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SHORT COMMUNICATIONS

Investigation of the alkylating action of 1,1-dimethylhydrazine

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THE CARCINOGENIC action of dimethylnitrosamine[1] has been correlated with the fact, that administration of this compound leads to the formation of 7-methylguanine in DNA and RNA of several tissues in rats.[2] According to Lijinsky *et al.*[3] the formation of diazomethane as an alkylating intermediate must be excluded. 1,1-dimethylhydrazine is a possible metabolite of dimethylnitrosamine, for it has been shown by Süss,[4] that *N*-nitrosomorpholine is metabolized to the corresponding hydrazine derivative by liver homogenates. 1,1-dimethylhydrazine is mutagenic[5] and is carcinogenic in mice,[6] but was found inactive[8] or only weakly active[7] in rats. We have tested whether ^{14}C-1,1-dimethylhydrazine acts as alkylating agent on the RNA of liver and on the RNA of the Yoshida transplantation tumor in rats.

^{14}C-1,1-dimethylhydrazine was synthetisized from ^{14}C-dimethylnitrosamine by reduction with zinc dust in acetic acid as described in Organic Synthesis.[9]

Male Sprague–Dawley rats (300–350 g) with solid growing Yoshida transplantation tumors of about 2–3 g were used. The animals were maintained at Altromin^{R}-diet and water *ad lib.* Three rats were injected intravenously with 80 mg/45 μCi/kg ^{14}C-1,1-dimethylhydrazine hydrochloride. Livers and tumors were removed 6 hr after application. The RNA was prepared by the modified method of Kidson, Kirby and Ralph[10, 11] and was hydrolized for 1 hr with 1 N HCl. The hydrolysate was chromatographed on a Dowex-column (WX 2 (H^+)) using a 1–3 N HCl gradient.

The RNA of the liver showed little incorporation of radioactivity whereas the RNA of the tumor was labelled. In both cases the labelling was due to the biological incorporation of the radioactivity into the purine bases. No 7-methylguanine was detected. It therefore must be concluded that even if 1,1-dimethylhydrazine is formed from dimethylnitrosamine, this compound is not an alkylating intermediate.

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