

ANGELICA SINENSIS: A MONOGRAPH

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Botanical Name:	<i>Angelica sinensis</i> (Oliv.) Diels
Family:	Apiaceae (Umbelliferae)
Pharmaceutical Name:	Radix Angelicae Sinensis
Mandarin:	Dang Gui
Japanese:	Toki
Korean:	Tanggwi
Pin Yin/English:	Tang Kuei Root

Botanical Description: Perennial herb with smooth erect stem; lower leaves tripinnate, superior leaves simply pinnate, segments oval or obovate, sharply toothed on long sheathed petioles; flowers are in umbels with 9-13 irregular rays. The root is much divided into numerous rootlets; when dried these are obtained peeled, in thin slices: the outer cortex pale yellow-brown, a deep bark layer with pronounced cambium line; the inner cortex is pale white with an amorphous consistency; fracture is short and granular. Odor is aromatic; taste is sweet and pungent.

(1)
Habitat: In high ground in cool and damp areas; mostly from the Chinese province of Szechuan and Kansu in southwestern China.

(2)
Collection: The root is grown for one year then harvested, peeled and dried in the shade (2), usually thinly sliced about the width of a penny before completely drying.

Varieties and Grading: The larger the taproot and the sweeter the taste, the better the quality. Dang gui is never just purely sweet but has a pungent flavor as well. In general the higher the alkaloid content the sweeter the roots taste. If it is very bitter it is of a low

quality and will not be of much benefit. Most Dang gui available is of an average grade and is mildly sweet to pungent. Do not purchase very small roots. Korean Dang gui is considered to be very weak. (2) *Angelica acutiloba*, *A. gigas*, and other species of the herb have been used as substitutes for *A. sinensis*; although the properties are the same, their actions are inferior.

Traditional Chinese Properties: Sweet, acrid, bitter, warm.

Meridians Entered: Heart, liver, spleen and kidney.

Text in which it first appeared: Divine Husbandman's Classic of the Materia Medica, *Shen Nong Ben Cao Jing*, authors unknown, circa later Han.

INTRODUCTION

Angelica sinensis is an ancient Traditional Chinese Herbal medicine (TCHM) that is classified within this system as a tonifying herb, specifically a tonifier of the blood. "Tonifying herbs are those that strengthen or supplement an area or process of the body that is insufficient or weakened." (3) Even though the tonic herbs strengthen the body's defenses against disease, they are not to be used when acutely ill, even if the illness is just a common cold. "Correct any acute ailments before starting to use the tonics, and suspend their use if and when you catch a

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cold or other acute illness." (2) In TCHM an External Pernicious Influence is the terminology for any agent causing an acute illness. Tonics strengthen various physiological processes of the body and supplement the body's insufficiencies, therefore they are primarily indicated to help patients recover who have been ill with chronic or degenerative diseases.

Chronic illness creates "deficiencies," a TCHM concept akin to systemic, constitutional degradation be it at the level of an internal organ, a bodily fluid or the immunological capacity. Deficiencies are usually treated by tonifying methods; herbs, needles, moxibustion or other methods. External pathogens generally cause an acute "excess" condition best addressed with reducing methods aimed not so much at the patient's physiological process with the disease, but at "killing the pest." A "tonic" is used to treat a deficiency condition. Most trained in a western physiotherapy model think of tonic or tonifying as providing missing nutrients to a compromised tissue or organ system (i.e., bitters to help stimulate HCL, promote enzymatic function, etc.). In TCHM a blood tonic builds the blood, while the heart controls the blood and houses the Spirit, the Liver stores the blood, the Spleen and Kidney produce the blood, and Circulation-Sex conducts the direction of the blood. Blood tonics are generally used to tonify the Yin elements of the organ systems and to balance or harmonize while enhancing their functions. Blood tonics promote healthy reproductive function and work in general to regulate the menstrual cycle, thus benefiting pregnancy and promoting healthy sexual functions. These same functions are indicated for males, but the herb is classically used to build the blood, clean the blood, and act as a hemotonic.

