OPINION OF THE SCIENTIFIC COMMITTEE ON COSMETIC PRODUCTS AND NON-FOOD PRODUCTS INTENDED FOR CONSUMERS

CONCERNING

WOOD TARS AND WOOD TAR PREPARATIONS

adopted by the SCCNFP during the 23rd plenary meeting of
of 18 March 2003

1. Terms of Reference

1.1 Context of the question

Crude and refined coal tars are currently listed in Annex II, n° 420 of Directive 76/768/EEC on cosmetic products. The regulation of coal tars was based on the opinion of the SCC on coal tar, adopted on 3 February 1995 and on the opinions of the SCCNFP concerning refined coal tar, adopted on 20 December 1996 and concerning refined coal tars by bi-distillation, adopted on 28 June 2000.
In its opinions, the SCC/SCCNFP concluded that crude and refined coal tars contain carcinogenic polycyclic hydrocarbons and are therefore not safe for use in cosmetic products.

A member State requested the Commission to include as well wood tar and wood tar preparations in Annex II of Directive 76/768/EEC on cosmetic products.
A thorough review of the safety of wood tar is a pre-requisite for the consideration of a possible inclusion into Directive 76/768/EEC.

1.2 Request to the SCCNFP

The SCCNFP is requested to answer the following questions :

* *Are wood tar and wood tar preparations safe to be used in cosmetic products?*

* *If yes, does the SCCNFP propose any restrictions or conditions for the use of wood tar and wood tar preparations in cosmetic products?*

1.3 Statement on the toxicological evaluation

The SCCNFP is the scientific advisory body to the European Commission in matters of consumer protection with respect to cosmetics and non-food products intended for consumers.

The Commission's general policy regarding research on animals supports the development of alternative methods to replace or to reduce animal testing when possible. In this context, the SCCNFP has a specific working group on alternatives to animal testing which, in co-operation with other Commission services such as ECVAM (European Centre for Validation of Alternative Methods), evaluates these methods.

The extent to which these validated methods are applicable to cosmetic products and its ingredients is a matter of the SCCNFP.

SCCNFP opinions include evaluations of experiments using laboratory animals; such tests are conducted in accordance with all legal provisions and preferably under chemical law regulations. Only in cases where no alternative method is available will such tests be evaluated and the resulting data accepted, in order to meet the fundamental requirements of the protection of consumer health.

2. Toxicological Evaluation and Characterisation

2.1. General

2.1.1. Primary name

Wood tar, Wood creosote, Wood oil, in some cases the source of products are used in the name; e.g. pine tar, beechwood creosote, cade oils

2.1.2. Chemical names

Not applicable

2.1.3. Trade names and abbreviations

Not applicable

2.1.4. CAS no.

Not available, except: pine tar: 8011-48-1, wood creosote: 8021-39-4, tar oils: 8002-29-7, cade oils: 8013-10-3

2.1.5. Structural formula

Not applicable

2.1.6. Empirical formula

Not applicable

2.1.7. Purity, composition and substance codes

Wood tar, creosote and oils are complex mixtures. The chief constituents are volatile terpene oils, neutral oils of high boiling point, and phenol, cresols, and guaiacol. Polycyclic hydrocarbons are present in different amounts. In the table presented below the content of benzo(a)pyrene varied from 1 to 15 ppm.

Table 1. *Content of specified polycyclic aromatic hydrocarbons in the wood tars and their carcinogenic classification.*

Substance	Carcino-gen category	Rice bran tar (2) (ppm)	Rice bran tar (3) (ppm)	Pine tar (2) (ppm)	Pine tar (3) (ppm)
Anthracene		56.5		9.5	
Benz(a)anthracene	2	18.4		6.0	
Benzo(a)pyrene	2	14.8	1.3	5.3	9.7
Benzo(b)fluoranthene	2	0.5			
Benzo(k)fluoranthene	2	0.5			
Pyrene		21.6		7.1	
Chrysene	2	38.7		1.5	
Fluoranthene		10.5		4.5	
Perylene		0.7		0.3	
Phenanthrene		74.1		18.5	

Ref.: 2, 3

As noted from the table, several of the PAH's have been classified in EU as carcinogens category 2. It should also be noted that the PAH content differed in Rice bran tar and Pine tar. Moreover, the PAH content differed in two different preparations of Rice bran tar and Pin tar. The results suggest that the PAH content may vary both with the source of the tar as well as in different preparations of tar.

