Trends in Ginseng Research in 2010

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A total of 470 papers directly related to research on the Panax species were retrieved by performing internet searches with the keywords Panax and ginseng as the search terms. The publications were categorized as follows: 399 research articles, 30 reviews, 30 meeting abstracts, 7 proceedings, and 4 letters. The majority of these publications were published by scientists from Korea (35.7%), China (32.3%), and the USA (11.3%). Scientists from a total of 29 nations were actively involved in conducting ginseng research. A total of 43.6% of the publications were categorized as pharmacodynamic studies. The effects of ginseng on cerebrovascular function and cancer were the two most common topics considered in the pharmacodynamic studies. More than half of the ginseng studies assessed the use of P. ginseng. A total of 23 countries participated in studies specifically related to P. ginseng, and more than 80% of these studies originated from Korea and China. A total of 50 topics within the pharmacodynamics category were examined in association with the use of P. ginseng.

Key words: Trends in ginseng research, 2010, Country of origin of research publications, Major research categories, Pharmacodynamics

INTRODUCTION

This review provides a comprehensive overview of the trends in ginseng research in 2010. A total of 588 scholarly works were retrieved when an internet search using the keywords Panax and ginseng as the search terms was performed. Brazilian (Pfaffia glomerata and P. paniculata), Indian (Withania somnifera L. Duanal Solanaceae) and Siberian ginseng (Eleutherococcus senticoccus) were excluded from this analysis even though the term 'ginseng' was used in their descriptions. Publications that had no direct relationship to ginseng research were also excluded. For example, articles on the identification of microbes isolated from fields used for field-cultivated ginseng were excluded from this study. However, an article that examines the microbially mediated bioconversion or degradation of ginsenosides by microorganisms isolated from a ginseng cultivation field was included. The country from which the research and publication originated was categorized based on the country of residence of the corresponding author. Research categories were defined based on the major research topics examined.

PUBLICATION CATEGORIES

A total of 470 publications retrieved by the internet search were reviewed and classified, according to their country of origin and main research topics (Table 1). There were 399 formal research articles, which accounted for 84.9% of these 470 publications. There were 30 review articles and 30 meeting abstracts, which each comprised 6.4% of the publications. The 4 letters and 7
proceedings papers together accounted for slightly less than 2.5% of all of the publications.

RESEARCH PUBLICATIONS

A total of 29 nations were actively involved in conducting ginseng research (Table 2). Korea ranked first in terms of the number of publications, contributing 168 papers (35.7%), and China ranked second with 152 publications (32.3%).

In the second tier, there were 53 papers that originated from the United States of America (USA), 16 papers from Japan, and 13 publications each from Taiwan and Canada. In the third tier, India, Russia, Hong Kong, Brazil, and Singapore published 9, 7, 4, 4, and 3 papers, respectively. Several other countries contributed 1 or 2 papers. Interestingly, the research output by Japanese scientists decreased dramatically in 2010 compared to previous years. On the other hand, several countries in the Middle East (Egypt and Iran), Europe (Turkey, Greece, Poland, and Slovakia) and South America (Uruguay) appear to have recently initiated ginseng research programs. A small number of scientists from Western Europe, including the United Kingdom, Italy, Switzerland, Austria, and Germany, showed some interest in ginseng research in 2010 as indicated by the research publication volume; the Scandinavian countries exhibited the least amount of interest.

MAJOR RESEARCH CATEGORIES AND THE CRITERIA FOR CATEGORIZATION

All of the 470 papers were sorted into research categories based on the following specific criteria (Table 3): publications detailing cultivation methods, tissue culture techniques, or plant pathology as the major research topic were placed into the ‘horticulture’ category; processing, bioconversion, extraction methods, and quality control

Table 1. Types of publications

| Publication type   | No. of papers | Percentage |
|--------------------|---------------|------------|
| Research articles  | 399           | 84.9       |
| Review papers      | 30            | 6.4        |
| Meeting abstracts  | 30            | 6.4        |
| Letters            | 4             | 0.9        |
| Proceedings papers | 7             | 1.5        |
| Total              | 470           | 100        |

