

PAEONIA

Paeonia lactiflora Pall.

Family

Paeoniaceae.

Parts Used

Root.

Description

Paeonia is a herbaceous perennial flowering plant popular with gardeners due to its appealing flowers. Paeonia is native to central and eastern Asia from eastern Tibet across northern China to parts of Siberia. Paeonia is now widely found outside Asia and grown in many countries as an ornamental plant, with many cultivars available. Paeonia has attractive flowers and foliage and decorative seedpods. The leaves are large, alternately arranged on the stems, and divided into oval to lance-shaped linear leaflets.

The foliage is often tinted bronze when new and takes on reddish tones in the fall. The blossom is very fragrant with five or more wide petals arranged in a single row around a centre of pollen bearing stamen. The roots of peonies are tuberous and are the part used medicinally. The tuberous roots are fleshy and plentiful and attached to a mass of underground tissue usually referred to as the crown. Paeonia, also known as white peony (Bai shao) root comes from cultivated *Paeonia lactiflora* and is provided by the root without the bark attached – giving a characteristic white colour to the bark – hence its name.

Traditional Use

Paeonia is named after the mythical Greek figure Paeon, who was said to be a student of Aesculapius, the great physician. Paeon used the peony plant



(various species also grow in Europe) to heal a wound for the god Pluto.

Peonies have a long and varied history in both the eastern and western worlds. Paeonia has a long history of use in Traditional Chinese Medicine – dating back to 1000 BC. The bark, red peony root, and paeonia root all have somewhat different properties in TCM. Dried versus charred roots also have been viewed as having different properties. In China, peonies were acclaimed for their medicinal and horticultural value. The best varieties commanded huge prices and peonies were often part of a dowry settlement.

Medicinally, paeonia was traditionally used in China to treat nervous complaints and those that involve spasm such as epilepsy, muscular cramps and hypertension. It was also used for painful periods or menstrual irregularity in women. It is thought to be bitter, salty and cold and has an affinity for the liver meridian. It is more nourishing than red peony and can supplement the spleen, nourish the liver blood and drain liver fire.

In the West, peonies were first grown for their medicinal uses, but their popularity quickly spread and they became a prized garden flower. People have used paeonia as sources of inspiration for their artwork and in their gardens. During the middle ages in Europe peonies were used for everything from childbirth to warding off evil spirits. Paeonia was recommended to cure gall stones, control epileptic seizures, soothe teething pain and cure jaundice.

Constituents

Paeonia contains proanthocyanidins, flavonoids, tannins, terpenoids, triterpenoids, and complex polysaccharides. It contains gallotannin and the unique glycosides paeoniflorin, benzoylpaeoniflorin, albiflorin and oxypaeoniflorin as well as paeonol, pentagalloylglucose, hexagalloylglucose, heptagalloylglucose, octagalloylglucose and a range of paeonilactones.

Actions

Antioxidant, anti-inflammatory, antispasmodic, anticonvulsant, analgesic, antithrombotic, steroid hormone modulator, hepatoprotective, immunomodulator, neuroprotective.

Pharmacological Activity

Paeonia contains a unique glycoside called paeoniflorin that has been most extensively studied. Much of the other research into paeonia looks at it in combination with other herbs as part of traditional Chinese formulas.

Hepatoprotective Activity

Glucosides from paeonia have been shown to have beneficial effects on induced hepatic fibrosis in rats. The extracts were able to inhibit collagen synthesis and decrease oxidative stress.¹

Paeoniflorin was shown to significantly protect against immunological liver injury induced by the bacillus Calmette-Guérin (BCG) and lipopolysaccharide in mice. The protective mechanism of paeoniflorin was partially related to modulation of TNF-alpha, IL-6, lipopolysaccharide binding protein and CD14 messenger ribonucleic acid expression in mouse liver.²

Paeoniflorin's role in preventing hepatic granuloma formation and fibrosis in mice infected with *Schistosoma japonicum* was examined. Paeoniflorin can exert antifibrogenic effects by inhibiting the proliferation of hepatic stellate cells and down-regulating gene expression and phosphorylation through transforming growth factor (TGF)-beta1 signalling.³ Paeoniflorin was also shown to significantly reduce hepatic granuloma formation and fibrosis due to schistosome eggs. It decreased the expression of TGF-beta1 and alpha smooth muscle actin in mice when it is given before praziquantel administration, which may be associated with the activation of hepatic stellate cells and the expression of TGF-beta1 in liver tissue.⁴

