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Ginseng Research in the Era of Systems Biology

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Guest Editor

Jian Yan

UTHSC-Molecular Resource Center, Memphis, USA

http://uthsc.edu/research/molecular_resource/

Issue infomation

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ABSTRACT

Invited Review: Ginseng is actually a collection of 11 distinct species of slow-growing perennial plants with fleshy roots, but *Panax ginseng* C.A. Meyer (*Araliaceae*) or Korean ginseng is the main one. The root of *P. ginseng* is a traditional medicine in Korea, China and Japan that has been shown to produce a variety of medicinal effects. The reported pharmacological activities of ginseng and its constituents are related to possess antistress and antioxidant effects. The excess of free radicals may lead to peroxidative impairment of membrane lipids and consequently disrupt cellular functions and cause their death. This review details the bibliography supporting the medicinal efficacy of ginseng and evidence has been closely linked to its

protective properties against free radicals.

ABSTRACT

Invited Review: The increased emergence of multi-drug and pandrug resistant bacteria necessitates the identification of new therapies. Although antibiotics are used to treat infections, the novel antibiotic discovery rate lags behind development of resistance. Antibiotics in clinical use combat infection through bactericidal or bacteriostatic action, which allows for selection of resistant strains. To impede or avoid resistance, treatments targeting microbial cell pathways critical for virulence and pathogenicity, but not essential for viability are being explored. One such signaling pathway is quorum sensing (QS) which regulates virulence factor expression in many pathogenic bacteria. Interference with this signaling pathway results in attenuation of pathogenicity and allows the host immune response system to eradicate the infection. Natural products have long been a rich source of antibiotic scaffolds as well as inhibitors of QS. *Panax ginseng* has been used as an herbal panacea for thousands of years, yet its ability to inhibit bacterial growth and QS is only beginning to be characterized. This review provides a brief outline of the microbial infection process, an overview of quorum sensing, an introduction to the use of natural products as alternative therapies, and a synopsis of the current literature describing the anti-bacterial and anti-QS activities of *Panax ginseng*.

ABSTRACT

Invited Review: Ginseng produces a variety of proteins and enzymes: alcohol dehydrogenase, catalase, chitnases, spermidine synthase, and glutamate decarboxylase, which are enzymes related with stress. Arginase and ginsenoside-β-glucosidase are hydrolytic enzymes whereas ribonuclease is an enzyme with defense activity. Polygalacturonase-inhibiting protein is a defense protein. Latex-like protein is a protein with osmoregulatory function. Medicinal peptide, radioprotective protein and antiproliferative tetrapeptides are proteins with medicinal activity. The PACAP-immunoreactive component increases cAMP in human neuroblastoma cells. Ginseng major protein and glutathione-related oligopeptides from ginseng do not have well defined functions as yet.

ABSTRACT

Invited Review: Ginseng is a famous herbal medicine. The major active ingredient of ginseng is ginsenoside, a ginseng saponin. After oral intake of ginseng, the major ginsenosides are hydrolyzed in the human intestinal tract into

the more active minor ginsenosides, and the converted minor ginsenosides are absorbed. The minor ginsenosides such as ginsenoside C-K, Rh2, Rh1, Rg3, and Rg2 have special physiological and therapeutic activities that are readily used for ginseng medicines and health foods. This review introduces the biotransformation of ginsenosides into minor ginsenosides and introduces four newly developed types of ginsenosidases (ginseng saponin-glycosidases) *i.e.*, ginsenosidase type I, which can hydrolyze multi-20-*O*-glycosides and 3-*O*-glycosides of the protopanaxadiol (PPD) type ginsenosides; ginsenosidase type II, which can hydrolyze multi-20-*O*-glycosides of the ginsenosides; ginsenosidase type III, which can hydrolyze 3-*O*-glucoside of the multi-PPD type ginsenosides; ginsenosidase type IV, which can hydrolyze multi-6-*O*-glycosides of the protopanaxatriol (PPT) type ginsenosides.

