SAFETY AND EFFICACY OF *PANAX GINSENG* DURING PREGNANCY AND LACTATION

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ABSTRACT

Background
There is a lack of basic knowledge on the part of both clinicians and patients as to the indications for use and the safety of herbs used by women during pregnancy and lactation. This is one article in a series that systematically reviews the evidence for herbs commonly used during pregnancy and lactation.

Objectives
To systematically review the literature for evidence on the use, safety and pharmacology of *Panax ginseng*, focusing on issues pertaining to pregnancy and lactation.

Methods
We searched 7 electronic databases and compiled data according to the grade of evidence that was found.

Results
Based on strong scientific evidence from a cohort study, *Panax ginseng* was not associated with adverse effects when used during pregnancy. *Panax ginseng* was misreported in the literature as causing androgenization, when, in fact, the case reported was due to an adulterant. There is *in vitro* evidence of teratogenicity with exposure to ginsenosides; however, this evidence is derived from animal embryos and is based on exposure to isolated ginsenosides at much higher levels than achievable through normal consumption in humans. There is also conflicting evidence as to whether or not *Panax ginseng* has estrogenic properties. In lactation, there are no human studies on the safety of *Panax ginseng*, only *in vitro* evidence based on three animal studies reporting minimal risk.

Conclusions
Panax ginseng should be consumed with caution during pregnancy, especially during the first trimester, and during lactation.

Key words: *Panax ginseng, asian ginseng, ginseng, pregnancy, lactation, breastfeeding, systematic review*

There are five main species of ginseng: American, Chinese, Korean, Japanese and Siberian (or Russian) and it is important to be able to distinguish between them. The commercially available product 'ginseng' usually refers to the dried root of *Panax ginseng*, commonly known as Korean or Asian ginseng. Preparations of *P. ginseng* include the steam-dried root that is called 'red ginseng', and the air-dried root that is called 'white ginseng'.[1] Fresh ginseng extract is also consumed, but is not generally the preparation available commercially.[2] *Panax ginseng* is a

popular herbal remedy that has been in use for thousands of years. It has been an important part of the pharmacopoeia of Traditional Chinese Medicine and is classified as an adaptogen that is thought to increase the body's overall resistance to stress and infection.[3] This herb has a wide base of application and is considered the most popular herbal medicine worldwide.[4] It has been used to treat a variety of disorders including: anaemia, insomnia, dyspnea, memory impairment, confusion, decreased libido, chronic fatigue, angina, diabetes mellitus and herpes simplex type-II infections.[2,5,6]

P. ginseng is not considered an herb specific to women's health issues. However, its broad base of popularity will invariably involve its usage by women of reproductive age and women who may be potentially pregnant. We conducted a systematic review of the literature to assess issues of efficacy, and potential safety for women who are pregnant, planning to become pregnant or those who are breast-feeding.

Synonyms/Common Names/Related Substances
Asian ginseng, Asiatic ginseng, Chinese ginseng, ginseng, ginseng asiatique, *Ginseng radix*, ginseng root, guigai, hong shen, Japanese ginseng, jen-shen, jinsao, jintsam, insam, Korean ginseng, Korean *panax ginseng*, Korean red ginseng, ninjin, Oriental ginseng, *Panax ginseng, Radix ginseng rubra*, red ginseng, ren shen, renshen, renxian, sang, seng, sheng shai shen, white ginseng[7]

Constituents
Triterpenoid Saponins: ginsenosides (Rg1, Rb1) Polyacetylenic constituents[8]: panaxynol, panaxydol, panaxytriol, Panaxagin[9], Essential oil[10], Phytosterol[10], Pectin[11], B vitamins[11], Flavonoids[11]

Part Used
Root and rhizomes[7]

METHODS

In keeping with the principles of evidence-based practice, we endeavoured to identify and analyse all the relevant scientific medical literature that provided information as to the safety, efficacy and pharmacology of *Panax ginseng* in pregnancy and lactation. Our search included the following databases from inception to June 2006: AMED, CINAHL, Cochrane CENTRAL, Cochrane Library, MedLine, Natural Database and Natural Standard. The common and the Latin names of the herb were used as the key words along with "pregnancy", "lactation" and "breastfeeding". In addition, we searched the Complete German Commission E Monographs by the American Botanical Council.