"The primary manifestations of Deficient Blood are pallid face and lips, dizziness, vertigo, diminished vision, lethargy, palpitations, dry skin, menstrual irregularities, pale tongue, and a fine pulse." (3) In TCHM the two organs most affected by deficient blood are the Heart and Liver. "From a modern biomedical perspective Deficient Blood patterns are not always due to anemia. They may arise from psychological causes, from heart failure or from chronic hepatitis, among other dis-

eases. Most of these herbs strengthen the body and improve nutritional status, thereby indirectly increasing the number of circulating blood cells." (3)

TCHM FUNCTIONS AND CLINICAL USE

Dang gui is used by many Chinese women to regulate menstrual function and as a sedative, but men can also use it to build the blood. It is thought to clean the blood by restoring and strengthening it. Millions of Asian women use Dang gui to tonify their sex organs and maintain normal reproductive functioning; it is used before, during and after pregnancy, benefiting the entire female hormonal system. Another TCHM function of this herb is to nourish, harmonize, and invigorate the blood and its circulation. It is also an important herb used to stop pain caused from congealed blood, such as bruises, menstrual clots or even uterine fibroids; classically *Angelica* is used for pelvic congestion. The whole root is said to harmonize the blood, which means that it contributes to healthy blood composed of the proper balance of elements.

PHARMACY

The root of Dang gui is described as three different parts: The head (the uppermost part), the tail (the part deepest in the soil), and the body (the part in-between). The head is said to be the most tonifying and least effective in promoting the circulation of the blood. The tail is said to be the least tonifying and able to move the blood most strongly. The body is just as tonifying as it is invigorating to the blood, preserving the internal organs while nourishing the blood. Usually the entire root is prescribed.

When cooked it is more tonifying than when taken raw and acts as a powerful blood tonic, warming up the visceral organs, improving circulation, beautifying the skin, hastening the healing of cuts and wounds, and acting as a sedative. (2) Traditionally it is fried with vinegar (which increases its ability to move the blood); toasted to ash (which increases its property of warming the Channels and stops bleeding); eaten raw after it is lightly steamed and allowed to dry (has a stronger regulatory effect on the female reproductive system and also heals the reproductive and vascular tissues). (2) In preparation of

the root, slightly steam then cut into small pieces and allow to dry for at least 24 hours, in a warm dry place out of the path of direct sunlight. Dosage is anywhere from 2 slices per day up to 3-10 grams per day. As a decoction use anywhere from 1 teaspoon to 1 tablespoon of cut root per one cup of hot water. Remember, that the root must be slightly boiled and then simmered from 2-5 minutes, then remove from the heat and let stand for 5-10 minutes. Taken in this way, dosage is usually 1 cup two to three times a day. As a tincture extraction of 55-65% alcohol in a 1:5 ratio, take 2-5 ml three times a day.

Some very famous commercial TCHM tonics such as Shou Wu Chih and Four Things Soup, have *Angelica* as the main component. In the Shou Wu Chih mixture, 1 tablespoon of the mix is added to a cup of boiling water and taken twice a day, once before breakfast and again at bedtime. It is a blood tonic that benefits the circulatory and reproductive systems and when taken for a few weeks, it helps to increase energy in the daytime while creating a deep and restful sleep at night. It also acts as a powerful tonic that increases sexual function so be aware! When recovering from an illness, *Angelica* root is added to chicken soup and consumed over a four day period, acting not only as a tonic but also as a nourishing herb. Four Things Soup is composed of equal parts of *Angelica sinensis*, *Rheum glutinosum*, *Peonia albiflora*, and *Rhizoma Ligusticum*. This is a widely prescribed women's tonic by TCHM herbalists. It is used to regulate and balance hormones and the menstrual cycle, balancing the reproductive cycle. The mix is traditionally cooked as a soup and eaten daily until the prescription runs out.

