



## Angelica sinensis (Dong quai)

### Description

*Angelica sinensis* (commonly known as dong quai) is a fragrant, perennial herb found in mainland China, Japan, and Korea. Other common names for dong quai include Chinese Angelica, dang gui (Chinese), toki (Japanese), tanggwi (Ko-

rean), and kinesisk kvan (Danish). A member of the Umbelliferae family, Angelica produces white flowers that bloom in umbrella-like clusters in June-July. A typical plant grows to a height of approximately six feet (two meters). The dried root is valued for its therapeutic properties. Its flavor is a distinct blend of bitter, sweet, and pungent, and its overall effect is warming in nature. Chinese herbalists have used Angelica for thousands of years to strengthen heart, lung, and liver meridians, as well as lubricate the bowel. It is considered a blood tonic, and has been used by generations of women for health concerns such as menstrual pain and regulating the menstrual cycle.

### Active Constituents

Dong quai root contains 0.4-0.7 percent volatile oil, the key components of which are n-butylidenephthalide, ligustilide, n-butylphthalide, ferulic acid, nicotinic acid, and succinic acid.<sup>1-3</sup> Significant amounts of vitamin A and carotenoids (0.675%), vitamin B12 (0.25-0.40 mcg/100 g), vitamin E, ascorbic acid, folic acid, biotin, various phytosterols (e.g., beta-sitosterol), calcium, magnesium, and other essential macrominerals are also found in dong quai root.<sup>1,3,4</sup> Other constituents include n-valerophenone-O-carboxylic acid, delta-2,4-dihydrophthalic anhydride, uracil, adenine, carvacrol, safrole, isosafrole, sesquiterpenes, beta-cadinene, n-dodecanol, n-tetradecanol, palmitic acid, angelic acid, myristic acid, sucrose (40%), and a polysaccharide with a molecular weight of approximately 3,000.<sup>1,4</sup>

Natural coumarin derivatives have been attributed to dong quai, but reports differ regarding which ones are truly present. The coumarin derivatives include angelol, angelicone, bergapten, oxypeucedanin, osthole, psoralen, and 7-desmethylnumbosin.<sup>1-3,5,6</sup>

### Mechanisms of Action

Due to its varied constituents, several pharmacological actions may be attributed to dong quai. Such characteristics include anticoagulation<sup>7</sup> and antiplatelet activity,<sup>1,2</sup> as well as hematopoiesis,<sup>4</sup> immune support,<sup>8,9</sup> and uterine tonicity.<sup>1,2,4,10</sup>

## Anticoagulant Activity

Coumarins and coumarin derivatives, natural anticoagulants in *Angelica* spp., have been associated with both the bioactivity and toxicity of the plants; however, *A. sinensis* contains a lower coumarin content compared to other closely related species.<sup>7</sup>

## Antiplatelet Action

Ferulic acid, one of the constituents of dong quai, can inhibit the polymerization of platelets in blood circulation. It retards platelet release of 5-hydroxytryptamine (5-HT) and adenosine diphosphate (ADP).<sup>1</sup> Both ferulic acid and an aqueous extract of dong quai were found to inhibit platelet aggregation and serotonin release.<sup>2</sup>

## Immune Support and Hematopoiesis

Lymphocyte proliferation assays indicate dong quai consistently exerts an immunostimulatory effect.<sup>8,9</sup> A high molecular weight polysaccharide found in dong quai has demonstrated immunostimulating activity and a blood tonifying effect by inducing hematopoiesis in the bone marrow. This is accomplished, in part, by either direct or indirect stimulation of macrophages, fibroblasts, erythrocytes, granulocytes, and lymphocytes, and can induce an increased secretion of human growth factors from muscle tissue.<sup>4</sup>

Hematopoiesis is further supported by the presence of significant amounts of vitamin B12, folic acid, and biotin in dong quai.<sup>4</sup>

## Antifibrotic Action

A mixture of dong quai and *Astragalus* demonstrated antifibrotic activity in a recent animal study. Rat models with chronic puromycin-induced nephrosis were treated with either a dong quai and *Astragalus* mixture (3 mL/day) or enalapril (10 mg/kg). The normal control group received saline, and another group received puromycin but no treatment.<sup>11</sup> After 12 weeks the untreated rats showed marked renal fibrosis. However, dong quai and *Astragalus* significantly retarded the progression of renal fibrosis and deterioration of renal histological damage, with effects comparable to enalapril.<sup>11</sup>

## Antispasmodic Activity

Ligustilide, butylidenephthalide, and butylphthalide were found to have antispasmodic activity against rat uterine contractions and in other smooth muscle systems. The components were characterized as non-specific antispasmodics with a mechanism different from papaverine.<sup>7,12</sup>

## Clinical Indications

### Cardiovascular Disease

Dong quai has demonstrated quinidine-like activity on the heart.<sup>2</sup> It can prolong the refractory period, lower blood pressure, and correct experimental atrial fibrillation induced by atropine, pituitrin, strophanthin, acetylcholine, or electrical stimulation.<sup>10</sup> Dong quai can dilate the coronary vessels, increase coronary flow, and reduce respiratory rate. An animal study using a water-based extract of dong quai demonstrated a marked protective effect against myocardial dysfunction and myocardial injury induced by ischemia.<sup>4</sup>

A recent histological study demonstrated a preparation of dong quai and *Ligusticum* significantly protected human umbilical vein endothelial cells against hydrogen peroxide damage, primarily by inhibiting reactive oxygen species formation and promoting endothelial nitric oxide synthase (eNOS) expression.<sup>13</sup> This might be the mechanism of the above-noted cardio-protective activity.

