Journal of Occupational and Environmental Hygiene, 4(S1): 237–244
ISSN: 1545-9624 print / 1545-9632 online
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DOI: 10.1080/15459620701289661

Review of Skin Permeation Hazard of Bitumen Fumes

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The potential for health hazards arising from dermal exposure and possible uptake of bitumen fume or components is unclear. In 2001 the German MAK committee has assigned a "H-notation" to bitumen fumes. However, the assignment of a skin notation to bitumen fumes is under debate. The American Conference of Governmental Industrial Hygienists (ACGIH®) concluded in 1999 that assigning a skin notation was not justified. NIOSH did not develop a conclusion on this aspect in their health hazard review of bitumen fumes in 2000. The present study aimed to update and review the strength of evidence of scientific knowledge on the skin permeation hazard of bitumen fumes among workers.

Keywords bitumen fumes, skin permeation, hazards

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INTRODUCTION

Bitumen is a black or brown solid or viscous liquid that is obtained from non-destructive vacuum distillation of crude petroleum oil. With mineral aggregates bitumen forms strong cohesive mixtures. Most of the bitumen is used as a binder in asphalt for road paving and roofing. Asphalt is in most cases heated during which bitumen vapors and aerosols are released that may contain various carcinogenic compounds including polycyclic aromatic hydrocarbons (PAH). In Europe, the term "asphalt" refers to the product called asphalt mix or hot mix asphalt in North America. Both are mixtures of mineral aggregate (sized stone fractions, sands, and a filler such as fine limestone) and a binder (bitumen and, historically, tar or coal tar pitch); in North America, "asphalt" refers only to the binder.

The potential for health hazards arising from dermal exposure and possible uptake of bitumen fume or components is unclear. In 2001 the German MAK committee assigned a "H-notation" to bitumen fumes. However, the assignment of a skin notation to bitumen fumes is under debate. The ACGIH® concluded in 1999 that assigning a skin notation was not justified. NIOSH did not develop a conclusion on this aspect in their health hazard review of bitumen fumes in 2000.

The present study aims to update and review the strength of evidence of scientific knowledge on the skin permeation hazard of bitumen fumes among workers.

METHODOLOGY

For this review we followed the following procedure:

Step 1: Screening of three recent reviews for relevant publications on both skin permeation hazards and occupational dermal exposure:

> ACGIH (1999)[1]: TLV-Documentation: Asphalt (Petroleum; Bitumen) Fumes, Draft: 2/17/1999.
>
> NIOSH (2000)[2]: Hazard Review—Health Effects of Occupational Exposure to Asphalt, December 2000.
>
> MAK (2001)[4]: Bitumen (Dampf und Aerosol). 32. Lieferung, 2001.

Step 2: Search in scientific bibliographic databases to identify recent publications that were not covered in the three reviews. This additional search, conducted in July 2003 and updated in May 2006, retrieved the following relevant studies and reports:

- a relevant human volunteer study[5];
- five cross-sectional studies on skin exposure among road-pavers [6–11];
- a draft review of health hazards of bitumen.[12]

Step 3. Critical assessment of the data on skin permeation hazards of bitumen fume.

RESULTS

Skin Notation Assignment

The skin notation refers to the potential contribution of the cutaneous route to the overall exposure to a substance, either in contact with vapors or by direct skin contact. Since limited quantitative data on dermal absorption currently exist, different criteria exist for the assignment of a skin notation to a substance.

The German MAKcommittee assigns a skin notation to substances when compliance of the MAK value for the substance is not sufficient to protect exposed persons from

adverse effects on health, i.e., when the systemic exposure may be increased by percutaneous absorption. Substances, independently of how readily they penetrate the skin, are not designated with a skin notation if toxic effects are not to be expected under workplace conditions.[13]

ACGIH assigns a skin notation when available data indicate that the potential for absorption via the hands and forearms during the workday could be significant. ECETOC[14] recommends assigning a skin notation when the amount of a substance absorbed through skin (hands: 2000 cm^2, 1 hour exposure) exceeds 10% of the inhaled dose after an 8-hour exposure at the occupational exposure limit (OEL), which is based on systemic toxic effects. The Scientific Committee Group on Occupational Exposure Limits of the European Commission[15] recommends assigning a skin notation if the total dermal absorption is 10% or more of the uptake from respiratory exposure at the 8-hour time-weighted average (TWA) OEL.