WESTERN FUNCTIONS AND CLINICAL USE

ACTIVE CONSTITUENTS

- Radix *Angelica sinensis* contains volatile oils which give it distinct actions and aroma. It also contains Vitamin B12, Nicotinic Acid, Vitamin E and sucrose. (2)
- *Angelica* contains butylidene phthalide, n-valerophenone-o-carboxylic acid dehydrophthalic anhydride, sucrose, Vitamin B12, carotene, b-sitosterol. (3)

- Using the *Leuconostoc citrovorum* growth factors evaluation the following vitamin groups were verified as compounds in *Angelica*: nicotinic acid, nicotinamide, pantothenic acid, folic acid, folinic acid, vitamin B12, and biotin. (4)
- An active ingredient found in the water extract of *Angelica* is sitosterol-D-glucoside. (4)
- An active polysaccharide of *Angelica* is AR-4E-2, and is composed of arabinose, galactose, and rhamnose in molar ratios of 3.3:1.0:0.7, and also contains 14.5% galacturonic acid and 3.2% protein. (5)
- Angelica* immunostimulating polysaccharide (AIP) is a polysaccharide fraction obtained from hot water extracts of *Angelica*. (6)
- An immunomodulator extracted from *Angelica* is composed of 90% sugar and 10% protein. The major polysaccharide of this compound is identified as a pectic substance and the main component of sugars are arabinose, glucose, and galacturonic acid. It is suggested that the protein constituent of the compound is also the mitogenic constituent, and it is heat stable, and protease resistant. (7)
- Volatile oil constituents of *Angelica* root show 16 monoterpene hydrocarbons, 13 sesquiterpene hydrocarbons, 12 monoterpene alcohols, 4 oxygenated sesquiterpenes, 11 esters, 3 lactones, 7 aliphatic carbonyl compounds and 4 aromatics. Twenty additional compounds identified were present only in the alcohol sample: ethyl ethers of monoterpene alcohols, ethyl esters of long chain fatty acids, and acetals. (8)
- An aqueous extract, administered orally to mice, inhibited both writhing and capillary permeability, suggesting an analgesic effect and an anti-inflammatory effect. The extract was 1.7 times more effective than sodium acetylsalicylate. (9)
- The water extract of *Angelica* can be used clinically as an antiphlogistic drug. The active ingredient traced was sitosterol-D-glucoside. (4)
- A cholinergic component was found in Japanese *Angelica* root. (10)
- Ligustilide, a component of *Angelica* root, has a spasmolytic effect and falcarnol, another component, has an anti-nociceptive effect. (10)
- Ligustilide and butylidenephthalide, two components of *Angelica* were shown *in vitro* to be anti-acetylcholine substances. (10)
- The active anodyne ingredients were not in the essential oil fractions but were isolated by hot water extraction method. They were identified as falcarnindiol, falcarninol, falcarninolone, choline, and scopoletin; these are polyacetylene compounds. (4)
- Two chalcones, xanthoangelol and 4-hydroxyderricin, were isolated from the root of *Angelica keiskei* Koidzumi. (11)
- Non polar extracts of *Angelica* have found the following constituents: two angular furanocoumarins, archangelicin and 8(S),9(R)-9-angeloyloxy-8,9-dihydrooroselol; three linear furanocoumarins, psoralen, bergapten and xanthotoxin; three chalcones, 4-hydroxyderricin, xanthoangelol and a novel chalcone named asitaba-chalcone. (12)
- Water soluble tannin and alcohol soluble ferulic acid are two constituents of *Angelica*. (13)
- The essential oils of roots and fruits of five species of *Angelica* examined gave 59 chemical compounds, of which α -pinene, myrcene and p-cymene are common to all five species. (14)
- Oxypeucedanin, imperatorin and isoimperatorin are constituents of *Angelica*. (15)
- Ferulic acid is a phenolic compound contained in *Angelica*. (16)
- Eight coumarins were isolated from *Angelica*: columbianetin, columbianetin acetate, columbiadin, osthol, isoimperatorin, bergapten, xanthotoxin and columbianetin- β -D-glucopyranoside. (17)
- AR-4E-2 (a polysaccharide of *Angelica*) contains a rhamnogalacturonan moiety in which 2,4-di-substituted rhamnose residues attach to 4-substituted galacturonic acid through position 2 of rhamnose. It also contains a highly branched 3,5-arabian and (1-4)-galactan. (5)

