EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate C - Public Health and Risk Assessment
C7 - Risk assessment

SCIENTIFIC COMMITTEE ON CONSUMER PRODUCTS

SCCP

Opinion on

Tea Tree Oil

Adopted by the SCCP
during the 2nd plenary meeting of 7 December 2004

TABLE OF CONTENTS

1. BACKGROUND

Tea Tree Oil and its components are not regulated in any of the annexes of the Cosmetic Directive 76/768/EEC.

In July 2003 the European Commission received a dossier on Tea Tree Oil provided by an Australian manufacturer. Recently, the European Commission received additional data on the identity, purity, contamination/impurities, toxicological data and allergies on the substance.

2. TERMS OF REFERENCE

* *On the basis of provided data the SCCP is asked to assess the risk to consumer when Tea Tree Oil is used in cosmetic products?*

* *Does the SCCP propose any restrictions or conditions for the use of Tea Tree Oil as an undiluted product?*

* *Does the SCCP propose any restrictions or conditions in terms of concentrations for the use of Tea Tree Oil in cosmetic products?*

* *Does the SCCP find it important, for safety reasons, to have a date of minimum durability on the Tea Tree Oil products?*

3. OPINION

3.1. Chemical and Physical Specifications

3.1.1. Chemical identity

The essential oil Tea Tree Oil is a complex mixture of compounds obtained by steam distillation from the leaves and twigs of the Australian tea tree (*Melaleuca alternifolia,* Myrtaceae). Sometimes, however, other essential oils from Leptospermum species and other Melaleuca species may be summarised under this name, like for instance cajuput oil obtained from *Melaleuca leucadendra* and niauli oil obtained from *Melaleuca viridiflora*. The European Inventory contains 3 Melaleuca-type ingredients (INCI names): *Melaleuca alternifolia* oil (antimicrobial), *Melaleuca cajuputi* extract (tonic), *Melaleuca leucadendron* extract (tonic).

Tea Tree Oil from *Melaleuca alternifolia* contains various mono- and sesquiterpenes as well as aromatic compounds. The monoterpenes terpinen-4-ol, γ-terpinene, α-terpinene, 1,8-cineole, p-cymene, α-terpineol, α-pinene, terpinolenes, limonene and sabinene account for 80-90 % of the oil. From about 100 terpenes found in Tea Tree Oil more than 60 individual substances have been identified. The natural content of the individual terpenes in Tea Tree Oil may vary considerably depending on the *Melaleuca alternifolia* population used, the climate, the leaf maceration, the age of the leaves and the duration of distillation. For terpinen-4-ol the concentrations measured varied from 28.6 % to 57.9 %, for γ-terpinene from 9.5 % to 28.3 %, for α-terpinene from 4.6 % to 12.8 %, for 1.8-cineole from 0.5 % to 17.7 %, for p-cymene from

0.4 % to 12.4 %, for α-terpineol from 1.5 % to 7.6 % and for limonene from 0.4 % to 3.1 %. The enantiomeric composition of the principal components was analysed: for terpinen-4-ol the enantiomeric ratio was 65:35 (+:-).

Ref.: 1, 2, 3, 4, 5, 6

In order to regulate the quality of Tea Tree Oil, requirements were imposed in the Australian Standard, in the International Standard ISO 4730 (ISO 4730, 1996 and ISO/FDIS 4730, 2004) and in a former issue of the German Drugs Code (DAC) with respect to the level of individual ingredients. The normative chromatographic profile set by ISO/FDIS 4730:2004 is given in Table 1.

Ref.: 7, 8

Table 1: Chromatographic profile of Tea Tree Oil according to ISO/FDIS 4730:2004

Component	**Minimum (%)**	**Maximum (%)**
α-Pinene	1	6
Sabinene	trace	3.5
α-Terpinene	5	13
Limonene	0.5	1.5
p-Cymene	0.5	8
1,8-Cineole (eucalyptol)	trace	15
γ-Terpinene	10	28
Terpinolene	1.5	5
Terpinen-4-ol	30	48
α-Terpineol	1.5	8
Aromadendrene	trace	3
Ledene (syn. viridoflorene)	trace	3
δ-Cadinene	trace	3
Globulol	trace	1
Viridiflorol	trace	1

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-cymene increases up to tenfold. Oxidation processes lead to the formation of peroxides, endoperoxides and epoxides. The main hydrolytic and oxidative degradation pathways are shown in Figure 1 (taken from Ref. 3).

