Fate in Rats of Heterologous Protein Labeled "Internally" by S^{35} and "Externally" by I^{131}

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The widespread use of radioactive labels to study protein metabolism prompted us to compare the fate of I^{131} attached as an "external" label to serum albumin with that of S^{35}-amino acids incorporated into the same protein molecule as an "internal" label. The doubly labeled protein was prepared by injecting guinea pigs with a yeast hydrolyzate containing S^{35}-amino acids (*1*), sacrificing the animals after 6 to 12 hr, isolating the serum albumin, and labeling it with traces of I^{131} *in vitro* (*2*). Nine days after the intravenous administration of the doubly labeled guinea-pig serum albumin to rats, the animals were sacrificed. Dry protein powders (*3*) were prepared from the liver homogenates, and the protein-bound radioactivity was determined repeatedly during a period of several weeks. An aliquot of the injected protein was treated similarly.

The activities resulting from I^{131} and S^{35} were calculated from the decay rate of 30-mg samples using the equations $R_0 = S_0 + I_0$ and $R_t = S_0 \times 0.5^{t/87} + I_0 \times 0.5^{t/8}$, where R_0 is the total activity (in counts per minute) and S_0 and I_0 the activities of S^{35} and I^{131} at zero time, respectively; R_t is the total activity at the time t. The results of two such experiments (*4*) are shown in Table 1.

We express our results by the ratio "percentage of persisting S^{35}/percentage of persisting I^{131}" in the proteins of the rat liver. Obviously, this ratio remains 1.0 when both isotopes are metabolized at the same rate. According to Table 1, the percentage of persisting S^{35} is, however, 72 or 58 times higher than that of persisting I^{131}. This may be caused by (i) partial deiodination of the injected protein and persistence of the deiodinated product in the liver; (ii) incorporation into the rat liver proteins of S^{35}-cystine, S^{35}-methionine, or peptides containing these amino acids; or (iii) a combination of these processes. In each of these cases, the percentage of guinea-pig serum albumin persisting in the rat liver will be quite different from the percentages of persisting I^{131} and/or S^{35}. If deiodination or loss of iodinated amino acids, as we believe, is the major factor responsible for our results, the amount of guinea-pig protein deposited in the rat liver would be many times higher than that indicated by the low I^{131} content.

Table 1. Radioactivity of I^{131} and S^{35} in doubly labeled guinea-pig serum albumin and in the liver homogenate of injected rats. (All activities are expressed as counts per minute on the 6th day after the rats were sacrificed.)

	Rat 4-WF	Rat 7-WF
Guinea-pig serum albumin		
Injection (mg)	10.4	8.0
S^{35} activity	40×10^3	67×10^3
I^{131} activity	11.2×10^6	13.3×10^6
Rat liver proteins		
Dry weight (g)	1.02	1.20
S^{35} (activity)	0.85×10^3	1.87×10^3
S^{35} (% of injection)	2.1	2.8
I^{131} (activity)	3.2×10^3	6.45×10^3
I^{131} (% of injection)	0.029	0.048
Ratio		
% S^{35}/% I^{131}	72	58

References and Notes

1. R. B. Williams and R. M. C. Dawson, *Biochem. J. (London)* **52**, 314 (1952).
2. S. Warren and F. Dixon, *Am. J. Med. Sci.* **216**, 131 (1948).
3. F. Haurowitz and C. F. Crampton, *J. Immunol.* **68**, 73 (1952).
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Goiter Production and Prevention in Rats

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Laboratory studies of the causes of dietary goiter have been handicapped by the lack of an experimental diet that would rapidly and reproducibly produce goiter in the absence of known goitrogenic chemicals. A low iodide diet is available commercially (*1*), prepared according to the recommendation of Remington (*2*). In rats this diet produces goiter very slowly. We have prepared low-iodide diets (*3*) with casein and sucrose as the basic components. These mixtures were not goitrogenic.

In June 1953 we received a communication from Eartly and Leblond (*4*) stating that a commercial cereal (*5*) was low in iodine content and could be used as a diet for rats. For the past 20 mo we have studied iodide metabolism of rats fed this cereal. In this report (*6*) the cereal is referred to as Cereal-G. Repeated analyses have shown that Cereal-G contained 0.015 to 0.035 μg of iodide per gram (*7–11*), and it was consistently goitrogenic.

The commercial Remington diet contained 0.08 μg (*7*) of iodide per gram according to our analyses, although Remington reported that his original mixtures were as low as 0.015 μg of iodide per gram. Our diets of sucrose with 13 and 26 percent casein (*3*) contained, respectively, 0.03 and 0.05 μg of total iodide per gram (*7*).

Groups of Long-Evans male rats, 60 to 100 g initial body weight, were fed one of the afore-mentioned diets for 6 wk to 2 yr. All diets were supplemented with distilled water, and the rats were main-