MECHANISMS OF ACTION

- Active constituents of Japanese *Angelica* root shifted to the aqueous layer with successive fractionation of the extract with hexane and BuOH, indicating a contribution of a hydrophilic principle. (10)
- Antagonistic experiments using atropine suggest that the uterotonic activities of *Angelica* are due to a cholinergic component. (10)
- Ferulic acid is a phenolic compound contained in *Angelica sinensis*. It showed an inhibitory effect on uterine movement when given perorally and intravenously to rats. (16)
- The herbal components of tokishakuyakusan (Peony, *Angelica*, *Alisma*, and *Cnidium*) increased progesterone secretion by effecting the corpora lutea. (18)
- Corpora lutea is stimulated to secrete progesterone without direct luteotropic or luteolytic effect and that the effect is due to tokishakuyakusan, of which Japanese *Angelica* root is a component. (19)
- The lowering of ocular pressure due to the administration of oral and intravenous 40% hot water extract was attributed to two causes: One was the inhibition of the production of chamber fluid as a consequence of the lowering of blood pressure when the extract was injected intravenously; the other was the inhibition of central pressure factors when it was administered orally. The central pressure factors inhibition lowered blood pressure and caused vasodilation which were attributed to extremal and central factors. The literature attributes the drop in blood pressure to an inhibition of arterial constriction, and in experiments.

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and ATP release induced by ADP, arachidonic acid, PAF, collagen, ionophore A23187 and thrombin in washed rabbit platelets. Osthole inhibited the thromboxane B2 formation caused by arachidonic acid, collagen, ionophore A23187 and thrombin in washed platelets, and also the thromboxane B2 formation caused by the incubation of lysed platelet homogenate with arachidonic acid. Inositol phosphates were generated in washed platelets caused by collagen, PAF, and thrombin which were all suppressed by osthole. PAF and thrombin were both suppressed by osthole. (21)

- When 40% hot-water extract was administered intravenously (0.5 ml/kg) or orally (2ml/kg) ocular pressure was lowered, paralleling the lowering of blood pressure as well as a marked lowering of the yield of eye chamber fluid. (4)

Summary: The actions on the vascular system that were observed have a vast range. *Angelica* was found to lower blood pressure, decrease blood flow, heart beat and pulse rate while having a vasodilatory effect. It was found that this herb also decreased arrhythmias while resolving premature ventricular contractions of the heart and relaxing the myocardium. Other observations such as a decrease in atherosclerotic plaque formation, increased absorption and utilization of vitamin E, while also being a mild analgesic, antiinflammatory, and anesthetic.

Uterotonic:

- Uterotonic effects noted *in vitro* included contractions *in situ uteri* and relaxation of uterine specimens. In some studies direct measurement of the myometrium after administration of Dang gui revealed the contractions of the uterus to be more orderly. In the opinion of some researchers, this may be the mechanism underlying its effectiveness in treating dysmenorrhea. The motility of both *in situ* intestines in rabbits and dogs as well as rabbit intestine specimens is relaxed. (3)

- Laboratory tests in rats have shown that Dang gui consumed raw or with alcohol relaxes the uterus and can result in developing an undeveloped uterus. It has been found to be a laxative and to relieve congestion of the tissues of the pelvic cavity. It has shown the ability to stabilize blood sugar levels and is used by eastern, and western physicians in the treatment of some menopausal symptoms, especially those with a vasomotor etiology. (2)
- Intraduodenal administration of 70% MeOH extract of Japanese *Angelica* root (3g/kg) increased uterine contractile activities. In *i.v.* route it produced contraction along with decrease of blood pressure, which was inhibited by pretreatment with atropine, suggesting participation of a cholinergic component. (9)
- The water extract possesses the action of tensing and contracting the smooth muscles of the intestinal tract and uterus, while the essential oil inhibited these movements. (4)
- Depending on the dosage, sexual hyperfunction was observed when the extract was administered orally. Persistent administration exhibited a tendency toward inhibition of the estrus rates in mice. (4)
- Incorporating *Angelica* into feed and administering to mice for observing the liver and uterus gave the following results: uterine weight increase, the nucleic acid in the liver and uterus (especially the content of DNA) increased markedly, glycogen increased, the consumption of glucose by the liver and uterus increased. Thus it was postulated that Dang gui promotes the development of the uterus and exhibits a therapeutic effect in mice deficient in vitamin E. (4)
- Water extract and petroleum ether extract, administered peritoneally, at doses of 50-200 mg/kg, had an estrogen-like action. (4)
- A mixture of Peony root, *Angelica* root and *Alisma*

