



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

MEDICAGO SATIVA EXTRACTUM

SUMMARY REPORT

1. *Medicago sativa* is the botanical name for alfalfa. Extracts or tinctures of *Medicago sativa* are used in both human and veterinary medicine for the treatment of a variety of disorders. In veterinary medicine, the extract may be administered topically to aid the healing of skin lesions. The amount applied depends on the size of the lesion.
2. The pharmacologically active substances present in *Medicago sativa* include acids (lauric, maleic, malic, malonic, myristic, oxalic, palmitic, quinic), alkaloids (stachydrine, homostachydrine), aminoacids (arginine, asparagine, cystine, histidine, isoleucine, leucine, methionine, tryptophan, valine), the non-protein aminoacid canavanine, coumarins (medicagol), isoflavonoids (coumestrol, biochanin A, genistein), saponins, steroids (campesterol, cycloartenol, β -sitosterol) and other constituents such as fructose, vitamins (A, B₁, B₆, B₁₂, C, E, K), pectin, chlorophyll, minerals and trace elements.
3. *Medicago sativa* contains many pharmacologically-active constituents some of which may give rise to unwanted effects if consumed in excess. It decreases plasma cholesterol levels and it helps to prevent the development of arterosclerosis. However, it also contains ingredients with potential oestrogenic and anticoagulant activity.
4. Alfalfa top (stem and leaves) saponins were administered in the diet to groups of rats and cynomolgus macaques. In the rat study the dietary concentrations of alfalfa top saponins were 1% for 6 months and 2% for 2 months. In the macaque study, the dietary concentrations of alfalfa top saponins were 1% and 1.2% and were fed for 6 months and 18 months. There was no evidence of toxicity and the serum lipid levels were lowered. When alfalfa top saponins were administered at the same dose levels to rats and monkeys which were also fed cholesterol, a reduction in the serum lipid level was observed.
5. A systemic lupus erythromatosus-like syndrome was reported in female monkeys fed alfalfa sprouts; this was attributed to canavanine, a non-protein amino acid constituent. Reactivation of quiescent systemic lupus erythromatosus in humans has been associated with the ingestion of alfalfa tablets which were found to contain canavanine on analysis. Alfalfa seeds may contain substantial amounts of canavanine (8.33 to 13.6 mg/kg) whereas the herb is stated to contain only minimal amounts.
6. In the target species, there were no reports of adverse effects from the use of veterinary medicines based on alfalfa. Cases of bloat have been reported after feeding large amounts of alfalfa to ruminants as fodder. This was attributed to the saponin constituents of the alfalfa.
7. Oestrogenic activity has been reported in ruminants fed large amounts of alfalfa as fodder and appeared to be associated with the coumestrol and isoflavone constituents of alfalfa. In humans, the consumption of alfalfa seeds has been reported to be lactogenic and to affect the menstrual cycle.

8. There was no evidence of mutagenicity when alfalfa was tested in an *in vitro* bacterial assay for gene mutation using *S. typhimurium* TA98 and TA100.
9. In human medicine, 5 to 10 g of the dried herb may be given orally 3 times daily. The same dose may be given as an infusion, or as a liquid extract (1:1 in 25% alcohol). When 15 human patients with hyperlipoproteinaemia were given 40 g of alfalfa seeds 3 times per day for 8 weeks, the drug helped to normalise the serum-cholesterol concentrations. Some diabetic patients obtained better control of the diabetes following treatment with alfalfa; it was considered that the manganese content of the alfalfa (45.5 mg/kg) was responsible for the hypoglycaemic effect. Alfalfa is contraindicated for use in humans with a history of systemic lupus erythromatosus and during pregnancy and lactation.
10. Alfalfa is widely used in foods and is listed by the Council of Europe as a source of natural food flavouring (category N2 and N3). These categories indicate that alfalfa can be added to foodstuffs in small quantities, with a limitation on the concentrations of an active ingredient in the final product (though no such limitation has been specified for alfalfa). In the USA, alfalfa is listed as GRAS (Generally Recognised As Safe).

Conclusion and recommendations

Having considered that:

- alfalfa is a normal constituent of the diet for both animals and humans,
- the uptake of canavanine by animals treated topically with extractum *Medicago sativa* was calculated to be insignificant compared with the normal uptake of canavanine by animals fed alfalfa in the diet;
- *Medicago sativa extractum* is administered topically only for individual animals and treated animals were unlikely to be sent for slaughter immediately after treatment,

the Committee considers that there is no need to establish an MRL for *Medicago sativa extractum* and recommends its inclusion in Annex II to Council Regulation (EEC) 2377/90 in accordance with the following table:

Pharmacologically active substance(s)	Target species	Other provisions
<i>Medicago sativa extractum</i>	All food producing species	For topical use only