The effects of paeoniflorin on liver fibrosis in rats induced by carbon tetrachloride has also been examined. Paeoniflorin significantly inhibited the progression of hepatic fibrosis induced by carbon tetrachloride. The inhibitory effect on hepatic fibrosis might be associated with its ability to scavenge free radicals, decrease the level of TGF-beta1 and inhibit collagen synthesis and proliferation.⁵

A study found that the extract prepared from the roots of both *Paeonia lactiflora* and *Astragalus membranaceus* demonstrated more efficient hepato-protective activity than the single herbs used individually.⁶

Immunoregulatory Activity

Paeoniflorin was found to induce apoptosis in both murine T-lineage cells and human T-cell leukaemia cells. The apoptosis was mediated through the reduction of mitochondrial membrane potential, activation of enzymes and fragmentation of DNA. Paeoniflorin also induced the generation of reactive oxygen species (ROS) and a reducing agent and a ROS scavenger which successfully attenuated the apoptosis.⁷

Paeonol was examined for its role in anaphylactic reactions and its mode of action. Paeonol significantly inhibited histamine release and IgE production in B cells and effectively downregulated the expression of IL-4. The study confirmed that paeonol effectively inhibited anaphylactic shock in mice by 90%, suggesting that paeonol has antianaphylactic activity by regulating histamine and TNF- α .⁸

The antiallergic effects of paeoniflorin and paeonol were evaluated *in vivo* for their inhibitory effects against passive cutaneous anaphylaxis (PCA) reaction and scratching behaviours induced by various compounds. The paeonia compounds potently inhibited PCA reaction and scratching behaviours in mice. Paeoniflorin exhibited the most potent inhibition against scratching behaviours and the acetic acid-induced writhing syndrome in mice. Paeonol most potently inhibited PCA reaction and mast cells degranulation.⁹

In a study, the effects of Paeoniflorin on inflammatory and immune responses in adjuvant arthritis in rats were investigated. The administration of paeoniflorin significantly diminished the secondary hind paw swelling and arthritis scores, reversed the changes of cytokines, and further decreased the lowered proliferation of lymphocytes in rats. Other results suggested that paeoniflorin might induce the Th1 cells immune tolerance, which then shift to Th2, Th3 cells mediated activities to take effect the anti-inflammatory and immunoregulatory effects.¹⁰

Paeonia combined with dong quai and Cnidium was found to be effective for the restoration of impaired immune functions in aged mice. Aging is known to reduce the Th1-like function, but not the Th2-like function, resulting in a Th1/Th2 imbalance. The herbal compound restored the Th1/Th2 balance

in the aged mice. The overall results suggest the herbs could be a good recommendation for immune restoration in elderly humans.¹¹

Paeonol has been found to be useful in resisting many species of bacteria and fungi. A study on rats showed that paeonol could enhance specific cellular immunity. These enhancing effects of the specific cellular immunity and the nonspecific phagocytosis functions of the immune system were thought to be one of the mechanisms of the antibacterial effects of paeonol.¹²

Another study examining herbal antifungal agents found that paeonia was effective against *Candida* spp.¹³

Anti-inflammatory and Antioxidant

Paeonia has been found to have anti-inflammatory and antioxidant actions.

Paeonia suppressed the damage to DNA induced by a chemical agent, and scavenged the superoxide and hydroxy radical generated by the chemical.¹⁴

The ethanol extract of the paeonia root as well as its major active components including gallic acid and methyl gallate were evaluated for their protective effects against free radical generation and lipid peroxidation. All components exhibited a significant free radical scavenging effect and an inhibitory effect on lipid peroxidation. The protection against oxidative DNA damage occurred without exhibiting any pro-oxidant effect.¹⁵

Another study indicated that different extracts of paeonia significantly inhibited LPS-induced nitric oxide production and COX-2 activity in LPS-activated macrophages, suggesting the herb might be a candidate for developing anti-inflammatory and cancer chemopreventive agents.¹⁶

The administration of paeoniflorin inhibited the inflammatory response and restored the weight of immune organs of rats with induced arthritis. Paeoniflorin inhibited abnormal proliferation of synoviocytes and inhibited the production of various inflammatory cytokines.¹⁷