Table 2. Sorting of publications by country of origin

| Origin of paper      | No. of papers | Percentage |
|----------------------|---------------|------------|
| Korea                | 168           | 35.7       |
| China                | 152           | 32.3       |
| USA                  | 52            | 11.3       |
| Japan                | 16            | 3.4        |
| Taiwan, Canada       | 13            | 2.8        |
| India                | 9             | 1.9        |
| Russia               | 7             | 1.5        |
| Hong Kong, Brazil, United Kingdom | 4 | 0.9  |
| Singapore, Australia | 3             | 0.6        |
| Italy, Turkey, Austria, Pakistan, Egypt, Switzerland | 2 | 0.4  |
| Uruguay, Slovakia, Greece, Germany, Poland, Iran, Vietnam, Thailand, Denmark, New Zealand | 1 | 0.2  |
| Total                | 470           | 100        |

Table 3. Research categories

| Category            | Area of research                                                                 |
|---------------------|----------------------------------------------------------------------------------|
| Horticulture        | Cultivation, tissue culture, plant pathology                                      |
| Manufacture         | Process, bioconversion, extraction methods, quality control                       |
| Analytical chemistry| Analysis of pesticide residues and ginsenosides                                   |
| Pharmacodynamics    | In vitro and in vivo biochemical and physiological studies; prevention of wrinkle formation and sunlight damage |
| Pharmacokinetics    | In vivo metabolism of active compounds                                            |
| Clinics             | Clinical and epidemiological studies, pharmacovigilance                           |
| Marketing surveillance | Market share                                                                     |
| Others              | Nutrition, cultivation of mushroom, genetics, identification of ginseng species, quality control, gene expression |
studies were categorized as ‘manufacture’ publications; analyses of pesticide residues and ginsenosides were categorized as ‘analytical chemistry’ research; in vitro and in vivo biochemical, pharmacological, and physiological studies and studies examining ginseng use for the prevention of wrinkle formation and sunlight damage were categorized as ‘pharmacodynamics’ publications; studies of the in vivo metabolism of active compounds were categorized as ‘pharmacokinetics’ research; clinical and epidemiological studies and pharmacovigilance studies were categorized as ‘clinics’ publications; and market share studies were categorized as ‘marketing surveillance’ research.

MAJOR RESEARCH CATEGORIES

A total of 205 papers related to pharmacodynamics research were published in 2010, accounting for 43.6% of the 470 ginseng-focused publications (Table 4). The second most abundant category was analytical chemistry, with a total of 72 publications (15.3% of all of the publications). There were 49 and 41 articles that were regarded as cultivation research and manufacture studies, respectively, accounting for 10.4% and 8.7% of all of the publications. Pharmacokinetic and clinical studies comprised 33 (7.0%) and 31 (6.6%) of the studies, respectively.

PHARMACODYNAMIC SUBCATEGORIES

The pharmacodynamics category was further sub-divided into several specific research areas (Table 5). Ginseng research related to cancer prevention and therapy was the most common topic, accounting for 39 of the 205 pharmacodynamic studies. The majority of the cancer research was confined to in vitro cellular studies.

PANAX GINSENG AND RELATED SPECIES

There were 268 studies, representing 57% of the total publications in 2010, that focused on Panax ginseng as the primary research topic (Table 6). There were smaller numbers of articles that primarily examined P. quinquifolium (49), P. notoginseng (36), and P. japonicus (5), while a total of 112 studies were performed using ginsenosides of obscure origins. Studies on P. japonicus were rare, and the number of publications devoted to P. ginseng was more than five fold greater than the number of studies that focused on P. quinquifolium. Many of the papers classified as ‘others’ were mechanistic studies conducted using a single ginsenoside.

PANAX GINSENG

Researchers from a total of 23 countries performed
studies focused on *P. ginseng*, but more than 80% of the studies originated from Korea and China (Table 7). Of the 268 papers published on *P. ginseng*, Korean and Chinese scientists published 154 (57.5%) and 68 papers (25.4%), respectively. Scientists from the USA and Japan each published 9 papers (3.4%). The numbers of publications by Japanese scientists decreased compared to prior years. In addition to the three main East Asian countries and the USA, scientists from other regions of Asia, the Americas, Europe, and the Middle East also conducted research on *P. ginseng*. Although scientists in New Zealand, Canada, India, Austria, Turkey, Hong Kong, Singapore, Pakistan, Denmark, Switzerland, Poland, Germany, Greece, Australia, and Uruguay only published one paper from each country, it appears that the interest in supporting *P. ginseng* research is increasing in these countries.