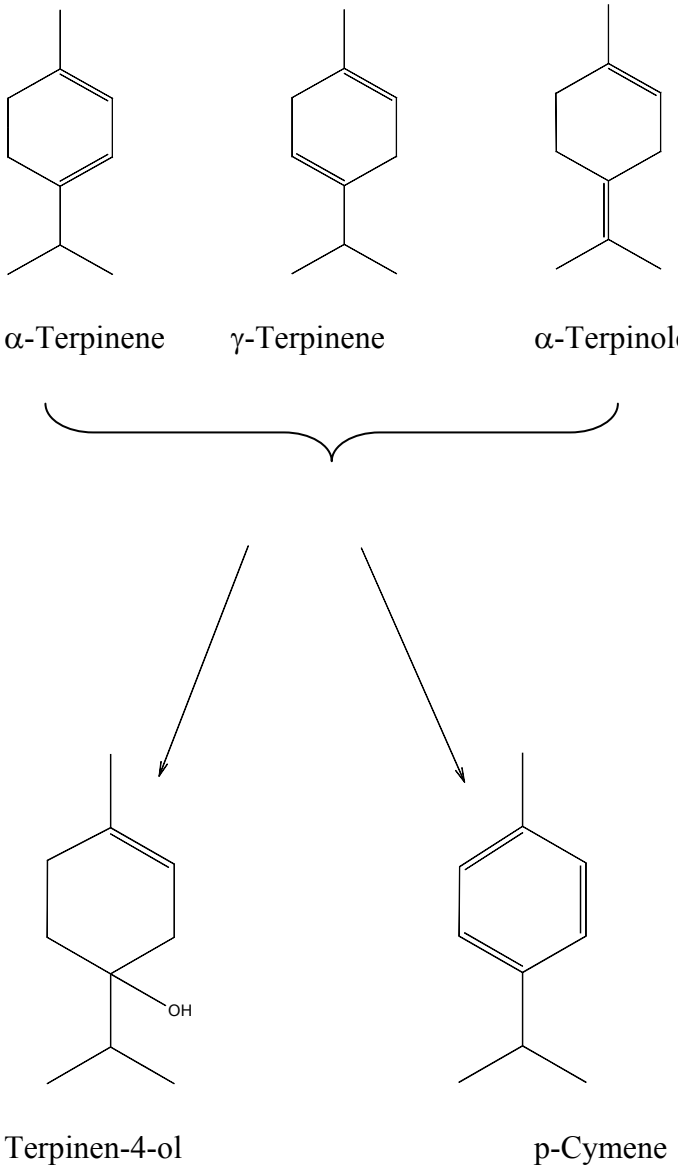


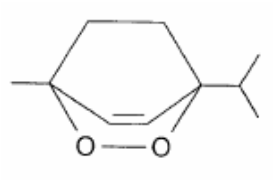
Figure 1: End products of hydrolysis and oxidation of Tea Tree Oil constituents

In Tea Tree Oil stored for 9 months under sunlight the formation of the endoperoxide ascaridole was proven using a GC-MS analytical procedure.

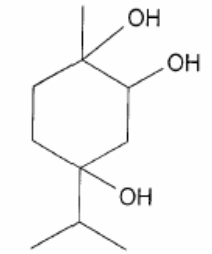
Ref.: 9

As a further oxidation product 1,2,4-trihydroxymenthane was identified.

Ref.: 10



ascaridole



1,2,4-trihydroxymenthane

3.1.1.1.	Primary name and/or INCI name

Melaleuca alternifolia oil (INCI)

3.1.1.2.	Chemical names

Not applicable

3.1.1.3.	Trade names and abbreviations

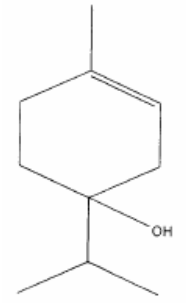
/

3.1.1.4.	CAS / EINECS number

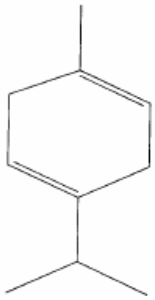
CAS no.: 85085-48-9
EINECS no.: 285-377-1

3.1.1.5.	Structural formula

main constituents:



Terpinen-4-ol (41 %)



γ-Terpinene (19 %)

3.1.1.6.	Empirical formula

not applicable

3.1.2. Physical form

Colourless to pale liquid

3.1.3. Molecular weight

Not applicable

3.1.4. Purity, composition and substance codes

See point 3.1.1.

