THE CYTOSTATIC EFFECTS OF PYRIMIDINE COMPOUNDS

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ABSTRACT

Thirteen derivatives of toxopyrimidine, which is thought to be a vitamin B6 antagonist, were found to be without significant antitumor activity against solid Sarcoma 180.

INTRODUCTION

Prompted by earlier reports on the inhibition of tumor growth by pyridoxine deficiency (1,2) or by vitamin B6-antagonists (3,4), A. Schellenberger, Kl. Winter and V. Müller, prepared several N-alkylated derivatives of toxopyrimidine similar to the known vitamin B6-antagonists (5,6). We studied these and related compounds on the mouse tumor Sarcoma 180 and observations are presented in this report.

MATERIALS AND METHODS

Experiments were carried out in female albino mice weighing 17-23 g. from the Institute’s random bred strains. The animals were fed a diet of "Nährkonzentrat" and water ad libitum. The strain of Sarcoma 180 has been kept in continuous passage at our Institute for several years. Implants of 0.2 ml. of tumor mash in saline were made subcutaneously in the dorsal region. Experimental and control animals were inoculated with the same original material and sacrificed on the 17th day. Tumors were excised and weighed for evaluation. Changes in body weight were observed throughout the experiment, and mean tumor weights recorded on the day of sacrifice. The significance of differences between experimental and control tumors was established by the "t" test.

The acute toxicity of every substance was determined in preliminary experiments (in general, 15 animals/substance). The daily experimental doses, based on these findings, were slightly smaller than a single well tolerated dose. Only the compounds with carboxylic acid groups were tolerated at doses as high as 500 mg/kg. All substances were injected intraperitoneally for five consecutive days, the first injection being made two hours after transplantation of the tumors. A different schedule was used in the case of 2-methyl-4-methylamino-5-hydroxymethylpyrimidine. This consisted of either ten treatments prior to tumor implantation, or five before and five after implantation.

RESULTS

Table I shows that under experimental conditions the average tumor weights of the experimental and control groups do not differ significantly in any case (p = 0.05). The variations of body weight are negligible.

1/ Director: Professor Dr. K. Pohle.
2/ The synthetic work was carried out in the Institute for Organic Chemistry, University of Halle, East Germany.

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REFERENCES


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<th>ENTRY NO.</th>
<th>DOSE (mg/day)</th>
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<th>AV. MGT WEIGHT (G)</th>
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**Vehicles:**

1. Saline + 1 drop 37% KCN/10 ml.
2. Saline + 1 drop 37% KCN/10 ml.

- Effect of compounds on Sarcina 120
- Number of injections before transplantation
- Treated/Controls
- Av. body wt.
- Av. mg wt.
- C. R. C.
- Effect of compounds on Sarcina 120

Matthies and Peters
Cancer Research Chemotherapy Screening Data
The Cytostatic Effects of Pyrimidine Compounds

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