A broad spectrum of pharmacodynamic studies were performed with *P. ginseng* as the main focus. There were at least 50 distinct topics studied that related to *P. ginseng*, including the following: its roles in the detoxification of anticancer agents, immune function, antioxidant activity, allergies, obesity, blood vessels, peptic ulcers, dermatitis, cytotoxicity, brain neurons, hepatic disease, lipid metabolism, cancer, AIDS, stress, inflammation, sexuality, diabetes, fatigue, neurotoxicity, viral infections, cosmetics, tumors, oxidative stress, apoptosis, granulocyte growth, platelet aggregation, hyperactivity, insomnia, cognitive functions, enzyme activity, skin aging, cardiovascular disease, gastritis, cardiac ischemia, nephrotoxicity, aging, brain ischemia, cardiovascular disease, vision, Alzheimer’s disease, bone necrosis, arthritis, metabolic diseases, hyperlipidemia, photosensitivity, diabetic memory loss, cardiovascular endothelial cells, physical activity, and radiation injuries.

**PANAX QUINQUEFOILUM**

A total of 49 publications that focused on the American ginseng, *P. quinquifolium*, were published in 2010. Scientists from 7 countries were actively involved in these studies (Table 8). American scientists published the largest proportion of the articles (46.9%) on this species, and the vast majority (91.8%) of the studies on *P. quinquefolium* were performed in the USA, China, and Canada. These studies originated from only a few countries. A relatively narrow spectrum of pharmacodynamic topics related to *P. quinquefolium* was examined, comprising the following 7 subjects areas: cardiovascular disease, cancer, antioxidant activity, radiation injury, diabetes, inflammation, and depression.

**PANAX NOTOGINSENG**

Chinese scientists performed almost all of the research concerned with *P. notoginseng*. Two groups from Korea and one group from Singapore also studied the effects of
**Table 9.** Country of origin of Panax notoginseng studies

| Host country | No. of papers | Percentage |
|--------------|---------------|------------|
| China        | 33            | 91.7       |
| Korea        | 2             | 5.6        |
| Singapore    | 1             | 2.8        |
| Total        | 36            | 100        |

*P. notoginseng* (Table 9). The *P. notoginseng* subspecies is not a common research subject outside of China. Although there were fewer pharmacodynamic studies that featured *P. notoginseng* compared to *P. ginseng*, a relatively broad spectrum of research topics was addressed in studies concerned with *P. notoginseng* compared to *P. quinquefolium*. A total of 15 topics within the pharmacodynamic research category were explored in the studies of *P. notoginseng*, including arteriosclerosis, arthritis, the cardiovascular system, bone fractures, antioxidant activity, inflammation, obesity, cancer, hyperlipidemia, osteoporosis, fibrosis of the liver, Alzheimer’s disease, cardiac ischemia, blood circulation, and cytotoxicity. In contrast, the pharmacodynamic studies of *P. japonicas* were limited to examinations of its effects on liver toxicity and α-glucosidase inhibition.