Each relevant journal article was collected and referenced in our database. The nature of the findings and the grade of evidence were then abstracted and compiled in the final report. The grade of evidence for indications was evaluated as displayed in Table 1. Evidence of harm was rated as displayed in Table 2.

RESULTS

Indications for Use

	Evidence Grade
Erectile dysfunction[12]	B1
Premature ejaculation[13]	B1
Type II diabetes [14]	B1
Influenza and the common cold[15]	B1
Memory improvement[16-18]	B2
Improved cognitive function[19-22]	B2
Enhanced physical function[23]	B2
Chronic bronchitis (with antibiotics)[24]	C
Cancer prevention[25,26]	C
Parkinson's disease[27]	E

Use and Safety during Pregnancy

	Level of evidence for potential harm
Non-estrogenic[28]	1
Treatment of intrauterine growth retardation[29]	2
Estrogenic[30]	3b
No evidence to support androgenization[31,32]	3b
Protection of neonatal brain against ethanol damage[33]	4
Teratogenicity[34-37]	4
Activates DNA polymerase delta in placenta[38]	4
Traditionally used during pregnancy[39]	4

A randomized controlled trial of 384 women receiving either ginseng extract or placebo for 16 weeks, showed that the beneficial effects in the treatment of menopause are most likely not mediated by hormone replacement-like effects, as physiological parameters such as FSH and estradiol levels, endometrial thickness, maturity index and vaginal pH were not affected by the treatment.[28]

On the other hand, there are case reports and animal studies indicating potential estrogenic activity due to ginseng. Evidence includes postmenopausal vaginal bleeding, increased serum ceruloplasmin oxidase activity and phytoestrogenic actions of ginsenoside Rb1.[40-46] A review article on the potential value of plants as sources of anti-fertility agents also reported that Korean ginseng has estrogenic activity.[30]

Zhang et al. (1994) conducted a comparison study on pregnant women with intrauterine growth retardation (IUGR).[29] One group of women received ginseng, while the other group was nutritionally treated as controls.[29] The height of fundus, fetal diparietal diameter, urinary estrogens/creatinine, serum human placental lactogen and neonatal weights approached normal pregnancy values.[29] The authors did not report any adverse effects associated with ginseng supplementation.[29]

A case was reported of a 30-year-old woman who gave birth to a full-term baby boy with signs of androgenization following ingestion of "ginseng" during her pregnancy.[32] After further investigation, the herbal preparation used by the mother appeared to be adultered by the herb silk vine (*Periploca sepium*).[31]

Okamura et al. (1994) reported that ginseng extract prevented an ethanol-induced reduction of neonatal brain weight in rats.[33] The ginseng saponins, including ginsenosides Rg1, Rb2, Rd, Rf and Re, were shown to stimulate a potent recovery of cerebellum growth.[33]

Chan et al. have demonstrated that ginsenosides Rb1, Rc and Re exert direct teratogenic effects on rat embryos.[34,37] A separate group of investigators also found embryotoxicity when rat and mice whole embryos cultures were exposed to high concentrations of the two ginsenosides, Rg1 and Rb1[35,36] Ginsenosides from *Panax ginseng* were found to activate DNA polymerase delta in bovine placenta.[38]

Researchers conducted a review of the herbs used during pregnancy in Singapore.[39] *Panax ginseng* was used in various combinations and in various amounts in herbal prescriptions during pregnancy.[39] The researchers could not confirm that the claims made by Chinese herbalists on the efficacy of *Panax ginseng* in pregnancy were real or not.[39] They concluded that there is no specific effect on pregnant women, but that it does not exclude the possibility of a beneficial psychosomatic effect.[39] The researchers also noted that the active principles can cross the placenta and reach the fetus.[39] The authors did not discuss if *Panax ginseng* was safe or contraindicated during pregnancy.[39]

