

Panax ginseng, Rhodiola rosea and Schisandra chinensis

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Abstract

Panax ginseng (Ginseng), *Rhodiola rosea* (Hong Jing Tian) and *Schisandra chinensis* (Wu Wei Zi) are well-known herbs in traditional Chinese medicine (TCM). Recently, there have been a number of studies on these 3 herbs. This review discusses their active components and major pharmacological effects. For *Panax ginseng*, it has been shown to have an anti-inflammatory activity, affects pulmonary function and erectile dysfunction, improves cognition in patients with Alzheimer's disease and promotes sexual arousal in menopausal women as well as prevent cancer. For *Rhodiola rosea*, its effectiveness on alleviating depression and reducing fatigue are summarized in this review. Additionally, anti-cancer and other clinical effects of *Schisandra chinensis* are also discussed. These 3 herbs are considered as adaptogens as they bear multiple functions and their effects were found to be very different in subjects depending on the circumstances (age, gender, environment, diet, season, etc.). Thus, in most cases, the art of the TCM practitioner is to prescribe these herbs after a complete evaluation of patients' overall health status.

Keywords: *Adaptogen, Panax ginseng, Rhodiola rosea, Schisandra chinensis, Traditional Chinese*

Medicine

Introduction

An organism which demonstrates a biochemical change in response to stressors or different environmental conditions is known as physiological adaptation. This adaptive ability conveys the organism from its normal steady state to a heightened level of dynamic equilibrium (Chrousos and Gold, 1992). It has been suggested that the heightened level of dynamic equilibrium could be achieved either by gradually training to withstand the effect of the stressor or by application of biological response modifiers, adaptogens (Panossian et al., 1999). An adaptogen is a substance that: (1) showed some non-specific effect, (2) has a normalizing influence on a pathological state, and (3) is innocuous and does not disturb body functions at a normal level (Brekhman and Dardymov, 1969). Plant adaptogens have been considered as substances that increase the ability of an organism to adapt to environmental factors and to avoid damage from stressors (Panossian et al., 1999). At the start of the twentieth century, the majority of people in developed countries were more health conscious and were willing to spend extra money on different functional foods or nutraceuticals in order to pursue healthy aging (Chan et al., 2010b). Therefore, the use of plant adaptogens to improve health has been a common practice in developed countries.

In traditional Chinese medicine (TCM), it is believed that food and medicine come from the same origin but with different uses and applications (Chan et al., 2010a). Therefore, it is common

for Chinese people to incorporate different TCM herbs into their diet to produce various “healthy” food recipes so as to achieve better taste, more attractive appearance and improved texture of the food and most importantly to improve health (Guo et al., 2008). In fact, most of the TCM herbs have an adaptogen-like effect. In this article, recent findings on the chemistry and pharmacology of three well-known plant adaptogens, *Panax ginseng* (Ginseng), *Rhodiola rosea* (Hong Jing Tian), *Schisandra chinensis* (Wu Wei Zi), used in TCM are reviewed.

***Panax ginseng* (Ginseng)**

Panax ginseng (Figure 1) is often described as the “king herb” which holds an important position in TCM and traditional Oriental medicine in many countries (Xie et al., 2005). It is a slow-growing perennial plant with fleshy roots, belonging to the *Panax* genus in the family Araliaceae. It grows in cooler climate regions of the Northern Hemisphere (mostly in northern China, Korea, and eastern Siberia). The earliest therapeutic use of *Panax ginseng* can be traced back approximately 2000 years ago (recorded in the oldest comprehensive materia medica, Shen Nong Ben Cao Jing) (Huang, 1999). Raw *Panax ginseng* could be processed by two major methods. It can be sun dried to form white ginseng or steamed to form red ginseng. In TCM theory, *Panax ginseng*, in general, is a substance rich in influences (Qi, in Chinese) and full of vigor. It is able to replace any deficiencies and prevent any loss of proper influences (positive energies). Thus, it is a good adaptogenic herb.

Different processing methods are believed to modify the therapeutic effects of *Panax ginseng*

(Keum et al., 2000). White ginseng is better for boosting fluids and is considered to be more balanced in temperature; while red ginseng is considered to be warmer and stronger for supplementing Qi. It has been shown that the chemical compositions of white and red ginseng are different so they have different biological effects (Park et al., 2001).

