Federal Institute for Risk Assessment (BfR)

Use of undiluted tea-tree oil as a cosmetic

Opinion of the Federal Insitute for Risk Assessment (BfR), 1th September 2003

Background

Recently there has been an increasing amount of reports on contact-allergic eczema in conjunction with the use of tea-tree oil. Tea-tree oil is sold as a pure natural product, highly concentrated and undiluted in cosmetics. Tea-tree oil is advertised as a universal remedy although there is no marketing authorisation as a pharmaceutical product.

Concentrated tea-tree oil has been classified as harmful according to the self-classification of the International Fragrance Association (IFRA) and is labelled with R-phrases R 22 (harmful if swallowed) R 38 (irritating to skin) and R 65 (may cause lung damage if swallowed) as well as the symbol Xn (harmful) (IFRA Labelling Manual 1, 2001). These indications of health hazards are also part of the safety data sheets of raw material suppliers.

At the 65th and 66th meetings of the Cosmetics Committee at the Federal Institute for Risk Assessment (BfR), health risks associated with the use of undiluted and highly concentrated tea-tree oil in cosmetic products were discussed extensively.

Result

Tea-tree oil is a mixture of various terpenes extracted from the Australian tea-tree. Undiluted tea-tree oil is a pure natural product. In the presence of atmospheric oxygen but also when exposed to light and higher temperatures, oxidation processes occur leading to the formation of peroxides, epoxides and endoperoxides which have a sensitising potency and may trigger allergic skin reactions. In humans allergic skin reactions are known to occur both after topical application and after the intake of tea-tree oil. Corresponding case studies are available. The risk of skin irritations and allergic reactions can, however, be minimised by diluting of the oil. In tests with volunteers a 1% tea-tree oil vaseline formulation was found to have no sensitising effect. The risk of allergic reactions to tea-tree oil in concentrations below 1% cannot, however, be ruled out in principle, particularly not for individuals who are already sensitised to tea-tree oil. 1% tea-tree oil probably does not possess a pharmacological effect. However, there are no data on this available to the Federal Institute for Risk Assessment.

The Federal Institute for Risk Assessment recommends limiting the concentration of tea-tree oil in cosmetic procucts to a maximum content of 1%. Cosmetic products containing tea-tree oil should, furthermore, be protected against light and admixed with antioxidants in order to avoid as far as possible any oxidation of the terpenes. Tea-tree oil as a natural ingredient in cosmetic products, is an example of a substance with a possible pharmacological effect, which has not obtained marketing authorisation as a pharmaceutical product but which may be used in cosmetics. In principle, a health risk from such substances cannot be excluded.

Explanation

Tea-tree oil is a terpene compound obtained by steam distillation from the leaves and twigs of the Australian tea tree (*Melaleuca alternifolia*). Sometimes, however, other essential oils from Leptospermum species and other Melaleuca species may be summarised under this name, like for instance cajeput oil obtained from *Melaleuca leucadendra* and niauli oil obtained from *Melaleuca viridiflora*.

Tea-tree oil from *Melaleuca alternifolia* is a mixture of various mono- and sesquiterpenes as well as from aromatic compounds. The monoterpenes terpinen-4-ol, γ-terpinene, α-terpinene, 1,8-cineol, p-cymen, α-terpineol, α-pinene, terpinolenes, limonene and sabinene account for 80-90 % of the oil. A total of more than 60 individual substances have been detected in tea-tree oil. The natural content of the individual terpenes in tea-tree oil may vary considerably depending on the *Melaleuca alternifolia* race used, the climate, the age of the leaves and the duration of distillation. For terpinen-4-ol concentrations measured vary between 28.6 and 57.9 %, for γ-terpines between 9.5 and 28.3 %, for α-terpines between 4.6 and 12.8 %, for 1.8-cineol between 0.5 and 17.7 %, for p-cymen between 0.4 and 12.4 %, for α-terpineol between 1.5 and 7.6 % and for limonene between 0.4 and 3.1 %. In order to regulate the quality of tea-tree oil, requirements were imposed in the Australian Standard, in the International Standard and in the German Drugs Code (DAC) with respect to the level of individual ingredients. According to the DAC a minimum level of 30 % terpinen-4-ol and a maximum level of 15% 1,8-cineol has to be maintained in tea-tree oil (DAC 1999).

