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World Health Organisation (WHO) REPORT ON Angelica Sinensis

Medicinal uses

Uses supported by clinical data

None. Although Radix Angelicae Sinensis has been alleged to be useful for the treatment of menopausal symptoms, a randomized, placebo-controlled clinical trial concluded that 4.5 g of the root daily for 24 weeks did not alleviate menopausal symptoms, such as hot flushes (*14*).

Uses described in pharmacopoeias and in traditional systems of medicine

Treatment of menstrual disorders such as irregular menstruation, amenorrhoea and dysmenorrhoea (*1*, *3*, *15-19*). As an analgesic for symptomatic treatment of rheumatic arthralgia, abdominal pain and in the management of postoperative pain (*1*, *20*). Treatment of constipation (*1*), anaemia (*1*, *20*), chronic hepatitis and cirrhosis of the liver (*20*).

Uses described in folk medicine, not supported by experimental or clinical data

Treatment of dehydration, lumbago, abnormal menstruation, menopausal symptoms (including hot flushes), hypertonia and nervous disorders (*18*, *21*).

Pharmacology

Experimental pharmacology

Smooth muscle contraction

Hot aqueous extracts of Radix Angelicae Sinensis stimulated smooth muscle contractions of the bladder, intestine and uterus when administered intravenously to dogs (10 g/kg body weight) (*22*). Intravenous administration of an aqueous or 95% ethanol extract of the roots to cats, rats and rabbits increased the strength of the contractions and tone of uterine smooth muscles (*4*). In vitro assays demonstrated that a decoction of the roots stimulated the H_1 receptor of mouse uterus (*23*). The active constituent responsible for this activity is an aqueous- and alcohol-soluble, non-volatile component, the structure of which is unknown (*4*). Conversely, ligustilide, a constituent of the essential oil of the roots, inhibited contractions of isolated uteri from various animal models (*20*, *24*). Intraperitoneal administration of ligustilide (0.14ml/kg body weight) to guinea-pigs inhibited asthmatic reactions induced by acetylcholine and histamine (*25*). Ligustilide (32.5-130.0 µl/ml) inhibited smooth muscle contractions induced by barium sulfate, acetylcholine and histamine in isolated guinea-pig trachea (*25*).

Antihepatotoxic activity

Intraperitoneal administration of a decoction of the roots (11ml/kg body weight) ameliorated galactosamine-induced hepatotoxicity in rats (*26*). Ferulic acid, a constituent of the roots, protected rat liver mitochondria against damage induced by oxygen free radicals (*27*). Intragastric pretreatment of mice

with sodium ferulate (100 mg/kg body weight) daily for 10 days alleviated liver toxicity induced by paracetamol (*28*) and prednisolone (*29*), and bromobenzeneinduced liver injury (*30*).

Cardiovascular activity

Cardiac haemodynamic studies demonstrated that intravenous administration of an aqueous root extract (2 g/kg body weight) to anaesthetized dogs increased coronary blood flow from 88 ml before administration to 128 ml (per 100g cardiac muscle/minute post-injection). Coronary vascular resistance and myocardial oxygen consumption also decreased, while the heart rate decreased or remained unchanged (*31*). An extract of the roots increased coronary blood flow in isolated guinea-pig hearts (*32*).

In animal models, both aqueous and ethanol extracts of the roots had an effect on arrhythmias induced by epinephrine, barium chloride and digitalis (*32*, *33*). Intravenous administration of an ethanol extract of the roots (4g/kg body weight) antagonized chloroform- and epinephrine-induced arrhythmias in cats (*34*). Ethanol extracts of the roots and ferulic acid restored normal sinus rhythm after ouabain-induced arrhythmia in isolated ventricular muscle from cats (*20*). Aqueous extracts of the roots reduced the action potential amplitude and maximal upstroke velocity of the Q phase, and prolonged the effective refractory period and the duration of the action potential in guinea-pig myocardium (*35*). Intravenous administration of an aqueous extract of the roots (50mg/kg body weight) to rabbits with ligation of the left anterior descending coronary artery provided protection against ischaemia- and reperfusion-induced myocardial dysfunction and injury (*36*). An aqueous extract of the roots bound to nitrendipine and diltiazem receptors, thereby demonstrating calcium channel blocking activity (*37*). A ligustilide dimer, isolated from the roots, inhibited [^{3}H]nitrendipine binding to dihydropyridine-sensitive calcium channels (inhibitory concentration of 50% [IC_{50}] 0.4 µmol/l) (*38*). Since calcium channel blockers are known to have pronounced effects on the cardiovascular system, this activity may explain some of the reported effects of root extracts on the cardiovascular system.