Chemical constituents

Panax ginseng is constituted of organic (80%–90%) and inorganic substances (approximately 10%) and consists of a number of active constituents, such as saponins or ginsenosides, carbohydrates, nitrogenous substances, phytosterol, essential oils, organic acids, amino acids, peptides, vitamins, and minerals (Attele et al., 1999; Gillis, 1997; Xie et al., 2005).

Pharmacological effects

The anti-inflammatory activity, effects on pulmonary function and erectile dysfunction, improvement of cognition in patients with Alzheimer's disease and sexual arousal in menopausal women as well as cancer prevention using *Panax ginseng* will be discussed.

Anti-inflammatory effect

The anti-inflammatory effect of *Panax ginseng* has been known for the past few decades. Ginsenoside Ro has been shown to inhibit any increases in vascular permeability in mice induced

by acetic acid and reduce an acute paw edema in rats induced by carrageenin (Matsuda et al., 1990).

A recent study using 70% ethanol-water extract of *Panax ginseng* significantly inhibited the transcription and secretion of an inflammatory gene CXCL-10 following TNF- α stimulation in U937 cells (human leukemic monocyte lymphoma cell line) (Lee et al., 2009). Interestingly, the CXCL-10 suppressive effect of individual ginsenosides was less than that of the crude extract or the mixture of ginsenosides. The CXCL-10 suppression could be attributed to the inactivation of ERK1/2 pathways by *Panax ginseng*. The anti-inflammatory function of *Panax ginseng* may be due to the combined effects of various ginsenosides, contributing in part to the diverse actions of ginseng in humans (Lee et al., 2009).

Pulmonary function in chronic obstructive pulmonary disease (COPD)

The pulmonary effect of *Panax ginseng* has been evaluated in 92 adults [randomly divided into the experimental (n = 49, Ginseng extract 100 mg) and placebo-control (n = 43) groups] with moderately-severe COPD (Gross et al., 2002). Patients receiving *Panax ginseng* extract (100 mg) for three months were tested in all parameters in Pulmonary Function Tests, Maximum Voluntary Ventilation, Maximum Inspiratory Pressure and Maximal Oxygen Consumption. It was found that this experimental group, but not the control group, test values increased significantly above the baseline (Gross et al., 2002). No side effects were observed within the treatment period (Gross et al., 2002).

Against erectile dysfunction

Panax ginseng is a traditional Asian medicine for stimulation of sexual function (Hong et al., 2002) and it has been shown to enhance penile corpus cavernous smooth muscle relaxation in rabbits with diabetic erectile dysfunction (Kang et al., 2004). Additionally, a recent double-blind, placebo-controlled study on mild or mild to moderate erectile dysfunction patients' response to Korean Red Ginseng (KRG) treatment was launched (de Andrade et al., 2007). The five-item version of the International Index of Erectile Function score after treatment was significantly higher in the KRG group compared with the scores before the treatment; while there was no difference before and after the treatment in the placebo group. The improvement in sexual function was in term of rigidity, penetration and maintenance in patients treated with KRG for 12 weeks (de Andrade et al., 2007).

Improves cognition in Alzheimer's disease (AD)

Alzheimer's disease (AD), a neurodegenerative disease, invokes a cascade of oxidative damages to neurons and is characterized by senile plaque deposition, neurofibrillary tangle formation and neuronal loss. Various natural compounds are effective in suppressing AD like pathology through their properties as anti-oxidants (Dos Santos-Neto et al., 2006; Frank and Gupta, 2005). Our team has even shown that *Panax ginseng* has a high content of anti-oxidants (Chan et al., 2010a; Chan et

al., 2008). *Panax ginseng*'s effect on cognitive performances were evaluated in consecutive AD patients (Lee et al., 2008). In the clinical study, patients were randomly assigned to the Ginseng (n=58) or the control group (n=39), and the *Panax ginseng* group was treated with *Panax ginseng* powder (4.5 g/d) for 12 weeks. Both Alzheimer's disease assessment scale (ADAS) and mini-mental state examination (MMSE) were used to monitor cognitive performances during 12 weeks of the *Panax ginseng* treatment and at 12 weeks after the *Panax ginseng* discontinuation. The results showed that after *Panax ginseng* treatment, the cognitive subscale of ADAS and the MMSE score began to show significant improvements and continued up to 12 weeks (Lee et al., 2008).