2.1.8. Physical properties

Genuine Pine tar 588

Subst. Code : /
Appearance : Viscous, blackish brown liquid
Melting point : /
Boiling point : /
Density : 1.05
Rel. vap. dens. : /
Vapour Press. : /
Log P_{ow} : /
Flash point : 120° C

Ref.: 4

Wood creosote

Subst. Code : /
Appearance : Almost colourless or yellowish, oily liquid
Melting point : Below -20° C
Boiling point : About 203° C
Density : Not less than 1.076
Rel. vap. dens. : /
Vapour Press. : /
Log P_{ow} : /
Flash point : 73.9° C

Ref.: 5

2.1.9. Solubility

Wood tar is soluble in ethanol and ether, slightly soluble in water.

Wood creosote is relatively soluble in water.

2.2 Function and Uses

Wood tar has been used by mariners as a preservative for wood and rigging for at least the past six centuries.

Wood creosote is extensively used as a wood preservative. It has been used as a disinfectant, in medicinal products and has been used in some cosmetic products.

TOXICOLOGICAL CHARACTERISATION

Only the carcinogenic and genotoxic potential of wood tar and its preparations have been considered in this opinion

2.3. Toxicity

Not considered, see above

2.4. Irritation & corrosivity

Not considered, see above

2.5. Sensitisation

Not considered, see above

2.6. Teratogenicity

Not considered, see above

2.7. Toxicokinetics (incl. Percutaneous Absorption)

Not considered, see above

2.8. Mutagenicity/Genotoxicity

IARC has reviewed the evidence in short-term tests for genetic activity of several of the aromatic polycyclic hydrocarbons in tar.

Ref. : 6,7

Benzo(a)pyrene is classified as a category 2 and chrysene as a category 3 mutagen in EU.

Phenol has been proposed to be classified as a category 3 mutagen in EU

Ref. : 8

2.8.1. Mutagenicity/Genotoxicity, *in vitro*

Beechwood creosote has been tested in the Ames assay using *Salmonella typhimurium* strains TA 97, TA98, TA100, TA102, TA104, TA1535, TA1537, and TA 1538, with and without metabolic activation. No mutagenic activity was found.

Ref. : 9

Pine tar resin induced a non-statistical increase of mutations in *S. typhimurium* TA100 both without and with S9, while no increase was found with TA98. No significant increase in SCE induction was observed in CHO cells after treatment with pine resin.

Ref. : 10

Evidence of covalent binding to DNA by components of coal-tar and juniper tar (cade oil) was sought in a) human skin biopsy samples from 12 psoriasis patients receiving therapy with these agents, b) human skin explants maintained in organ culture and treated topically with the tars, and c) the skin and lungs of mice treated with repeated doses of the formulations following the regimen used in the clinic. 32P-Post-labeling analysis revealed the presence of aromatic DNA adducts in the biopsy samples at levels of up to 0.4 fmol total adducts/microgram DNA. Treatment of human skin in organ culture produced similar levels of adducts, while treatment with dithranol, a non-mutagenic therapeutic agent, resulted in chromatograms indistinguishable from those from untreated controls. In mouse skin, coal-tar ointment and juniper tar gave similar DNA adduct levels, with a similar time-course of removal: maximum levels (0.5 fmol/microgram DNA) at 24 h after the final treatment declined rapidly to 0.05 fmol/microgram at 7 d, thereafter declining slowly over the succeeding 25 d. However, while coal-tar ointment produced only very low levels of adducts in mouse lung (less than 0.03 fmol/microgram DNA), juniper tar produced adducts at a high level (0.7 fmol/microgram DNA) that were persistent in this tissue. The authors point out that the results provide direct evidence for the formation of potentially carcinogenic DNA damage in human and mouse tissue by components of these therapeutic tar preparations.

Ref. : 11

Guaiacol has not induced mutations in S. *typhimurium* TA98, TA100, or TA102 neither without nor with metabolic activation.

Ref. : 12

Guaiacol has induced SCE in human lymphocytes *in vitro.*

Ref. : 13

2.8.2. Mutagenicity/genotoxicity, *in vivo*

32P-Post-labeling analysis revealed the presence of aromatic DNA adducts in the biopsy samples from psoriasis patients receiving therapy with juniper tar (see above)

Ref. : 11

General conclusion

Wood tar and wood tar preparations contain genotoxic polycyclic aromatic hydrocarbons. Moreover, phenol a constituent has been proposed to be classified as a category 3 mutagen. Beechwood creosote and pine tar resin have not been found to induce mutations in *S. typhimurium*.