ABSTRACT

Invited Review: Ginseng has been used as a traditional medicine in Asian countries for thousands of years. The main molecular components responsible for the actions of ginseng are ginsenosides. It is thought that the activities are mainly carried out by the minor ginsenosides which are obtained via the hydrolysis of the sugar moieties in the major ginsenosides using hydrolytic acid, heating or microbial transformation. Due to the significant region- and stereoselectivities of biotransformation, there is a profound potential for ginsenoside structural modification. In this article, the biotransformation methods of ginsenosides by fungi and bacteria, and the enzymes involved, are reviewed.

ABSTRACT

Invited Mini-Review: Ginseng is a slow-growing, deciduous perennial plant that belongs to the Araliaceae family and the *Panax* genus. There are a variety of species but the two main types are *Panax ginseng* C.A Meyer (Asian ginseng) and *Panax quinquefolius* (American ginseng). Asian ginseng is further subdivided by drying method of the root into either red or white ginseng. Traditionally, both Asian and American ginsengs have been used for a wide array of preventive and therapeutic purposes. Ginsenosides or dammarane triterpenoids are plant secondary metabolites and are thought to be the major active constituents of the *Panax* species. Ginsenosides are primarily classified into two groups, which are the 20(S)-protopanaxadiol (PD) and the 20(S)-protopanaxatriol (PT), which is based on their chemical structural differences. Differences in ginsenosides chemical structure are due to the type, position, and the number of sugar moieties attached by glycosidic bonds. Both Asian and American ginsengs generally contain a similar ginsenosides profile but vary in terms of amount of individual compounds. Rare ginsenosides which may not naturally be present in ginseng extracts can be obtained via processing methods such as steaming, microbial or enzymatic transformation. The detection and generation of rare ginsenosides can produce ginsenosides such as Rg3, Rh2, IH-901 (K), 25-OH-PD, 25-OCH3-PD among others and this has increased the interest into the biological activity of ginseng. This review focuses on the recent developments in ginseng research.

ABSTRACT

Invited Mini-Review: In traditional Chinese medicine, *Panax ginseng* C.A. Meyer (PG) invigorates “qi” of kidney, spleen and lung, promotes body fluids production, calms the mind to promote intelligence, while *P. quinquefolium* L. (PQ) supplies “qi”, nourishes “Yin”, clears fire and promotes body fluid production, both are classified as “restoratives”. *P. notoginseng* (Burk.) F.H. Chen (PN) removes blood stasis, stops bleeding, promotes blood circulation with analgesic effect, and is classified as “hemostatics”. The major bioactive principles of *Panax* species, ginseng saponins, are classified into dammarane, oleanane, and ocotillol types. PQ contains all three types of ginseng saponins. PG contains dammarane and oleanane types. PN contains only dammarane type, and a peptide like substance dencichine is the major active component to stop bleeding. PN contains the highest level of ginseng saponins (6.24-10.32%), followed by PQ (4.50-6.45%) and PG (3.50-4.84%). Besides ginseng saponin in which the chemistry and biological effects have been studied in detail, the polysaccharides, polypeptides and fatty acids are also investigated by many scholars. In this paper, the separation and identification of ginseng saccharides, immuno-modifier, anti-inflammatory, anticancer, anti-ulcer or antiadhesive, anti-diabetic and anti-hyperlipidemic effects of such saccharides are reviewed, while the causes of succession cropping obstacle and future ways for the development of *Panax* species are discussed and suggested.

ABSTRACT

Invited Review: Despite introduction of highly active antiretroviral therapy, the AIDS pandemic continues to spread across the world. Although the development of an effective vaccine is urgently required, we still do not have any vaccine. In this regard, we need to look back towards alternative ways based on history and the recent scientific literature. Immunotherapy is currently receiving great attention as supporting treatment modalities in the management of cancer and AIDS patients whose immune function is compromised. Ginseng has long been used to maintain the vitality of man in the Orient. Recent studies have shown that ginseng has significant potential as an immune modulator and adjuvant. We have reported the beneficial effects of Korean red ginseng (KRG) in HIV-1-infected individuals since 1991. Several patients have remained healthy for up to 23 years in the absence of HAART. Of note, most patients treated with KRG reveal significantly high frequency of genetic defects in HIV-1 genes of as well as attenuation of chronic immune activation. A series of our data and literature show the possibility that ginseng could be a safe and effective medicine for treating AIDS patients.