Sexual arousal in menopausal women

Climacteric symptoms, including impairment of sexual function, are commonly reported by menopausal women. In a clinical study, the effect of Korean Red Ginseng (KRG) extract on improving sexual function was assessed in 28 menopausal women (51.2 ± 4.1 years old) with a mean menopausal duration of 37.4 ± 2.9 months (Oh et al., 2010). The result was that KRG extract significantly improved scores on the Female Sexual Function Index in the sexual arousal domain (Oh et al., 2010).

Preventing cancer

During the development of tumors, very large amounts of nutrients (oxygen and nutrients) are required to sustain the rapid proliferation of tumor cells. However, tumor cells can still survive under extreme conditions such as low oxygen and carbohydrate availability due to their relatively high tolerance to hostile environments. Similar to other herbs (Li et al., 2009; Li et al., 2007), *Panax ginseng* has reported to have anticancer effects both *in vitro* and *in vivo* (Lee et al., 2010; Ni et al., 2010; Qi et al., 2010). The ability of *Panax ginseng* on cancer prevention was illustrated by a recent cohort study, in which Korean Red Ginseng (KRG) extract powder (1 g) was administered orally to each patient (n=643) with atrophic gastritis per week for 3 years and reports were followed up for 8 years (Yun et al., 2010). Also, the development of various cancers in subjects in the KRG group was compared to the placebo group. Twenty-four cancers of various organs were diagnosed from these subjects in 11 years: eight lung cancers, six stomach cancers, two colorectal cancers, two liver cancers and one cancer each of the esophagus, nasopharynx, urinary bladder, prostate, pancreas and gallbladder. Results show that KRG appeared to have a cancer protective effect in males with a relative cancer risk of 0.35 (95% confidence interval, 0.13-0.96; $P = 0.03$) compared to the male placebo group (Yun et al., 2010).

***Rhodiola rosea* (Hong Jing Tian)**

Rhodiola rosea (Figure 2) has been used among Chinese people (especially Tibetan people) and Russians for over 1000 years. It belongs to the plant family Crassulaceae and the genus *Rhodiola*. This herb grows on the mountain regions up to 3500 to 5000 m above sea level throughout the Arctic, Europe and Asia (Bawa and Khanum, 2009; Hung et al., 2011; Kelly, 2001). *Rhodiola rosea* has shown to have effects on improving mood, alleviating depression and treating opioid addiction (Mattioli and Perfumi, 2011; Panossian et al., 2010). The effects are potentially mediated by changes in serotonin and dopamine levels due to monoamine oxidase inhibition and its influence on opioid peptides such as β -endorphins. Additionally, *Rhodiola rosea* and/or its major active ingredients have been reported to induce cell-cycle arrest and apoptosis in human breast cancer cells (Hu et al., 2010), reduce high-altitude sickness and mental problems (Gupta et al., 2010). It protects neuronal cells from oxidative stress (Qu et al., 2009; Yu et al., 2010; Zhang et al., 2010), reduces or abolishes bingeing-related eating disorders (Cifani et al., 2010) and suppresses adipogenesis and lipid accumulation (Lee et al., 2011). Because of the multiple functions of this herb, it is included among a class of plant derivatives called adaptogens.

Chemical constituents

So far, approximately 140 compounds have been isolated from *Rhodiola rosea*. They are monoterpene alcohols and their glycosides, aryl glycosides, cyanogenic glycosides, phenylethanoids, phenylpropanoids and their glycosides, flavonoids, flavonlignans,

proanthocyanidins and gallic acid derivatives (Panossian et al., 2010)..

Pharmacological effects

Being an adaptogen, *Rhodiola rosea* bears various pharmacological effects. It is particularly useful in that it does not interfere with other drugs nor have any adverse effects in the course of clinical trials (Panossian et al., 2010). In the upcoming sections, *Rhodiola rosea*'s effectiveness on anti-depression and anti-fatigue are reviewed further.

