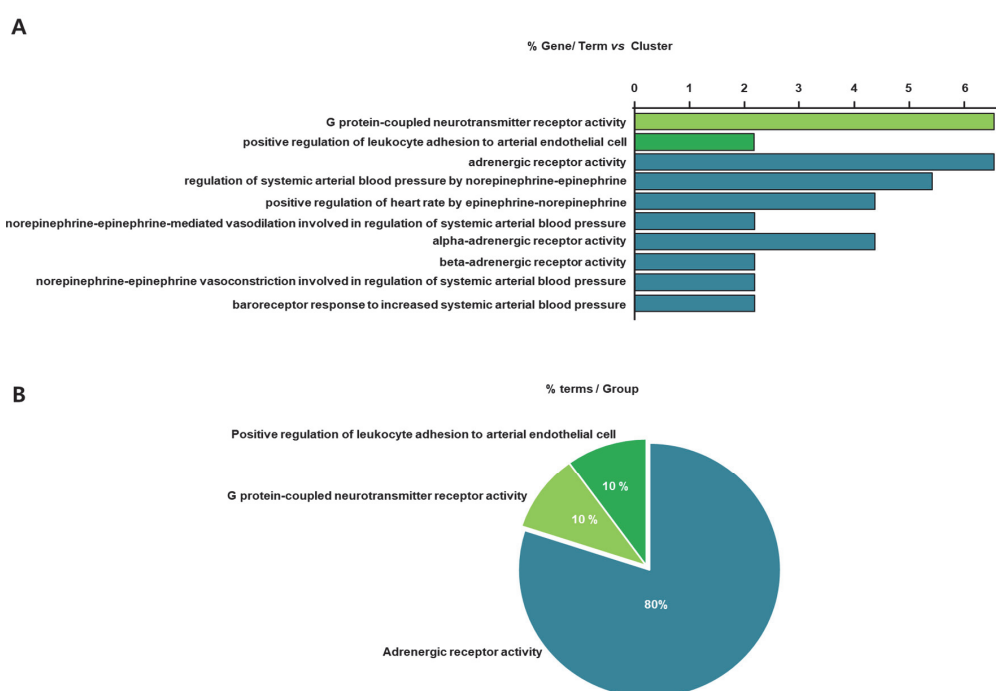
**Figure 2.** Gene ontology (GO) analysis of differentially expressed genes through 21 active compounds of *Panax ginseng*. (A) Highly expressed genes and (B) muscle-related genes Twenty-one active compounds of *P. ginseng* were identified using Cytoscape. Significantly enriched GO terms are shown with Benjamini–Hochberg FDR-corrected *P*-values <0.01.

Table 3. Top 10 enriched biological process of GO analysis using Cytoscape.

Category	Term	Molecule name	P-value	Gene
GOTERM_BP	GO:0099528	G protein-coupled neurotransmitter receptor activity	2.0 E-11	ADRB1, CHRM1, CHRM2, CHRM3, CHRM4, CHRM5
GOTERM_BP	GO:1904999	positive regulation of leukocyte adhesion to arterial endothelial cell	2.5 E-6	ALOX5, TNF
GOTERM_BP	GO:0004935	adrenergic receptor activity	2.0 E-11	ADRA1A, ADRA1B, ADRA1D, ADRA2A, ADRB1, ADRB2
GOTERM_BP	GO:0001993	regulation of systemic arterial blood pressure by norepinephrine-epinephrine	2.0 E-11	ADRA1A, ADRA1B, ADRA1D, ADRB1, ADRB2
GOTERM_BP	GO:0001996	positive regulation of heart rate by epinephrine-norepinephrine	2.0 E-11	ADRA1A, ADRA1B, ADRA1D, ADRB1
GOTERM_BP	GO:0002025	norepinephrine-epinephrine-mediated vasodilation involved in regulation of systemic arterial blood pressure	2.0 E-11	ADRB1, ADRB2
GOTERM_BP	GO:0004936	alpha-adrenergic receptor activity	2.0 E-11	ADRA1A, ADRA1B, ADRA1D, ADRA2A
GOTERM_BP	GO:0004939	beta-adrenergic receptor activity	2.0 E-11	ADRB1, ADRB2
GOTERM_BP	GO:0001994	norepinephrine-epinephrine vasoconstriction involved in regulation of systemic arterial blood pressure	2.0 E-11	ADRA1A, ADRA1D
GOTERM_BP	GO:0001985	negative regulation of heart rate involved in baroreceptor response to increased systemic arterial blood pressure	2.0 E-11	ADRA1A, ADRA1D