Bee venom (BV) was used to induce nociception and hypersensitivity to examine the role of Paeoniflorin in rats. When compared with saline control, systemic pre- and post-treatment with paeoniflorin resulted in an apparent antinociception

against both persistent spontaneous nociception and primary heat hypersensitivity. The paeoniflorin-produced antinociception was likely to be mediated by endogenous opioid receptors because of its naloxone-reversibility.¹⁸

Antispasmodic and Anticonvulsant Activities

Paeonia has been studied for its role in preventing spasm during colonoscopy. One study looked at using TJ-68, a combination of paeonia and liquorice, in comparison to saline. The preparation was sprayed on to the bowel mucosa and spasm was monitored. The spraying of TJ-68 on the colonic mucosa suppressed colonic spasm and the researchers suggested that it may be useful during colonoscopy when anticholinergic agents are contraindicated.¹⁹

Another study examined the inhibitory effects of antibiotic drugs on the antispasmodic action of Paeoniflorin. A traditional analgesic formulation containing paeonia is often used together with antibacterial synthetic drugs, such as amoxicillin in peptic ulcer therapy. However, gut bacteria are responsible for converting paeoniflorin into its antispasmodic metabolite, paeonimetabolin-I and thus concomitant use of antibiotics can impede this conversion through depletion of healthy gut bacteria. The researchers found that repetitive administration of the paeonia formula was useful in restoring the beneficial action of paeoniflorin.²⁰

The co-administration of the laxative (sodium picosulfate) has also been shown to impact on the paeoniflorin metabolizing activity of intestinal bacteria in rat faeces. The laxative reduced the bacterial activity to 34% of initial levels and took approximately 6 days to recover. However, repeated administration of the herbal formula (paeonia and liquorice) after the sodium picosulfate pretreatment significantly shortened the recovery period to around 2 days. The muscle relaxant activity of the formula was thought to relieve the pain associated with colonoscopy.²¹

Paeonia was examined for its vasodilator effect and mechanisms of action *in vitro* and was found to relax prostaglandin F_{2a}-precontracted aortic ring preparations of isolated rat aorta – but only in those that contained endothelium. Paeoniflorin was not responsible for the vasodilator effect in this

study. The active component was thought to be gallotannin and galloylglucoses.²²

Paeoniflorin and total flavones extracted from the traditional paeonia containing formula Qixue Bingzhi were examined for their impact on vascular smooth muscle cells and the expressions of platelet-derived growth factor. The extracts had an inhibitory effect on these parameters that was thought to be beneficial to the prevention and treatment of arteriosclerosis.²³

The effects of paeoniflorin and glycyrrhizin (from paeony and liquorice) on contractile and non-contractile calcium ions were examined. The Ca²⁺ transients of the nerve-stimulated skeletal muscle of mice were measured in the presence of neostigmine. Paeoniflorin prolonged the duration of non-contractile Ca²⁺ transients but did not affect contractile Ca²⁺ transients. Glycyrrhizin depressed contractile Ca²⁺ transients without affecting non-contractile transients. The results suggested that paeonia and liquorice may have complementary effects on intracellular Ca²⁺ mobilization to block the neuromuscular transmission.²⁴

The anticholinergic action of paeonia root was examined in an *in vivo* experiment with rats to determine the presence of analgesic, antispasmodic and antidiarrhoeal properties. The 50% methanol extract of paeonia root was found to be effective. Paeoniflorin was one of the active constituents showing an anticholinergic action *in vivo*, but had no effect *in vitro* on the contractile responses of isolated rat proximal colon to agents such as potassium chloride.²⁵

A study examined the effect of paeoniflorin on neonatal maternal separation-induced visceral hyperalgesia in rats. A dose-dependent analgesic effect was produced by paeoniflorin and was maximal at 30 minutes after administration. The effect may be mediated by kappa-opioid receptors and alpha(2)-adrenoceptors in the central nervous system. These results suggest that paeoniflorin might be potentially useful in clinical therapy for irritable bowel syndrome to alleviate visceral pain.²⁶

Steroid Hormone Modulation

Paeonia has been shown to have binding activity in both oestrogen and glucocorticoid receptors.