Anti-depression

Depression is a serious public mental disease and sometimes creates a great social burden. The mechanism of depression is complex. Many synthetic chemical antidepressants have been introduced, such as tricyclic antidepressants, selective serotonin reuptake inhibitors and so on. However, their therapeutic effects also come with a variety of side effects such as psychomotor impairment and dependence liability (Sarko, 2000). Thus, searching for new therapeutic products from medicinal plants for the treatment of depression is a possible solution such as using *Rhodiola rosea* where there have been encouraging results. A clinical trial showed a significant effect using *Rhodiola rosea* extract (340–680 mg/day) in male and female patients from 18 to 70 years old with mild to moderate depression (Darbinyan et al., 2007). Several mechanisms of action possibly contributing to this clinical effect have been identified. They include interactions with

hypothalamic-pituitary-adrenal system (cortisol-reducing), protein kinases p-JNK, nitric oxide and defense mechanism proteins (e.g. heat shock proteins Hsp 70 and FoxO/DAF-16) (Panossian et al., 2010).

Anti-fatigue

Fatigue is known to be accompanied by a feeling of extreme physical or mental tiredness, resulting from severe stress and hard physical or mental work. It can be divided into two types: physical fatigue caused by forced exercise or swimming; mental fatigue caused by sleep deprivation (Akazawa et al., 2010; Chen et al., 2009). *Rhodiola rosea* has shown to have both anti-physical fatigue (De Bock et al., 2004; Huang et al., 2009) and anti-mental fatigue (Tokunaga et al., 2007).

In a randomised, double-blind, placebo-controlled, parallel-group study, after four weeks of repeated administration of standardised extract of *Rhodiola rosea*, it has been demonstrated to exert an anti-fatigue effect that increases mental performance, particularly the ability to concentrate, in healthy subjects and burnout patients with fatigue syndrome (Olsson et al., 2009). In another study by Parisi et al., 14 trained athletes (male) underwent a cardio-pulmonary exhaustion test and blood samples were taken to evaluate their antioxidant status and other biochemical parameters (Parisi et al., 2010) following a chronic supplementation with Hong Jing Tian for 4 weeks. It was found that there was a significant reduction in both lactate levels and parameters of skeletal muscle damage after an exhaustive exercise session in the treatment group. Moreover, this supplementation seems

to ameliorate fatty acid consumption (Parisi et al., 2010).

***Schisandra chinensis* (Wu Wei Zi)**

Schisandra chinensis (Figure 3) belongs to the family *Schisandraceae* and the genus *Schisandra*.

The plant of *Schisandra chinensis*, a climbing plant widely distributed in the region of the Russian Far East, Korea, Japan and northeastern China, is often considered as an example of a medicinal plant used for anti-aging, sedative and tonic agents in TCM (Huang et al., 2005). The name of *Schisandra chinensis* in Chinese tells us a great deal about the qualities of this herb. It means “Five Taste Fruit”. In TCM theory, the five tastes mean 1) sour, 2) bitter, 3) sweet, 4) spicy and 5) salty. Thus, the fruit possesses the essence of all five of the elemental energies (wood, fire, earth, metal and water). According to an overview of ancient Chinese and Korean books, only plants with black berries growing in the northern regions of China possessed curative properties, whilst the southern varieties with red berries were not considered to be effective (Panossian and Wikman, 2008). Current scientific findings suggest that lignans of *Schisandra chinensis*, the active ingredients can stimulate liver regeneration, prevent liver injuries and inhibit hepatocarcinogenesis as well as lipid peroxidation in rats (Hikino et al., 1984; Kubo et al., 1992). Also, other pharmacological effects such as lowering the serum glutamate-pyruvate transaminase level, inhibiting platelet aggregation, and anti-oxidative, calcium antagonism, anti-tumor and anti-HIV (human immunodeficiency virus) effects of *Schisandra chinensis* can also be attributed to its lignan constituents, particularly the

dibenzocyclooctadiene-type lignans (Lu and Chen, 2009).