This means that only the latter two organizations use quantitative data when assigning a skin notation to compounds. (NO INDENT) ACGIH concluded in 1999 that assigning a skin notation to bitumen fume was not justified according to their criteria. In 2001 the German MAK committee in 2001 assigned a skin notation to bitumen fume based on the fact that animal studies have shown that carcinogenic substances in bitumen fume are able to permeate skin. In a recent draft report of the Dutch Expert Committee on Occupational Standards (DECOS) it is stated that although data on skin carcinogenesis are weak, it cannot ruled out that chronic exposure to bitumen fume causes skin cancer. And that this may warrant a skin notation.[12] DECOS in The Netherlands generally applies the ECETOC criteria for skin notation assignment.

Evaluation of Hazard of Dermal Exposure of Bitumen Fume

In-Vitro and Animal Studies

There is convincing evidence from in-vitro experiments and animal studies that (markers of) compounds in bitumen fume, such as PAH, may permeate skin and that DNAadducts may be formed in vivo after dermal application.[16–21]

The bioavailability of BaP in bitumen decreases with increasing viscosity.[3] The genotoxic potential in vivo after topical application of bitumen extract is relatively low in comparison with other oilproducts.[20]

There are indications that compounds other than the known carcinogenic native PAHs, e.g., methylated PAH or thiopenes contribute to the genotoxicity[22,23] and/or carcinogenicity of bitumen fumes.[24,25]

Experiments with coal tar on blood-perfused pig ear skin[26] show that when pyrene is used as marker compound the percutaneous absorption of PAH with a higher molecular weight (e.g., benzo(a)pyrene is overestimated 7–100 times).

The animal carcinogenicity data (skin tumors) are in dispute due to the method of laboratory generation of asphalt fume condensate. ACGIH considers the available data from animal studies as inconsistent and inconclusive.[1] DECOS concludes in their draft report of July 2005 that animal data are too limited to conclude whether bitumen fume exposure will result in lung and skin cancer.[12] Based on these animals studies, however, NIOSH concludes that there is "sufficient evidence" that roofing asphalt fume is a potential occupational carcinogen.[2] Based on animal studies the German MAK concludes that a classification of bitumen fume as category2 carcinogen is justified.[4]

In a recent review on benzo(a)pyrene and PAH from coal-derived sources, DECOS concludes that PAH mainly act as local carcinogens. This means that PAH induce tumors at the site of contact. DECOS states that there are no data published suggesting that inhalation or dermal exposure to single PAH of PAHmixtures may lead to cancer at other sites than the lungs and skin, respectively.[27] This suggests that for risk assessment it is necessary to establish route-specific cancer potency estimates for PAHs. Recently, Knafla et al. have reported the development of a cancer slope factor for dermal exposure to benzo(a)pyrene based on experiments in mice. They also identified dermal potency equivalence factor values for other carcinogenic PAH.[28]

Biological Effects in Exposed Workers

Several research groups studied genotoxic effects in workers exposed to bitumen fume. Elevated PAH-albumin adducts,[29] DNAadducts in white blood cells,[30,31] DNA strand breaks and cross-links,[31] were reported in roofers. However in each of these studies the roofers might have been exposed to coal-tar products during roofing repair.

In workers that were exposed to bitumen "fume and probably not to coal tar, Toraason[32] reported "slightly elevated" DNA-strand breaks in roofers, but no oxidative DNAdamage or lipid peroxidation. Hatjian[33] reported elevated SCE frequencies, although within the range of normal human values, in roofers and road pavers. Järvholm[34] did not detect an increase of SCE frequencies and micronuclei in peripheral lymphocytes of road pavers. Zhou[35] reported no, or only marginal, effects of bitumen exposure in road pavers on the formation of DNAadducts in exfoliated urothelial cells.

Epidemiological Studies

Partanen and Boffetta[36] reviewed 20 epidemiological studies from various countries investigating the cancer risk in asphalt workers and roofers. They calculated the aggregated relative risk (RR) for different cancers, including skin cancer. The aggregated relative risk for non-melanoma skin cancer in roofers was 4.0 (95% CI: 0.8–12.0). In road pavers and highway maintenance workers a relative risk for skin cancer of 2.2. (95% CI: 1.2–3.7) was calculated. However, the authors conclude that it is difficult to associate the elevated cancer risks with bitumen because of confounding co-exposure to coal tar and solar radiation.

ACGIH,[1] NIOSH,[2] MAK,[4] and DECOS[12] consider the available epidemiological data as insufficient to draw conclusions on the carcinogenicity of bitumen fume in humans.

There are questions concerning confounding exposures (e.g., tobacco, coal tar and asbestos) with all of the reviewed epidemiological studies.