Antithrombotic activity

In vitro and in vivo studies have shown that extracts of the roots inhibit platelet aggregation and have antithrombotic activity (*20*). Aqueous extracts of the roots (200 mg/ml) or ferulic acid (0.4 mg/ml) inhibited platelet aggregation induced by ADP or collagen in vitro (*39*). A hot aqueous extract of the roots (500mg/ml) or ferulic acid (1 mg/ml) inhibited thrombin-induced platelet aggregation and release of [^{3}H]5-hydroxytryptamine from labelled platelets in vitro (*39*). An aqueous extract of the roots inhibited both ADP- and collagen-induced platelet aggregation when administered intravenously to rats (200 mg/ml) (*20*, *39*). The mechanism of action appears to be via inhibition of cyclooxygenase and thromboxane A_2 synthase by ferulic acid, leading to decreased production of thromboxane A_2 (*40*). The antithrombotic activity of the drug is associated with inhibition of platelet aggregation, reduction in the concentration of plasma fibrinogen, changes in cell surface charge and a decrease in blood viscosity (*20*).

Intraperitoneal administration of polysaccharides isolated from the roots increased haematopoiesis in mouse bone marrow, as determined by an increase in colony-forming units in the marrow cells (*12*, *41*). The polysaccharides promoted the proliferation and differentiation of haematopoietic progenitor cells in healthy and anaemic mice (*13*). Results of this study indicated that the polysaccharides may enhance haematopoiesis by stimulating macrophages, fibroblasts and lymphocytes in haematopoietic and muscle tissue to secrete haematopoietic growth factor (*13*).

Clinical pharmacology

Menstrual disorders

Although there are a number of case reports concerning the clinical use of Radix Angelicae Sinensis in the treatment of amenorrhoea and dysmenorrhoea, these studies were published between 1899 and 1910 (*15-18*). Randomized, controlled clinical trials are needed to confirm these observations. In these early case studies, female patients were treated with 5 ml of a fluidextract of the roots three times daily before meals for 1 week before menstruation. The treatment relieved premenstrual pain and induced menstrual flow in most cases. No abortifacient activity was observed in two pregnant women treated with the same fluidextract (*15*). In other studies, the fluidextract was used for the treatment of dysmenorrhoea in nulliparous women, and of severe bleeding in multiparous women. Administration of 5 ml of the fluidextract three times daily for 1 week before menstruation was effective in decreasing menstrual pain and chronic endometritis (*16*). Successful treatment of amenorrhoea and dysmenorrhoea in female patients was further reported after administration of the same fluidextract (5 ml, three times daily) (*17*, *18*). In another report, 112 women with dysmenorrhoea were treated for 3-7 days with ligustilide dimer isolated from the roots. The efficacy rate was 77%. Minor side-effects were nausea and dizziness, which disappeared after the treatment stopped (*42*).

Smooth muscle contraction

Decoctions of the roots reportedly stimulated uterine smooth muscle in female patients, but the doses used and the conditions being treated were not stated (*19*). A decoction of the roots lowered whole blood viscosity after administration to six patients (*11*).

Contraindications

Radix Angelicae Sinensis should not be administered to children or patients with diarrhoea, haemorrhagic diseases or hypermenorrhoea, and should not be used during pregnancy or lactation (*4*).

Warnings

No information available.

Precautions

Drug interactions

Decreased prothrombin times were reported in rabbits that received both a single subcutaneous dose of warfarin (2 mg/kg body weight) and a repeated oral dose of Radix Angelicae Sinensis (2g/kg body weight twice daily for 3 days) (*43*). Therefore, patients receiving anticoagulant therapy should be advised against taking Radix Angelicae Sinensis without medical supervision.

Pregnancy: teratogenic effects

See Contraindications.

Pregnancy: non-teratogenic effects

See Contraindications.

Nursing mothers

See Contraindications.

Paediatric use

See Contraindications.

Other precautions

No information available on general precautions or precautions concerning drug and laboratory test interactions; or carcinogenesis, mutagenesis and impairment of fertility.

Adverse reactions

Oral administration of Radix Angelicae Sinensis is generally regarded as having few side-effects; however, headaches may occur in sensitive individuals (*14*, *19*). No adverse reactions were reported in 40 people who received an aqueous root extract by intravenous administration (240 ml/person) for 30 days (*19*).

Dosage forms

Powdered crude drug and fluidextracts (*4*). Store in an airtight container in a cool, dry place protected from moisture (*1*).

Posology

(Unless otherwise indicated)

Daily dosage: 4.5-9 g crude drug (*1*).

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