Evidence of covalent binding to DNA by components of juniper tar (cade oil) was found in :

a) human skin biopsy samples from psoriasis patients receiving therapy with juniper tar;
b) human skin explants maintained in organ culture and treated topically with the tar, and
c) the skin and lungs of mice treated with repeated doses of juniper tar.

2.9. Carcinogenicity

2.9.1. Animal studies

Previously, several polycyclic aromatic hydrocarbons present in wood tar and wood tar preparations have been classified in EU as category 2 carcinogens or evaluated by IARC with the conclusion that there *is sufficient evidence* for carcinogenic effects in animals.

Ref. : 6, 7

Already back in 1920's the development of squamous cell carcinoma in 1 of 30 rabbits was observed after applying Pityrol (rice bran tar) on the ears for a period of 100 or more days.

Ref.: 14

The carcinogenicity of tar-containing skin drugs, Pityrol (rice bran tar; 145 ppm BaP), Glyteer (oil-extracted soybean tar; 129 ppm BaP), Ichthammol (sulfatation and ammoniation of distillate from mineral deposits), Pine tar (48 ppm BaP), and Metashal (18% Colorado shale oil; 80 ppm BaP) was investigated in experiments with CF1 female mice. The skin drugs were dissolved in acetone and applied to back of mice, interscapular region, 3 times a week for whole span of the experiment. The experiment was started 8-9 weeks after birth of mice and ended at death or after 630 days when the experiment was terminated. The control group consisted of 40 mice, while the exposed group consisted of 60 mice. The results are shown in table 2. It is apparent that both rice bran tar (Pityrol) and Pine tar induced not only skin papilloma, but also skin squamous carcinoma. In the case of rice bran tar a number of the skin carcinomas gave rise to metastasis.

Table 2. *Histological results of skin painting of CF1 mice with tar-containing skin drugs*

Preparation	First appearance of tumour[a] (weeks)	Effective No. of mice[b]	Skin papilloma No.	%	Skin Squamous carcinoma No.	%	Lung adenoma	Others
Pityrol	18	50	32	64[c]	18(8[d])	36[e]	2	malig. lymphoma (1) forestomac pap (7)
Glyteer	24	55	39	71	22(7)	40	4	malign. lymphoma (1) hepatoma (4) adenomatous polyp (1) forestomac pap (1)
Ichthammol	38	46	4	9	-	-	1	spindle cell sarcoma (2) hepatoma (1) malign. lymphoma (2) leukaemia (1) reticulum cell sarcoma (1)
Pine tar	33	31	7	23	2	6	2	thyroid adenoma (1) liver cell carcinoma (1)
Metashal	15	55	35	64	12(5)	22	1	malign. lymphoma (2) forestomac pap (2)
Control	-	-	-	-	-	-	1	-

a) Time interval in weeks between the initiation of the treatment and the first appearance of tumour.

b) Number of animals surviving when first tumour appeared.

c) Proportion of tumour-bearing mice to the effective number of mice.

d) Number of mice with metastasis to lung, liver, spleen, lymph nodes, etc.

The results are summarised in fig. 1 which shows skin tumour after skin painting with the different tar drugs in relation to the content of benzo(a)pyrene. The results demonstrate that the frequency of skin tumours increases nearly linearly with the concentration of benzo(a)pyrene in the tar containing drug.