**SUMMARY OF THE MAJOR FINDINGS OF SELECTED PUBLICATIONS**

Scholey *et al.* [1] studied the effects of *P. quinquefolium* on neurocognitive function using a double-blind, placebo-controlled method and found a significant improvement in the performance of the working memory, reaction time and decision making processes, as well as increased calmness. Wang *et al.* [2] suggested that the administration of *P. ginseng* can significantly reverse learning impairments induced by scopolamine. Hao *et al.* studied the hepatic cytochrome P450-catalyzed metabolism of ginsenosides [3]. Cui *et al.* [4] performed antibody array experiments on precancerous colon cells and found that the consumption of ginseng maintains the environment of the colon in metabolic equilibrium. Cheng [5] reported that the ginsenoside Rb1, aids in preventing and treating diabetic disorders. Park *et al.* [6] found that Korean red ginseng is clinically effective for treating dry mouth. Chung *et al.* [7] reported that Korean red ginseng improves vascular stiffness in patients with coronary artery disease. Musende *et al.* [8] attempted to treat prostate cancer patients with a combination of the ginsenoside Rb1 and docetaxel, a chemotherapeutic agent. Sakamoto *et al.* [9] successfully expressed a single-chain variable fragment antibody against the ginsenoside Re in silkworm larvae to establish an enzyme-linked immunosorbent assay to measure total ginsenosides for quality control purposes. Reay *et al.* [10] presented data that indicate that *P. ginseng* can improve certain aspects of the working memory and induce calmness in healthy young adults. Kim *et al.* [11] suggested that the anti-stress effects of *P. ginseng* are mediated via the down-regulation of the expression of the tyrosine hydroxylase and dopamine β-hydroxylase genes in an animal model of repeated immobilization stress. Li *et al.* [12] analyzed decocting-induced chemical transformations based on a chemical profiling method using UPLC-Q-TOFMS/MS techniques. Using an *in vitro* test, Qi *et al.* [13] attempted to describe the cytotoxic activity of *P. quinquefolium* after it had been processed into red ginseng. Zhao *et al.* [14] established and validated a quantitative analytical procedure for detecting the levels of the ginsenoside Rg3, in plasma and urine that can be used in comparative pharmacokinetic studies. Yan *et al.* [15] elucidated the biotransformation pathway of the ginsenoside Rb1 to compound K in the presence of the glucosidase from Paecilomyces Brallnier sp. 229. Xue *et al.* [16] developed an X-ray phase contrast microscopy technique to identify wild ginseng by comparing the microstructures of ginseng roots. Sahashi *et al.* [17] analyzed the bioactive compounds in *P. ginseng* using nanoparticle-assisted laser desorption/ionization (nano-PALDI) mass spectrometry by preparing manganese oxide nanoparticles and developing a nano-PALDI MS method to analyze the ginsenosides in ginseng extracts. Li *et al.* [18] found that *P. quinquefolium* suppresses oxidative stress and oxidative stress-induced cell death in cardiomyocytes via the activation of the Nrf2 pathway in the murine heart. Baek *et al.* [19] demonstrated the antidiarrheal effect of ginseng using an *in vitro* model of rotavirus infection, which is the leading cause of severe diarrhea, and identified two pectic polysaccharides that are important contributors to this effect. Liu *et al.* [20] suggested that the administration of *P. notoginseng* saponins can attenuate atherogenesis through their anti-inflammatory action and their regulation of the blood lipid profile. A Brazilian scientist studied the sensory acceptance of a *P. ginseng* extract supplemented with nectar and determined that the optimal effect was observed when the extract was administered at a concentration of 20 mg per 100 mL of nectar [21]. Chan *et al.* [22] identified the α-glucosidase inhibitors contained in *P. japonicas*, including four polyacetylenes, five phenolic compounds, one sesquiterpenoid, and one sterol glucoside. Zhao *et al.* [23] of Yunnan Ag-
ricultural University in China reviewed the biosynthetic pathways of triterpenoid saponins. Son et al. [24] of the College of Pharmacy at Chungnam National University in Korea determined the glycemic index of Korean red ginseng in human subjects and found that ginseng is beneficial for patients with metabolic disorders. Lei et al. [25] studied the allelopathic effects of ginsenosides on the in vitro growth and antioxidant activity of the ginseng callus and found that all of the ginsenosides examined inhibited the growth of the ginseng callus; the addition of the total ginsenosides mixture increased the enzymatic antioxidant activity of the ginseng callus. Shin et al. [26] studied the effect of Korean red ginseng on neonatal hypoxia-induced hyperactivity in rats and found that Korean red ginseng improved the hyperactivity phenotype without an incremental decrease in the locomotor activity in normal animals. Lee et al. [27] suggested that black ginseng improves the memory of mice with scopolamine-induced amnesia. Ma et al. [28] found that the ginsenoside Rg1 promotes peripheral nerve regeneration in a crush-injury rat model. Ha et al. [29] found that the ginsenoside Rg1 prevents UVB-induced cytotoxicity in a concentration- and time-dependent manner by increasing