

Chen

A PROGRESS REPORT FOR THE STUDIES ON THE RADIATION - INDUCED
URINARY EXCRETION OF DEOXYRIBONUCLEIC ACID COMPONENT

1. Deoxycytidine (CdR) metabolism.

Our experimental results indicate that CdR uria is a sensitive biological indicator for radiation dose in rats but not in man. It was thought that some differences in CdR metabolism in these two species might be partially responsible for the discrepancy in the radio-sensitivity of CdR-urea.

(a) CdR-deaminase

We have now demonstrated that CdR deaminase, which is capable of converting CdR to deoxyuridine, is present in man but was not detectable in rats. Thus CdR in man can be deaminated and metabolized further whereas CdR in rats is excreted into urine unchanged. CdR deaminase activity in serums of cancer patients before and after they were treated with gamma radiation showed an initial drop shortly after irradiation. The deaminase activity started to increase after the initial drop and approximately a two-fold increase in the activity was observed in the serum obtained 24 hours after irradiation. The enzyme activity returned to the preirradiation level 42 hours after irradiation. The deaminase activity in rat serums was still not detectable even after they were exposed to radiation.

(b) Metabolism of isotopically labelled CdR

Our comparative study of CdR deaminase activity in rat and human suggest that CdR is metabolized differently in these two species.

Studies on the differences in CdR metabolism in rats and humans are of importance because they may provide us further insights into the metabolic origin of radiation induced urinary CdR and may lead us to obtain more sensitive biological indicators of radiation injury to man.

In the study using CdR specifically labelled with H-3 on the carbon-5 of the cytosine, we found that irradiated rats (200R) excreted about 21% of total radioactivity injected whereas only 13% of radioactivity was excreted by unirradiated rats. Specific radioactivity of CdR isolated from the urine of irradiated rats decreased about 2 to 6 folds as compared with that of CdR in the urine of unirradiated rats, indicating the increase in the pool size of free CdR in irradiated rats. Our preliminary results of the analyses of radioactive compounds excreted in urines indicate that the urine of irradiated rats contains a radioactive compound or compounds which chromatographically behaved differently from the radioactive compounds isolated from the urine of unirradiated rats.

We have showed that the same animal can serve as its own control in the study mentioned above. This result is especially helpful when human subjects are involved, because the number of individual receiving radioactive material can be reduced. Studies on humans are now in preparation.

2. Various enzyme activities in serums of irradiated cancer patients β -glucuronidase and acid phosphatase activities in serums

of 4 cancer patients before and after irradiation were studied, using phenolphthalein glucuronide and p-nitriphenyl phosphate, respectively, as substrates. The results so far obtained showed no significant change in pre- and post- irradiation activities. Assays of other lysosomal enzymes in blood as well as in urine are in progress at present.

3. Effects of radioprotective compounds on urinary CdR excretion

Effects of serotonin creatine sulfate and L-cysteine hydrochloride hydrate on the radiation induced urinary excretion of CdR were studied in the hope that further insight into the mechanism of radiation injury could be obtained. It was found that injection of these chemicals into rats could suppress the radiation induced urinary excretion of CdR. Dose reduction factor (DRF) was derived in terms of 24 hour urinary excretion of CdR for chemically protected and non-protected rats. DRF of 1.7 and 1.5 were obtained, respectively, for serotonin and L-cysteine. These values are within 7% of DRF values reported by other investigators using LD₅₀ as the response criterion.

Submitted by:

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1. Chen, I. W., Kereiakes, J. G., Friedman, B. I. and Saenger, E. L.: Colorimetric Analysis of Deoxycytidine in Urine After Separation by Ion-exchange Column Chromatography. Anal. Biochem., 23,230 (1968)
2. Chen, I. W., Kereiakes, J. G., Friedman, B. I., and Saenger, E. L.: Radiation-Induced Urinary Excretion of Deoxycytidine by Rats and Humans. Radiology, 91,343 (1968)
3. Chen, I. W., Wrede, E. D., Kereiakes, J. G. and Saenger, F.L.: Radiation Effect on the Metabolism of Isotopically-labeled Deoxycytidine in Rats. (Abstract) Radiation Research, 1969 (In Press)