Use and Safety during Lactation

	Level of evidence for potential harm
Minimal risk[47-49]	4

Cows with subclinical mastitis caused by *Staphylococcus aureus* were given subcutaneous injections of an extract of the *Panax ginseng* root.[47] Based on blood leukocyte measurements, ginseng treatment was found to activate the innate immunity of cows and contribute to the cow's recovery from mastitis.[47] The authors did not report any adverse effects associated with the use of *Panax ginseng* during lactation.[47] Two other studies by the same authors, conducted in lactating cows, found similar results where *Panax ginseng* increased leukocyte activity and no adverse effects were reported.[48,49]

Toxicity and Adverse Effects

Very low incidence of toxicity has been observed in ginseng clinical trials using well-characterized preparations.[50] When used inappropriately, *Panax ginseng* has been noted to cause hypertension, diarrhea, sleeplessness, mastalgia, eruptions and vaginal bleeding.[1] Siegel has coined a condition called "ginseng abuse syndrome", in reference to the long-term effects of ginseng use. This 'syndrome' is characterized by hypertension, nervousness, sleeplessness, skin rash, diarrhea, confusion, depression or depersonalization.[51]

Pharmacology

It is clear that *Panax ginseng* is pharmacologically active. While it is uncertain to what extent isolated constituents are biologically active, the ginseng saponins (or ginsenosides) are considered to be responsible for a majority of this species' biological activity.[52] Ginsenosides are unique to *Panax ginseng* and over 30 of these compounds have been identified.[1] Some of the known pharmacological effects are detailed in Table 3, and attest to the wide range of potential therapeutic applicability of this incredibly popular and seemingly potent herbal medicine.

Drug Interactions

There is some evidence of potential interactions between ginseng and prescription drugs; however, most of the evidence is derived from preclinical assays. Confirmation from pharmacokinetic studies should be conducted to establish true interactions. Current evidence requires that *Panax ginseng* be used with caution in conjunction with the following agents:

- Anitcoagulent drugs[53,54]
- Antidiabetic drugs[55]
- Antipsychotic drugs[56]
- Caffeine[57]
- Furosemide[58]
- Immunosuppressants[26]
- Insulin[57]
- Monoamine Oxidase Inhibitors[59,60]
- Stimulant Drugs[61]
- Warfarin (Coumadin)[53,54,62]

DISCUSSION

Panax ginseng is frequently used as a general tonic or "adaptogen" to fight stress, and possibly to enhance physical and mental performance. This herb is not specifically used during pregnancy and lactation in the same way that ginger might be used to treat nausea and vomiting, or how horse chestnut seed extract might be used to treat varicose veins.[63,64] However, the fact that it is one of the most commonly used herbs worldwide, inevitably women will end up taking the herb during pregnancy or while breastfeeding. As such, it is critical that both women and clinicians be aware of the possible risks attendant to such usage and to be able to plan and advise accordingly.

There is no high-grade evidence demonstrating that *P. ginseng* is unsafe during pregnancy and lactation. Observations during a cohort, and from traditional use, have not uncovered any adverse events from ginseng with respect to pregnancy and lactation. A single case report was found in the literature that reported on a potential link between *P. ginseng* use by a pregnant woman and the death and androgenization of her fetus.[31] It was determined that the ginseng-containing-product was adulterated, however, and as such, we cannot infer that ginseng was the causative agent. In addition, this is an isolated case and the anecdotal nature of the evidence does not provide anything beyond speculation. Of somewhat greater concern, however, are the repeated findings of teratogenicity in mice and rats when exposed to ginsenosides. Again, this evidence must be interpreted with caution, as it is derived from animal embryos and is based on exposure to isolated ginsenosides at much higher levels than achievable through normal consumption in humans. Evidence regarding phytoestrogenic activity of *P. ginseng* is conflicting; some concern may be justified regarding this possibility, especially with respect to exposure during early fetal development.

Our study is limited primarily by the lack of evidence available. Given the vulnerabilities of a developing fetus and newborn child, and the fact that their metabolism can vary substantially from the adult, extreme caution is required in making recommendations for women of child bearing age. The totality of the evidence that we analysed in our systematic review indicates that *Panax ginseng* may well be safe for consumption during pregnancy; however, to ensure safety to the developing fetus, consumption of this herb is best avoided, especially during the first trimester.

