https://doi.org/10.3176/oil.1992.2.11

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CARCINOGENICITY OF OIL SHALE PROCESSING PRODUCTS

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КАНЦЕРОГЕННОСТЬ ПРОДУКТОВ ПЕРЕРАБОТКИ ГОРЮЧИХ СЛАНЦЕВ

The possibility that oil shale derived products can be the cause of malignant tumours in humans has been attentively considered ever since the report of the carcinogenic action of Scottish shale oils was published in 1922 [1] and the skin cancer cases in workers were observed. Historical surveys of studies on carcinogenicity of oil shale processing products have been published repeatedly [2—4]. Results of experiments in laboratory animals elucidating the carcinogenic action of various materials derived from the Estonian (Baltic) oil shale kukersite have been shortly reviewed [5] and analyzed more in detail by a special Working Group of international experts [4] in 1984. Discussions and decisions of this Working Group based on the critical examination of existing scientific publications on the subject can be considered as a turning-point in the studies on the biological effects of oil shale derived products. According to internationally accepted criteria used by the experts the following statement of evaluation was made [4]:

"There is *sufficient evidence* for the carcinogenicity in experimental animals of high-temperature crude shale oils, low temperature crude shale oils, fractions of high-temperature shale oil, crude shale oil distillation fractions, shale oil bitumens and commercial blends of shale oils.

There is *limited evidence* for the carcinogenicity in experimental animals of raw oil shale, spent oil shale and a residue of shale oil distillation.

There is *sufficient evidence* that shale oils are carcinogenic to humans."

Some comments can be made to these evaluations. As to the experimental data unanimous judgement was not difficile to reach as most experiments had been conducted with the Estonian oil shale products during a period of over 30 years using standard methods [3, 5]. The evaluation of limited evidence of carcinogenicity was assented to a residue of shale oil distillation. This definition adopted by the Working Group means that available experimental data suggest a carcinogenic effect but they are limited because — a) the studies involve a single species, strain or experiment, b) the experiments were inadequate (dosage levels, duration of experiment, too few animals or poor survival etc.), c) the produced neoplasms often occur spontaneously and in the past have been difficult to classify them as malignant by histological criteria alone. In fact in experiments according to which this evaluation was made [6] a distillation residue also called shale oil coke was tested as a 15 % (w/v) benzene solution containing 9.2 μg/ml (9.2 ppm) benzo(a)-pyrene (BP). Skin application experiments in mice showed a clear carcinogenicity — 48 mice out of 50 animals developed skin tumours among them 44 mice had malignant neoplasms. The fact that the same coke

as a suspension in physiological saline in doses of 3 and 0.5 mg weekly for 15 and 30 weeks did not induce lung tumours in hamsters after intratracheal instillation was considered as decisive for the evaluation as positive results were obtained in only one animal species. It is not excluded that if another application method or vehicle or animal species would have been used sufficient evidence of carcinogenicity could have resulted.

The most important conclusion reached by the Working Group concerns carcinogenicity of shale oils for humans. This evaluation was made on the basis of numerous statistical data and observations in Great Britain where shale oils were produced and widely used. In Estonia, an epidemiological study [7] was carried out in which significantly elevated rates of skin cancer were found in a cohort of 2003 shale oil workers but cancers at other sites were not of elevated rate. A study from the USA reported an excess of total and colon cancer but only in maintenance and miscellaneous workers of oil shale enterprises, not in miners or retortmen. Commenting these data it should be mentioned, as indicated earlier [8], that most of the lubricating oils used in Great Britain and related to the cases of "mule-spinners" cancer and scrotal cancer, contained Scottish shale oils, but usually the workers were exposed to used oil, which contains due to pyrolytic processes carcinogenic compounds. It has been demonstrated [9] that used petroleum derived oils contain up to two orders of magnitude more BP compared with the new oil.

The deliberations at the Working Group revealed that short-term tests with oil shale products were carried out only in the USA and that Estonian products had not been studied from the aspect of genotoxicity. A scarcity of epidemiological data was noted as well.