rhizome significantly increased progesterone secretion. (18)

- Ferulic acid, a phenolic compound in *Angelica*, shows an inhibitory effect on uterine movement when given orally and intravenously, thus inhibiting uterine contractions. (16)

Summary: *Angelica* was observed to regulate uterine contractions making them more unified and conformed, while also having the ability to relax the uterus and even inhibit spasmodic uterine contractions. It relaxes pelvic congestion, acts as a mild laxative and stabilizes serum glucose levels. The water extract (tea) was found to regulate the tensing and contraction of the smooth muscle of the intestines and uterus, while the essential oils had the opposite effect on the tissue. An increase in sexual function and libido was observed with consumption of large doses of the root. *Angelica* has a phytohormonal effect on both estrogen and progesterone fractions, while also showing an effect in aiding the development of the uterus.

IMMUNOREGULATORY AND ANTI-TUMOR ACTIVITY

- Dang gui has been demonstrated to have bactericidal action against *Bacillus dysenteriae* and *Staphylococcus* spp. Extracts of the herb have also shown *in vitro* and *in vivo* antiviral and antifungal activity. (2)
- One study demonstrated an antibiotic effect *in vitro*: inhibition of *Streptococcus* and *Shigella* spp. (3)
- Immunosuppressive activity is observed by both oral and intraperitoneal administration of the extract; this effect was not reduced by dialysis. When treated with daily doses of extract, serum titers of antibodies were significantly lower. The extract had little to no effect on passive anaphylaxis reaction of the release of histamine from sensitized lung fragments. (26)
- *Angelica* immunostimulating polysaccharide (AIP) was tested on murine lymphocytes participating in antibody response. AIP was injected concomitantly into mice

immunized with antigens: immunoglobulin M (IgM) and IgG-Antibody responses against sheep erythrocytes (SRBC) increased significantly, but IgM responses against T-Independent antigens such as trinitrophenylated lipopolysaccharide (TNP-LPS) and TNP-Picoil did not augment.

Murine B lymphocytes were polyclonally activated *in vitro* and *in vivo* by AIP fraction to differentiate into antibody-forming cells as functionally mature cells. The differentiation of B lymphocytes to an intermediate stage capable of responding to helper T lymphocytes was also stimulated by the administration of AIP fraction. A concomitant injection of AIP fraction with SRBC for carrier priming resulted in the increase of anti-TNP IgM antibody response in culture, reconstituted with unprimed B and SRBC-primed T-lymphocytes, indicating that AIP fraction can stimulate T lymphocytes. (27)

- AIP stimulated the uptake of tritiated thymidine into murine and human spleen cells in a dose-dependent manner. Murine B cells were activated polyclonally by AIP and differentiated to antibody-forming cells even in the absence of either helper T cells or macrophages. The primary antibody response to sheep erythrocytes was markedly augmented by an intraperitoneal injection of AIP. AIP also showed an anti-tumor activity in terms of prolongation of the survival period of intraperitoneally inoculated mice bearing Ehrlich ascites cells. (6)
- The polysaccharide fraction from the root of *Angelica* shows a potent antitumor activity against ascitic form of Sarcoma-180, IMC carcinoma, and Meth A fibrosarcoma as well as the solid form of MM-46 tumor. (5)
- A preparation of *Angelica* was given to DDY mice in their drinking water before and after transplantation of Ehrlich tumors. Survival rates were good and sometimes a complete cure was observed. (24)