the activity of the DNA repair system, possibly by modulating the levels of the proteins involved in the p53 signaling pathway. Zhang et al. [30] proposed a new method for grading the quality of ginseng with the aid of 2D-IR correlation spectroscopy. Kim and Lee [31] suggested that pretreatment with panaxatriol ameliorates ischemia/reperfusion-induced myocardial damage and that this healing property is caused by a reduction in oxidative stress. Khalid et al. [32] of the Department of Anatomy at the University of Health Science in Pakistan studied the histological changes in the fetal brain of albino mice after maternal treatment with P. ginseng. Dai and Orsat [33] proposed a microwave-assisted extraction method to improve the efficiency of ginsenoside extraction from fresh American ginseng root. Wang et al. [34] presented data suggesting that administration of the ginsenoside Rb3 from P. ginseng protects against isoproterenol-induced myocardial injury and heart function impairment in the rat and that the mechanism of pharmacological action is related to the antioxidant activity of this Rb3. Sharma et al. [35] proposed that a synaptic mutation in the herbaceous perennial P. sikkimensis was responsible for male sterility in this species. Shen et al. [36] proposed that P. notoginseng saponins might be an alternative medicine for the prevention and treatment of postmenopausal osteoporosis. YoKang et al. [37] of the Institute of Natural Medicine at Toyama University in Japan provided evidence that the 20(S)-ginsenoside Rg1 prevents the progression of renal damage and dysfunction in type 2 diabetic rats by inhibiting oxidative stress and the formation of advanced glycation end products. Dewir et al. [38] of the Department of Horticulture at Kafrelsheikh University in Egypt suggested that linolenic acid is an elicitor of ginsenoside accumulation in ginseng adventitious root cultures. Kim et al. [39] investigated the association between the pattern of dietary supplement use and the sociodemographic and lifestyle characteristics of Korean consumers and found that women use dietary supplements more regularly than men, but males preferred ginseng to other supplements. Jager et al. [40] of the Department of Medicinal Chemistry at the University of Copenhagen in Denmark found that P. ginseng added to dairy products can be pasteurized without significant changes in the ginsenoside patterns. Lee et al. [41] suggested that an American ginseng extract can protect lymphocytes obtained from healthy individuals against radiation injury. Huang et al. [42] proposed that the compounds K and Rg1 can stimulate glucose uptake in 3T3-L1 cells, suggesting a potential application of ginseng for diabetic individuals because of its hypoglycemic properties. Xu et al. [43] investigated the effectiveness of a nutritional mixture containing a P. ginseng extract against aging. Their report suggested that the administration of the mixture in the early-midlife years significantly decreases age-related mitochondrial functional decline and preserves physical performance. Kim et al. [44] discovered the efficacy of the ginsenoside Rg1, for the treatment of restraint-stressed animals. Li et al. [45] found that the ginsenoside Rb1 from P. ginseng relieves cerebral vasospasms and potentially protects against stroke and subarachnoid hemorrhaging and that the underlying mechanism may be partly related to the inhibition of the p53- and Bax-dependent proapoptosis pathways by Rb1. Jovanovski et al. [46] demonstrated that Korean red ginseng can improve arterial stiffness and that the principal pharmacological active agent might be the ginsenosides. Leonti et al. [47] of the Institute of Biochemistry and Molecular Medicine at the University of Bern in Switzerland studied the feasibility of reducing dermatitis by applying falcarniol (panaxynol, carotatoxin), which can be found in carrots, parsley, celery and P. ginseng. Chai et al. [48] of the Department of Surgery at Stanford University in the USA demonstrated that the ginsenoside Rb1 attenuates homocysteine-augmented guide wire injury-induced intimal hyperplasia in mice. These authors also suggested the potential of using ginseng to control homocysteine-related vascular injuries. Dickman et al. [49] of
the University of Wisconsin in the USA warned that the chronic intake of American ginseng can cause oxidative damage in postmenopausal women, based on an increase in oxidative damage markers (plasma malondialdehyde and urine 8-hydroxydeoxyguanosine) and erythrocyte antioxidant enzyme activities (superoxide dismutase and GSH reductase). Oh et al. [50] of the Department of Urology in the School of Medicine at Chonnam National University in Korea demonstrated that the administration of Korean red ginseng to menopausal women can improve sexual arousal. Chang et al. [51] of the College of Medicine at Taiwan National University in Taiwan suggested that the ginsenoside Rg1 from P. ginseng possesses a remarkable potential for treating osteonecrosis of the femoral head. These authors further confirmed the angiogenic effect of Rg1 by demonstrating tube formation in human umbilical vein endothelial cells. Zhang et al. [52] demonstrated the usefulness of ginsenosides against glycerol-induced acute renal failure and the activation of catecholaminergic neurons in the locus coeruleus of rats.