The results from the more recent IARC epidemiological study of cancer risk among European asphalt workers, which were not available at the time of the reviews of ACGIH, NIOSH, and MAK, suggest that there is a statistically significant increase in lung cancer mortality when workers exposed to bitumen fume are compared with the national population. This was only evident with increasing average exposure to bitumen fume, but not in the case of increasing duration or cumulative exposure. However, confounding exposure to other agents within the asphalt industry, exposure to carcinogens in other industries, and from tobacco smoking and other life style factors cannot be ruled out. The results for cancer of the head and neck were similar to those of lung cancer although most dose-response analyses were not statistically significant. There was no suggestion of an association between bitumen exposure and any other neoplasm, including skin cancer.[37]

Volunteer Studies

A study by Knecht et al.[5] with volunteers exposed to bitumen fumes in an exposure chamber (with and without breathing masks) indicates that dermal absorption of PAH-markers like pyrene, chrysene and phenantrene contribute substantially to the internal dose of PAHs. They estimate that approximately 50% of the total internal dose is absorbed through skin. However, there are some drawbacks in the study design such as the low number of controls (n = 2) and the efficiency of the breathing masks used in the experiments was not reported. Furthermore, no data are presented to quantify the internal dose and allow comparison with exposure to PAHs in other industry sectors.

By wearing only shorts, bitumen fume was deposited on a very large skin surface area. This experiment probably overestimates the absorption of dermally deposited bitumen fume in workers. On the other hand there was no direct skin contact with contaminated surfaces as is common among exposed workers.

Skin Contamination Among Bitumen Exposed Workers

Different techniques are applied to estimate the contamination on skin of bitumen-exposed workers: exposure pads (made from polypropylene, cotton, or paper), skin wipes and hand wash methods. There are no standardized and validated methods for skin contamination measurements.[38]

Exposure pads only estimate the dermal contamination and provide no indication of the rate of dermal flux (in ng/m^3/hour). Skin wipes and hand-wash techniques only measure the remaining PAH contamination on skin. Data on the adsorption properties of the material of the exposure pad (mostly polypropylene filter) in comparison to the adsorption of bitumen fume to natural skin are limited. Also, the removal efficiency of skin wipes and handwashing techniques has not been well studied.

Skin contamination measurements by Zhou,[35] McClean,[7] and Väänänen[10] among road pavers exposed to bitumen fume, indicate that the average amount of pyrene on wrist and hands after a working day ranges between 0.1 and 20 ng/cm^2 per working day. The amount of benzo(a)pyrene on the wrist is often non detectable and <2.5 ng/cm^2. McClean reports that of the 59 wrist samples 48% were below detection limit for pyrene (2.6 ng/cm^2) and 88% were below the limit of detection for benzo(a)pyrene = 0.6 ng/cm^2). The PAH contamination on the wrists depends on paving job function and, according to McClean,[7] the used amount of recycled asphalt product. Väänänen[10] reports statistically significant higher PAH skin contamination during remixing (hot recycling at the paving site) than during non recycled asphalt paving. The application of coal fly ash as filler had no statistical significant effect on workers' dermal PAH exposure.

Väänänen[10] compared two techniques for the measurement of PAH contamination on skin: exposure pad on the wrist and a hand washing method (using sunflower oil and wiping with Kleenex tissues). The PAH contamination measured with these two methods were equivalent and showed a strong correlation ($r = 0{,}76$, $P < 0.001$, $n = 23$).

According to Sciarra et al.,[6] the total skin contamination of 19-PAH varies between 14 and 360 μg/day (is equivalent with 0.8–20 ng/cm^2 skin). These estimates are based on analyses of PAH contamination on polypropylene pads applied on 9 skin sites and in hand wash samples. The authors do not indicate how the total skin contamination was calculated and how they dealt with pads where levels were non detectable. The estimated amount of daily inhaled 19-PAH varied between 1 and 21 μg/day.

Cirla et al.[9] report a median dermal dose rate of PAH of 2905 ng/h in asphalt workers (n = 88). The median dermal dose rate of pyrene was 239 ng/h (this is equivalent with app. 0,1 ng/cm^2 per working day). Benzo(a)pyrene on the skin pads was below the limit of detection (0,02 ng/sample). The skin contamination among road construction workers (not exposed to bitumen fume) is approximately 2–3 times lower (n = 28). These estimates are based on skin contamination measurements of 16-EPA PAH on polypropylene pads pasted on 6 skin sites. Cirla et al. did not find important differences in contamination of the different body regions. The estimated median inhalatory PAH dose rate of asphalt workers was 897 ng/h (assuming inhalation of 30 L/min).

