COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

LESPEDEZA CAPITATA

SUMMARY REPORT

1. The stem (the herb) of Lespedeza capitata (Round-headed bush clover) is used in medicinal products. Its main constituents are flavonoids, which are contained up to 0.1% in fresh plants: Lespedesin (kämpferitrin), n-pentacosane, n-hexacosane, n-hentriacontane and n-tritriacontane.

2. In veterinary medicine Lespedeza capitata is used in mono-preparations as an extract, tincture, powder, in form of injections (intravenous, subcutaneous), and drinking solutions and tablets. It is used as a diuretic and for treatment of hyperazotaemia. Doses of the finished product usually administered to animals are 8 ml/100 kg of a 15% solution prepared from a tincture of Lespedeza capitata. Target species are cattle, sheep, goats and pigs.

In human medicine a medicinal product for oral administration containing a 15% alcoholic solution of Lespedeza capitata is used to stimulate renal water excretion.

Flavonoids, constituents of Lespedeza capitata, are belonging to a naturally occurring group of phenolic compounds many of which are plant pigments and thus natural constituents of the animal and human diet.

3. The pharmacodynamic properties of Lespedeza capitata include increase of diuresis and decrease of the blood urea nitrogen concentration without modification of electrolyte balance.

In tests on rabbits, rats, dogs and cats it was shown that the diuretic efficacy of preparations containing Lespedeza capitata was equal to theophylline and theobromine but longer lasting. The urinary flow was doubled to tripled.

Four of five rabbits with experimentally induced uraemia showed significant reduction of urea blood levels when 1 ml/kg bw of the tincture was administered via gavage.

The administration of 1 ml tincture (containing 1.5 mg flavonoids) via gavage in rats increased the urinary flow (24 hour rate) from 7.3 ml in untreated animals to 14.1 ml in treated ones.

Dogs and cats showing symptoms of liver and kidney failure were treated with 1 ml/kg bw once or twice per day through several days or weeks. Oliguria and albuminuria disappeared and urea concentration decreased significantly.

4. Flavonoids are absorbed by passive diffusion. Pharmacological activity (increased diuresis) is noted within the first hour after administration and increases for 7 hours (peak activity). With autoradiographs, using 14C flavonoids, it was shown that these compounds are rapidly distributed and predominantly found in the bile, in the liver, and to a lesser extent in the kidneys, muscles and bones. After oral administration there is partial degradation by the intestinal microflora thus liberating polyphenol derivatives. After intraperitoneal administration a hydroxylation in the liver takes place and 2 major metabolites are formed.
Elimination of the flavonoids occurs in the urine as sulphate- and glucuronide-conjugates, but also as the parent compound in the bile. In healthy animals, 25 to 45% of the product is eliminated within 24 hours. Faecal elimination is important during the first two hours.

5. Using the injectable solution (concentration not stated), the intraperitoneal LD$_{50}$ in mice was 32 ml/kg bw.

6. Subacute toxicity was tested in 10 mice, 10 rats, 10 guinea pigs, 6 rabbits 3 cats and 2 dogs by intramuscular administration of 5 ml/kg bw/day (five times the therapeutic dose) during one month (concentration not stated). No clinical signs or changes in blood cells were observed. No effect on body weight was observed. No pathological signs could be found in the main organs at the histopathological examinations.

   Chronical toxicity was tested in the same dosage and number of animals as above for a period of 90 days. The findings were the same as in the former tests.

7. No data on reproductive toxicity and embryotoxicity including teratogenicity in laboratory animals were provided.

8. No data on mutagenicity or carcinogenicity in laboratory animals were provided.

Conclusions and recommendations

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

- the active substances of *Lespedeza capitata* (flavonoids) are natural constituents in the animal and human diet,
- *Lespedeza capitata* is used only for occasional treatment of individual animals,
- animals are unlikely to be sent for slaughter immediately after treatment;

the Committee concludes that there is no need to establish an MRL for *Lespedeza capitata* and recommended its inclusion in Annex II to Council Regulation (EEC) No. 2377/90 in accordance with the following table:

<table>
<thead>
<tr>
<th>Pharmacologically active substance(s)</th>
<th>Animal species</th>
<th>Other provisions</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Lespedeza capitata</em></td>
<td>All food producing species</td>
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