Chemical constituents

Schisandra chinensis contains various forms of lignans, including schisandrol A, gomisin J, schisandrol B, tigloylgomisin H, angeloylgomisin H, schisandrin A, γ -schisandrin, gomisin N and schisandrin C (Ding et al., 2010; Gnabre et al., 2010; Panossian and Wikman, 2008). A group of nortriterpenoids including pre-schisanartanin and schindilactones A–C, schinrilactones A and B and wuweizidilactones A–F have been isolated and identified (Huang et al., 2007; Panossian and Wikman, 2008).

Pharmacological effects

Schisandra chinensis bears various pharmacological effects. In the following sections, its anti-cancer and other clinical effects are reviewed.

Anti-cancer

Recently a group from Johns Hopkins isolated lignans from *Schisandra chinensis* and demonstrated its anti-proliferative activity in human colorectal carcinoma (Gnabre et al., 2010) and cytotoxicity against colon cancer cell line LoVo (Smejkal et al., 2010). Their effects were reported on structure-activity relationships (Gnabre et al., 2010). It is also interesting to note that *Schisandra*

chinensis extract significantly inhibited P-glycoprotein substrate timolol in humans (Fan et al., 2009). This provides further scientific evidence for the adjuvant effect of *Schisandra chinensis* on cancer therapy. However, patients receiving the *Schisandra chinensis* extract may require dose adjustments when treated with drugs primarily transported by P-glycoprotein (Fan et al., 2009).

Other clinical effects

Schisandra chinensis is renowned as a beauty tonic and is considered to be a youth preserving herb in China. It is also said to be a powerful stimulant in sexual weakness/impotence and to treat spermatorrhoea, nocturnal emission, gonorrhoea, protracted diarrhoea, dysentery, frequent urination, enuresis, impairment of body fluids, night sweating, spontaneous sweating, cough, phlegm, jaundice, wheezing, shortness of breath, asthma, thirst, feeble pulse, urinary tract disorders, exhaustion, diabetes as well as body weakness caused by internal heat, palpitation and insomnia (Panossian and Wikman, 2008). In healthy subjects, *Schisandra chinensis* increases endurance and accuracy of movement, mental performance and working capacity, and generates alterations in the basal levels of nitric oxide and cortisol in blood and saliva with subsequent effects on the blood cells, vessels and CNS. Numerous clinical trials have demonstrated the beneficial effects of *Schisandra chinensis* on various body systems (Panossian and Wikman, 2008) such as the nervous system, where it helps neurologic and psychiatric (neurosis, psychogenic depression, astheno-depressive states, schizophrenia and alcoholism) disorders. Its neuroprotective effects may

be due to the attenuation of ROS production and the modulation of the apoptotic signal pathway through Bax and caspase-3 in neuronal cells (Song et al., 2011). In the cardiovascular system, it counteracts hypertension and cardiotoxic disorders. In the skin, it reduces allergic dermatitis and in the gastrointestinal system, it alleviates acute gastrointestinal diseases, gastric hyper- and hypo-secretion, chronic gastritis, stomach and duodenal ulcers, wound healing and trophic ulcers (Panossian and Wikman, 2008).

Conclusion

Despite the beneficial effects of *Panax ginseng* (Ginseng), *Rhodiola rosea* (Hong Jing Tian) and *Schisandra chinensis* (Wu Wei Zi), in most cases, the use of these herbs is based on the TCM practitioner's evaluation on the patients' condition. Traditionally, in TCM, most of the herbs like *Panax ginseng* and *Schisandra chinensis* are almost never used alone but in combination with the aim of increasing activity, tolerance and safety. One of the well-known TCM prescriptions is Shengmai San which is comprised of the medicinal herbs of *Panax ginseng*, *Schisandra chinensis* and *Ophiopogon japonicas*. Shengmai San has been used for patients with coronary heart disease for long-time clinically (Yao et al., 2008). Although *Rhodiola rosea* is a TCM, the use of it in TCM prescriptions is not common. It is because the origin of *Rhodiola rosea* is from Tibet and it is usually use as a single herb. The current body of evidence supporting the use of *Panax ginseng*, *Rhodiola rosea* and *Schisandra chinensis* has been reviewed. These 3 herbs are considered as adaptogens as they bear multiple functions and their effects were found to be very different in subjects depending on certain criteria (age, gender, environment, diet, season, etc.).