No human evidence could be found regarding the safety of consuming *Panax ginseng* while breastfeeding. Nonetheless, there is *in vitro* evidence based on three animal studies that *Panax ginseng* was of minimal risk when consumed by lactating cows. Research is necessary to determine if ginsenosides and other potentially active compounds are carried in the human breast milk, and also how this might affect a newborn child.

There is evidence to support the use of *Panax ginseng* in the treatment of male sexual dysfunction; care of type II diabetics; amelioration of symptoms from influenza and the common cold and to enhance cognitive and physical function; however, more research is necessary to establish its use in these areas as well as to establish safety during pregnancy and lactation.

TABLE 1 Levels of Evidence for Efficacy

GRADE	LEVEL OF EVIDENCE
A	**VERY STRONG SCIENTIFIC EVIDENCE** Statistically significant evidence of benefit from one or more systematic reviews/ meta-analysis.
B1	**STRONG SCIENTIFIC EVIDENCE** Statistically significant evidence of benefit from one or more properly conducted random control trials (RCTs).
B2	**GOOD SCIENTIFIC EVIDENCE** Statistically significant evidence of benefit from one or more RCTs. The RCTs, however, are either of small sample size OR have discrepancies in their methodologies.
C	**WEAK SCIENTIFIC EVIDENCE** Statistically significant evidence of benefit from one or more cohort studies OR case control studies.
D	**VERY WEAK SCIENTIFIC EVIDENCE** Evidence from case series OR case reports.
E	**INDIRECT EVIDENCE** Expert opinion OR laboratory studies.
F	**HISTORICAL OR TRADITIONAL EVIDENCE** Historical or traditional use by medical professionals, herbalists, scientists or aboriginal groups.

TABLE 2 Levels of Evidence for Harm

LEVEL	EVIDENCE
1	**STRONG SCIENTIFIC EVIDENCE** Statistically significant evidence from one or more systematic reviews or RCTs.
2	**ACCEPTABLE SCIENTIFIC EVIDENCE** Statistically significant evidence from one or more well designed cohort studies OR case control studies.
3a	**WEAK SCIENTIFIC EVIDENCE** Evidence from one or more case series.
3b	**VERY WEAK SCIENTIFIC EVIDENCE** Evidence based on case reports.
4	**INDIRECT SCIENTIFIC EVIDENCE** Evidence based on scientific studies conducted on animals, insects or microorganisms OR laboratory studies on human cells.
5	**THEORETICAL EVIDENCE** Evidence based on scientific theory OR expert opinion.
6	**UNKNOWN** No available information.

TABLE 3 Pharmacological Actions Attributable to *Panax Ginseng*

SYSTEM	PHARMACOLOGICAL ACTION
Adrenal	• Ginsenosides increase serum cortisol levels, stimulate adrenal function and in women, increase dehydroepiandrosterone sulfate (DHEA-S)[65-68]
Cardiovascular	• Ginsenoside Rb1 may lowers blood pressure and acts as a CNS depressant[11] • Ginsenosides interfere with platelet aggregation and coagulation[47] • *Panax ginseng* may lower cholesterol and triglycerides[18]
Antiinflammatory and antiinfective	• Ginsenosides have analgesic and anti-inflammatory effects[18] • *Panax ginseng* has shown inhibitory activity on Helicobacter pylori[69] • *Panax ginseng* promotes the growth of normal intestinal flora while inhibiting Clostridial species[70] • The protein isolate panaxagin may have antiviral and antifungal activity where it appears to inhibit HIV reverse transcriptase and ribosomal activity of some fungi[9]
Neurocognitive	• Ginsenosides potentiate nerve growth factor and may have a neuroprotective effect through nicotinic activity[11,71] • *Panax ginseng* increases penile vibratory threshold and reduces the amplitude of penile somatosensory evoked potentials[13]
Pulmonary	• Ginsenosides have anti-asthmatic effects through the relaxation of human bronchial smooth muscle by stimulating the release of nitrous oxide from airway epithelium[72]
Endocrine system	• *Panax ginseng* may prevent insulin resistance and change gene expression in Type II diabetes[73] • Some studies report that *P. ginseng* has phytoestrogenic properties[40-46]