Rosner [53] of the Department of Analytical Chemistry at the BAM Federal Institute of Material Research and Testing in Germany developed a method for validating the provenance of ginseng by analyzing strontium isotope ratios (Sr87/Sr86) using ICP-MS. Yoo et al. [54] discovered the effectiveness of Sun-ginseng, a heat processed form of ginseng consisting primarily of the Rg3, Rk1, and Rg5 ginsenosides, for the treatment of prostate cancer in an animal model by inhibiting cyclin and regulating the expression of the TNFRSF25 and ADRA2A genes. Wahid et al. [55] suggested that Korean red ginseng is useful for improving the optical process in the eyes of bullfrogs, which suggests the potential for the use of Korean red ginseng as a treatment for certain ophthalmic diseases in humans. Sagar [56] of the Juravinski Cancer Center in Canada studied the efficacy of Asian botanicals, including P. ginseng, for radiotherapy on tumor tissues. These authors showed an increase in the efficacy of the radiotherapy, which allowed for a reduction in the radiation doses applied to normal tissues. Ginseng selectivity protected normal tissues or increased tissue repair following radiation therapy. These results strongly suggest that ginseng agents are promising candidates for clinical trials. Kim et al. [57] suggested the usefulness of Korean red ginseng that is rich in the ginsenosides Rg1, Rk1, and Rg5 for the treatment of collagen-induced arthritis. Thomson [58] examined the science-based medical evidence supporting the use of traditional Asian medicinal plants, including P. ginseng, and suggested that ginseng is an important medicinal plant based on the strong support from medical efficacy trials. Ock et al. [59] of the College of Medicine at the Catholic University in Korea found that the most commonly used dietary supplement in Korea was P. ginseng. Abdel-Wahhab et al. [60] of the National Research Center in Egypt suggested that the consumption of P. ginseng extract can protect against aflatoxin B-1- and fumonisin-induced hepatic precancerous lesions in rats. Shin et al. [61] evaluated the toxicity of Korean red ginseng against embryonic implantation and mortality and fetal body weight gain at doses of up to 2,000 mg/kg/d, which is approximately 200 fold greater than the clinical dose recommended by the Korean Food and Drug Administration. The authors concluded that the consumption of ginseng did not cause embryo-fetal death or abnormalities. Wen et al. [62] attempted to degrade the residual fungicides in American ginseng by gamma irradiation. Quan et al. [63] tried to eliminate organochlorine pesticide residues from ginseng using a supercritical fluid extraction method. Lin et al. [64] developed a method for determining the ages of cultivations of P. ginseng with the aid of H1 NMR fingerprint analysis. Kim et al. [65] of the Korea Research Institute of Standards and Science succeeded in creating a pure certified reference material for the ginsenoside Rg1 [65]. Gravas et al. [66] of the School of Medicine at the University of Thessalia in Greece recommended the discontinuation of herbal medication for up to 15 days prior to surgery. Li et al. [67] demonstrated that the ginsenoside Rd from P. ginseng can prevent glutamate-induced apoptosis in rat cortical neurons. These results provide further evidence for the potential of voltage-independent Ca2+ channel blockers as novel neuroprotective drugs for the prevention of neuronal apoptosis and death by cerebral ischemia. Kim et al. [68] determined the efficacy of P. ginseng against the intestinal damage induced by gamma irradiation in mice.

CONCLUSION

A total of 470 papers (399 research articles, 30 reviews, 30 meeting abstracts, 7 proceedings and 4 letters) were published in 2010 by scholars from 29 nations. The majority of these publications were contributed by scientists from Korea, China, and the USA. P. ginseng was the predominant species examined in the pharmacodynamic studies.

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