3.1.5. Impurities / accompanying contaminants

See point 3.1.1.

3.1.6. Solubility

Insoluble in water, miscible with ethanol 85% (v/v)

3.1.7. Partition coefficient (Log P_{ow})

No data submitted

3.1.8. Additional physical and chemical specifications

-	organoleptic properties	:	myristic odour
-	flash point	:	/
-	vapour pressure	:	/
-	boiling point	:	/
-	density at 20 °C	:	0.885-0.906
-	viscosity	:	/
-	pKa	:	/
-	UV absorption spectrum	:	/
-	Refractive index at 20 °C	:	1.4750-1.4820

Ref.: 8

3.2. Function and uses

Tea Tree Oil is considered 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. According to a recent review on the use of plants in cosmetics Tea Tree Oil is widely employed in skin care for the treatment of sores, blisters, spots, rashes, warts, burns and acne. Its antimicrobial activity is well known.

Ref.: 1, 2, 3, 11, 12, 13, 14

Tea Tree Oil is not currently subject to any constraint for the use in cosmetic products. It is sold undiluted and highly concentrated to the public. Furthermore, the oil is used as ingredient of cosmetics, e.g. skin and body care products, toothpaste, mouthwash and in bath oils as well as in products for aromatherapy. A monograph on Tea Tree Oil as an active ingredient being used in cosmetic products was prepared in 2001 by the Norwegian delegation to the Council of Europe Committee of experts on cosmetic products. The following cosmetic usage was evaluated: up to 0.5 % in toothpaste and mouth washes, up to 2 % in creams for chapped skin, hands and nails and in deodorants, up to 3 % in bath preparations, shampoos and special detergents. The Swedish MPA has registered three Tea Tree Oil containing products as "natural medicinal products".

Ref.: 15

In Germany, 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.

The European Cosmetic Toiletry and Perfumery Association (COLIPA) in 2002 published the following recommendation:

"*COLIPA recommends that Tea Tree Oil should not be used in cosmetic products in a way that results in a concentration greater than 1 % oil being applied to the body. When formulating Tea Tree Oil in a cosmetic product, companies should consider that the sensitisation potential increases if certain constituents of the oil become oxidised. To reduce the formation of these oxidation products, manufacturers should consider the use of antioxidants and/or specific packaging to minimise exposure to light.***"**

3.3. Toxicological Evaluation

3.3.1. Acute toxicity

3.3.1.1. Acute oral toxicity

Guideline	:	/
Species/strain	:	Sprague Dawley rats
Group size	:	5 males + 5 females
Test substance	:	Tea Tree Oil in peanut oil
Batch no	:	88/375
Purity	:	/
Dose	:	0.83, 0.92, 1 ml/kg bw, once by gavage (SPF animals) 0.34, 0.43, 0.53, 0.56 0.6 ml/kg bw, once by gavage (non SPF animals)
GLP	:	/

Results SPF rats:
Animals exhibited lack of tonus in the forelimbs. The LD_{50} was calculated to be 2.6 ml (= 2.3 mg) per kg bw.

Results Non-SPF rats:
The animals showed similar symptoms. The LD_{50} was calculated to be 1.9 ml (=1.7 mg) per kg bw.

Ref.: 16

Reports on human poisoning

There are a few case reports of intoxication caused by Tea Tree Oil in humans.

A 4-year-old boy ingested a small quantity of Tea Tree Oil and became ataxic and progressed to unresponsiveness. But 24 h after admission the child had recovered.

Ref.: 17

A 17-month-old male child developed ataxia and drowsiness following ingestion of less than 10 ml Tea Tree Oil.

Ref.: 18

A 23-month-old boy became confused and was unable to walk 30 minutes after ingesting less than 10 ml of a commercial product containing 100 % melaleuca oil. 5 h following ingestion the child was asymptomatic.

Ref.: 19

A man aged 60 swallowed about half a teaspoonful of Tea Tree Oil and had a dramatic rash accompanied by leukocytosis.

Ref.: 20

One person 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.

Ref.: 21

Pursuant to § 16 Chemicals Act the predecessor of the German Federal Institute for Risk Assessment (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.