REFERENCES

1. Radad K, et al. Use of ginseng in medicine with emphasis on neurodegenerative disorders. J Pharmacol Sci 2006;100(3):175-86.
2. Bahrke MS, Morgan WR. Evaluation of the ergogenic properties of ginseng: an update. Sports Med 2000;29(2):113-33.
3. Boon H, Smith M. The complete natural medicine guide to the 50 most common medicinal herbs. 2004, Toronto: Robert Rose.
4. Blumenthal M. Asian ginseng: potential therapeutic uses. Adv Nurse Pract 2001;9(2):26-8, 33.
5. Coon JT, Ernst E. Panax ginseng: a systematic review of adverse effects and drug interactions. Drug Saf 2002;25(5):323-44.
6. Vogler BK, Pittler MH, Ernst E. The efficacy of ginseng. A systematic review of randomised clinical trials. Eur J Clin Pharmacol 1999;55(8):567-75.
7. Jellin JM, Batz F, Hitchens K. Natural medicines comprehensive database 3rd Edition. 2002, Stockton, CA: Therapeutic Research Faculty. 1530.
8. Moon J, et al. Induction of G(1) cell cycle arrest and p27(KIP1) increase by panaxydol isolated from Panax ginseng. Biochem Pharmacol 2000;59:1109-16.
9. Ng TB, Wang H. Panaxagin, a new protein from Chinese ginseng possesses anti-fungal, anti-viral, translation-inhibiting and ribonuclease activities. Life Sci 2001;68:739-49.
10. Foster S. Panax ginseng. American Botanical Council, 1996.
11. Leung AY, Foster S. Encyclopedia of Common Natural Ingredients Used in Food, Drugs and Cosmetics. 2nd ed. 1996, New York, NY: John Wiley & Sons. 649.
12. Hong B, et al. A double-blind crossover study evaluating the efficacy of korean red ginseng in patients with erectile dysfunction: a preliminary report. J Urol 2002;168(5):2070-3.

