Alfalfa

Species (Family)

Medicago sativa L. (Fabaceae/Leguminosae)

Synonym(s)

Lucerne, Medicago, Purple Medick

Part(s) Used

Herb

Pharmacopoeial and Other Monographs

BHP 1996[G9]
Martindale 32nd edition [G43]
PDR for Herbal Medicines 2nd edition[G36]

Legal Category (Licensed Products)

GSL[G37]

Constituents[G19,G22,G41,G64]

Acids Lauric acid, maleic acid, malic acid, malonic acid, myristic acid, oxalic acid, palmitic acid and quinic acid.

Alkaloids Pyrrolidine-type (e.g. stachydrine, homostachydrine); pyridine-type (e.g. trigonelline) in the seeds only.

Amino acids Arginine, asparagine (high concentration in seeds), cystine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan and valine. The non-protein toxic amino acid canavanine is present in leaves (0.9–1.2 mg/g), stems (0.6–0.9 mg/g) and seeds (5–14 mg/g).[G19]

Coumarins Medicagol.

Isoflavonoids Coumestrol, biochanin A, daidzein, formononetin and genistein.

Saponins 2–3%. Hydrolysis yields aglycones, medicagenic acid, soyasapogenols A–F and hederagenin.[1] Sugar chain components include arabinose, galactose, glucuronic acid, glucose, rhamnose and xylose.

Steroids Campesterol, cycloartenol, β-sitosterol (major component), α-spinasterol and stigmasterol.

Other constituents Carbohydrates (e.g. arabinose, fructose, sucrose, xylose), vitamins (A, B_1, B_6, B_{12}, C, E, K), pectin methylesterase, pigments (e.g. chlorophyll, xanthophyll, β-carotene, anthocyanins), proteins, minerals and trace elements.

See reference G22 for more detailed chemical information.

Food Use

Alfalfa is widely used in foods and is listed by the Council of Europe as a source of natural food flavouring (categories N2 and N3). These categories indicate that alfalfa can be added to foodstuffs in small quantities, with a possible limitation of an active principle (as yet unspecified) in the final product.[G16] In the USA, alfalfa is listed as GRAS (Generally Recognised As Safe).[G41]

Herbal Use

The herb was not valued by ancient civilisations and is not detailed in classical herbals. Herbal use probably developed in the USA where claims have been made for it in the treatment of arthritis, high cholesterol, diabetes and peptic ulcers.[2,G19,G32] Reputedly, the herb has bactericidal, cardiotonic, diuretic, emetic, emmenagogue and oestrogenic properties.[2] Commercial preparations including teas, tablets and capsules are available.[G19] Alfalfa is stated to be a source of vitamins A, C, E and K, and of the minerals calcium, potassium, phosphorus and iron. It has been used for avitaminosis A, C, E or K, hypoprothrombinaemic purpura, and debility of convalescence.[G7,G64]

Dosage

Dried herb 5–10 g as an infusion three times daily.[G7]

Liquid extract 5–10 mL (1 : 1 in 25% alcohol) three times daily.[G7]

Pharmacological Actions

In vitro and animal studies

Alfalfa top (stem and leaves) saponins have been reported to decrease plasma cholesterol concentrations without changing high-density lipoprotein (HDL) cholesterol concentrations, decrease intestinal absorption of cholesterol, increase excretion of neutral steroids and bile acids, prevent atherosclerosis and induce the regression of atherosclerosis.[3]

Hypocholesterolaemic activity has been reported for root saponins, when given to monkeys receiving a high-cholesterol diet.[4] Alfalfa herb fed to monkeys reduced hypercholesterolaemia and atherosclerosis; the effect may be partially due to the saponin constituents.[G19] In mice fed with alfalfa (6.25% of diet) for 12 days before administration of streptozotocin, hyperglycaemia was reduced compared with values for control animals.[5]

Oestrogenic activity in ruminants has been documented for coumestrol and the isoflavone constituents.[G22,G41]

An investigation into the effect of various herbs on hepatic drug metabolising enzymes in the rat, showed that alfalfa potentiated the activity of aminopyrine *N*-demethylase but had no effect on glutathione *S*-transferase or epoxide hydrolase activities.[6]

The seeds are reported to contain trypsin inhibitors.[G41] Saponins isolated from the aerial parts have been reported to stimulate the lipolytic activity of neopancreatinum (a mixture of porcine pancreatic enzymes including lipase, amylase and proteases).[7]

Alfalfa root saponins have been documented to exhibit selective toxicity towards fungi.[1,8,9] A medicagenic acid glycoside with low haemolytic activity, isolated from alfalfa root, was found to exhibit both strong inhibitory and fungitoxic activities towards several medically important yeasts including *Candida* species, *Torulopsis* species, *Geotrichum canadidum* and *Rhodotorula glutinis*.[8] It has been proposed that the antimycotic activity of alfalfa saponins is related to their ability to complex steroids and that fungi sensitive to the saponins may contain relatively more steroids in their membranes.[8] Antifungal properties have also been documented for medicago.[G41]

The saponin constituents are documented to be haemolytic and to interfere with vitamin E utilisation, and are believed to be one of the causes of ruminant bloat.[G41] Haemolytic activity is associated with the medicagenic acid glycosides and not the hederagenin and soyasapogenol glycosides.

