



Monograph

PEONY (*PAEONIA SPP*)

Introduction

Peonies have provided useful medicine and attractive ornamental flowers for over 3,000 years in China and at least 500 in Europe.¹ There are four species of this Ranunculaceae family plant that are utilized in traditional Chinese medicine (TCM) under the general rubric of peony: *Paeonia suffruticosa* (tree peony), *Paeonia lactiflora* (Chinese peony), *Paeonia veitchii* (Chinese peony), and *Paeonia obovata* (Chinese peony).

For millennia, peony root has been used to treat wounds, fungal infections, pain, and spasmodic conditions in TCM.¹ In recent times, peony root has received growing research attention, primarily in Japan and China. It has a long history of use in Europe as well, particularly for spasmodic conditions.²

Description and Constituents

All three Chinese peony species are perennial and achieve heights up to nine meters (the tree peony is somewhat larger). They have alternate, elliptical, smooth-edged leaves growing on smooth stems bearing two or more flowers. The large blossoms of the Chinese peony can have a range of color and are generally 4-6 cm in diameter.¹ The roots of all peonies are large, straight, and firm with easily peeled bark that reveals a powdery underlayer when removed.

There are three possible medicines that are produced from peony plants in TCM.³ *P. suffruticosa* (tree peony) bark of root provides *mu dan pi*, referred to below as tree peony. *P. lactiflora*, *P. veitchii* and *P. obovata* root with bark attached provides *chi shao*, referred to below as red peony. The root without the bark of these same three plants provides *bai shao* (white peony), although most often this medicine is derived from *P. lactiflora*. The color designation does not refer to the flowers of these plants (which are most commonly pink, red, purple, or white) but to the color of the root after processing.

White, red, and tree peony contain glycosides (most notably paeoniflorin), flavonoids, proanthocyanidins, tannins, terpenoids, triterpenoids, and complex polysaccharides that may all contribute to its medicinal effects.³ Paeoniflorin has received the most research attention.

Mechanisms of Action

The exact mechanisms of action of peony constituents have not been determined in their entirety. Paeoniflorin, monoterpenoids, and other constituents in white and red peony have been shown to be spasmolytic. This is in part achieved by interfering with acetylcholine release into neuromuscular junctions (NMJ) associated with gut smooth muscle tissue.⁴

There is a great deal of synergism of activity between white or red peony and licorice (*Glycyrrhiza uralensis*, for which *G. glabra* can be substituted) – the two components of shakuyaku-kanzo-to, a formula commonly used in Japanese and Chinese herbal medicine. One animal study found that peony extracts interfere with acetylcholine release into the NMJ while licorice extracts interfere with acetylcholine's activity in the NMJ.⁵ An *in vitro* study found concentrations of paeoniflorin and glycyrrhizin (a major active glycoside in licorice) that individually were too low to inhibit muscle contraction were very active when applied simultaneously.⁴

Other actions possessed by peony extracts and their constituents in preclinical studies include the following: (1) improvement of memory;^{6,7} (2) antioxidant activity;^{8,9} (3) hepatoprotection;¹⁰ (4) anti-atherosclerotic effects associated with lipid peroxidation inhibition;¹¹ (5) inhibition of hydrochloric acid secretion;¹² (6) anti-epileptic activity;¹³ (7) appetite suppressant and metabolism stimulating activity;¹⁴ (8) antimutagenic properties;¹⁵ (9) protection of endothelium from negative effects of hyperlipidemia;¹⁶ (10) platelet aggregation inhibition;¹⁷ and (11) anticoagulation and fibrinolysis.^{18,19} The complex polysaccharides of peony exert immunomodulating effects *in vitro*.²⁰

Clinical Indications

Muscle Cramps

The efficacy of white peony for relieving muscle cramps of various types, particularly combined with licorice in the formula shakuyaku-kanzo-to, is supported by several clinical trials. In a double-blind, placebo-controlled trial involving 101 patients with muscle cramps due to hepatic cirrhosis, dried extract of shakuyaku-kanzo-to was significantly superior to placebo in relieving symptoms over a two-week period.²¹ The dose in this study – 2.5 g three times daily before meals – was sufficiently high to induce signs of pseudoaldosteronism (edema and weight gain) in five patients (9%) receiving shakuyaku-kanzo-to, due to the high intake of licorice. Other uncontrolled trials have shown that shakuyaku-kanzo-to can help relieve muscle cramps in people with diabetes mellitus,²² those undergoing dialysis,²³ in alcoholics,²⁴ and in people with cerebrovascular disease.²⁵