13. Choi HK, et al. Clinical study of SS-Cream in patients with lifelong premature ejaculation. Urology 2000;55:257-61.
14. Sotaniemi EA, Haapakoski E, Rautio A. Ginseng therapy in non-insulin dependent diabetic patients. Diabetes Care 1995;18:1373-5.
15. Scaglione F, et al. Efficacy and safety of the standardised Ginseng extract G115 for potentiating vaccination against the influenza syndrome and protection against the common cold [corrected]. Drugs Exp Clin Res 1996;22(2):65-72.
16. Wesnes KA, et al. The memory enhancing effects of a Ginkgo biloba/Panax ginseng combination in healthy middle-aged volunteers. Psychopharmacology (Berl) 2000;152(4)353-61.
17. Scholey AB, Kennedy DO. Acute, dose-dependent cognitive effects of Ginkgo biloba, Panax ginseng and their combination in healthy young volunteers: differential interactions with cognitive demand. Hum Psychopharmacol 2002;17(1):35-44.
18. The Review of Natural Products by Facts and Comparisons. 1999, St. Louis, MO: Wolters Kluwer Co.
19. Sorensen H, Sonne J. A double-masked study of the effects of ginseng on cognitive functions. Curr Ther Res Clin Exp 1996;57:959-68.
20. D'Angelo L, et al. A double-blind, placebo-controlled clinical study on the effect of a standardized ginseng extract on psychomotor performance in healthy volunteers. J Ethnopharmacol 1986;16(1):15-22.
21. Reay JL, Kennedy D, Scholey A. Effects of Panax ginseng, consumed with and without glucose, on blood glucose levels and cognitive performance during sustained 'mentally demanding' tasks. J Psychopharmacol 2006;20(6):771-781.
22. Reay JL, Kennedy DO, Scholey AB. Single doses of Panax ginseng (G115) reduce blood glucose levels and improve cognitive performance during sustained mental activity. J Psychopharmacol 2005;19(4):357-65.
23. Kim SH, et al. Effects of Panax ginseng extract on exercise-induced oxidative stress. J Sports Med Phys Fitness 2005;45(2):178-82.
24. Scaglione F, Weiser K, Alessandria M. Effects of the standardized ginseng extract G115 (Reg.) in patients with chronic bronchitis: A nonblinded, randomized, comparative pilot study. Clin Drug Invest 2001;21:41-5.
25. Yun TK, Choi SY. Non-organ specific cancer prevention of ginseng: a prospective study in Korea. Int J Epidemiol 1998;27(3):359-64.
26. Shin HR, et al. The cancer-preventive potential of Panax ginseng: a review of human and experimental evidence. Cancer Causes Control 2000;11:565-76.
27. Van Kampen JM, Robertson HA. A possible role for dopamine D3 receptor stimulation in the induction of neurogenesis in the adult rat substantia nigra. Neuroscience 2005;136(2):381-6.
28. Wiklund IK, et al. Effects of a standardized ginseng extract on quality of life and physiological parameters in symptomatic postmenopausal women: a double-blind, placebo-controlled trial. Int J Clin Pharmacol Res 1999;19:89-99.
29. Zhang WY, Teng H, Zheng Y. [Ginseng saponin treatment for intrauterine growth retardation]. Zhonghua Yi Xue Za Zhi 1994;74(10):608-10, 646.
30. Farnsworth NR, et al. Potential value of plants as sources of new antifertility agents II. J. Pharm Sci. 1975;64(5):717-753.
31. Awang DV. Maternal use of ginseng and neonatal androgenization. JAMA 1991;266(3):363.
32. Koren G, et al. Maternal ginseng use associated with neonatal androgenization. JAMA 1990;264:2866.
33. Okamura N, et al. Protective effect of ginseng saponins against impaired brain growth in neonatal rats exposed to ethanol. Biol Pharm Bull 1994;17(2):270-4.
34. Chan LY, Chiu PY, Lau TK. An in-vitro study of ginsenoside Rb1-induced teratogenicity using a whole rat embryo culture model. Hum Reprod 2003;18(10):2166-8.
35. Liu P, et al. Developmental toxicity research of ginsenoside Rb1 using a whole mouse embryo culture model. Birth Defects Res B Dev Reprod Toxicol 2005;74(2):207-9.
36. Liu P, et al. Effects of ginsenoside Rg1 on postimplantation rat and mouse embryos cultured in vitro. Toxicol In Vitro 2006;20(2):234-8.
37. Chan LY, Chiu PY, Lau TK. Embryotoxicity study of ginsenoside Rc and Re in in vitro rat whole embryo culture. Reprod Toxicol 2004;19(1):131-4.
38. Cho SW, Cho EH, Choi SY. Ginsenosides activate DNA polymerase delta from bovine placenta. Life Sci 1995;57(14):1359-65.
39. Wong HB. Effects of herbs and drugs during pregnancy and lactation. J Singapore Paediatr Soc 1979;21(3-4):169-78.
40. Palmer BV, et al. Gin Seng and mastalgia [letter]. BMJ 1978;1:1284.
41. Hopkins MP, Androff L, Benninghoff AS. Ginseng face cream and unexplained vaginal bleeding. Am J Obstet Gynecol 1988;159:1121-2.
42. Greenspan EM. Ginseng and vaginal bleeding [letter]. JAMA 1983;249:2018.
43. Hammond TG, Whitworth JA. Adverse reactions to ginseng [letter]. Med J Aust 1981;1:492.
44. Punnonen R, Lukola A. Oestrogen-like effect of ginseng. Br Med J 1980;281:1110.