Ref.: 22

3.3.1.2.	Acute dermal toxicity

Guideline	:	OECD 402
Species/strain	:	Albino rabbits (NZ whites)
Group size	:	5 males + 5 females
Test substance	:	Tea Tree Oil
Batch no	:	88/375
Purity	:	/

Dose	:	2000 mg/kg bw, once for 24 h
GLP	:	not in compliance

Results
The animals were observed for 14 d. With the exception of slight diarrhoea (1 animal) the animals exhibited no signs of toxicity.

Ref.: 23

3.3.1.3.	Acute inhalation toxicity

No data submitted

3.3.2.	Irritation and corrosivity

3.3.2.1.	Skin irritation

Guideline	:	/
Species/strain	:	Albino rabbits (NZ whites)
Group size	:	6
Test substance	:	Tea Tree Oil
Batch No.	:	88/375
Purity	:	/
Dose	:	0.5 ml
GLP	:	not in compliance

The Draize irritation index was found to be 5.0, indicating a severe irritant.

Ref.: 24

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. For Tea Tree Oil the Draize Index for skin irritation in rabbits was determined at 5.0.

Ref.: cited in 25

Human study

Tea Tree Oil has been investigated for skin irritancy using an occlusive patch test on 25 human subjects for 21 days and compared with 1,8-cineole in concentrations of 0 %, 3.8 %, 8 %, 12 %, 16 %, 19.9 %, 24 %, and 28.1 % in soft white paraffin. 8 Tea Tree Oil preparations containing similar 1,8-cineole concentrations (from 1.5 % to 28.8 %) and the 1,8-cineole-treated groups did not show skin irritation. 3 of 28 panellists exhibited an allergic response. They were further tested (see 4.3).

Ref.: 26

3.3.2.2.	Mucous membrane irritation

Hen's egg test on the chorio-allantoic membrane (HET-CAM assay)

Guideline : /
Species/strain : fertilised fresh chicken eggs (white leghorn)
Group size : substance treated 6, controls 2
Test substance : Tea Tree Oil several oral products (see Table)
Batch number : 6081 and 871
Purity : pharmaceutical grade
Dose : 0.1 g / egg, controls: 300 µl / egg.
GLP : In compliance

Results

Substance	Mean irritation index	Evaluation
Negative control (0.9% NaCl solution)	0.0	non-irritant
Tea Tree Oil batch no. 6081	16.1	severe
Tea Tree powder	0.0	non-irritant
Tea Tree ground leaf	0.0	non-irritant
water-soluble Tea Tree Oil	14.7	severe
Placebo (0 % Tea Tree Oil) 10 % surfactant	10.3	severe
25 % Tea Tree Oil 5 % surfactant	9.8	severe
5 % Tea Tree Oil 8 % surfactant	4.5	slight
10 % Tea Tree Oil 10 % surfactant	12.1	severe
Positive control (0.1 N NaOH)	19.3	severe
Positive control (1 % SDS)	11.3	severe

Neat Tea Tree Oil and 25 and 10 % solutions in surfactant as well as 10 % surfactant are severe irritants in the assay while 5 % is only slightly effective. Tea Tree powder and ground leaf are non-irritant.

Comment
The description of the analysed substances is poor. The identity of the used surfactant is not indicated and the reasoning of the used dilutions is not clear. Historical control data on the range of response to positive control agents are included. The HET-CAM assay has been extensively used and is showing promise as a potential alternative assay for eye irritation. However, it has not yet been validated.

Ref.: 27

3.3.3.	Skin sensitisation

Human studies

The method was based on the skin sensitisation study of Draize 1965. 6 Tea Tree Oil products were investigated which consisted of 100 % Tea Tree Oil and 25 % and 5 % Tea Tree Oil in cream, ointment or gel formulation. Cream base was used as negative control. 151 adult male and female panellists were selected. They gave their consent in conformance with the Declaration of Helsinki. On day 1, 100 µl of the respective product was placed in Finn chambers onto the upper arm or the back. After 48 h the chambers were removed and the skin was assessed. If needed, the volunteers returned 48 h later for a further assessment. Skin reaction was assessed on a 5-graded scale. The test products were applied to the skin 9 times over a 3 week period and any response for irritancy was recorded (induction). After a 2 week rest phase the products were applied on a new site (challenge). 2 days later and - if necessary - again after 4 days the skin reaction was assessed. Any doubtful results were repeated 2 weeks later.