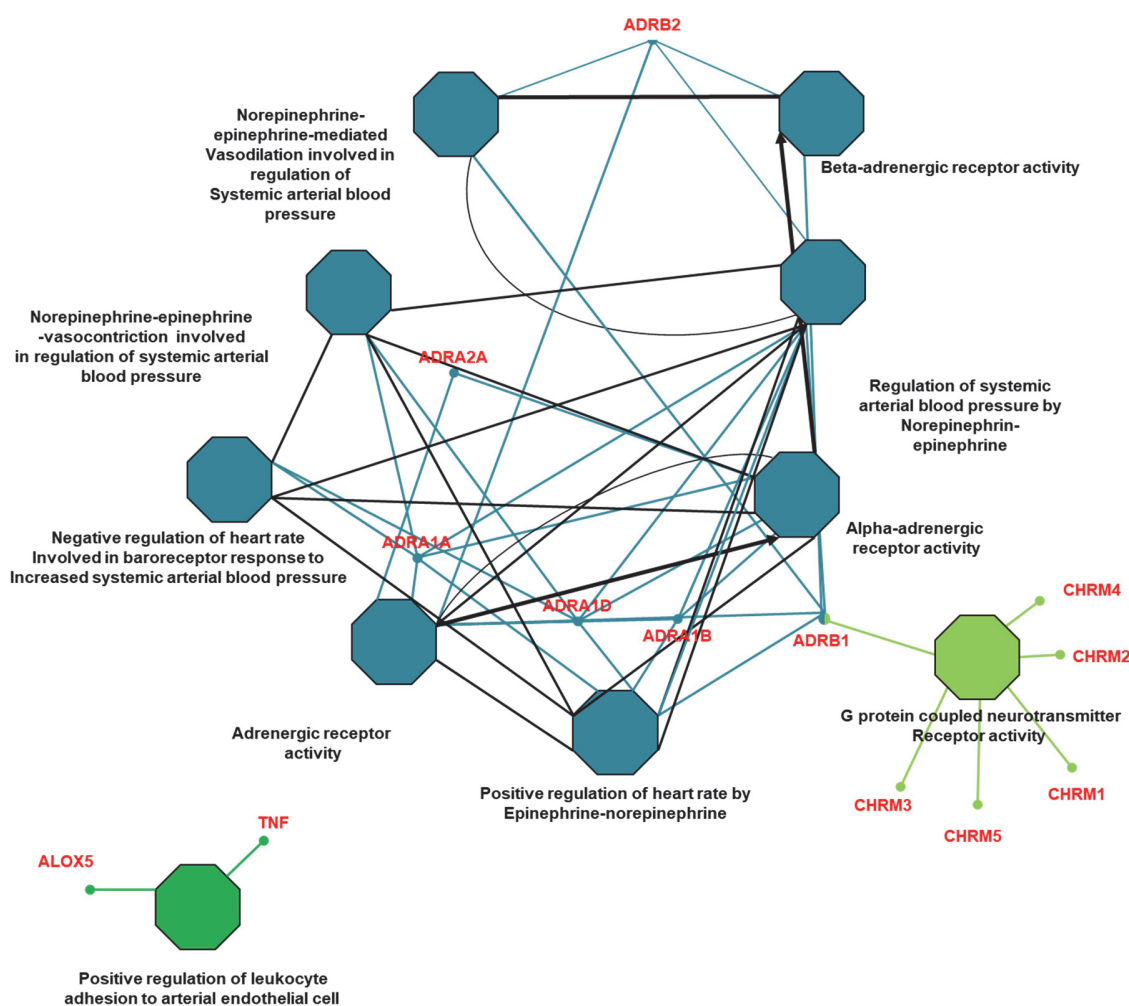


Figure 3. Biological processes of GO by compound-target of *Panax ginseng*. The enriched network of compound-target includes G protein-coupled neurotransmitter receptor activity, adrenergic receptor activity, and positive regulation of leukocyte adhesion to arterial endothelial cell. The target genes related to corresponding pathways are marked in red letter, and show in biological network. The thicker the connected solid line, the higher the relationship. ADRB1: beta-1 adrenergic receptor.