A study in rabbits found that herbal extracts from paeonia and liquorice influence steroid effects by glucocorticoid and mineralocorticoid receptors and to a lesser extent by oestrogen receptors or serum sex hormone-binding globulin and corticosteroid-binding globulin.^{27,28}

Bupleurum and paeonia formula (Jia Wei Xiao Yao San) is a herbal formula used for the treatment of menopausal syndrome and menstrual irregularity. Researchers examined the formula's phytoestrogen content and found that pre-treatment of oestrogen cells with the botanical formula produced a 5-fold increase in cell activity and that the response was oestrogen specific. Pre-treatment of the cells with tamoxifen effectively blocked the activation of the oestrogen receptor by the botanical formula.²⁹

Paeonia and liquorice treatment was examined with antipsychotic-induced hyperprolactinemia in women with schizophrenia. The herbal formula produced a significant decrease in serum prolactin levels, without exacerbating psychosis and changing other hormones. The decrease was similar to those achieved with bromocriptine yet more patients receiving herbal treatment compared to bromocriptine had a reduction in adverse effects associated with hyperprolactinemia. The herbal therapy can yield additional benefits while having comparable efficacy in treating individuals with schizophrenia.³⁰

Paeonia and liquorice treatment has also been shown to lower high serum testosterone levels in oligomenorrhoeic or amenorrhoeic women, and that some of these sterile women conceive. The testosterone production by ovaries was significantly decreased the treated group in comparison with the control. However, the delta 4-androstenedione (delta 4-A) production by ovaries was increased in each treated group. The ratio of T to delta 4-A was significantly lower in each treated group than in the control. The oestradiol production by ovaries in each treated group was not changed in comparison with the control.³¹

Other results confirmed that paeoniflorin, glycyrrhetic acid and glycyrrhizin affect the conversion between delta 4-androstenedione and testosterone. This could inhibit testosterone synthesis and stimulate the aromatase activity to promote oestradiol synthesis by the direct action on the rat ovary.³²

Twenty-five women suffering with either amenorrhoea, anovulatory cycles or luteal phase dysfunction were treated with paeonia and liquorice. Blood was taken to monitor levels of LH, FSH, prolactin, E2, progesterone and testosterone. The treatment initiated menstruation in four of the seven amenorrhoeic women, half the women with anovulatory cycles were shown to ovulate and 10 of the women with luteal phase dysfunction improved with seven women reporting normal progesterone levels, with 4 among them conceiving. The results were thought to be due to paeonia and liquorice's effects on hypothalamic-pituitary function and secondary ovarian effects. Although a direct effect on the ovary may not be excluded.³³

The Chinese formula Keishi-bukuryo-gan (TJ-25) contains *Paeonia lactiflora* along with four other herbs. A study investigated the effects of TJ-25 on levels of LH, FSH and E2, and on uterine wet weight and thymidine kinase (TK) activity in immature rats. Administration of TJ-25 for 14 days decreased plasma levels of LH, FSH and E2 by 94%, 67% and 50%, respectively, compared to controls. Uterine wet weight and TK activity were reduced to 65% and 64% that of controls, respectively. The overall results obtained indicate that TJ-25 may act as a LH-RH antagonist and/or as a weak antioestrogen.³⁴ The same formula was used in a study with 110 premenopausal patients with uterine myomas. Clinical symptoms of hypermenorrhoea and dysmenorrhoea were improved in more than 90% of the cases with shrinking of uterine myomas in roughly 60% of the cases.³⁵

Cognition Enhancement and Neuroprotective

A traditional Chinese medicine, Shimotsu-to, consisting of four herbs: angelica, cnidium, paeonia and rehmannia, has been reported to improve spatial working memory in rats. One study found that Paeoniflorin and tetramethylpyrazine (TMP) extracted from peony root and cnidium rhizome, respectively, were the candidates for enhancing cognitive function.³⁶

The antioxidative and neuroprotective effects of *Paeonia lactiflora* were examined. The protective effect of paeonia against induced oxidative damage to cells was investigated. Paeonia was found to increase cell survival and greatly suppressed apoptosis suggesting that paeonia could be a

candidate for a new antioxidant against neuronal diseases.³⁷

Delayed neuronal death induced by ischemia may be concerned with energy metabolism disorders and decrease of nitric oxide formation. A study in rats found that paeoniflorin may play the role of antagonising cerebral ischemia by adjusting cerebral energy metabolism and nitric oxide formation.³⁸