Internal Dose Measurements

Several studies report that the level of urinary 1-hydroxypyrene in exposed road pavers or roofers exposed to bitumen fume (and not coal-tar pitch) may increase approximately two-fold compared to controls[6,9,11,34,35] The level of urinary 1-hydroxypyrene in workers exposed to petroleum-derived products are generally 1- to 5-fold elevated in comparison to non exposed workers. Workers exposed to coal tar derived products, e.g., in coke ovens, primary aluminum industry, tar distillation and creosote impregnation, show

TABLE I. Overview of Studies with an Estimation of the Uptake of PAH due to Dermal Exposure to Bitumen Fume

Reference	Job/function	Marker compound	Estimated contribution of dermal exposure to total internal dose	Comments	Relevance for assessment of dermal uptake
Zhou, 1997[35]	Road pavers	Pyrene	50–62%	Based on calculation of the average dietary pyrene intake and inhalation in relation to average 1-hydroxypyrene excretion	Very low
Rinehart, 2000[38]	Roofers	4- and more ring PAH	Multiple regression with presented model indicates that: a 2-fold increase in dermal PAH (on wrist) results in a 1.4-fold increase in post-shift 1-hydroxypyrene. A 2-fold increase in BSF air concentrations results in a 1.25-fold increase.	Based on a mixed model multiple linear regression analysis. All roofers were exposed to dust from old roofs (coal-tar). The model is based on multiple consecutive post shift 1-hydroxypyrene samples from a limited number of workers (so the observations are not independent). Interaction between air concentration and skin contamination is not studied in the model.	Low
Knecht, 2001[5]	12 Human volunteers in exposure chamber	Pyrene, phenantrene and chrysene	About 50% of the total internal dose was caused by dermal exposure	Only 2 of the volunteers were both dermally and inhalatory exposed to bitumen fume. The protection factor of the breathing masks used in the experiments was not given. It is questioned whether the applied fume generation method results in bitumen fume that is comparable with the workplace. The volunteers were exposed to high levels of fume, over the full body surface so may overestimate the dermal absorption under normal working conditions.	Medium/High
Sciarra et al., 2002[6]	Asphalt mixing workers and pavers	Pyrene	10 times higher than inhalation	The draft publication did not explain how the analysis of data was done to draw the conclusion that the external skin contamination was a more important route.	Low

McClean, 2004[8]	Road pavers (n = 20) and millers (n = 6)	Pyrene	Based on "distributed lag models" the authors conclude that dermal exposure during the preceding 32 h had a statistically significant effect on urinary 1-OH-pyrene, while the effect of inhalation exposure was not significant. The "impact" of dermal exposure on urinary 1-OH-pyrene is approximately 8 times that of inhalation exposure.	Skin contamination estimates are based on wrist-patches only. The researches only sampled 70 wrist patches of the intended total number of 156 samples (each worker 2 wrist-patches per day during 3 days). Of these 70 samples, 31 samples were below the detection limit of pyrene. In the applied model the effect of smoking appeared statistically non significant (P = 0,09). It remains unclear whether the reported 'impact of dermal exposure' indeed means that the dermal absorbed amount of pyrene substantially adds to the total internal dose.	Medium
Cirla, 2005[9]	Asphalt workers (88), ground construction operators (28)	16 EPA-PAH	The cutaneous dose rate is about threefold higher than the inhalatory dose rate. Based on in-vitro toxicokinetic information the authors estimate, however, that the dermal absorption of PAH is lower in comparison to the inhalatory absorption.	Skin contamination measurements reveal no differences between different body regions. The number of PAH-analyses that were under the detection limit is not given. A clear description of the calculations of the absorbed amounts of the 16 PAH through either skin or inhalation, is not presented. The calculations are based on in-vitro toxicokinetic parameters of PAHs. A comparison of the estimated uptake of pyrene through skin and via the lung with urinary 1-hydroxypyrene levels is not presented.	Unclear

1-hyfroxypyrene levels that are approximately 10 to 100 fold higher than in non-exposed controls.

Estimations of the Uptake Due to Dermal Exposure of Bitumen Fume

The studies, in which the relative contribution of dermal exposure to the internal dose of bitumen-exposed workers was estimated, are listed in the Table I. Comments are added. There are, as yet, little data available on the quantitative aspects of dermal absorption.