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Figures:



Figure 1

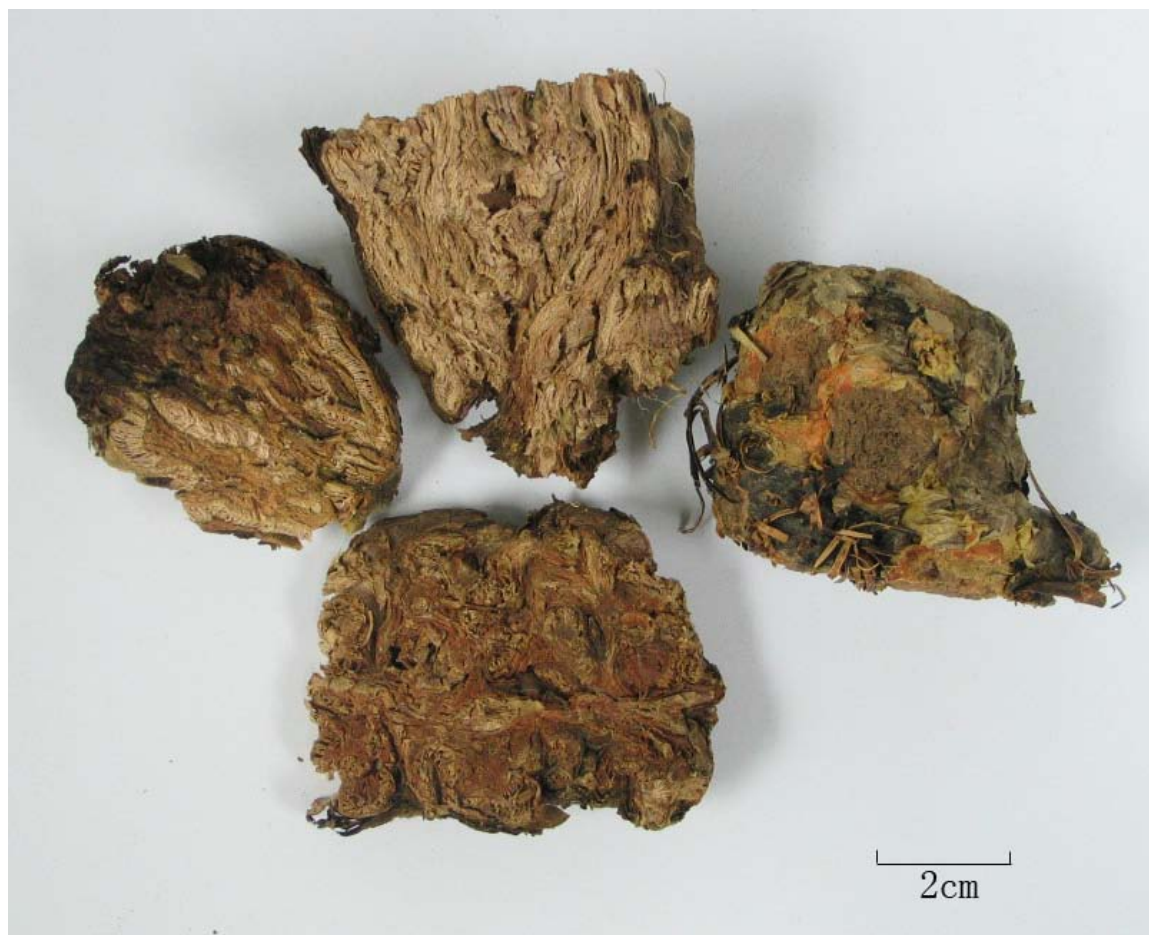


Figure 2



Figure 3

Figure legends

Figure 1: Photo of *Panax ginseng* (Ginseng).

Figure 2: Photo of *Rhodiola rosea* (Hong Jing Tian).

Figure 3: Photo of *Schisandra chinensis* (Wu Wei Zi).