Ref: 2

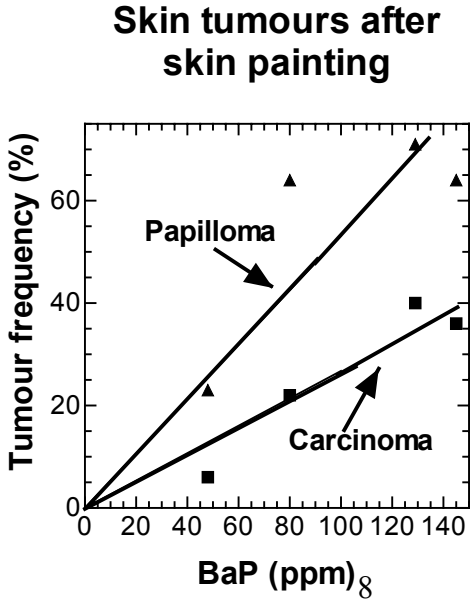

Fig 1. Tumours as a function of the BaP concentration in the skin drug

Experiments with coal tar and coal creosote are sited in the opinion on "Refined coal tar by bi-distillation." One recent experiment with two different preparations of coal creosotes containing 10 ppm and 275 ppm is also relevant for the present Opinion. In the experiment groups of 62 male mice were treated with the two creosote preparations for 78 weeks. The experiment is described in the Opinion mentioned above. Here will only two of the conclusions be repeated. "*Evaluation of the results showed an almost linear relationship between tumour rate and BaP content of the solution applied to the animals' skin. No evidence was found for the existence of a threshold dose, below which dermal exposure shows no carcinogenic effect. A most probably value of 4.9 x 10-3 tumours/(animal x µg BaP) was found for the slope of the curve which for both samples of creosote, describes the relationship between the increased number of skin tumours compared with the control, and the total amount of BaP (creosote) applied during the course of treatment. The life-time risk is obtained by multiplication with the particular life-time dose of BaP. Of particular interest is the linear course of the dose-effect relationship down to the lowest dose rates, which support the view that there is no threshold value."* and "*It is clear that two test samples of creosote, despite their different BaP contents, showed the same dose-effect relationship based on BaP. This led to the conclusion that BaP was a suitable reference substance for the risk assessment of different creosotes. The result showed that BaP alone is about 5 times less effective than as a component of one of the two creosotes. This is understandable considering that apart from BaP, creosote also contains other carcinogenic PAH such as benz(a)anthracene, benzo(b)fluoranthene, benzo(j)fluoranthene, benzo(k)fluoranthene, chrysene, dibenz(a,h)anthracene and ideno(1,2,3-cd)pyrene."*

Ref. : 1

***In vitro* morphological transformation of Syrian hamster embryo cells**

Coal tar and Beechwood creosote was tested in the Syrian hamster embryo cell transformation assay. The results are presented in Table 3.

Table 3 *In vitro morphological transformation of Syrian hamster embryo cells by coal tar and beechwood creosote*

Substance	Concentration µg/ml	Cloning efficiency	Colonies No	Transformation No	Transformation frequency (%)
Beechwood creosote	5 40	30 15	270 135	3 1	1.1 0.7
Coal tar	5 40	32 26	240 234	1 5	0.4 2.1
Control	-	36	303	0	0

The results demonstrate that beechwood creosote induces transformation of Syrian hamster embryo cells. Actually Beechwood creosote was on a weight basis more potent than coal tar. The toxic effect of beechwood is probably the reason that the frequency of transformation was higher at the low concentration than at the high concentration.

Ref : 15, 16

2.9.2. Human studies

No data are available for the wood tar and wood tar preparations.

Several studies have demonstrated tumour induction in relation to tar and creosote. However, it is clear that most of these studies involve products from coal. It is unclear whether some studies may involve wood tar or preparations from wood tar.

General conclusion

Wood tar and wood tar preparations contain genotoxic carcinogens. Wood tar preparations are demonstrated to induce both benign and malignant skin tumours in mice. The data available indicate that wood tar and wood tar preparations may induce tumours by a non-threshold mechanism.

Treatment of psoriasis patients with a wood tar preparation has induced DNA adducts in the skin.

2.10. Groups at extra risk

Not considered, see above

2.11. Safety evaluation

2.11.1. Assessment of human exposure

Not considered, see above

2.11.2. Effects of concern

Genotoxic and carcinogenic effects

Although, no mutagenic effects were found with the wood tar or wood tar preparations tested, it is known that it contains genotoxic substances. Treatment of psoriasis patients with a wood tar preparation has induced DNA adducts in the skin. In a skin painting mouse with wood tar and wood tar preparations evidence was obtained that no thresholds exists for skin tumour formation and that even very small exposure will represent a small but definite risk for tumour formation.

In a mouse skin painting experiment with coal creosotes, it was concluded that the most probable value for the tumour risk was 4.9×10^{-3} tumours/(animal x µg BaP).

Ref. : 1

2.12. Opinion

SCCNFP is of the opinion that wood tar and wood tar preparations do pose a health risk when used in cosmetic products.

Wood tar and wood tar preparations contain polycyclic aromatic hydrocarbons which are genotoxic carcinogens. Wood tar preparations have been found to induce both benign and malignant skin tumours in mouse skin and to form DNA adduct in human skin. The products may represent risk of skin cancer.

2.13. References

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