Results
Irritancy: 148 of 151 panellists were evaluated. The average daily score for irritancy was 0.1922 for the neat Tea Tree Oil. The other samples showed scores from 0.0000 to 0.0060.
Sensitization: 150 of 151 panellists were evaluated. 3 out of 150 (2 %) became sensitized to Tea Tree Oil.

In a second follow-up trial the number of panellists was increased to a joint number of 306 (irritancy) and 308 (sensitization). The second study confirmed the results of the first one but no details were presented.

Ref.: 28

3 of 28 panellists of a skin irritancy study exhibited an allergic response to Tea Tree Oil. They were further tested for allergic responses with major constituents of Tea Tree Oil. 3 positive reactions were seen against a sesquiterpenoid hydrocarbon fraction and 1 against α-terpinene

Ref.: 26

1216 patients were patch tested in a Swiss dermatology clinic. 7 cases showed an allergic contact dermatitis due to Tea Tree Oil while 2 of them also exhibited a type IV hypersensitivity towards fragrance-mix or colophony.

Ref.: 29

A case of positive patch testing with 1 % Tea Tree Oil solution was reported on a 74-year-old man with a history of blistering dermatitis who had treated warts with Tea Tree Oil as wart paint.

Ref.: 30

An immediate systemic hypersensitivity reaction of a 38-year-old man associated with topical application of Tea Tree Oil was observed. The patient had placed a drop of Tea Tree Oil on his finger and had applied this to psoriatic lesions on his leg.

Ref.: 31

A case of an allergic contact dermatitis to Tea Tree Oil with erythema multiforme-like ‘id’ reaction was reported.

Ref.: 32

A further case report of a contact allergy to Tea Tree Oil and cross-sensitization to colophony origins from Norway.

Ref.: 33

In Wales a combined contact allergy to Tea Tree Oil and lavender oil complicating chronic vulvovaginitis was observed.

Ref.: 34

A case of contact dermatitis (face eczema) to Tea Tree Oil was reported which was explained by the use of Tea Tree Oil against pimples. The epicutaneous testing of the patient revealed positive reactions to α-terpinene, terpinolene and ascaridole.

Ref.: 35

7 patients were seen in a dermatology clinic during a 3-year period reactive to a 1 % solution of melaleuca oil. 6 of them also reacted to limonene, 5 to α-terpinene and aromadendrene, 2 to terpinen-4-ol and 1 to p-cymene and α-phellandrene.

Ref.: 36

Recently, contact dermatitis was observed with a 12-year-old boy who had applied Tea Tree Oil on his face to treat a minimal skin infection.

Ref.: 37

The case reports in the literature were summarized and the potentially causative substances were discussed.

Ref.: 25, 38

In a Danish dermatology clinic from 2001-2002 (1. study) and in 2003 (2. study) 217 and 160 consecutive patients were patch tested with the European standard series and in addition with 10 % Tea Tree Oil in petrolatum (study 1) and commercial lotions containing 5 % Tea Tree Oil (study 1 and 2). In the 1st study only 1 person with a relevant positive patch test to 5 % and 10 % neat Tree Oil. In the 2nd study no allergic but 3.1 % (5/160) irritant reactions were seen.

Ref.: 39

In an Italian study of 725 consecutive patients were patch tested with undiluted, 5 %, 1 % and 0.1 % Tea Tree Oil in petrolatum. While in 5.9 % of the patient positive reactions were observed to undiluted Tea Tree Oil only 1 patient was positive with the 1 % dilution, none with 0.1 %.

Ref.: 40

An increase in sensitization to oil of turpentine between 1992 and 1997 was found in a multicenter study on 45,005 patients from the German-Austrian information network of departments of dermatology (IVDK). Oil of turpentine is a mixture of terpenes including α-pinene, carenes and β-pinene. While between 1992 and 1995 the prevalence rate was as low as 0.5 % in the years 1996 and 1997 a dramatic increase was observed showing a sensitization rate of 4.8 %. It was hypothesized that the increase in the use of Tea Tree Oil may be responsible due to cross-reaction with turpentine.