Genotoxicity tests with the contemporary oil shale product, the low-temperature retorting (semicoking) oil from the 1000 t/d ("Kiviter") shale oil generator were conducted later [10]. It was demonstrated that the total (crude) oil was mutagenic and clastogenic in short-term tests *in vitro*. The total oil and an industrial distillation residue tested for comparison induced skin tumours in mice and showed a broader spectrum of genotoxicity than the fractions which did not induce tumours.

A study of death certificates [11] showed that in a cohort of 2181 oil shale processing plant workers from Kohtla-Järve and Kiviõli with an occupation record of over 10 years 29 % had cancer of various sites, lungs ranking first, stomach second and intestines third. The proportion of death caused by cancer in the general population was 16 %. Epidemiological studies to disclose more particular correlations should certainly be envisaged.

Published results of experiments and epidemiological data can give indications which may be helpful in future studies and in considering cancer control action.

It is definitely clear that high-temperature retorting of oil shale produces a more carcinogenic oil than processing at lower temperatures. Shale oil retorted at 1000—1200 °C in chamber ovens had a strong carcinogenic action. Even blended products containing about 40 % of chamber oven oil in low-temperature material were in mouse skin experiments strongly carcinogenic. In a study benzene solutions containing 5, 10, 15 and 20 % chamber oven oil (w/v) were tested in four equal groups of 105 mice. It was found that the carcinogenic effect of all four solutions was similar, only the latent period of tumours induced by the 5 % solution was about twice as long as in the other three groups. Obviously workers exposed to blends or having had short periods of exposure run into smaller risk to get an earlier cancer. High-temperature retorting of oil shale has been terminated in 1988, but the latent period of cancer

induction, which is not precisely known and is certainly very variable individually, may reach many decades. This means that cases of cancer in workers having been earlier exposed to chamber oven oil or products containing it are by no means impossible.

Low-temperature (semicoking) oils retorted in shale oil generators had a significantly weaker carcinogenic action. Some controversial results of experiments were however noticed. For example a fraction of a generator oil from Kiviõli retorted at 450—600 °C induced during 18 months in 17 mice out of 68 $CC_{57}Br$ mice skin tumours, in six mice these were malignant. Other samples of generator oils induced only benign tumours or were inactive.

An approximate correlation was noted between the carcinogenic potency and the concentration of BP in investigated shale oils. Oil samples, blends or fractions containing 500—2800 ppm (mg/kg) BP induced in the majority of mice skin tumours and most of them became malignant. In some experiments the relationship was less evident, e.g. a generator residue mixed 1 : 1 with olive oil, containing only 10 ppm BP induced in 22 out of 50 mice skin tumours, which were malignant in 15 mice [5]. In the most recent experiments [10] the oil of the high capacity 1000 t/d shale oil generator was studied and it appeared that the total (crude) oil, containing 56 ppm BP was clearly carcinogenic whereas the laboratory residue with a BP concentration of 82 ppm did not induce any tumours. An industrial distillation residue of a blend of oils, which contained 590 ppm BP was only slightly more carcinogenic compared with the total oil. Similar paradoxical results were obtained in our earlier experiments with cool-fractionation products from low-temperature shale oils [12].

Interesting results were obtained in bioassays designed to compare the carcinogenic action of various fractions of a chamber oven oil sample which were received by repeated chromatographic separation on silica gel and alumina. The aromatic fraction containing 2000 ppm BP, was strongly carcinogenic in mice, the latent period of skin tumour induction was however much longer than in a control group of mice painted with a solution of the same dose of BP in benzene. This indicates the presence of an inhibitor of BP action in the aromatic fraction. Another BP-free fraction induced skin tumours obviously due to other aromatic compounds which were not identified. A third fraction also without BP did not induce skin tumours but potentiated the carcinogenic action of another moderately carcinogenic fraction. These fractions were also painted on the skin of rabbits, who reacted differently e.g. a fraction free of BP produced benign skin tumours in rabbits but no tumours in mice and another fraction which induced malignant skin tumours in mice provoked in rabbits only benign tumours. The possibility of obtaining incomparable and sometimes even contradictory results in different animal species and even in different strains of one species has to be taken into account when evaluating experimental carcinogenicity data. Differences were also observed depending on the site of administration of fractions. One BP-free fraction which was moderately carcinogenic in mouse skin painting experiments did not induce tumours at the site of intramuscular injection but gave rise to remote tumours in the lungs of mice.