### Nephrotic Syndrome

An herbal preparation of *Astragalus* and dong quai has long been used in China to treat nephrotic syndrome, as it was thought to elicit antifibrotic effects. In a recent animal study the *Astragalus*/dong quai mixture was found to retard the progression of renal fibrosis and deterioration of renal function with an effect similar to the drug enalapril.<sup>11</sup>

### Dysmenorrhea

Two general components of dong quai affect uterine smooth muscle in opposite ways. The antispasmodic component of the herb is attributed to constituents of the volatile oil, such as

ligustilide, butylidenephthalide, and butylphthalide. As a balance, the uterine stimulating aspect is attributed to the water-soluble, non-volatile constituents of the herb.<sup>1,2,4,10</sup>

Animal experiments *in vivo* have demonstrated increased excitability of the uterus, where the contractive rhythm of uterine smooth muscle changed from fast, weak, and irregular to slower, stronger, and more coordinated (more rhythmic), depending on uterine tone. This is believed to be the pharmacological basis for use of dong quai during dysmenorrhea.<sup>1</sup> The root does not exert estrogenic activity.<sup>10,14</sup>

### Menopause

One of the most common applications for dong quai in the United States is for relief of vasomotor symptoms associated with menopause. Such symptoms include hot flashes, skin flushing, perspiration, and chills. The mechanism of action, however, is still unclear. In a randomized, double-blind, placebo-controlled clinical trial, 71 postmenopausal women received either dong quai root (4.5 g) or placebo daily for 24 weeks.<sup>14</sup> There were no differences in vasomotor symptoms between the two groups, and there appeared to be no estrogen-like effects on vaginal epithelial tissue. The use of dong quai alone can be criticized because traditional Chinese practitioners never prescribe it alone, but rather in combination with several other herbs. The researchers chose to study dong quai alone because many women in the United States who take it to relieve menopausal symptoms purchase the herb over-the-counter as a single entity. Women should be discouraged from using dong quai alone for the relief of menopausal complaints.

An herbal mixture containing *Angelica sinensis* root, *Paeonia lactiflora* root, *Ligusticum rhizome*, *Atractylodes rhizome*, *Alismatis rhizome*, and *Sclerotium poria* has been reported to reduce menopausal disturbances, including vasomotor symptoms by 70 percent.<sup>10,14</sup>

### Drug-Botanical Interactions

Dong quai may potentiate the therapeutic and adverse effects associated with antiplatelet medication. A small pharmacokinetic study conducted on rabbits observed the interaction between dong quai and warfarin. Single subcutaneous doses of warfarin (2 mg/kg) were administered with or without oral dong quai extract (2 g/kg, twice daily for three days). The dong quai treatment did not effect prothrombin time on its own, but significantly lowered the value three days after co-administration with warfarin. No significant variation in the pharmacokinetic parameters of warfarin were observed after dong quai treatment for either single-dose administration or steady-state concentrations of warfarin.<sup>2,15</sup>

In a case report, a 46-year-old woman, who had been taking 5 mg/day warfarin for nearly two years and had an international normalized ratio (INR) stabilized at 2-3, experienced an increase in her INR to 4.9 over the course of approximately two months.<sup>16</sup> Changes in medication regimen, diet, alcohol consumption, or other lifestyle factors that may affect INR were sufficiently ruled out. However, the patient stated that for the past four weeks she had been taking dong quai for perimenopausal symptoms as recommended by an herbalist, and had forgotten to mention this earlier. The dosage was one 565-mg tablet 1-2 times/day. The patient was instructed to discontinue dong quai, and within four weeks her INR declined to the therapeutic range of 2.48. In view of this information, caution is advised for patients receiving chronic treatment with warfarin.

### Side Effects and Toxicity

Although no reported side effects have occurred with the use of authentic dong quai, various sources continue to warn of potential photosensitivity reactions due to psoralen and bergapten content.<sup>7</sup> Both psoralen and bergapten are furanocoumarins widely studied for their photosensitizing properties.<sup>17</sup> Other related species of *Angelica* (e.g., *A. gigas*, *A. dahurica* and *A. pubescens*) pose a greater risk than dong quai due to their higher furanocoumarin content.<sup>7</sup>

There has been one isolated case of a man who developed gynecomastia (mammary glandular hyperplasia) after taking dong quai capsules daily for approximately one month.<sup>18</sup> The label on the bottle indicated “100% dong quai (*Angelica sinensis*) root powder. No fillers or additives.” The patient discontinued the “dong quai” pills and his gynecomastia had regressed completely when examined three months later. It is important to note that the pills in question were not properly analyzed to confirm or refute the purity of the product. Consequently, the authors could not rule out presence of a pharmacologically active contaminant that may have contributed to the patient’s condition.<sup>19</sup>

The oral LD<sub>50</sub> of a concentrated (8:1 to 16:1) dong quai extract in rats was measured at 100 g/kg body weight.<sup>2</sup> Intravenous administration of the essential oil to animals at doses of 1 mL/kg can cause a drop in blood pressure and depression of respiration.<sup>4</sup>

## Contraindications

Dong quai is contraindicated in pregnancy, particularly in the first trimester, due to potential uterine stimulant and relaxant effects.<sup>2,17,20</sup>

## Dosage

Dong quai is available in several different forms, and dosages vary accordingly. Typical oral dosages<sup>2,5,7,17</sup> are as follows:

- Dried root: 3-15 g daily by decoction
- Powdered root: 1-2 g 3 times daily
- Tea: 1 cup 1-3 times daily (1 g per cup)
- Tincture (1:2): 4-8 mL (1-2 tsp) per day
- Capsules/Tablets: 500 mg 1-6 times daily

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