The histologic observations revealed that liver structure was preserved. Hypertrophy of histiocytes and liver cells, vacuolization with scarce lipid storage, phagocytosis of hyaline body by Kuppfer's cells, and an increase in the number of binucleated cells, were the most frequent findings in the sedormid treated rats. The AIA treated rats showed the same histologic picture described in another work[1].

Discussion. The formation of the glucoronide is an obligatory step in the excretion of bilirubin in the bile of rats, since rats of the Gunn strain, which cannot form bilirubin glucoronide from UDPG[5], are unable to excrete free bilirubin, although they can excrete bilirubin glucoronide at the normal rate[6,7]. Since the inhibitory effect of one of these drugs (sedormid) on the UDPG-glucoronyl transferase activity has been demonstrated[1], these observations present further evidence that the drugs employed produce an impairment on the enzyme system involved in the conjugation of bilirubin with glucoronic acid. It should be noted that bile urobilin output and concentration were decreased at the same time as that of bilirubin. It is not known how urobilin is transported and excreted by the liver, but these findings might indicate that the liver uptake and excretion of urobilin is an active process.

Resumen. La administración de sedormid o AIA durante cuatro días, o una sola inyección de AIA reducen las excreciones de bilirubina y urobilinas en ratas. El mecanismo probable de la falla de la excreción de estos pigmentos puede ser atribuída a una inhibición de la actividad de la UDPG-glucoronil transferasa.

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Influence of Serotonin on the Radiation Sensitivity of Lactate Dehydrogenase[1]

Recently we have shown[2] that glycerol protects lactate dehydrogenase (LDH) against radiation damage when added to the enzyme solution prior to irradiation. In these experiments all of the results obtained, including an optimum concentration for the protective effect (approx. 5 λ/10 ml), are similar to results obtained using glycerol to protect catalase. In order to explain this protective effect we proposed a chelating mechanism by which glycerol forms a complex with the metal ions present in the LDH molecule. This metallo-enzyme has been found to contain zinc bound coordinately[3].

If the protective action of glycerol can be attributed to this mechanism, then it should also be possible to produce a modification in the radiation response of this enzyme with other compounds which exhibit a close interaction with bound metal ions. In a previous investigation[4] we could show by means of electron spin resonance and optical absorption studies that serotonin creatinine sulfate (5-HT) forms a complex with metal ions. Such a complex with Fe^{3+}, the active site of catalase, was thought to be responsible for the radioprotective effect observed with this enzyme. In our present investigation, the action of 5-HT on LDH was studied.

12 λ of a rabbit muscle LDH stock solution (49 mg/ml) (Mann Research Laboratories, New York, New York) were diluted to 100 ml with 0.035 M phosphate buffer, pH 7.4, making a final LDH concentration of $4.3 \cdot 10^{-8} M$. 5-HT (Nutritional Biochemical Corporation, Cleveland, Ohio) was dissolved in the LDH solution prior to irradiation. The 5-HT concentrations used are mentioned in Figure 1. The reduced form of diphosphopyridine nucleotide, NADH (Mann Research Laboratories, New York, New York), was used as a substrate in a concentration of $3.45 \cdot 10^{-4} M$.

1 ml samples of LDH solution were irradiated in open Lucite containers with different exposure doses ($0–9 \cdot 10^5$ R). The irradiations were done with a beryllium-window X-ray tube (100 kV, 12 mA, HVL 0.064 mm Al;

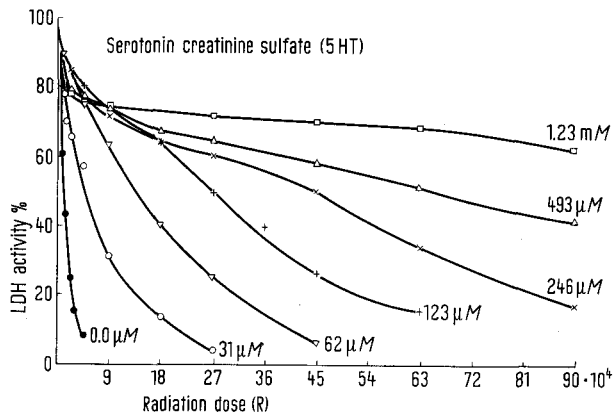

Fig. 1. The influence of different concentrations of serotonin creatinine sulfate (5-HT) on the radiation sensitivity of lactate dehydrogenase.

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Philips Electronics Inc., Mount Vernon, New York). The exposure rate was about $9 \cdot 10^4$ R/min. The X-ray output was calibrated with an air-wall ionization chamber.