The effects of polysaccharides from medicago on mice lymphocytes *in vitro* indicated immunopotentiating activity.[10]

Clinical studies

In a short-term study involving three normolipidaemic individuals given alfalfa seeds (80–60 g daily), serum cholesterol concentrations were reported to be reduced.[G19] In another small study in which heat-treated alfalfa seeds (40 g three times daily for eight weeks) were taken by eight type-IIA hyperlipoproteinaemic patients and three type IIB patients, a significant decrease was noted in total serum cholesterol concentrations, low-density lipoprotein (LDL) cholesterol and apolipoprotein B. The LDL cholesterol concentration fell by less than 5% in two of the 11 patients.[11]

The manganese content of alfalfa (45.5 mg/kg) is reported to be the active principle responsible for a hypoglycaemic effect documented for the herb.[12] A diabetic patient, treated with soluble insulin but poorly controlled, found that an alfalfa extract adequately controlled his diabetes. When administered separately, only small doses of manganese chloride (5–10 mg) were required to have a hypoglycaemic effect. However, no effect was seen on the blood sugar concentrations of non-diabetic controls or of other diabetic patients, who were also administered manganese. It was concluded that manganese lowered the blood sugar concentration in this particular diabetic patient because he was unable to utilise manganese stored in his body.[12]

Side-effects, Toxicity

Both alfalfa seed and herb have been reported to induce a systemic lupus erythematosus (SLE)-like syndrome in female monkeys.[3,13,G19,G32] This activity has been attributed to canavanine, a non-protein amino acid constituent which has been found to have effects on human immunoregulatory cells *in vitro*.[14] Reactivation of quiescent SLE in humans has been associated with the ingestion of alfalfa tablets which, following analysis, were found to contain canavanine.[15] It was not stated whether the tablets contained seed or herb material. Canavanine is known to be toxic to all animal species because it is a structural analogue of arginine and may interfere with the binding of this amino acid to enzymes and its incorporation into proteins.[16,G19] Alfalfa seeds are reported to contain substantial quantities of canavanine (8.33–13.6 mg/kg), whereas the herb is stated to contain amounts that are considerably less.[16,17]

Pancytopenia has been associated with human ingestion of ground alfalfa seeds (80–160 g/day),

which were taken to lower plasma cholesterol concentrations.[18]

Dietary studies using alfalfa top saponins (ATS) in the diet of rats and monkeys showed no evidence of toxicity and serum lipid concentrations were lowered.[3,19,20] In addition, when ATS were given to cholesterol-fed animals, a reduction in serum lipid concentrations was observed.[3,19,20] ATS are reported to be free of the SLE-inducing substance that is present in the seeds.[3]

Negative results were documented for alfalfa when tested for mutagenicity using *Salmonella* strains TA98 and TA100.[21]

Contra-indications, Warnings

Individuals with a history of SLE should avoid ingesting alfalfa. Ingestion of large amounts of alfalfa (exceeding amounts normally consumed in the diet) should be avoided in view of the documented oestrogenic activity and potential anticoagulant activity. Excessive doses may interfere with anticoagulant therapy and with hormonal therapy, including the oral contraceptive pill and hormone replacement therapy. Alfalfa may affect blood sugar concentrations in diabetic patients because of the manganese content.

Pregnancy and lactation Alfalfa seeds are reputed to affect the menstrual cycle and to be lactogenic.[G30] Although the safety of alfalfa herb has not been established, it is probably acceptable for use during pregnancy and lactation provided that doses do not exceed the amounts normally ingested as a food. Alfalfa seeds should not be ingested during pregnancy or lactation.

Pharmaceutical Comment

The chemistry of alfalfa is well documented and it does appear to be a good source of vitamins and minerals, thereby supporting the herbal uses. However, normal human dietary intake of alfalfa is low and excessive ingestion should be avoided in view of the many pharmacologically active constituents (e.g. canavanine, coumarins, isoflavones and saponins), which may give rise to unwanted effects if taken to excess. Oestrogenic effects are generally associated with the ingestion of large amounts of the herb, such as in fodder for poultry and cattle. Reports of a possible SLE-inducing capacity for alfalfa, particularly the seeds, also suggests that excessive ingestion is not advisable. In view of the reports of arthralgia, alfalfa should not be recommended for the treatment of arthritis.

References

See also General References G5, G9, G16, G19, G22, G24, G30, G31, G32, G36, G37, G41, G43 and G64.

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