cells (GO:1904999). The list of related genes in the corresponding pathways is displayed in Table 3. The biological network of compound-target genes was then constructed. The network diagram of “core target-signaling pathways” is displayed in Figure 3. In the network, the red letters indicate the target genes of the active compounds and the corresponding pathways are designated by black letters and an octagon. The lists of GO terms and target genes in Table 3 are connected to the node. The light green node represents G protein-coupled neurotransmitter receptor activity, the blue nodes represent adrenergic receptor activity and its related pathways, and the green node represents positive regulation of leukocyte adhesion to arterial endothelial cells; the network contains 23 nodes. The connections between the active compounds and their corresponding pathways demonstrate a core network. The biological response centered on adrenergic receptor activity showed a close relationship with G protein through the reactivity of the beta-1 adrenergic receptor (ADRB1) gene, the key core node (Figure 3). ADRB1 has been suggested to regulate cardiovascular responses to exercise in healthy subjects¹⁷. Therefore, through a systematic analysis of its pharmacological function, ginseng may exert its druggable activity by regulating GPCR pathways, resulting in the enhancement of exercise performance.

DISCUSSION

The TCMSP is a platform that can check the correlation between drug target substances and diseases. This database contains information on drug–target networks; drug–target–disease networks; and pharmacokinetic properties of natural compounds, including oral bioavailability, drug-likeness, and intestinal epithelial permeability¹⁸. This is a groundbreaking *in silico* approach that can identify the correlations with target substances of various drugs and is a widely used method in traditional medicine and natural product studies¹⁹. However, despite the widespread use of these useful analyses, most studies are limited to nutrition and oriental medicine. Therefore, this study aimed to identify the potential active ingredients of ginseng and its related target genes through network pharmacological analysis and present basic exercise nutrition data. In particular, this study demonstrates that the integration of an exercise-enhancing GPCR and associated protein expression analysis. The network analysis of ginseng intake provides a useful approach to gain system-level insight into pharmacological efficacy and cardiovascular modulators.

Since ginseng has long been recognized for promoting health, many studies have been conducted on its effects^{20,21}. Ginseng has a number of applications as a functional health food. Rather than extracting individual compounds to produce exercise supplements, such as caffeine^{22,23}, capsaicin^{24,25}, and taurine²⁶, ginseng is extracted and utilized as a whole. As it contains various active compounds (ginsenosides), it delivers multiple benefits such as antioxidant²⁷, anti-obesity²⁸, and anti-fatigue²⁹, unlike the exercise supplements that exhibit only a single effect³⁰. Recently, various

studies have been conducted on the effects of exercise and complex intake on angiogenesis^{31,32}, immune response³³, antioxidant³⁴, and anti-fatigue³⁵. For this reason, ginseng has recently been evaluated as a potential candidate for improving exercise performance. However, these reported effects are variable^{36,37}; the reason behind this being problems associated with the exercise protocol, dose, and duration of intake. However, because the compounds in ginseng are diverse, it is not known which gene has the most interaction. Therefore, it is necessary to understand the molecular approaches for various parameters.

A recently published meta-analysis detailing the anti-fatigue efficacy of ginseng, indicated the effective dose in animal studies ranged from 50 mg to 800 mg/day and in clinical studies, 100 mg to a maximum 3.6 g/day³⁸. An animal study conducted over 30 days, where ginseng was administered to a range to animals that swam for exercises, reported that the mid-range dose of 300 mg/kg resulted in a superior anti-fatigue effect than the highest dose (600 mg/day)³⁹. In clinical studies, a quantity of ginseng less than 200 mg/day is demonstrated to improve cognitive and anaerobic performance in untrained young or older subjects⁴⁰. Ginseng has been reported to have an anti-fatigue effect in both aerobic and anaerobic exercise, and it has been reported that ginseng supplementation effects (anti-fatigue, anti-oxidant, anti-inflammatory, etc.) are relevant across a range of exercise intensities rather than a single, specified intensity⁴¹.