- *Angelica sinensis* increases the production of murine IL-2, showing that *Angelica* is an immuno-modulating agent. (28)
- Extract of Chinese *Angelica* exhibited antibacterial action toward 6 gram negative bacteria such as *Bacillus dysenteriae*, and 3 gram positive bacteria such as hemolytic *Streptococcus*. (4)
- The two chalcones isolated from *Angelica* root showed antibacterial activity against gram-positive plant pathogenic bacteria. (11)

Summary: The root of *Angelica* was observed to be antiviral, antifungal, and antibacterial to both gram positive and gram negative bacteria. *Angelica* provokes an increase of lymphocyte activity into polyclonal activity to form mature antibody forming cells, while also increasing IL-2 formation. It was also observed to increase the B cells' capability of responding to T helper cells and stimulating the overall T lymphocyte production. The polysaccharide constituents of the root showed the strongest antitumor ability.

OTHER CLINICAL EFFECTS:

- Effect on the liver was shown in a study when mice were fed a 5% preparation of Dang gui which increased the oxygen consumption of the liver without affecting the amount of nucleic acids present. It is thought that perhaps this is due to *Angelica* generally increasing the metabolism. It also has a protective effect on livers exposed to carbon tetrachloride. (3)
- On the central nervous system it acts as a mild sedative. Treatment of pain showed that injections into acupuncture points to treat various types of pain including neuralgias, ischemic pain, and arthritis had good results. In one trial of 50 patients with occipital neuralgia 33 were cured and the remainder experienced some relief. This form of therapy is not recommended for sprains and other acute conditions or for pain from tumors or infections. (3)
- The EtO Ac fraction of the roots of *Angelica* inhibits adrenaline-induced lipolysis in

rat fat cells, while having no effect on ACTH-induced lipolysis. The MeOH fraction inhibited ACTH-induced lipolysis but not adrenaline-induced lipolysis. The two furocoumarins, psoralen and bergapten, were found to enhance ACTH- and adrenaline-induced lipolysis in fat cells. A coumarin derivative of khellactone type, isopteryxin, was found to inhibit the adrenaline-induced lipolysis but with no effect on ACTH-induced lipolysis and insulin-induced lipogenesis from glucose. The other coumarin of khellactone type, 3'(R),4'(R)-3'-epoxyangeloyloxy-4'-acetoxy-3',4'-dihydroreseline, was found to inhibit the insulin-induced lipogenesis from glucose but had no effect on adrenaline- and ACTH-induced lipolysis. (29)

- Korean Dang gui has been used for treating diabetes; thirty minutes after it was administered the value of the blood sugar rose, but three hours later it declined precipitously. Six hours after administration the value of the blood sugar continued to be slightly lower than normal. (4)

NATUROPATHIC IMPLICATIONS

From this extensive literature search one can find many therapeutic uses for *Angelica sinensis*. The empirical uses, in both eastern and western medicine, have been validated with the scientific experimentation on each of the implicated therapeutic indications. Some of the more well indicated clinical uses for *Angelica sinensis* are to relieve dysmenorrhea, prepare the uterus for conception, ripening, labor, and post partum effects while also acting as a mild laxative and reducing pelvic congestion. Research has shown that it acts as a uterine relaxant while also stimulating and regulating uterine contractions. The root reduces the elevated blood pressure of essential hypertension and slows the pulse rate by relaxing the cardiac muscle. *Angelica* also acts as a mild but effective bactericidal agent and research has shown that the extracts of the root have both an *in vivo* and *in vitro* antiviral and antifungal effect. *Angelica* also has been shown to modulate blood sugar and the immune system, help

aid in detoxifying the liver and absorption of vitamin E, and perhaps even help stimulate tumor necrosis factor in controlling certain cancerous tumor growths. Although most of these studies have been on animals, they have given us the first set of data for the scientific validation of our empirically derived information regarding the clinical uses of *Angelica*. This author suggests that the next course of action should be extensive clinical trials on the effect of this herb on humans, to further validate and understand its vast applications on the whole human system. Such efforts will also further validate the existing scientific data and our empirical and anecdotal evidence for the use of this herb.

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