



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

VISCUM ALBUM

SUMMARY REPORT

1. *Viscum album* L. (synonyms: *Viscum*, mistletoe) is a common bushy plant of the family *Viscaceae* (*Loranthaceae*), which grows as an epiphyte on the branches of deciduous trees. *Viscum album* is widely distributed in tropical and subtropical Africa, in Asia and in Europe. The homeopathic mother tincture is prepared of the fresh younger twigs with leaves and berries according to homeopathic pharmacopoeias.

The main constituents of *Viscum album* are lectins, a mixture of high-molecular-weight polypeptides (mistletoe lectins I, II, III). The amount of mistletoe lectins in the range of 340 to 1000 µg/g dried plant material, and viscotxins (0.05% to 0.1%), a mixture of low-molecular-weight polypeptides. Further constituents of *Viscum album* are polysaccharides, cyclitols and flavonoids, phenylpropane derivatives, triterpenoids like amyirin, betulinic acid and oleanolic acid, phytosterols (approximately 0.2%), amino acids, alkaloids, cyclic peptides and amines like histamine and acetylcholine, and proteins (9.3%) are constituents.

2. In veterinary homeopathy the mother tincture of *Viscum album* and dilutions thereof are intended for use in all food-producing animals. The use follows the principles of homeopathic therapy where animals are diagnosed on basis of the individual pattern of clinical signs. The recommended maximum parenteral dose for large animals is 10 ml/animal. Treatment may be repeated but a fixed dose schedule is not common in homeopathy.

Viscum album is also used in human homeopathy as mother tincture as well as in lower concentrations for treatment of high blood pressure, dizziness, and arthritis. Advers effects are described for dilutions up to 1:10⁷ after parenteral application. In phytotherapy mistletoe is considered to posses hypotensive, cardiac depressant and sedative properties. It may also have a weak antitumour effect. The recommended oral dose is 2 to 6 g, or as infusion 3 times daily.

The branches and berries of *Viscum album* are listed by the Council of Europe as natural sources of food flavouring (category N3). This category indicates that mistletoe may be added to foodstuffs in the traditionally accepted manner.

3. Documented pharmacological studies have concentrated on the cytotoxic, cardiotoxic and immunostimulant properties of *Viscum album*. The crude plant juice has been reported to exert cytotoxic activity *in vitro* and *in vivo*. Also significant antitumour activity has been observed. These pharmacological activities have been attributed to the basic amino acids and to some cytotoxic alkaloids. The demonstrated immunostimulant activity may be due to the polysaccharide fraction of the mistletoe extract. Intact lectins and viscotoxins have been shown to bind to a number of cells including erythrocytes, lymphocytes and macrophages and to agglutinate them. Therefore, the lectins are responsible for the cytotoxicity of mistletoe. However, after oral application no toxic effects of mistletoe could be demonstrated. This is most likely due to the limited or absent oral absorption and systemic availability of the protein toxins (lectins, viscotoxins) in their native form, as a result of effective denaturation and enzymatic proteolysis in the gastrointestinal tract.

4. The following LD₅₀-values for intraperitoneal administration of *Viscum album* to mice were reported: 32 mg/kg bw for the crude plant juice; more than 2.25 mg/kg bw for the polysaccharide fraction of the berries; 80 µg/kg bw for the mistletoe lectin fraction and 0.7 mg/kg bw for viscotoxin. No intoxications of humans or animals after oral ingestion of mistletoe or respective plant extracts have been reported.
5. In a preliminary risk evaluation procedure by the Committee for Veterinary Medicinal Products, considering all defended old substances used in veterinary homeopathy in concentrations greater than 1:10 000, the use of *Viscum album* and its individual constituents was considered as not giving rise to specific health concerns. There are prominent differences in pharmacological and toxicological activity after parenteral and oral use of *Viscum album*. Search of published literature did not provide any further evidence for pharmacological or toxicological properties of *Viscum album* alerting to specific health risks which may result from oral intake of residues in food producing animals following the intended uses. Special emphasis was also put on identification of any suspicion pointing to genotoxicity or other potential of serious health effects of plant constituents.

Conclusions and recommendation

Having considered the criteria laid down by the Committee for Veterinary Medicinal Products for the inclusion of substances in Annex II of Council Regulation (EEC) No 2377/90 and in particular that:

- oral absorption and systemic bioavailability of *Viscum album* constituents of possible concern, like the protein lectins and viscotoxins, was considered negligible as shown by absence of any oral toxicity in humans at high therapeutic doses of several grams,
- with the exception of the presence of the orally inactive plant toxins, *Viscum album* and constituents thereof did not give rise to consumer health concern which may result from veterinary homeopathic uses in food producing animals,
- *Viscum album* is used only in a small number of individual animals for non-regular treatments,
- animals are unlikely to be sent for slaughter during or immediately after treatment;

the Committee for Veterinary Medicinal Products concludes that there is no need to establish an MRL for any plant constituents of *Viscum album* following homeopathic uses and recommends its inclusion in Annex II of Council Regulation (EEC) No 2377/90 as follows:

Pharmacologically active substance(s)	Animal species	Other provisions
<i>Viscum album</i>	All food producing species	For use in homeopathic veterinary medicinal products prepared according to homeopathic pharmacopoeias at concentrations corresponding to the mother tincture and dilutions thereof only