EFFECT OF DIMETHYL SULFOXIDE AS THE CARCINOGEN SOLVENT ON INDUCED CARCINOGENESIS OF THE SKIN IN MICE

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The effect of dimethyl sulfoxide (DMSO) as the solvent for 20-methylcholanthrene (MC) on induced carcinogenesis of the skin was investigated in male CBA × C57BL hybrid mice. MC was used as a 0.25 and 0.5% solution in benzene or DMSO and applied in a dose of 0.2 ml to the previously shaved skin of the interscapular region once a week until the end of the experiment. The following parameters were determined: the time of appearance of the first papilloma and the first carcinoma, the mean latent period of development of the two types of tumor. After application of a 0.25% solution of MC in DMSO only a tendency toward the acceleration of carcinogenesis was observed, but if the MC concentration was doubled, the acceleration of carcinogenesis became significant.

Investigations have shown [2, 7, 8] that the choice of solvent of the carcinogen is an important factor in chemical carcinogenesis. Dimethyl sulfoxide (DMSO), with its great penetrating power, promotes the absorption of chemicals dissolved in it by the skin [6]. However, the use of DMSO as the solvent for carcinogens in experiments to study the induction of tumors of the mucous membrane of the retrobuccal pouch in hamsters [3, 4, 10] and of the skin in rats [11] has been shown sometimes to potentiate, sometimes to inhibit carcinogenesis.

Since the effect of DMSO as the solvent of the carcinogen applied to the skin of mice has not hitherto been investigated, the effect of DMSO as the solvent for 20-methylcholanthrene (MC) on induced carcinogenesis of the skin was studied in mice.

EXPERIMENTAL METHOD

Experiments were carried out on male CBA × C57BL hybrid mice weighing 20-22 g at the beginning of the experiment. MC was used as 0.25 and 0.5% solutions in benzene or DMSO, which were applied in a volume of 0.02 ml to the previously shaved skin of the interscapular region once a week until the end of the experiment. The following parameters were determined: the time of appearance of the first papilloma and of the first carcinoma, the mean latent period of development of each type of tumor, and the mean number of papillomas per mouse.

The mice of group 1 were treated with a 0.25% solution of MC in DMSO, and those of group 2 (control to group 1) with a 0.25% solution of MC in benzene. The mice of group 3 were treated with a 0.5% solution of MC in DMSO, and those of group 4 (control to group 3) with the same concentration of MC in benzene.

EXPERIMENTAL RESULTS

The results given in Table 1 show that the first papilloma in the animals of group 1 was discovered 3 weeks earlier, and the first carcinoma one week earlier than in the corresponding control group (2). The mean latent period was 0.8 week less for the papillomas and 0.4 week less for the carcinomas, but these differences are not statistically significant. In group 3, with twice the MC concentration, the appearance

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TABLE 1. Effect of MC Dissolved in Dimethyl Sulfoxide and Benzene (0.25 and 0.5% solutions) on Carcinogenesis of the Skin in Mice

Group	Experimental conditions	No. of mice	Time of appear. of 1st papilloma (in weeks)	Mean latent period of development of papillomas (in weeks)	Difference (in weeks)	Time of appear. of 1st carcinoma (in weeks)	Mean latent period of development of carcinomas (in weeks)	Difference (in weeks)
1	Application of 0.02 ml 0.25% MC solution in DMSO once a week	49	10	16,0±0,31	−0,8 $P<0,1$	15	23,0±0,40	−0,4 $P<0,5$
2	The same but with MC in benzene	39	13	16,8±0,34		19	23,4±0,33	
3	Application of 0.02 ml 0.5% soln. of MC in DMSO once a week	44	10	14,1±0,28	−1,0 $P<0,05$	15	21,2±0,33	−1,0 $P<0,05$
4	The same but with MC in benzene	43	11	15,1±0,34		16	22,2±0,33	

of the first papilloma and the first carcinoma was observed 1 week sooner and the mean latent period was significantly shorter (also by 1 week) for both papillomas and carcinomas. No significant differences were found in the mean number of papillomas per mouse between the control and experimental groups.

After application of a 0.25% solution of MC in DMSO there was thus only a tendency for carcinogenesis to be speeded up, but a twofold increase in the MC concentration was accompanied by a more definite acceleration of carcinogenesis. The accelerating action of DMSO on cutaneous carcinogenesis in this experiment can be explained by the increase in the effective dose of the carcinogen resulting from its more rapid penetration through the stratum corneum of the skin and also by the fact, demonstrated recently [5], that DMSO increases the uptake of radioactive thymidine in tissue culture, for tissues with increased DNA synthesis are known to be more sensitive to the action of carcinogens [1, 9].

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