Women's Health

Both white and red peony are commonly used for various women's health problems in TCM. There is evidence from preliminary clinical trials supporting their use in dysmenorrhea and polycystic ovary syndrome (PCOS). The TCM formula toki-shakuyaku-san – containing white peony, *Atractylodes lancea* (red atractylodes) rhizome, *Alisma plantago-aquatica* (alisma; water plantain) rhizome, *Poria cocos* (hoelen) sclerotium, *Cnidium monnieri* (cnidium) rhizome, and *Angelica dahurica* (Chinese angelica) radix – has been reported to alleviate pain in patients with primary dysmenorrhea in one double-blind clinical trial.²⁶ Shakuyaku-kanzo-to reduced dysmenorrhea in 60 percent of women with uterine fibroids in an open trial.²⁷ Shakuyaku-kanzo-to helped increase fertility in women with PCOS in another open clinical trial.²⁸ More research is warranted to clarify the exact role and degree of efficacy of white peony by itself and in combination formulae for these and other women's health concerns, particularly luteal dysfunction and menopausal symptoms.²⁹

Chronic Viral Hepatitis

Both red and white peony are traditionally utilized in Asia to treat people with chronic viral hepatitis. In one small, open clinical trial using red peony (doses could not be determined but said to be “heavy”) over a three-month period, 77 percent of patients with cirrhosis or chronic active hepatitis experienced improvement in liver histology based on repeat biopsy results.³⁰ A case series also reported the efficacy of this approach.³¹ Until more research is conducted to determine effectiveness of red or white peony for chronic hepatitis, these agents should be combined with other, better-established therapies.

Cardiovascular Disorders

Numerous lines of evidence suggest tree, red, and white peony may be beneficial in people with atherosclerosis and/or hypertension. Various extracts and constituents of these herbal medicines have shown antiplatelet and anti-atherosclerotic properties. One open trial found a *Paeonia obovata* extract decreased platelet aggregation in humans.³² A combination of Chinese angelica and peony was found helpful in an uncontrolled trial of women with pregnancy-induced hypertension.³³ There is also at least one open clinical trial suggesting tree peony can reduce blood pressure in humans.³ The exact role of peony in atherosclerosis and hypertension remains unknown.

Miscellaneous Indications

There is preclinical evidence suggesting peony might be helpful in people with dementia, Alzheimer’s disease, infectious disease, epilepsy, peptic ulcer, obesity, and cancer. However, no clinical trials or reports were found discussing the use of peony for any of these conditions. One review article did suggest an open trial was conducted in Japan showing benefits of toki-shakuyaku-san in Alzheimer’s disease patients, but the specifics of this trial could not be located.²⁹

Dosage and Toxicity

Peony is generally available as dried crude herb or dried aqueous extract, either in capsules or as powders. The usual dose of white peony is 1.5-4 grams three times daily. The usual dose of red peony and tree peony is 1-3 grams three times daily. The usual dose of the shakuyaku-kanzo-to and toki-shakuyaku-san formulae is 2.5 grams three times daily.

At the doses indicated above, peony has not been associated with any adverse effects other than occasional gastric upset in susceptible individuals. Shakuyaku-kanzo-to, on the other hand, can cause pseudoaldosteronism with symptoms of hypertension, edema, and weight gain. This is due to the licorice in the formula and is not attributed to peony.

The safety of peony in pregnancy and lactation is unknown. However, as noted above, it has been used without obvious ill effect in one open trial to treat women with pregnancy-induced hypertension.³³ Until further safety studies have been conducted, caution should be exercised during pregnancy.

Drug Interactions

Peony has been shown to reduce sexual dysfunction in men, reportedly caused by neuroleptic-induced hyperprolactinemia.^{34,35} Women with dysmenorrhea and/or amenorrhea due to use of the neuroleptic drug risperidone benefited from shakuyaku-kanzo-to according to another report.³⁶ No published reports suggest any lessening of efficacy of neuroleptics when combined with peony.

Toki-shakuyaku-san has been reported effective in relieving menopausal symptoms as well as frozen shoulder syndrome in some women treated with gonadotropin-releasing hormone superagonists

such as leuprolide (Lupron®).³⁷ Estrogen levels were not affected by the formula. It is unknown if this formula would help men taking these drugs for treatment of prostate cancer.

Toki-shakuyaku-san showed additive effects in improving pregnancy rates in infertile women treated with clomiphene.³⁸ When clomiphene was given alone in this uncontrolled trial, 21 percent of study volunteers became pregnant compared to 34 percent who took clomiphene with toki-skakuyaku-san. There was no sign of additive adverse effects.

The anticoagulant and antiplatelet effects of peony suggest it might potentiate anticoagulant drugs such as warfarin and antiplatelet drugs such as aspirin. No published reports have yet appeared confirming this possibility, but caution is warranted.

In a small open trial of cancer patients who suffered muscle pain due to paclitaxel (Taxol®) and carboplatin therapy, adding shakuyaku-kanzo-to to the second course relieved the pain in 7 of 10 patients.³⁹ In an animal trial, oral shakuyaku-kanzo-to reduced diarrhea due to intravenous cisplatin administration.⁴⁰ Further study is warranted on the effect of peony and formulae containing it in cancer patients undergoing chemotherapy.

Finally, peony may not combine well with antibiotics. The gut flora is responsible for cleaving the aglycones of peony glycosides and thereby activating these constituents.⁴¹ Damage to the gut flora by antibiotics might interfere with this process, theoretically decreasing peony's efficacy. Clinical trials will be necessary to determine the importance of this possible interaction.

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