

Rate of Uptake of ^{75}Se , as Selenourea- ^{75}Se , in Rats in vivo

A study on the function of selenourea as a radioprotective substance was initiated in our laboratories. Some preliminary data¹ suggest the possible utilization of organic derivatives of selenium for the purpose of blocking the formation of free radicals produced by radiation. This kind of protective effect is mostly produced by formation of mixed selenium bridges, as organic disulphides. Having scarce knowledge on the distribution of organic derivatives of selenium in the organs of animals in vivo² and on the limit of toxicity of the selenium as introduced in the form of organic compounds which are easier to metabolize³, it was decided first to investigate the rate of uptake of selenourea for a more rational utilization of this derivative as a radioprotector.

The present paper reports data on the rate of uptake of the selenium in different organs of rats in vivo and for variable doses of the said compound.

The selenourea was prepared according to the method of HOPE⁴ and radioactivated by a reaction (n, γ) in the nuclear reactor at Harwell (England) to a radioactivity of 0.6 mC/0.5 g of compound and crystallized from a hydroalcoholic solution.

We used 10 male albino rats of Wistar race for every series of experiments and every rat was injected i.p. with 1 ml of solution either 0.4 mg/ml, 0.8 mg/ml, 1.6 mg/ml, or 3.0 mg/ml.

2 rats were sacrificed after each time interval of 6, 12, 24 and 72 h, and 14 days after injection, and the radioactivity of different organs determined by γ -scintillation technique.

The Table summarizes the ^{75}Se content of the various organs per gram of net tissue as % of the amount administered.

From the data indicated one may suggest some conclusions on the times of metabolism.

One may notice a different distribution of ^{75}Se depending upon the amount of organic and inorganic selenium present and strictly correlated to the physiological activity of the organs and to the catabolism of urea. The distribution is fundamentally identical in the first two series of experiments. In the fourth series, one may notice variations, linked to the phenomenon of chemical and radiochemical toxicity due to the injected compound⁵. This phenomenon takes place particularly in the spleen. The liver indicates a rate of uptake and a particular fast exchange of ^{75}Se , while the blood and the lungs follow a slower but similar process. For the lungs this process could be attributed to the blood present in the internal vessels.

A biological half-life of ^{75}Se was deduced from the mean data of the distribution after 24 h. Only the first two series are considered, where the ^{75}Se is at subtoxic level so that we have physiological and not pathological conditions.

The half-life for the liver is approximately 30 h, for the lungs 36 h, for the heart 4 days and for the other organs longer (5-6 days). These half-lives suggest that the liver is the principal organ for biological assimilation and exchange of selenium from selenourea to biological selenium, which is part of the protein systems⁶.

The ^{75}Se protein system has a slower time of turnover in comparison with free biological selenium. In fact the biological half-life of the selenourea is shorter than that of other derivatives such as selenomethionina⁷, which participates directly without an intermediate transformation to the protein synthesis and remains longer in the tissues.

Distribution of selenium in rat organs at various times after i.p. administration of selenourea, % of amount administered per g of tissue

Series	Organ	Time after injection				
		6 h	12 h	24 h	72 h	14 days
1 (0.4 mg/rat)	Blood	0.40	0.44	0.40	0.22	0.18
	Heart	0.85	0.63	0.44	0.24	0.15
	Kidney	1.26	1.10	0.98	0.65	0.12
	Spleen	0.57	0.57	0.64	0.63	0.14
	Lung	0.30	0.30	0.27	0.10	0.03
	Liver	1.00	0.90	0.95	0.23	0.09
2 (0.8 mg/rat)	Blood	0.38	0.49	0.46	0.28	0.11
	Heart	0.40	0.24	0.24	0.15	0.06
	Kidney	0.58	0.40	0.33	0.30	0.09
	Spleen	0.42	0.36	0.49	0.39	0.06
	Lung	0.18	0.05	0.12	0.05	0.01
	Liver	0.43	0.35	0.61	0.13	0.06
3 (1.6 mg/rat)	Blood	0.37	0.39	0.45	0.26	0.10
	Heart	0.45	0.25	0.27	0.25	0.03
	Kidney	0.47	0.40	0.41	0.15	0.05
	Spleen	1.85	0.71	0.35	0.35	0.05
	Lung	0.05	0.06	0.11	0.05	0.02
	Liver	0.78	0.48	0.18	0.09	0.03
4 (3.0 mg/rat)	Blood	0.33	0.28	0.33	0.26	0.14
	Heart	0.28	0.12	0.14	0.13	0.04
	Kidney	0.75	0.38	0.33	0.28	0.10
	Spleen	1.57	0.38	0.18	0.48	0.27
	Lung	0.10	0.11	0.11	0.06	0.06
	Liver	0.60	0.29	0.29	0.22	0.11

Zusammenfassung. Die Geschwindigkeit der Verteilung und Fixierung des Selenharnstoff- ^{75}Se wurde in diversen Rattenorganen in vivo und bei Stoffwechselzeiten von 6 h bis zu 14 Tagen untersucht. Die Selenharnstoffmengen variierten zwischen 0,4 und 3,0 mg pro Tier.

A. BRECCIA⁸, A. TRENTA, R. BADIELLO, S. MORETTI, and M. MATTII

III Sezione del Centro Nazionale di Chimica delle Radiazioni e dei Radioelementi del C.N.R., Istituto Chimico «G. Ciamician» dell'Università di Bologna, and Istituto di Radiologia dell'Università di Bologna (Italy), December 24, 1965.

¹ F. SHIMAZU and A. L. TAPPEL, *Science* 143, 369 (1964).

² D. B. SODEE, L. RENERTS, G. HILL, and B. DISTEFANO, *Nucleonics* 23, 78 (1965).

³ G. D. ZUIDEMA, M. KIRSH, I. G. TURCOTTE, W. D. GAISFORD, W. POWERS, and R. KOWALCZYK, *Ann. Surg.* 158, 894 (1963).

⁴ H. HOPE, *Acta chem. scand.* 18, 1800 (1964).

⁵ R. BADIELLO, A. TRENTA, S. MORETTI, and M. MATTII, *Nature*, in press.

⁶ K. P. MCCONNELL, *Agric. Food Chem.* 11, 385 (1963).

⁷ M. BLAU, R. F. MANSKE, and M. A. BENDER, *J. nucl. Med.* 3, 202 (1962).

⁸ The authors wish to thank Dr. H. HOPE (Kjemisk Institut, Universitet i Oslo, Norway), for supplying the first selenourea used in these experiments.