

# Influence of 2,3-Dimercapto Propanol (BAL) on the Induction of Skin Tumors in Mice by 3,4-Benzpyrene

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Among the many agents influencing the rate of induction of skin tumors in mice with a standard carcinogen, hydrolyzing chlor-compounds (1), bromobenzene (2) and unsaturated dibasic acids (3) have been shown to either delay or prevent tumor formation. In attempting to explain why such diverse compounds have a common anti-carcinogenic effect, Crabtree (3) has suggested that their influence is mediated through a disturbance in sulfur metabolism. More specifically, he suggests that these three types of inhibitors react with sulfhydryl groups of the cell by the chemical process of condensation, oxidative coupling, or addition, thus making the sulfhydryl groups unavailable for normal cellular metabolism. Crabtree further postulates that the initial phase involved in the production of skin tumors with a standard carcinogen is the fixation of the carcinogen to the cell through combination with free sulfhydryl groups. If these free -SH groups have been previously blocked by an anti-carcinogen or if the anti-carcinogen competes with the carcinogen for cellular fixation, the carcinogen will be eliminated without producing its characteristic effects.

It was believed that additional evidence to support this theory could be obtained by another approach, namely, to supply the tissue with additional -SH groups which would compete with cellular -SH groups for reaction with the carcinogen. The compound 2, 3-dimercapto propanol (BAL) is known to possess the property of competing with tissue -SH groups for chemicals forming stable -SH complexes (4). Therefore, the effect of BAL on the rate of induction of skin tumors in mice with 3,4-benzpyrene was studied.

## EXPERIMENTAL

Albino mice, predominantly males, (National Institute of Health "Swiss") were used in these experiments. The mice were allowed water and Purina special laboratory chow at all times and were housed in an animal room maintained at a uniform temperature. All mice were treated as follows: Three days prior to the first treatment,

the hair was clipped from the scapular region. Twice a week, on Monday and Thursday, a 0.3 per cent solution of 3,4-benzpyrene in ether containing 2 per cent liquid paraffin was applied to the interscapular region with a No. 3 brush. In certain of these mice 24 hours after the 3,4-benzpyrene treatment, that is, Tuesday and Friday of each week, 5 per cent BAL in an ointment base consisting of a mixture of "Carbowaxes" was applied

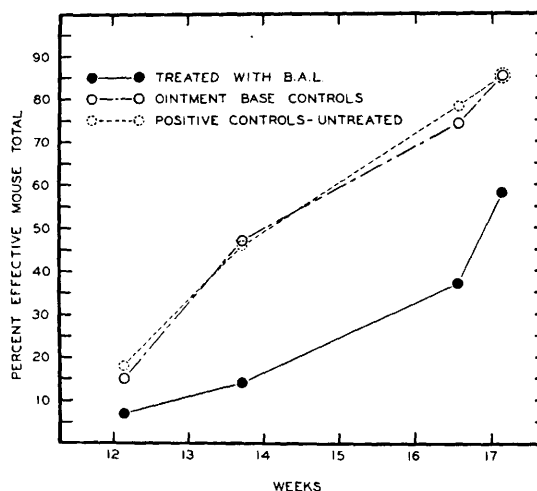


FIG. 1.—Incidence of tumors in mice skin painted with 3,4-benzpyrene.

over the scapular region. A quantity of 0.08 cc. of the BAL ointment measured from a 0.25 cc. syringe was used for each application.

In a preliminary experiment 70 mice were treated with the 3,4-benzpyrene of which 35 also received applications of 5 per cent BAL ointment. After 14 weeks of treatment, fewer mice receiving the 3,4-benzpyrene plus the BAL showed tumors than did those receiving the carcinogen alone. In order to check the apparently favorable results of BAL treatment obtained in this exploratory experiment and also to rule out any possible physical or chemical effects of the ointment base alone, the following experiment was started: Three com-

parable groups of 55 mice each were selected and were carried on experiment for 17 weeks. In addition to the 3,4-benzpyrene applications which all groups received, one of these groups was treated with BAL ointment as described above. The second group was treated with the ointment base without BAL, while the third group received no further treatment.

#### RESULTS AND CONCLUSIONS

The final results are shown in Table I. The progression of the experiment can be seen in Fig. 1.

TABLE I: INFLUENCE OF BAL ON INCIDENCE OF SKIN TUMORS AT 17 WEEKS IN MICE TREATED WITH 3,4-BENZOPYRENE

Treatment	No. of mice at start	No. survived 17 weeks	No. with tumors	Percentage with tumors
BAL ointment, 5%	55	40	23	57.5*
Control, ointment base	55	34	28	82.4
Control, untreated	55	48	41	85.4

\*Reduction in tumor incidence is statistically significant. ( $p < 0.01$  by  $\chi^2$  test).

The results obtained clearly show the inhibitory influence of BAL on the induction of skin tumors in mouse skin treated with 3,4-benzpyrene. Whether the mechanism of this inhibition is explained by the removal of the carcinogen by -SH groups supplied by the BAL or whether the in-

hibition is due to a more nonspecific toxic effect of BAL can not be definitely stated. However, the observation of tumor inhibition by this agent deserves mention.

#### SUMMARY

The incidence of skin tumors in mice painted with 0.3 per cent 3,4-benzpyrene twice weekly for 17 weeks was materially reduced when these mice were treated with 5 per cent BAL ointment 24 hours after each painting with the carcinogen. Only 23 of 40 mice showed tumors after BAL treatment while 41 of 48 mice not treated with BAL showed tumors. Twenty-eight of 34 mice treated with the ointment base developed tumors, thus showing that the physical or physiological effects of constituents of the ointment base were not responsible for the reduced incidence of tumors after BAL.

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