45. Eagon PK, et al. Medicinal herbs: modulation of estrogen action. in Era of Hope Mtg, Dept Defense. 2000. Atlanta, GA: Breast Cancer Res Prog.
46. Lee YJ, et al. Ginsenoside-Rb1 acts as a weak phytoestrogen in MCF-7 human breast cancer cells. Arch Pharm Res 2003;26:58-63.
47. Hu S, et al. Effect of subcutaneous injection of ginseng on cows with subclinical Staphylococcus aureus mastitis. J Vet Med B Infect Dis Vet Public Health 2001;48(7):519-28.
48. Concha C, Hu S, Holmberg O. The proliferative responses of cow stripping milk and blood lymphocytes to pokeweed mitogen and ginseng in vitro. Vet Res 1996;27(2):107-15.
49. Hu S, et al. Ginseng-enhanced oxidative and phagocytic activities of polymorphonuclear leucocytes from bovine peripheral blood and stripping milk. Vet Res 1995;26(3):155-61.
50. Chang YS, et al. Panax ginseng: a role in cancer therapy? Integr Cancer Ther 2003;2(1):13-33.
51. Siegel RK. Ginseng abuse syndrome. Problems with the panacea. JAMA 1979;241(15):1614-5.
52. Attele AS, Wu JA, Yuan CS. Ginseng pharmacology: multiple constituents and multiple actions. Biochem Pharmacol 1999;58(11):1685-93.
53. Janetzky K, Morreale AP. Probable interaction between warfarin and ginseng. Am J Health Syst Pharm 1997;54:692-3.
54. Cheng TO. Ginseng-warfarin interaction. ACC Current Journal Review 2000;9(1):84.
55. Sotaniemi EA, Haapakoski E, Rautio A. Ginseng therapy in non-insulin dependent diabetic patients. Diabetes Care 1993;Jan;16(1):8-15, 1995;18:1373-5.
56. Newall CA, Anderson LA, Phillipson JD. Herbal medicines: a guide for health-care professionals. 1996, London, UK: Pharmaceutical Press 296.
57. Brinker F. Herb Contraindications and Drug Interactions. 2nd ed. 1998, Sandy, OR: Eclectic Medical Publications.
58. Becker BN. Ginseng-induced diuretic resistance. JAMA 1996;276(8):606-7.
59. Shader RI, Greenblatt DJ. Phenylzine and the dream machine-ramblings and reflections. J Clin Psychopharmacol 1985;5:65.
60. Jones BD, Runikis AM. Interaction of ginseng with phenelzine. J Clin Psychopharmacol 1987;7:201-2.
61. McGuffin M, et al. American Herbal Products Association's Botanical Safety Handbook. 1997, Boca Raton, FL: CRC Press. 231.
62. Zhu M, et al. Possible influences of ginseng on the pharmacodynamics of warfarin in rats. J Pharm Pharmacol 1999;51:175-80.
63. Steiner M. Untersuchungen zur odemvermindernden und odemportektiven wirking von ro kastaniensamenextrakt. Phlebol Prokto 1990;19:239-42.
64. Vutyavanich T, Kraisarin T, Ruangsri R. Ginger for nausea and vomiting in pregnancy: randomized, double-masked, placebo-controlled trial. Obstet Gynecol 2001;97(4):577-82.
65. Tode T, et al. Effect of Korean red ginseng on psychological functions in patients with severe climacteric syndromes. Int J Gynaecol Obstet 1999;67:169-74.
66. Hiai S, et al. Stimulation of pituitary-adrenocortical system by ginseng saponin. Endocrinol Jpn 1979;26:661-5.
67. Kase Y, et al. Mechanisms by which Hange-shashin-to reduces prostaglandin E2 levels. Biol Pharm Bull 1998;21:1277-81.
68. Robbers JE, Speedie MK, Tyler VE. Pharmacognosy and Pharmacobiotechnology. 1996, Baltimore, MD: Williams & Wilkins.
69. Belogortseva NI, Yoon JY, Kim KH. Inhibition of Helicobacter pylori hemagglutination by polysaccharide fractions from roots of Panax ginseng. Planta Med 2000;66:217-20.
70. Schulz V, et al. Rational Phytotherapy: A Physician's Guide to Herbal Medicine. 3rd ed. 1998, Berlin, GER: Springer.
71. Lewis R, et al. Non-ginsenoside nicotinic activity in ginseng species. Phytother Res 1999;13:59-64.
72. Tamaoki J, Nakata J, Kawatani K. Ginsenoside-induced relaxation of human bronchial smooth muscle via release of nitric oxide. Br J Pharmacol 2000;130:1859-64.
73. Pan SJ, Ding Z, Ivy JL. Ginseng's effects on glucose tolerance and mRNA profiles in an animal model of Type II diabetes. Alt Ther 2001;7:S26.