Paeonol was examined for its role in reducing oxidative stress, cognitive impairment and neurotoxicity in d-galactose (D-gal)-induced aging mice. The results showed that paeonol significantly improved the learning and memory ability of mice. The effect of paeonol on improvement of cognitive deficit was related to its ability to inhibit the biochemical changes in brains of the mice. Paeonol increased acetylcholine and glutathione levels, restored superoxide dismutase activities. Furthermore, paeonol ameliorated neuronal damage in both hippocampus and temporal cortex in D-gal-treated mice. These results suggest that paeonol possesses antiaging efficacy and may have potential in treatment of neurodegenerative diseases.³⁹

Other results showed that paeonol reduced cerebral infarct and neuro-deficit in rat, suggesting paeonol might play a similar role in reducing cerebral infarction in humans. Paeonol suppresses and scavenges superoxide anion, and inhibits microglia activation and IL-1beta in ischemia-reperfusion injured rats.⁴⁰

The protective effects of paeonia against cerebral ischemia-reperfusion injury in gerbils was examined. The effects of paeonia on brain oedema index, superoxide dismutase (SOD) activity and malonaldehyde (MDA) concentration of the cerebral tissue and pathology of the brain were examined. Compared with the controls, the treatment group significantly relieved brain oedema, enhanced SOD activity and lowered MDA concentration in the gerbils. Pathological examination showed that the gerbils with paeonia treatment had milder injury of the cells in the hippocampal region.⁴¹

Cardiovascular Activities – Vasodilatation and Antithrombosis

Paeonia was examined for its vasodilator effect and mechanisms of action *in vitro* and was found to relax prostaglandin F2a-precontracted aortic ring preparations of isolated rat aorta – but only in those that contained endothelium. Paeoniflorin was

not responsible for the vasodilator effect in this study. The active component was thought to be gallotannin and galloylglucoses.⁴²

The effect of paeonia on endothelial function and the activity of superoxide dismutase (SOD) of erythrocytes in rats administered a high-fat diet was studied. Administration of the extract of paeonia significantly increased the endothelium-dependent relaxation and the activities of SOD compared with high the cholesterol group. Hypercholesterolaemia induced an increase of endothelial superoxide anion and endothelial dysfunction. Paeonia was thus suggested to have a protective effect on endothelial cells and their function.⁴³

Paeoniflorin and total flavones extracted from the traditional paeonia containing formula, Qixue Bingzhi, were examined for their impact on vascular smooth muscle cells and the expressions of platelet-derived growth factor. The extracts had an inhibitory effect on these parameters that was thought to be beneficial to the prevention and treatment of arteriosclerosis.⁴⁴

The antithrombotic effect of paeoniflorin was evaluated and the results showed that it could significantly prolong thrombosis time. The antithrombotic effect of paeoniflorin was thought to relate to the inhibition of arachidonic acid metabolism, the increase of tissue plasminogen activity, and the protective effect against free radicals.⁴⁵

Paeonol was studied for its influence on levels of intercellular adhesion molecule-1 (ICAM-1), one of the key molecules in the development of atherosclerosis. Paeonol inhibited the production of ICAM-1 and also inhibited nuclear factor-kappaB translocation into the nucleus. The compound was thus thought to be beneficial in the treatment of cardiovascular disorders such as atherosclerosis.⁴⁶

Indications

- Dysmenorrhoea, premenstrual syndrome, endometriosis and adenomyosis
- Polycystic ovarian syndrome, ovulatory failure, infertility, androgen excess, mastalgia and menopausal symptoms
- Hyperprolactinaemia

- Headaches and muscular spasm
- Hepatic injury and toxicity
- Cardiovascular disease (including angina, atherosclerosis and thrombosis)
- Oxidative stress and inflammatory disorders
- Memory impairment
- Pre and post operative pain and spasm (colonoscopy)

Energetics

Bitter, salty, cold.

Use in Pregnancy

Paeonia appears safe in pregnancy and lactation.

Contraindications

No contraindications have been documented.

Drug Interactions

Caution with phenytoin (a medicine used to treat epilepsy). Monitor with anticoagulant/antiplatelet (such as warfarin) drugs.

Administration and Dosage

Liquid Extract: 1:1

Alcohol: 45%

Weekly Dosage: 15 to 30mL

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