Ref.: 41

In a parallel guinea-pig and human study freshly distilled as well as oxidised Tea Tree Oil and some fractions were analysed and compared as to their sensitizing properties. Photo-oxidation of Tea Tree Oil was demonstrated by an increase of the p-cymene content (2.0 % to 11.5 %) accompanied by a decrease in the content of α-terpinene (11.2 % to 5.0 %), γ-terpinene and terpinolene. Simultaneously, the peroxide number increased from < 50 ppm to > 500 ppm.
All Tea Tree Oil-sensitive 11 patients reacted also positively to terpinolene, 9/11 to ascaridole and 7/11 to α-terpinene. Experimental sensitization in guinea pigs showed a low sensitizing capacity for fresh Tea Tree Oil while photo-oxidised oil was revealed to be 3 times stronger sensitizing. Also the monoterpene fraction obtained by fractional distillation elicited a positive response as well as p-cymene.

Ref.: 42

1,2,4-Trihydroxymenthane was shown to be an oxidation product of Tea Tree Oil formed from terpinen-4-ol. By epicutaneous patch testing of 15 patients sensitive to Tea Tree Oil 11 of them reacted positively to 1,2,4-trihydroxymenthane.

Ref.: 10

3 out of 28 normal healthy volunteers tested strongly positive to patch testing with Tea Tree Oil. All 3 reacted positive to a sesquiterpenoid fraction of the oil, 1 of them to α-terpinene.

Ref.: 43

In the draft monograph submitted to the Council of Europe by the Norwegian delegation data of the Swedish MPA (Medicinal Products Agency) on adverse effects induced by Tea Tree Oil in Sweden was mentioned. The reports concerned mainly contact dermatitis and eczema (27 out of 33 cases). Only products having a concentration of 2 % or more seem to cause skin reactions.

Ref.: 15

In a multicenter study with 11 dermatological departments in Austria and Germany 36 out of 3375 patients (1.1 %) reacted positive to a 5 % solution of Tea Tree Oil in diethylphthalate. Great regional differences in frequencies were found (0 to 2.3 %). 10 of 10 positively tested persons also reacted positive to terpinolene, ascaridole and α-terpinene, 9 of 10 to 1,2,4-trihydroxymenthane. 14 of these 36 persons (38.9 %) also showed a positive response to oil of turpentine.

Ref.: 44

In a recent review on cutaneous effects of Tea Tree Oil prevalence rates for allergic contact dermatitis reactions were cited. In an Australian study conducted with 219 volunteers 2.9 to 4.8 % reacted positively when patch-tested with Tea Tree Oil dilutions. Within the subjects with previous exposure to Tea Tree Oil the rate rose to 4.3 to 7.2 %. The same authors report on personal communications related to a study of the North American Contact Dermatitis Group. 0.5 % of patients reacted to oxidized Tea Tree Oil (5 % in petrolatum) on patch testing.

Ref.: 45

Allergic skin reactions related to oral intake of Tea Tree Oil have also been documented. After initial external treatment of an atopic dermatitis with undiluted Tea Tree Oil a man ingested the oil. This resulted in obvious exacerbation of the dermatitis.

Ref.: 46

A case of Tea Tree Oil dermatitis associated with linear IgA disease was described. The patient had applied Tea Tree Oil to her recently pierced umbilicus.

Ref.: 47

An airborne allergic contact dermatitis was observed following inhalation of the vapors of a hot aqueous solution of Tea Tree Oil.

Ref.: 48

3.3.4. Dermal / percutaneous absorption

No data submitted

3.3.5. Repeated dose toxicity

3.3.5.1. Repeated Dose (28 days) oral / dermal / inhalation toxicity

No data submitted

3.3.5.2. Sub-chronic (90 days) oral / dermal / inhalation toxicity

No data submitted

3.3.5.3. Chronic (> 12 months) toxicity

No data submitted

3.3.6. Mutagenicity / Genotoxicity

Reverse Mutation Testing Using Bacteria

Guideline	:	/
Test substance	:	Tea Tree Oil
Batch no	:	/
Purity	:	no data
Test system	:	*Salmonella typhimurium* TA98, TA100 and TA102
Vehicle	:	DMSO
Metabolic act.	:	S9 from rat liver homogenate (Aroclor 1254-induced)
Doses	:	100, 250, 500, 100, 1500 µg per plate
Replicate	:	yes
GLP	:	/

Results
No sufficient details were reported, the study is inadequate.

Comment
Tea Tree Oil has antimicrobial properties. Therefore, the test is of limited value.