ABSTRACT

Invited Mini-Review: The root of ginseng, *Panax ginseng*, has been heat-processed to improve its medicinal efficacy in Korea. Ginsenosides have been regarded as the main active components responsible for the pharmacological activities of ginseng. Although the Maillard reaction is known as a major source of compounds related to enhanced antioxidant activity by heat treatment in various crude drugs or foods, the chemical and free radical scavenging activity changes of ginsenosides brought about by the Maillard reaction have not yet been elucidated. To demonstrate the Maillard reaction of ginsenosides by heat-processing in ginseng, we heat-processed the two ginsenosides Rb_1 and Rb_2 with glycine as an amino acid, and the hydroxyl radical (•OH) scavenging activity was measured with an electron spin resonance spectrometer. Rb_1 and Rb_2 were gradually changed into 20(*S*)-Rg_3, 20(*R*)-Rg_3, Rk_1, and Rg_5 by heat-processing, and the sugar moieties at carbon-20 were separated. The •OH scavenging activities of 20(*S*)-Rg_3 and Rg_5 were stronger than that of Rb_1, but 20(*R*)-Rg_3 and Rk_1 showed weak or no •OH scavenging activities. The generation of Maillard reaction products, although limited to the reaction between the glucosyl moiety and glycine, were positively correlated with the •OH scavenging activity. However, certain amino acids such as L-arginine block the structural change of ginsenosides, leading to a stronger •OH scavenging activity. Based upon chemical and •OH scavenging activity tests using Maillard reaction model experiments, the scientific evidence underlying the increase in free radical scavenging activity of ginseng induced by heat-processing was elucidated.

ABSTRACT

Invited Mini-Review: Ginsenoside Re (G-Re), a single compound extracted from ginseng, shows multifaceted pharmacological activities. Reports have demonstrated that one of the most important pharmacological functions of G-Re is antihyperglycemia, including decreased blood glucose, improved glucose tolerance, and improved insulin resistance. The mechanism of the anti-diabetic effect of G-Re, however, is not entirely understood. The possible mechanism may be through several complex bioactive procedures, such as molecular biological and antioxidant mechanisms *etc*. In this mini-review, we will discuss the antihyperglycemic property of G-Re and its possible mechanisms.

ABSTRACT

Invited Mini-Review: Ginseng, which contains protopanaxadiol and protopanaxatriol ginsenosides as major constituents, has been used as a herbal medicine for more than 2000 years. When ginseng is orally administered to humans or experimental animals, its protopanxadiol ginsenosides are transformed predominantly to compound K by intestinal bacteria, and its protopanaxatriol ginsenosides are transformed to ginsenoside Rh1, ginsenoside F1, and protopanaxatriol by gastric juices and intestinal microflora. The fecal compound K-forming activity profile of ginseng extract in ginseng-treated individuals is proportional to that of the area under the blood concentration curve for compound K. Furthermore, compound K, ginsenoside Rh1 and protopanaxadiol may be absorbed into blood. These

metabolites exhibit more potent pharmacological effects, such as, anti-tumor, anti-inflammatory, anti-diabetic, anti-allergic and neuroprotective effects, than the parental ginsenosides, such as ginsenoside Rb1, Rb2 or Re, according to *in vitro* studies, parentally administered ginsenosides and their metabolites exhibit these biological effects *in vivo*. Based on these findings, intestinal microflora probably play an important role in the pharmacological action of orally administered ginseng.

ABSTRACT

Original Research Paper: Here, efficient plantlet regeneration via somatic embryogenesis from *Panax quinquefolium* hairy roots was reported. Callus development was optimal on MS medium containing 2,4-dichlorophenoxyacetic acid (1 mg l^{-1}) and α-naphthalene acetic acid (1 mg l^{-1}). After a 4-week growth, calli were transferred onto MS medium with different combinations of plant growth regulators (PGRs). The highest embryogenesis frequency (~55%) of the calli occurred with 0.5 mg l^{-1} 2,4-dichlorophenoxyacetic acid after an additional 2-month culture. During embryos germination, different media with 3 mg l^{-1} gibberellin were evaluated for plantlet rooting. It was indicated that the suitable medium was 1/2 MS among the media tested. Furthermore, different PGRs were appraised for plantlet rooting using 1/2 MS medium. The data implicated that abscisic acid (0.5 mg l^{-1}) could play a role in promoting plantlet rooting.