The composition of tea-tree oil changes particularly in the presence of atmospheric oxygen but also when the oil is exposed to light and higher temperatures. The levels of α-terpinene, γ-terpinene and terpinolene decrease whereas the level of p-cymen increases up to tenfold. Oxidation processes lead to the formation of peroxides, endoperoxides and epoxides. Limonene can undergo oxidation to carvone, limonene oxide and caveol. Terpinen-4-ol-peroxide and 1,2,4-trihydroxymenthane may crystallise.

Tea-tree oil is not currently subject to any constraint for the use in cosmetic products. It is sold undiluted and highly concentrated for cosmetic purposes. Furthermore, the oil is used as ingredient of skin and body care products, toothpaste, mouthwash and in bath oils as well as in products for aromatherapy.

Tea-tree oil is considered to be a universal remedy for acne, eczema, skin infections like herpes, wounds, warts, burns, insect bites and nail mycosis. Other indications mentioned are colds, sore throat and gingival infections, haemorrhoids and vaginal infections.

The antibacterial effect of tea-tree oil could be proven *in vitro*. For various bacterial strains, including skin bacteria and acne pathogens, a minimum inhibitory concentration between 0.25 % and 0.5 % was shown. An antiviral effect on tobacco mosaic virus was reported. Additionally, there are patient reports about the promotion of healing of lip blisters (*Herpes simplex* virus) and shingles (*Varizella zoster* virus).

In clinical trials the efficacy of an aqueous gel with 5% tea-tree oil was tested against acne and compared with a 5% benzoyl peroxide lotion. Like benzoyl peroxide, tea-tree oil induced a significant reduction in inflamed and non-inflamed lesions. Side effects like smarting, itching, dry skin and erythema were mentioned by 79% of patients treated with benzoyl peroxide and 44% of patients treated with tea-tree oil.

A statistically significant improvement of symptoms was found following treatment of athlete's feet with a cream containing 10% tea-tree oil. The number of negative cultures at the end of treatment was, however, comparable with the number from the placebo group.

Tea-tree oil does not have marketing authorisation as a pharmaceutical product since a positive clinical effect has not yet been proven according to valid criteria for clinical trials on the efficacy of pharmaceutical products. It can, however, be assumed that consumers use tea-tree oil externally and internally for therapeutic purposes.

Toxicity

Acute toxicity data are available for tea-tree oil. The LD_{50} after oral application amounts to 1.9 to 2.6 g per kg body weight in rats depending on the strain examined. In rabbits no toxic effects could be observed after dermal application of up to 2 g per kg body weight. There are case reports of intoxication caused by tea-tree oil in humans. One patient lapsed into a coma for 12 hours after ingesting half a cup of pure tea-tree oil and suffered disturbances of consciousness for another 36 hours. 30 minutes after taking 10 ml pure tea-tree oil, a two-year-old boy had difficulties in co-ordinating his limbs and was confused. Allergic skin reactions related to tea-tree oil have also been documented. After the intake of 3 ml pure tea-tree oil, one man developed reversible skin symptoms within 24 hours involving swelling of the face, one hand and the feet. Additionally there are reports of intoxication in pets. Dogs and cats, which were given high or frequent doses of tea-tree oil on the skin showed symptoms of depression, weakness, muscle tremors, co-ordination problems and ataxia.

Pursuant to § 16 Chemicals Act the predecessor of the BfR, the former Federal Institute for Health Protection of Consumers and Veterinary Medicine (BgVV) received a total of seven intoxication notifications involving tea-tree oil between 1996 and 2002. In two infants symptoms of nausea, tiredness and vomiting appeared following the oral intake of tea-tree oil; another infant did not develop any symptoms. One adult suffered nausea, stomach pain, loss of appetite and eructation after taking tea-tree oil capsules. In three other cases allergic reactions were observed after dermal application (see below).

For tea-tree oil the Draize Index for skin irritations in rabbits was determined at 5.0. A skin irritation test in rabbits was conducted with 25% tea-tree oil in paraffin oil and the solution was repeatedly applied over 30 days to the shaved rabbit skin. Minor initial irritations declined; however, skin changes were found microscopically. In the patch test under semi-occlusive conditions according to OECD 404, 12.5% and 25% tea-tree oil was not irritating, while 50% was minimally and 75% tea-tree oil was slightly irritating in rabbits; undiluted tea-tree oil in the patch test triggered irritations within 24 hours.

