



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

MYRISTICAE AETHEROLEUM

SUMMARY REPORT

- Myristicae aetheroleum* is the volatile oil is obtained by steam distillation of the seed of *Myristica fragrans* Houtt (synonym of the seed: nutmeg). Also the arillus can be included for the distillation. It contains monoterpenes (82 to 87%), monoterpene alcohols (5.5 to 9.8%) and phenylpropanoids (6.5%). The monoterpene fraction is composed of sabinene (39%), α -pinene (13%), β -pinene (9%), α -phellandrene (4%), limonene (4%), γ -terpinene (1%), *p*-cymene (1%) and terpinols (1%). The monoterpene alcohol fraction consists of 1,8-cineol (3.53%), terpinen-4-ol (1.96%), geranylacetate (0.90%) *trans*-sabinene hydrate (0.84%), *cis-p*-menth-2-en-1-ol (0.82%), terpinene-4-yl acetate (0.57%) and linalool (0.56%). Among the phenylpropanoids the main components are myristicine (2.3 to 7%) and elemicine (maximum 2.6%). Other phenylpropanoids are safrole (2.4%), methyl-eugenol (0.6%) and small amounts of methoxy-eugenol, isoeugenol, eugenol and isolemicin. Oil from the East Indies contains 1.9 to 2.9% safrol and 14 to 16% myristicin while oil from the West Indies contains 0.3 to 0.4% safrol and 2.6% myristicin.
- Myristicae aetheroleum* is contained in a veterinary medicinal product together with 9 other active principles. The percentage of the oil in the product is 0.02%. The product is used as a nose-spray to facilitate breathing in new-born animals of all food producing species. 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 0.06 mg of *Myristicae aetheroleum*. The treatment may be repeated after 10 to 15 seconds, if necessary.

Myristicae aetheroleum has been used in human medicine internally for treatment of stomach disorders at doses of 0.05 to 0.2 ml, and, topically in a liniment containing 10% oil, for treatment of rheumatism, neuralgia and catarrhs of the respiratory tract. Internal use is, however, not recommended in one EU Member State.

Myristicae aetheroleum is also widely used as a flavouring agent in human medicinal products (e.g. products for dental and oral care), in cosmetics (soaps, creams, lotions and perfumes at concentrations from 0.005 to 0.8%) and in food (baked goods, puddings, pickles, alcoholic beverages).
- Myristicae aetheroleum* has antimicrobial activity. It is an *in vitro*-inhibitor of the thromboxane synthesis. It also inhibits arachidonic acid induced aggregation of blood platelets. The main active components are eugenol and isoeugenol. The hallucinogenic activity of nutmeg is among others attributed to the content of myristicin, which is also contained in *Myristicae aetheroleum*.
- No information on the pharmacokinetics of *Myristicae aetheroleum* was provided.
- The oral LD₅₀ for *Myristicae aetheroleum* in rats is 3.64 g/kg bw. Oral doses of 8 to 21 g of the oil kill rabbits within 13 hours to 5 days. A lethal intravenous dose of *Myristicae aetheroleum* for dogs (6 to 20 kg bw) is 0.8 g to 1.75 g.
- No information on the long term toxicity of *Myristicae aetheroleum* was provided.

7. The following summary information on the effects of *Myristicae aetheroleum* on reproduction was available. Oral doses of *Myristicae aetheroleum* of 60, 80, 100 and 400 mg/kg bw given to male C3H-mice in corn oil for 8 weeks, caused a dose-related decrease in fertility in all dose groups. In the directly treated animals of the study no reciprocal chromosomal translocation was observed, however, in offspring of the F1-generation hereditary translocations were in the 60, 80 and 100 mg/kg bw dose groups. In rats a single oral dose of *Myristicae aetheroleum* of 300 mg/kg bw given on day 8 of gestation or injected directly into the uterus induced deformation of the foetuses (not further specified) and a bodyweight decrease. No information on other aspects of reproduction and teratogenicity was provided.
8. No information on the mutagenicity of *Myristicae aetheroleum* was provided. Safrole, which is contained in a concentration of about 0.2 to 3% in the volatile oil, is known to have mutagenic effects in some test systems. The available summary information reports induction of DNA strand breaks in rat hepatocytes, induction of DNA repair in liquid-scintillation assays for unscheduled DNA synthesis (UDS) but not in an autoradiographic assay, equivocal results in Chinese hamster ovary cells, while *in vivo* tests in *Drosophila* and an *in vivo* micronucleus test in mice did not show mutagenic effects. No further details were provided.
9. No information on the carcinogenicity of *Myristicae aetheroleum* was provided. Safrole, which is contained in a concentration of about 0.2 to 3% in the volatile oil, known to be carcinogenic, however no further details were provided.
10. Undiluted *Myristicae aetheroleum* did not irritate the back skin of pigs or nude mice. Applied to the intact or shaved skin of rabbits under occlusion for 24 hours it was moderately irritating.
11. *Myristicae aetheroleum* has a narcotic effect on humans when taken in bigger amounts. Vomiting and headache as well as epileptic convulsions can appear. No sensitising potential of *Myristicae aetheroleum* in a concentration of 8% in paraffin was observed in a maximisation test in male and female volunteers. The same concentration does also not irritate the skin in a 48-hour closed patch test.
12. The use of *Myristicae 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:

- *Myristicae aetheroleum* is obtained from the seed of *Myristica fragrans* which is used as a spice in human food,
- *Myristicae aetheroleum* is used only for newborn animals,
- the animals are unlikely to be sent to slaughter immediately after treatment;

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

Pharmacologically active substance(s)	Animal species	Other provisions
<i>Myristicae aetheroleum</i>	All food producing species	For use in newborn animals only