The LDH activity was determined spectrophotometrically using the decrease in optical density of NADH at 340 mμ as a function of time after mixing enzyme and substrate. A Cary 14 Spectrophotometer (Allied Physics Corp., Monrovia, California) was used for the determination. 1 ml of $1.14 \cdot 10^{-3} M$ pyruvic acid (Matheson, Coleman and Bell, Norwood, Cincinnati, Ohio) was rapidly injected with a syringe into 1 ml each of the LDH solution and the NADH solution. All solutions were prepared fresh daily and all measurements and irradiations were done at room temperature.

The radioprotective effect exhibited by 5-HT is shown in Figure 1. Non-irradiated samples were used for control values and their activity was taken as 100%. The activities of the LDH solutions irradiated with varying X-ray exposure doses are shown relative to the control value. As can be seen from Figure 1, 5-HT exhibits a good radioprotective effect. It should be noted from the experimental results using high 5-HT concentrations that at lower exposure doses the protective effect was less than that observed for smaller concentrations. At higher exposure doses the extent of protection seemed to be proportional to the 5-HT concentration.

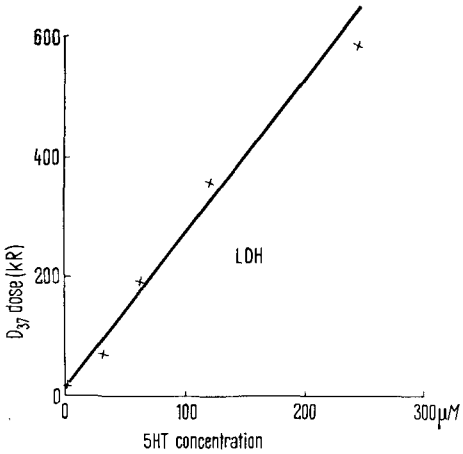

Fig. 2. D_{37}-dose values as a function of 5-HT concentrations (values from Figure 1).

The radiation dose which was required to reduce the LDH activity to 37% is plotted in Figure 2 as a function of the 5-HT concentration using the results from Figure 1. No 37% values could be obtained for the highest 5-HT concentrations used due to the high exposure doses required. As can be seen from the results, a linear relationship exists between the ED_{37} exposure dose and the 5-HT concentration. Unfortunately, higher 5-HT concentrations could not be used due to optical limitations. The ED_{37} for a 5-HT concentration of 246 μM is about 34 times larger than that of the control.

From the results obtained, especially the very large protective effect, it may be concluded that the 5-HT-metal complex mechanism might be applicable for the protection of LDH. The best protection seems to be obtained with agents which interact with metal ions present in biological systems.

Zusammenfassung. Die Veränderungen in der Strahlenempfindlichkeit von Milchsäuredehydrogenase durch Serotonin, gebraucht als Serotonin-Kreatinin-Sulfat, wurden spektralphotometrisch untersucht. Die Bestrahlungsdosen variierten zwischen $0–9 \cdot 10^5$ R. Die Serotonin-Konzentrationen variierten zwischen 0–1,23 mM. Die D_{37}-Dosis für eine Serotonin-Konzentration von 246 μM ist ca. 34mal grösser als für die Kontrollen. Der Schutzeffekt kann durch eine Komplexbildung zwischen Serotonin und den Metallionen, die im Enzym-Molekül vorhanden sind, erklärt werden.

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Abbau von Quarz mit Brenzkatechin

Kieselgel, verschiedene Silikate und selbst Quarz werden durch Brenzkatechin in leicht alkalischem Milieu langsam gelöst[1]. *o*-Diphenole bilden mit Si in alkalischem Milieu sehr stabile Komplexe, in denen das Si die Koordinationszahl 6 aufweist: $[Si(O_2C_6H_4)_3]^{2-}$ [2]. Beim Abbau der Si-Mineralien setzt das Brenzkatechinat wohl an ≡Si–OH an, worin das Si mit dem Gitter weniger verbunden ist. Die Koordinationszahl des Si wird dabei erhöht, und die Bindungen des Si zum Gitter werden geschwächt. Dazu kommt der Elektronendonatoreffekt des Brenzkatechinats, der die Bindungen des Si zu den O des Gitters stärker polar macht und dadurch weiter schwächt. Schliesslich wird der Abbau des Gitters durch die hohe Stabilität des entstehenden Chelats begünstigt[3].

In einer früheren Arbeit[3] haben wir der Geschwindigkeit des Abbaus von Quarz, Orthoklas und Nephelin durch ammoniakalische Brenzkatechinlösung untersucht. Dabei zeigte sich unter anderem, in Übereinstimmung mit Löslichkeitsbestimmungen in Wasser[4,5], dass frischgemahlener Quarz bedeutend rascher abgebaut wird als Quarz, dessen gestörte Oberflächenschicht mit HF weggelöst war. Um die Abbaugeschwindigkeit des eigentlichen Quarzgitters zu erfassen, haben wir in der vorliegen-

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