1,8-cineol and p-cymen, which are ingredients of tea-tree oil, were also examined for irritating effects: 25% 1,8-cineol in paraffin did not induce any skin irritation in the patch test under occlusive conditions over 21 days in 25 volunteers; undiluted 1,8-cineol displayed no skin-irritating effect. P-cymen induced initial minor skin irritations in patch test under occlusion in volunteers (4% p-cymen in vaseline) as well as erythema, dryness and defatting of the skin (undiluted p-cymen). The application of undiluted p-cymen to intact skin showed also minor irritations in the patch test under occlusion in rabbits after 24 hours.

The skin-sensitising potential of tea-tree oil was examined in guinea pigs. The oil was applied twice intradermally and once epidermally. No sensitisation could be induced through 30% tea-tree oil two weeks after application.

In a double blind, placebo-controlled study, tea-tree oil in a 1%, 2.5%, 5% and 10% cream was applied to the healthy skin of volunteers over a period of three weeks. Only in the case of the 10% cream minor skin irritations were observed; 5 of the 28 volunteers developed minor erythema. In tolerance tests with a 5% hand and body lotion, three out of 32 volunteers reacted with itching and skin irritation. In a two-hour patch test under semi-occlusive conditions in voluntary test persons, skin irritations and erythema were observed at concentrations above 25%.

In humans there are known cases of contact allergies in conjunction with the application of tea-tree oil. Up to 1997 the Swedish authorities received notifications of 22 cases of contact allergy eczema caused by tea-tree oil. The Information Network of Dermatological Clinics

(Schnuch et al. 2001) has noted an increase in allergies to turpentine oil, (also a compound of various terpenes) which is attributed to augmented use of tea-tree oil (Treudler et al. 2000). Two cases of allergic skin reactions after dermal application of tea-tree oil have been reported to BgVV within the framework of intoxication notifications as well as one case in which a shower lotion containing tea-tree oil led to skin irritation.

Tests in volunteers with various individual substances confirm that the monoterpenes α-terpinene, α-phellandrene, ascaridol, terpinolene, d-limonene and aromadendrene are the main sensitising ingredients in tea-tree oil whereas terpinen-4-ol and α-pinene showed only a slight to moderate effect and p-cymen and 1,8-cinoel a minor or no sensitising effect (Beckman & Ippen 1998, Hausen et al. 1999). Ascaridol, which has an anthelmintic effect, is formed in tea-tree oil during storage, probably through autooxidation from α-terpinen (Harkenthal et al. 1998). In ageing experiments with tea-tree oil it was shown that in particular the influence of atmospheric oxygen may increase the sensitising potential of tea-tree oil up to three-fold. Artificial ageing led to an increase in the peroxide number from 25 ppm to up to 500 ppm within six weeks. A correlation between the peroxide number and allergic skin reactions is known from other essential oils.

The skin irritating and sensitising effect of tea-tree oil can be reduced by dilution. In a closed patch test with 1% tea-tree oil in vaseline, no irritations could be observed after 48 hours in 22 test persons. However, the small number of cases does not permit any definitive statement that tea-tree oil no longer has a sensitising effect under 1%. Additionally, 1 % tea-tree oil probably does not have a pharmacological effect. However, the Federal Institute for Risk Assessment does not have any scientific data to support this.

Exposure, risk characterisation and measures

Undiluted tea-tree oil is a pure natural product and marketed as a cosmetic. Tea-tree oil does not have marketing authorisation as a pharmaceutical product. Given its description as a universal remedy, it is to be assumed that consumers undertake both a topical and systemic application of undiluted or highly concentrated tea-tree oil. Dermal application of the oil may lead to skin irritations. In particular old products or oils, which have not been stored adequately, have sensitising potential and may trigger allergic skin reactions when used repeatedly.

The Federal Institute for Risk Assessment, therefore, recommends limiting the concentration of tea-tree oil in cosmetic products to a maximum of 1%. The European Cosmetic, Toiletry and Perfumery Association (COLIPA) has published a recommendation with the same requirements for limiting of tea-tree oil in cosmetics (COLIPA 2002). Furthermore, cosmetic products containing tea-tree oil should be protected from light and admixed with antioxidants in order to largely avoid the oxidation of the terpenes. Tea-tree oil, a natural ingredient in cosmetic products, is an example for substances with a possible pharmacological effect which has not obtained marketing authorisation as a pharmaceutical product but which may be used in cosmetics. In principle, a health risk from such substances cannot be excluded.

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