Ref.: 49

3.3.7. Carcinogenicity

No data submitted

3.3.8. Reproductive toxicity

3.3.8.1. Two generation reproduction toxicity

No data submitted

3.3.8.2. Teratogenicity

No data submitted

3.3.9. Toxicokinetics

No data submitted

3.3.10. Photo-induced toxicity

3.3.10.1. Phototoxicity / photoirritation and photosensitisation

No data submitted

3.3.10.2. Phototoxicity / photomutagenicity / photoclastogenicity

No data submitted

3.3.11. Human data

No data submitted

3.3.12. Special investigations

The *in vitro* cytotoxicity of Tea Tree Oil in cultured human epithelial and fibroblast cells was investigated and compared with three resin acid analogues. Tea Tree Oil showed a lower level of toxicity in the neutral red bioassay.

Ref.: 50

Cases of Tea Tree Oil toxicosis have been reported in dogs and cats following dermal application for therapeutic reasons. Typical signs of neurotoxicity were observed (depression, weakness, incoordination, ataxia, muscle tremors etc.).

Ref.: 51, 52

In single-blinded randomized trial the treatment with a Tea Tree Oil shampoo was found to be more effective against dandruff than a placebo shampoo.

Ref.: 53

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.

Ref.: 54

There are more publications on possible therapeutic uses and side reactions. They can be found in a recent review.

Ref.: 45

3.3.13. Safety evaluation (including calculation of the MoS)

Not applicable

3.3.14. Discussion

At room temperature and under the influence of light and oxygen Tea Tree Oil was shown to degrade rapidly. Under these conditions the p-cymene and terpinen-4-ol contents considerably increase. In addition, oxidation processes lead to the formation of peroxides, endoperoxides and epoxides.

Acute toxicity data is 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 were observed after dermal application of up to 2 g per kg body weight. There are a few case reports of intoxication caused by Tea Tree Oil in humans.

No experimental data on percutaneous absorption were provided. But, due to the lipophilic nature of the main constituents it is assumed that they are readily absorbed through the skin. This is confirmed by systemic neurotoxic reactions following topical application.

No data on repeated dose toxicity, subchronic and chronic toxicity, carcinogenicity and reproductive toxicity are available. Only one inadequate study on genotoxicity was provided (Ames test). No conclusion can be drawn as to the mutagenicity and carcinogenicity of Tea Tree Oil. Since no data on percutaneous absorption and subchronic toxicity are available no safety evaluation can be performed.

Undiluted Tea Tree Oil is a severe irritant to the skin of rabbits while a 25 % solution is not. In a HET-CAM assay neat Tea Tree Oil as well as 25 and 10 % solutions in surfactant are severe irritants in the assay while 5 % is only slightly irritant.
Neat Tea Tree Oil is a sensitiser in humans. In a study including 9 treatments, 3 of 150 volunteers became sensitized.

The prevalence for allergic contact dermatitis exhibits regional differences. In a Swiss study 7 of 1216 (0.6 %) patch tested patients reacted positive to Tea Tree Oil. In a multicenter study with 11 dermatological departments in Austria and Germany 36 out of 3375 patients (1.1 %) reacted positive to a 5 % solution of Tea Tree Oil. It is not fully understood which of the constituents is

responsible. Terpinolene, α-terpinene, a sesquiterpenoid fraction, limonene and/or oxidative degradation products like ascaridole, 1,2,4-trihydroxymethane, peroxides and epoxides were discussed. Oxidised Tea Tree Oil is 3 times more potent than fresh oil. The sensitising potency may also be influenced by the content of irritants such as p-cymene and 1,8-cineole. Only products having a concentration of 2 % or more seem to cause skin reactions.

4. CONCLUSION

The sparse data available suggest that the use of undiluted Tea Tree Oil as a commercial product is not safe. The safety dossier of Tea Tree Oil is incomplete.
The stability of Tea Tree Oil in cosmetic formulations is questionable. A standardized method for the specification of Tea Tree Oil is needed. Industry should develop an analytical testing method based on typical degradation products to ensure and control the stability of the material.

Skin and eye irritation was not assessed by adequate methods. There are relevant data gaps with regard to subchronic toxicity, percutaneous absorption, genotoxicity/carcinogenicity and reproductive toxicity. The safe use of Tea Tree Oil as cosmetic ingredient cannot be assessed.

A complete dossier of a representative standardized material to all relevant toxicological endpoints is required by the end of 2005; an opinion based on the information available at that time will be given.

5. MINORITY OPINION

Not applicable

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