Exercise ability, nutrients, and supplements are all closely related. The human body can continue to exercise for a long period by muscles that utilize energy to resynthesize ATP from the food intake and ADP⁴². A total of 21 active ginseng ingredients were identified in this study (Table 1). However, 17 active substances that regulate the target genes were investigated (Figure 1, Table 2). Ginsenosides are divided into two groups: panaxadiols (Rb₁, Rb₂, Rb₃, Rc, Rd, Rg₃, Rh₂, and Rh₃) and panaxatriols (Re, Rf, Rg₁, Rg₂, and Rh₄)⁴³. Ginsenoside-Rh4 belonging to the proto-panaxatriol group has been reported to have anticancer effects. Ginsenoside-Rh5 is a minority deglycosylated ginsenosides, which has been reported to have multiple biological properties such as anti-cancer, cardioprotective, anti-diabetic, anti-inflammatory and neuroprotective⁴⁴. The gomisins family is known for its hepatoprotective action, but the sole effect of gomisins B is unknown. β -Sitosterol having diverse biological effects, is commonly used for heart disease, hypercholesterolemia, and immune system modulation. Alexandrin is a standard substance included in traditional medicines that plays an important role in the prevention and treatment of microbial diseases. Chrysanthemaxanthin is a golden yellow natural xanthophyll pigment found in small quantities in plants, and its direct action on physiological activity is unknown. Seventeen active substances (deoxyharringtonine, beta-sitosterol, Rh4, Dipo, arachidonate, alexandrine, inermine, girinimbine, suchilactone, dianthramine, panaxadiol, fumarine, stigmaterol, kaempferol, and fruinnone A) determined the compound targeting network in our study (Figure 1). Pharmacologically, active substances absorbed in a short period can be affected by various factors, such as exercise

time and physical strength³⁰. Therefore, through GO analysis, we suggest that the compounds present in ginseng may improve athletic performance. Continuous exercise is known to improve immune function and relieve inflammation. However, sudden high-intensity exercise or exercise until exhaustion can have the opposite effect. The top 17 active ginseng substances investigated in this study have antioxidant and anti-inflammatory functions, so if we focus on antioxidant and anti-inflammatory research, it will be of great help in maximizing the effects of exercise.

In contrast, Marshall et al.⁴⁵ reported a report on mitogen-activated protein kinase (MAPK) signaling in body metabolism regulation through exercise. A variant of GPCR is currently under pharmacological development for its gene expression actions, and GPCR has been shown to be closely related to exercise⁴⁶. Adenylate cyclase can be considered an important effector that ultimately transmits a signal that finely modulates the cAMP concentration through the G protein-coupled receptor in response to various stimuli outside the cell. It is known to influence ion channels or protein kinases as downstream signals by enabling interactions with G protein subunits or signals by extracellular hormones⁴⁷. Moreover, many types of G protein-coupled receptors activate MAPK-related signaling pathways; therefore, extracellular signal-regulated kinases (ERKs), Jun amino-terminal kinase/Stress-activated protein kinase, and p38, the fact that it activates MAPK, has been reported⁴⁸. MAPK regulates vascular smooth muscle cell proliferation in atherosclerosis, a representative cardiovascular disease⁴⁹. The physiologically active substances of ginseng identified in this study demonstrated having low physiological functions by regulating the GPCR signaling system. Therefore, we hypothesized that the 17 physiologically active substances in ginseng can improve exercise capacity by acting on the cardiovascular system, and this possibility was confirmed through GO analysis. We propose that ginseng intake during exercise can improve athletic performance and aid in cardiovascular diseases through GPCR and MAPK regulation.

In conclusion, we identified 21 bioactive substances in ginseng through network pharmacological analysis. Furthermore, we confirmed a close relationship between GPCR, which is a gene that can improve exercise performance, and ginseng. However, additional *in vitro* and *in vivo* studies to identify the effect of ginseng at the genetic level and determine any relationship with exercise are required. We propose that the analysis of the association between ginseng and exercise will generate data that will aid the improvement in athletic performance.

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