Environmental Health Perspectives
Vol. 30, pp. 177–178, 1979

Cocarcinogenicity of Phenols from Estonian Shale Tars (Oils)

by P. A. Bogovski* and H. I. Mirme*

Many phenols have cocarcinogenic activity. The Estonian shale oils contain up to 40 vol % phenols. The promoting activity after initiation of phenols of Estonian shale oils was tested in mice with a single subthreshold dose (0.36 mg) of benzo(a)pyrene. $C_{57}Bl$ and $CC_{57}Br$ mice were used in skin painting experiments. Weak carcinogenic activity was found in the total crude water-soluble phenols recovered from the wastewater of a shale processing plant. In two-stage experiments a clear promoting action of the total crude phenols was established, whereas the fractions A and B (tanning reagents), obtained by selective crystallization of the total phenols exerted a considerably weaker promoting action. Epo-glue, a commercial epoxy product produced from unfractionated crude phenols, had no promoting activity, which may be due to the processing of the phenols involving polymerization.

The mechanism of action of the phenols is not clear. According to some data from the literature, phenol and 5-methylresorcinol reduce the resorption speed of BP in mouse skin, causing prolongation of the action of the carcinogen.

Various thermal processing products of Estonian oil shale, shale tars, contain up to 40 vol % phenols, which can be separated from the oil or recovered from the wastewater of the shale processing plant.

Shale phenols are being widely used as raw material for the chemical industry for manufacture of various coatings, mastics, adhesives, tanning reagents, and drugs. Chemically the crude phenols represent a complicated mixture of mainly alkyl derivatives of monophenols and diphenols.

A number of phenols have been found to possess a distinct cocarcinogenic action as shown in two-stage carcinogenicity experiments (*1*). Some volatile phenols have been determined in concentrations up to 5.6 mg/m^3 in the air of various departments of the oil shale processing plants (*2*). As contact with phenols and phenol-containing products can occur in workers handling carcinogenic material like shale oils, a study was undertaken to determine the promoting action of some shale phenols occurring in various real situations.

Material and Methods

The following products were tested: (1) water-soluble crude phenols recovered from the wastewater of the Kohtla-Yarve shale processing plant, (2) two products of selective crystallization of crude phenols, fraction A and B, used as tanning reagents (Table 1); (3) 5-methylresorcinol, the main component of the fractions; and (4) a commercial product, Epo-glue manufactured from epoxy resins produced from shale phenols.

$C_{57}Bl$ and $CC_{57}Br$ mice were used in skin painting experiments. The hair in the intrascapular area was clipped and a single subthreshold dose of 0.36 mg benzo(a)pyrene (BP) (Fluka, Switzerland) dissolved in benzene was applied to the skin. After an interval of 10 days the same area was painted twice weekly (50 times) with 1:1 (per weight) solutions of phenols, fractions A and B, and orcinol in acetone or benzene. The experiments carried out are summarized in Table 2.

Table 1. Chemical composition of fractions A and B of water-soluble shale phenols.

Component	Fraction A	Fraction B
Resorcinol, wt %	0.1	0.7
5-Methylresorcinol (orcinol), wt %	44.1	62.8
2,5-Dimethylresorcinol, wt %	29.4	8.6
5-Ethylresorcinol, wt %	3.9	5.8
4,5-Dimethylresorcinol, wt %	6.9	12.6
2,4,5-Trimethylresorcinol, wt %	9.0	3.8
Others, wt %	6.3	5.7

* Institut Eksperimental'noĭ i Khimicheskoĭ Meditsing, Tallinn, Est. S.S.R.

Table 2. Carcinogenicity and promoting activity of some shale phenols and their products.

Group	Product[a]	BP, ppm	Pretreatment with BP[b]	Strain of mice	Initial no. of mice	Effective no. of mice	Time to first tumor, weeks	No. of mice with skin tumors	No. of mice with malignant skin tumors
I	Total phenols	10	+	$CC_{57}Br$	70	68	8	33	26
II	Total phenols	10	–	$CC_{57}Br$	70	67	28	2	1
III	Total phenols	10	+	$C_{57}Bl$	40	32	34	8	6
IV	Total phenols	10	–	$C_{57}Bl$	50	—	—	—	—
V	Fraction A	—	+	$CC_{57}Br$	70	64	22	6	4
VI	Fraction B	—	+	$CC_{57}Br$	70	69	18	14	7
VII	5-Methylresorcinol (orcinol)	—	+	$CC_{57}Br$	40	36	41	3	—
VIII	Epo-glue[c]	—	+	$CC_{57}Br$	40	—	—	—	—
IX	Epo-glue[c]	—	–	$CC_{57}Br$	40	—	—	—	—

[a] Treatment with product as 50% solution in acetone; 50 times twice weekly.
[b] Pretreatment with 0.36 mg PB.
[c] Treatment with undiluted product, 50 times twice weekly.

Results and Discussion

The total crude water-soluble shale phenols have a weak carcinogenic action on $CC_{57}Br$ mice; only two skin tumors developed, one of which was malignant, whereas in $C_{57}Bl$ mice no carcinogenicity was revealed. This effect may be due to the impurities of crude phenols, which contain a few per cent of shale oils and up to 10 ppm BP. The promoting action of phenols in two-stage carcinogenicity experiments is clearly demonstrated in both strains of mice. A single dose of 0.36 mg PB did not exhibit carcinogenic activity in $C_{57}Bl$ mice (group VIII) unless the Epo-glue has an anticarcinogenic action. Fractions A and B show a slightly different degree of promoting activity, both fractions having a considerably weaker promoting effect than the total crude phenols, which contain apparently more active fractions. It is difficult to evaluate the relative cocarcinogenic potency of 5-methylresorcinol, as testing has been carried out only in $C_{57}Bl$ mice, which appear to be less susceptible in our experiments. However, it seems that the promoting action of either fraction A or B can not be attributed to 5-methylresorcinol alone. The negative results in groups VIII and IX indicate that the Epo-glue produced mainly from total water-soluble phenols has no promoting activity at all; this may be due to the processing of phenols involving polymerization. The mechanism of the promoting action of phenols is not known. Karu et al. (*3*) have shown that phenol and 5-methylresorcinol reduce the resorption speed of BP in mouse skin causing the prolongation of action of the carcinogen, resulting in the promoting effect.

REFERENCES

1. Boutwell, R. K., and Bosch, D. K. The tumor-promoting action of phenol and related compounds for mouse skin. Cancer. Res. 19: 413 (1959).
2. Blinova, E., Veldre, I., and Jänes, H. Toxicology of Shale Oils and Phenols. Valgus, Institute of Experimental and Clinical Medicine, Tallinn, 1974.
3. Karu, T. I., Kirso, U. E., and Andrianov, L. A. Dynamics of resorption of benzo(a)pyrene with phenols from mice skin. Voprosy Onkol. 19: No. 5, 80 (1973).