



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

CINNAMOMI CEYLANICI AETHEROLEUM

SUMMARY REPORT

1. *Cinnamomi ceylanici aetheroleum* is the volatile oil of the bark of *Cinnamomum verum* J.S. Presl. (synonym: *Cinnamomum zeylanicum* Blume, cinnamon bark), Lauraceae, obtained by steam distillation. It mainly contains cinnamaldehyde (55 to 76%), eugenol (5 to 18%), and safrole (up to 2%). Seventy other components have been identified, among others cinnamic alcohol, cinnamic acid, o-methoxy-cinnamic aldehyde and cinnamyl acetate.
2. *Cinnamomi ceylanici aetheroleum* is contained in one veterinary medicinal product in combination with 9 other active principles. The percentage of the oil in the product is 0.008%. The product is intended to be used as a nose-spray to facilitate breathing in new-born foals, calves, sheep, goats and piglets. The dose is 0.1 to 0.3 g of the product, depending on the size of the animal. This corresponds to a maximal single dose of 0.024 mg of *Cinnamomi ceylanici aetheroleum*. The treatment may be repeated after 10 to 15 seconds.

In human medicine *Cinnamomi ceylanici aetheroleum* is used against dyspeptic troubles. The daily dose of the oil is 50 to 200 mg.

Cinnamon bark, which contains 0.5 to 2.5% *Cinnamomi ceylanici aetheroleum*, is widely used as a spice. *Cinnamomi ceylanici aetheroleum* is used for flavouring human foodstuffs (chewing gum, non-alcoholic beverages, meat sausages) and as a fragrance in the cosmetic industry.

3. The oil is a cyclo-oxygenase inhibitor. The active compound is probably eugenol. The oil has antibacterial and antifungal activity. Cinnamaldehyde has a hypotensive effect in anaesthetised dogs and guinea pigs. Cinnamaldehyde is an inhibitor of stomach peristalsis in anaesthetised rats (5 to 20 mg/kg bw intravenous) and of the peristalsis in the gut of mice (250 mg/kg bw intraperitoneal). Cinnamaldehyde stimulates bile secretion in rats (500 mg/kg bw), has CNS-stimulating activity in rabbits (10 to 20 mg/kg bw intraarterial) and inhibits motor activity in mice (250 to 1000 mg/kg bw oral doses). Cinnamaldehyde caused positive inotropic and chronotropic effects in isolated guinea pig heart preparations. Repeated application resulted in cardiac depression. Intravenous doses of 5 to 10 mg/kg bw and concentrations of 10 to 100 mg/l in organ preparations were used. Cinnamaldehyde (100 mg/l) has a papaverin-like spasmolytic effect on the isolated guinea-pig ileum and isolated mouse ileum.
4. No information on pharmacokinetics of *Cinnamomi ceylanici aetheroleum* was provided.
5. In human medicine *Cinnamomi ceylanici aetheroleum* is used against dyspeptic troubles. Daily dose: 50 to 200 mg.
6. The oral LD₅₀ for *Cinnamomi ceylanici aetheroleum* in rats is 4160 mg/kg bw. For cinnamaldehyde the oral LD₅₀ in rats is 2220 mg/kg bw and in mice the intra peritoneal LD₅₀ is 200 mg/kg bw. The dermal LD₅₀ for the oil is 690 mg/kg bw. Other reports state the dermal LD₅₀ as 0.69 mg/kg bw for the oil and 0.59 mg/kg bw for cinnamaldehyde.

7. No information on the repeated dose toxicity of *Cinnamomi ceylanici aetheroleum* was provided. For its main constituent the following summary information was available. Rats tolerated oral doses of 70 mg cinnamaldehyde for 8 weeks without any symptoms of toxicity. Cinnamaldehyde added to the feed for rats at 1000 and 2500 mg/kg feed for 16 weeks caused no adverse effects. At 10 000 mg/kg feed slight swelling of the hepatic cells and slight hyperkeratosis of the squamous portion of the stomach were observed.
8. No studies on the effects of *Cinnamomi ceylanici aetheroleum* on reproduction were provided. In humans, cinnamon and preparations thereof are in older literature reported to have abortifacient effect. It must be taken into account that in old sources cinnamon (cassia) was confused with *Cassia fistulosa*, which contains anthraquinones.
9. The following summary information on the mutagenicity of *Cinnamomi ceylanici aetheroleum* was available. Cinnamon oil is positive in the *Bacillus subtilis*-DNA repair test. In most experiments with the Ames test negative results have been obtained. For cinnamaldehyde both positive and negative results are reported. Cinnamon oil and cinnamaldehyde gave positive results in chromosomal aberration tests using Chinese hamster cell cultures and in *Drosophila* test systems. Negative results were reported with the *in vivo* micronucleus test in the mouse (125 to 500 mg/kg bw intraperitoneal). The results of the *in vitro* bacterial mutagenicity tests must be interpreted with caution as the concentrations used were within the dose range where antimicrobial effects of cinnamaldehyde or cinnamon oil have been demonstrated. Also for the *in vitro* tests with mammalian cell cultures it must be taken into account that cinnamon extracts and cinnamaldehyde have cytotoxic effects. Taking also into consideration the negative results of the *in vivo* micronucleus test, the positive *in vitro* findings can be considered of no concern.
10. No information on the carcinogenicity was provided. However, this is not considered necessary due to the above conclusion on the mutagenicity.
11. No data on immunotoxicity were provided, but *Cinnamomi ceylanici aetheroleum* is known to cause allergic reactions.
12. In humans, cinnamaldehyde is the leading substance responsible for allergic reactions caused by cosmetics and perfumes. Allergic reactions have also been caused by toothpaste containing cinnamaldehyde.
13. The ADI of cinnamaldehyde was set by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) to 0.7 mg/kg bw in 1984 but was not extended further in 1992 because of incomplete toxicity data. The ADI of eugenol is up to 2.5 mg/kg. The bark (oil content up to 4%) is used for food flavouring and is listed by the Council of Europe (1973) as a natural source of food flavouring, category N2. This category indicates that cinnamon can be added to foodstuffs in small quantities, with a possible limitation of an active principle in the final product. The bark is listed as “Generally Recognised As Safe” in the USA.
14. The use of *Cinnamomi ceylanici aetheroleum* in the doses recommended is unlikely to result in residues in edible tissues posing a risk to the health of the consumer.

Conclusions and recommendation

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

- *Cinnamomi ceylanici aetheroleum* is a normal component of the human diet,
- *Cinnamomi ceylanici aetheroleum* is used 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 *Cinnamomi ceylanici aetheroleum* and recommends its inclusion in Annex II of Council Regulation (EEC) No. 2377/90 according to the following table:

Pharmacologically active substance(s)	Animal species	Other provisions
<i>Cinnamomi ceylanici aetheroleum</i>	All food producing species	