ABSTRACT

Original Research Paper: In the newly established immunostaining method, Eastern blotting, we developed a new way to separate the ginsenoside molecule into two functional parts using a simple and well-known chemical reaction. The sugar parts were oxidized by $NaIO_4$ to give dialdehydes, which reacted with amino groups of the protein and covalently bound to the adsorbent PVDF membrane. The MAb bound to the aglycon part of the ginsenoside molecule for immunostaining. Eastern blotting indicated the specific staining of ginsenoside (G)-Rb1 together with other ginsenosides, G-Rc and -Rd of which cross-reactivities were 0.02% compared with H_2SO_4. When the mixture of anti-G-Rg1 and -Rb1 MAbs and the pair of substrates were tested for staining of ginsenosides, all ginsenosides, G-Rg1, -Re, -Rd, -Rc and -Rb1 were stained as a blue and a purple color, respectively. As an application we analyzed several Alariacean plants by Eastern blotting using anti-G-Rb1 MAb resulting in the isolation of G-Rb1 from *Kalopanax pictus*. We succeeded one-step isolation of G-Rb1 from the crude ginseng extract using immunoaffinity column combined with anti-G-Rb1 MAb. It became evident that the washing fraction contained all of components except antigen, G-Rb1 giving a knockout extract named by us. As other application we purified and identified two known ginsenosides from the crude extract of *P. japonicus* using Eastern blotting and immunoaffinity column combined with anti-G-Rb1 MAb.

ABSTRACT

Original Research Paper: The protopanaxatriol-type of ginsenosides isolated from the leaves of American ginseng mainly contained Rg1 and Re by High Performance Liquid Chromatography. Then isolation and purification of ginsenoside Rg1 and ginsenoside Re were carried out by repeated crystallization and silica gel column chromatography. And the purity of both ginsenoside Rg1 and ginsenoside Re were higher than 95%. *In vitro* experiment, assayed the effect of ginsenoside Rg1, ginsenoside Re and the protopanaxatriol-type of ginsenosides isolated from the leaves of American ginseng on porcine pancreatic lipase activity. It was determined by measuring released free fatty acids after incubating in substrate emulsions containing bile salts and phosphatidylcholine by water bath heating at 37°C. The absorbance of extreme colouration solutions on pancrestic lipase activity was measured at 480 nm. Both the protopanaxatriol-type of ginsenosides and ginsenoside Rg1 had no effect on inhibiting the pancreatic lipase activity, while ginsenoside Re had little effect. In order to clarify whether the protopanaxatriol-type of ginsenosides isolated from American ginseng leaves had anti-obesity effect *in vivo* or not, we examined the anti-obesity activity by testing the saponins preventing the obesity induced by feeding a high-fat diet to mice for 8 weeks. Body weight, food intake, organ weight, adipose tissue weight, serum parameters and liver lipids were measured and analyzed. The results demonstrated that the protopanaxatriol-type of ginsenosides isolated from American ginseng leaves had no inhibition activity of pancreatic lipase *in vitro*, however, it played an important role in preventing obesity, fatty liver and hypertriglyceridemia in mice fed with a high-fat diet during the long-term experiment.

ABSTRACT

Original Research Paper: Compound K (CK) is one of the principal metabolites of ginseng in human body which has been reported to exert diverse pharmaceutical activities including anticarcinogenic and antitumor effects on different lineages of cancer cells. However, the effect and mechanism of CK on colon cancer cells are not fully understood. In the present study the screening process was conducted with 12 different ginsenosides and metabolites, which showed CK was the most potent growth inhibitory compound against HT-29 colon cancer cells. The IC_{50} value of CK was 12.7 μM at 72 h. Cellular responses and growth pattern was analyzed simultaneously after CK treatment by Real Time Cellular Analysis (RTCA) method. CK treatment at specific concentration and time-point represented characteristic cytostatic stage in growth profile of HT-29 cells, and flow cytometric analysis showed that CK induced G_1 phase arrest in cell cycle distribution followed by apoptosis. The G_1 phase arrest was accompanied by down-regulation of cyclin D3, CDK6, and up-regulation of $p21^{WAF-1/CIP1}$, and apoptosis was evidenced by inactivation of p-Bcl-2 and p-Akt. These results demonstrated that CK caused growth inhibition of HT-29 cells by blocking cells in G_1 phase and inducing apoptosis.