All these variations of biological activity of the chamber oven oil fractions may not have any immediate practical significance and are more of academic interest, but they illustrate the multitude of potential bioactive groups of compounds in the most complex chemical composition of oil shale processing products.

Comparison of results of numerous experimental studies and epide-

miological data permits to derive as principal conclusion the validity of animal experiments as warning signals of existing carcinogenic hazards. Epidemiological data have in many other cases too confirmed experimental evidence. The second important inference of the carcinogenicity studies of oil shale processing products is the possibility that low-temperature retorting of oil shale can produce carcinogenic oils. This feature is apparently specific for oil shale as it has been demonstrated [13] that in the course of thermal destruction of oil shale, especially the Estonian (Baltic) variety kukersite, BP is formed in considerable amounts already at temperatures below 400 °C, whereas in other solid fuels formation of BP occurs as a result of pyrolysis of volatile products not below 700 °C.

Finally it should be pointed out that evidently the measurement of BP concentrations provides only approximate indication of potential carcinogenicity. Numerous compounds are known which potentiate the action of small amounts of distinct carcinogens which in such combinations represent a considerable hazard. Short-term genotoxicity tests for orientation and full scale bioassays have to be applied in such cases to permit evaluation of potential hazards. Taking into account further development of oil shale processing technology, especially the new shale oil generator with circular retorting chamber [14], new materials which may have passed various temperatures, will be produced and have to be tested for carcinogenicity as soon as the technology will be sufficiently constant.

РЕЗЮМЕ

На возможную связь между сланцепродуктами и злокачественными опухолями у человека впервые было указано в 1922 г., когда появились первые публикации по этой теме, и с тех пор названная проблема не утрачивает актуальности.

В 1984 г. в Международном агентстве по изучению рака этот вопрос обсуждала Рабочая группа компетентных экспертов. Они пришли к следующему заключению:

а) Имеются *достаточные основания* считать канцерогенными для подопытных животных высокотемпературные и низкотемпературные сырые сланцевые масла, фракции высокотемпературных масел, битумы и смеси сланцевых масел.

б) Имеются *ограниченные основания* считать канцерогенными для подопытных животных сырой сланец, сланцевую смолу и остаток дистилляции (кокс).

в) Имеются *достаточные основания* считать канцерогенными для человека сланцевые масла.

В публикуемое статье комментируются основания для этих оценок.

Поскольку до обсуждения, проведенного Рабочей группой, генотоксичность продуктов переработки эстонских горючих сланцев (кукерситов) не исследовалась, соответствующие работы были осуществлены впоследствии. Кроме того, с учетом высказанного Рабочей группой мнения о недостаточности эпидемиологических данных, было проведено изучение причин смерти стажированных рабочих сланцевой промышленности, в результате которого был выявлен более выраженный удельный вес злокачественных новообразований по сравнению с их долей в случае остального населения.

Несколько общих положений, выявленных в проведенных исследованиях, заслуживают внимания.

Ясно, что высокотемпературные продукты термической деструкции горючих сланцев более канцерогенны, чем низкотемпературные, и их наличие в разных смесях повышает канцерогенность последних. Однако и низкотемпературные продукты вызывают опухоли в опытах на животных. Следует обратить внимание на возможность очень длительного скрытого периода возникновения опухолей. Это обстоятельство надо иметь в виду несмотря

на прекращение высокотемпературной переработки горючих сланцев в Эстонии.

Своеобразным действием обладали различные хроматографические фракции ароматической части камерной смолы. Содержание бензо(а)пирена (БП) лишь ориентировочно указывает на возможность и степень канцерогенного действия неизвестного вещества.

Поскольку при термической деструкции горючих сланцев БП образуется при низких температурах, остается актуальным изучение биологического действия новых продуктов полукоксования горючих сланцев, в том числе и полученных в генераторах с кольцевой камерой, как в краткосрочных тестах на мутагенность, так и в полноценных опытах на животных.

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Presented by I. Öpik
Received 15 June 1991

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