Several workplace studies report correlations between skin contamination and internal dose markers among road pavers or roofers.[6,7,10,35,39] A correlation between skin contamination and an internal dose marker does not necessarily mean that dermal exposure substantially adds to the internal dose. A strong correlation between skin contamination and air concentration might hamper conclusions on the relevance of either the inhalation or the dermal route of exposure. That skin contamination and air concentrations are no independent determinants of bitumen exposure is shown by Väänänen et al.[10] They report that skin contamination of phenanthrene and pyrene correlate statistically significant with both air and urinary metabolite concentrations.

CONCLUSIONS

1. Animal experiments show that compounds in bitumen may permeate the skin and can cause genotoxic effects in the skin and other tissues.
2. Genotoxic effects are not clearly confirmed in workers exposed dermally to bitumen fume, due to concomitant exposure to coal-tar products and/or limitations in study design.
3. Animal data on skin carcinogenesis indicate that chronic exposure to bitumen fume may cause skin cancer. However, available epidemiological data reveal no conclusive evidence of an association between bitumen exposure and skin cancer in workers.
4. Five studies report a two-fold increase of urinary 1-hydroxypyrene in post-shift urine of workers exposed to bitumen fume. The 1-hydroxypyrene levels in workers exposed to bitumen fume are generally low compared to other industries with PAH exposures.
5. An exposure chamber study with volunteers wearing only shorts shows that about 50% of the uptake of 3-4 ring PAH from bitumen fume may have been absorbed through skin. This study underlines the potential for dermal uptake of bitumen fume components.
6. Recent cross-sectional field studies do not present conclusive data that confirm the relative significance of skin absorption of pyrene in bitumen fume exposed workers.
7. Experiments with coal tar on blood-perfused pig ear skin show that pyrene as a marker compound may strongly overestimate the dermal absorption of PAH with a higher molecular weight, such as benzo(a)pyrene (1 to 2 orders of magnitude).
8. In risk assessment of PAH exposure, it is generally accepted that PAH act mainly as local carcinogens and primarily induce tumors at the site of contact.

DISCUSSION

Gaps in Knowledge

As long as there is no international consensus on criteria for the assignment of a skin notation to substances, the debate on assigning a skin notation to bitumen fume will continue.

Urinary 1-hydroxypyrene is a sound marker of the body burden of PAH, however, it is not clear how the exposure expressed as urinary 1-hydroxypyrene is related to genotoxic responses in bitumen fume exposed workers.

The methods for the determination of the actual dose rate due to dermal exposure of workers are not yet validated. Aspects such as (i) transfer rate to the pseudo skin pads or patches compared to real skin transfer are not known, (ii) the estimation of the total body dose is not standardized, (iii) data on permeation coefficients of carcinogenic compounds through human and animal skin are limited, (iv) the effect of the matrix (fume, fume condensate, etc.) and the effect of diesel fuel or other solvents used for washing, on the absorption process are not yet understood, and (v) it is not known which part of the 8-hour contamination on workers skin becomes available in target tissues.

Adequate quantitative data of the dermal uptake of bitumen fume among exposed workers, relative to the inhalatory dose, are still lacking.

A route specific cancer potency estimate for dermal exposure to bitumen fume is not yet available.

RECOMMENDATIONS

Although there is currently no evidence that occupational exposure to bitumen fume, either via inhalation or absorbed through the skin, causes systemic toxicity, it appears prudent, in view of the presence of genotoxic components in bitumen fume, to limit both exposure routes via observance of good occupational hygiene practices. Whereas in the past this has already been identified for inhalation exposure, the data reviewed in this report suggest that further attention should be given to dermal protection. It is noted that measures directed towards reduction of ambient fume levels will contribute to limitation of dermal exposure.

Any newly developed skin protection programs for exposed workers should be thoroughly tested, preferentially in intervention studies of exposed workers with a crossover study design and with attention to skin of different body regions.

To enable a better assessment of the relative importance of dermal versus inhalation exposure, further quantitative data on uptake of bitumen fume via the skin would be needed. This would require well-designed field studies with small groups of exposed workers either (i) solely skin exposed or (ii) solely with inhalation and (iii) a group with both dermal and

inhalatory exposure. The body dose would need to be assessed with different biomarkers of exposure.

Quantitative data on dermal uptake of bitumen fume among exposed workers, relative to the inhalatory dose will enable a health risk assessment, but only if route specific cancer potency estimates for bitumen fume are established.

ACKNOWLEDGMENTS

This study is financially supported by EUROBITUME, Brussels. The authors acknowledge members of CONCAWE's Toxicology subgroup for their assistance and critical review of draft reports.

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