ABSTRACT

Original Research Paper: Ginseng is a traditional Chinese herb commonly used in the formulation of tonics. There are 2 main varieties: Oriental (*Panax ginseng*) and American ginsengs (*Panax quinquefolius*). Traditional means of authenticating ginseng have become less reliable since they are being processed into various formulations such as tablets, capsules, powder and tea. These products are sometimes also adulterated. This study employed SDS-PAGE as a technique for differentiating between the 2 varieties of ginsengs. Ginseng proteins were separated using a 12% polyacrylamide gel with a three-step electrophoresis: 18 mA for 15 mins, 24 mA for 30 mins and 34 mA for 30 mins. Five bands were identified as potential markers for the ginsengs. Among these, 3 bands at median molecular weights of ~19.47 kDa (interquartile range (IQR) 18.81–20.11 kDa), ~34.42 kDa (IQR 33.75–35.14 kDa) and ~47.35 kDa (IQR 46.16–48.16 kDa) were common to both ginsengs. The band at ~13.23 kDa (IQR 12.78–13.42 kDa) was unique to American ginseng, and the band at ~29.54 (IQR 29.27–29.69 kDa) was unique to Oriental ginseng. This study shows the potential of SDS-PAGE as a proteomic tool in the analysis of ginseng proteins. We hope that these findings can provide an insight to the differences in protein profiles of the 2 ginseng species, and benefit other researchers who are also doing proteomic research on this herb.

ABSTRACT

Research Note: In this trial, *Panax ginseng* has been checked for its efficacy in treatment of attention deficit hyperactivity (ADHD) patients. Four 14-17-year old male psychiatric outpatients, diagnosed with ADHD were rated at baseline and while taking *Panax ginseng* or placebo respectively to determine its efficacy as a treatment for ADHD. Improvement was valuated using comparisons of Conners' parent ratings. Patients' mean scores improved for Conners' Hyperactivity, Inattention and Immaturity factors. Although the sample size is very small and therefore generalization is very difficult, this observation indicates that *P. ginseng* might also be a slightly effective treatment for ADHD.

Maria Victoria Naval

Complutense University of Madr... · Facultad de Farmacia

Publications

Publications · 5

Article: Neuroprotective effect of individual ginsenosides on astrocytes primary culture.

M Victoria Naval López, M Pilar Gómez-Serranillos Cuadrado, Olga M Palomino Ruiz-Poveda, Angel M Villar Del Fresno, M Emilia Carretero Accame
[Show abstract]
Biochimica et Biophysica Acta 10/2007; 1770(9):1308-16. · 4.66 Impact Factor

Article: Neuroprotective effect of a ginseng (Panax ginseng) root extract on astrocytes primary culture.

M V Naval, M P Gómez-Serranillos, M E Carretero, A M Villar
[Show abstract]
Journal of Ethnopharmacology 07/2007; 112(2):262-70. · 2.94 Impact Factor

Article: Radical scavenging ability of spanish red wine

S Martin, MP Gómez-Serranillos, OM Palomino, MV Naval, T Ortega, ME Carretero
Planta Medica - PLANTA MED. 01/2007; 73(09).

Article: Value of high-performance liquid chromatographic analysis of amino acids in the determination of Panax ginseng radix extract effect in cultured neurons.

M V Naval, M P Gómez-Serranillos, M E Carretero, C De Arce
[Show abstract]
Journal of Chromatography A 08/2006; 1121(2):242-7. · 4.26 Impact Factor

Article: Influence of grape variety and their phenolic composition on vasorelaxing activity of young red wines

Teresa Ortega, Elena De La Hera, M. Emilia Carretero, Pilar Gómez-Serranillos, M. Victoria Naval, Angel M. Villar, Marin Prodanov, Visitación Vacas, Teresa Arroyo, Teresa Hernández, Isabel Estrella
[Show abstract]
European Food Research and Technology 227(6):1641-1650. · 1.39 Impact Factor