The European Agency for the Evaluation of Medicinal Products
Veterinary Medicines and Information Technology Unit

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COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

CINNAMOMI CASSIAE CORTEX

SUMMARY REPORT

1. *Cinnamomi cassiae cortex*, is the stembark of *Cinnamomum aromaticum* Nees (synonym: *Cinnamomum cassia* Blume). The main constituent of *Cinnamomi cassiae cortex* is the volatile oil (1 to 4%), which mainly contains cinnamaldehyde (75 to 90%), *o*-methoxy-cinnamaldehyde (10 to 11%), coumarin and 32 other compounds in low concentration. The bark also contains tannins and diterpenes such as Cinnzeylanol and Cinnzeylanin, which have insecticidal effect. Other diterpene derivatives are the Cinncassiols A - E, which are present as glycosides and free aglycones. Various organic acids such as ferulic acid, salicylic acid, vanillic acid and syringic acid have also been identified. Mucilage is also present in a concentration of 4 to 5%.

2. An extract is used in veterinary medicine, but no further information has been obtained.

   In human medicine *Cinnamomi cassiae cortex* is used as an appetite stimulant and as a carminative. *Cinnamomi cassiae cortex* is widely used as a spice. The volatile oil (*Cinnamomi cassiae aetheroleum*) is used for flavouring foodstuffs and as a fragrance in the cosmetic industry.

3. The essential oil (*Cinnamomi cassiae aetheroleum*) has antibacterial and antifungal activity. Cinnamaldehyde has a hypotensive effect in anaesthetised dogs and guinea pigs and is an inhibitor of stomach peristalsis in anaesthetised rats (5 to 20 mg/kg bw intravenously) and the peristalsis in the gut of mice (250 mg/kg bw intraperitoneally). Cinnamaldehyde stimulates bile secretion in rats (500 mg/kg bw), has CNS-stimulating activity in rabbits (10 to 20 mg/kg bw intra-arteriallly) and inhibits motor activity in mice (250 to 1000 mg/kg bw oral). Cinnamaldehyde caused positive inotropic and chronotropic effects in isolated guinea pig heart preparations. Repeated application resulted in cardiac inhibition. 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. Cinnamaldehyde is fungotoxic.

   Cinnamomi cassiae aetheroleum is also used in veterinary medicine. It has previously been assessed by the Committee for Veterinary Medicinal Products and included in Annex II of Council Regulation (EEC) No 2377/90 for all food producing species.

4. No information on pharmacokinetics of *Cinnamomi cassiae cortex* was provided.

5. No information was provided on the acute toxicity and on repeated dose toxicity of *Cinnamomi cassiae cortex*. The volatile oil and particularly its content of cinnamaldehyde, is the compound of toxicological interest. For cinnamaldehyde the oral LD_{50} in rats is 2220 mg/kg bw and in mice the intraperitoneal LD_{50} is 200 mg/kg bw. 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.

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6. No studies on the effects of *Cinnamomi cassiae cortex* 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.

7. No reports on the mutagenicity of *Cinnamomi cassiae cortex* were provided. The following summary information on the mutagenicity of *Cinnamomi cassiae 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.

8. No information on the carcinogenicity was provided. Compare, however, the above information on the lack of mutagenicity of the essential oil.

9. *Cinnamomi cassiae cortex* is known to cause allergic reactions, due to the content of the volatile oil, particularly cinnamaldehyde which is the leading substance responsible for allergic reactions caused by cosmetics and perfumes. Allergic reactions have also been caused by toothpaste containing cinnamaldehyde. Aqueous extracts of *Cinnamomi cassiae cortex* inhibits complement-allergic reactions of the types II and III whereas reactions of type IV were not affected.

10. A temporary ADI of 0.7 mg/kg bw was set for cinnamaldehyde by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in 1984 but was not extended further in 1992 because of incomplete toxicity data. 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 United States of America.

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 cassiae cortex* is a normal component of the human diet,
- *Cinnamomi cassiae cortex* is used for occasional treatment of individual animals,
- animals are unlikely to be sent for slaughter immediately after treatment,
- *Cinnamomi cassiae aetheroleum*, the main active constituent of *Cinnamomi cassiae cortex* is already included in Annex II;

the Committee concludes that there is no need to establish an MRL for *Cinnamomi cassiae cortex* 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
Cinnamomi cassiae cortex standardised extracts and preparations thereof	All food producing species	