Further Observations on *in vivo* Radioprotection of Rats by Selenourea

Roberto Badiello *, Enrico Gattavecchia **, Mario Mattii ***, and Maurizio Tamba *

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This paper deals with a study of some tests in rats *in vivo* after gamma irradiation in the presence and in the absence of selenourea. The factors considered were the total protein content, the protein pattern, and some serum enzymes, like GOT, GPT and AP. The result shows that the preadministration of selenourea modifies favourably the changes induced by ionizing radiation.

Some chemical considerations have suggested that selenium-containing compounds should be good radioprotectors.

Shimazu and Tappel reported that the seleno-analogues of cystine and methionine were effective in the radioprotection of proteins and amino acids in solution [1]. Earlier investigations in our laboratories have shown that selenourea has a radioprotective effect in chemical systems [2], in rats [3, 4] and in bacteria [5]. In particular in rats, selenourea was able to reduce the lethality, some clinical symptoms of radiation injury and the severity of haematological syndrome (depression of white cell count and of neutrophiles in blood).

This paper reports further investigations and new results on the effect of selenourea in irradiated rats. The parameters investigated were the total protein content and the protein pattern of serum and some changes in the activity of plasma enzymes like alkaline phosphatase (AP), glutamate oxalacetate transaminase (GOT) and glutamate pyruvate transaminase (GPT).

Groups of eight male Wistar rats of an average weight of 150 g were exposed to 750 R (about LD 50) total body gamma irradiation by means of a ^{60}Co therapy apparatus with a dose rate of 30 R/min. Selenourea, at a single dose of 1 mg/ml of physiological solution, was injected intraperitoneally to a group of rats 10 min prior to irradiation. At fixed time after the irradiation, from the animal, subjected to cardiopuncture following Nembutal anaesthesia, were taken blood samples for the biochemical analysis. The serum proteins were separated by means of paper electrophoresis technique and the enzymatic analysis were carried out with the standard methods described in the literature [6]. The administration of selenourea in unirradiated rats does not cause any change in the investigated parameters.

Table I shows the effect of selenourea on the radiation-induced changes in protein content and in protein pattern of rat serum. Data on the effect of cysteine, a well known radioprotective agent, are also given for comparison. The mean values are summarized together with the standard errors for the means. In the irradiated control rats the total protein values of the serum were significantly decreased and the concentration of albumin decreases much more than that of globulins. These modifications are in agreement with other published works [7]. The modifications induced by the presence of

Table I. Effect of selenourea and cysteine on the protein content and protein pattern of serum of rat irradiated with 750 R.

	Before Irradiation	After Irradiation 8 hours			16 hours			24 hours		
		Control	Seleno-urea	Cysteine	Control	Seleno-urea	Cysteine	Control	Seleno-urea	Cysteine
Total proteins	7.5±0.5	4.8±0.6	7,6±0.2	6.9±0.5	4.0±0.6	7.3±0.2	7.2±0.3	3.5±0.1	6.5±0.3	6.5±0.5
Albumin	39.6±1.0	28.9±0.5	36.0±0.5	37.6±1.0	30.0±0.3	37.0±0.2	36.5±0.5	29.1±0.6	36.2±0.4	36.7±0.7
Globulin										
α_1	5.0±0.5	9.8±0.2	9.0±0.2	9.1±0.3	12.1±0.3	8.8±0.2	7.6±0.3	11.5±0.2	9.5±0.4	8.9±0.6
α_2	14.2±0.7	19.6±0.5	12.1±0.3	12.8±0.3	15.8±0.4	13.1±0.3	14.0±0.2	15.4±0.3	13.2±0.5	14.1±0.5
β	23.0±1.0	30.3±0.1	24.9±0.6	23.4±0.4	32.5±0.6	22.2±0.5	23.9±0.3	32.6±0.5	23.1±0.2	23.0±0.6
γ	18.0±0.2	11.2±0.2	17.8±0.3	17.1±0.3	11.6±0.5	18.8±0.1	18.8±0.5	11.3±0.2	18.0±0.2	17.2±0.2
Ratio albumin/globulin	0.396	0.289	0.360	0.376	0.300	0.370	0.365	0.291	0.362	0.367

* Laboratorio di Fotochimica e Radiazioni di Alta Energia (CNR) Bologna, ** Cattedra di Chimica Generale ed Inorganica, Facoltà di Farmacia, Università di Bologna, *** Istituto di Radiologia e del Radio, Università di Bologna

Requests for reprints should be sent to Dr. R. Badiello, Laboratorio di Fotochimica e Radiazioni d'Alta Energia (CNR), Via Castagnoli 1, *40126 Bologna*, Italy.

Table II. Effect of selenourea on changes of some serum enzymes of rats irradiated with 750 R. The GOT and GPT activities are expressed in U/ml, the AP activity in King-Armstrong units. Normal values are given within brackets.

Before irradiation		After Irradiation 6 hours		12 hours		24 hours	
		Control	Selenourea	Control	Selenourea	Control	Selenourea
GOT (60–90)	70±4	128±4	90±4	129±3	86±4	98±4	88±5
GPT (8–25)	20±2	27±3	20±2	20±2	19±2	22±2	20±2
AP (60–90)	70±2	94±3	61±2	94±2	65±2	95±2	61±2

selenourea and cysteine are similar and in both cases the treatment decreases drastically the effect of irradiation. In particular the total proteins and the different fractions are within normal values. Table II shows the effect of selenourea on some plasma enzymes, (GOT, GPT and AP) after irradiation. A strong increase of the GOT activity was observed in the animals, particularly between 6 and 12 hours after the irradiation (about 45%), in good agreement with other published data [8–10]. The GPT and the AP activities do not show significant change; both increase by a small factor and are, therefore, of scarce diagnostic value. The results demonstrate that the administration of selenourea before the irradiation produces a smaller increase in the GOT activity which remains practically within normal values.

Previous observations [3, 4] have shown that selenourea provides a significant amount of protection in rats following gamma rays exposure and in particular this chemical prevents lethality and depression of white cell count. The present new results show that other radiation induced changes of biological and physiological significance are favourably modified by pretreatment with selenourea.

As to the mechanism of radioprotection, we can only say that a physiological action by selenourea is rather unlikely since the postirradiation administration of the compound is uneffective. A tentative explanation could be given by the rapid incorporation of selenourea in the radiosensitive tissues of the organism [11] and its ability in scavenging free radicals, as it was shown by pulse radiolysis study [12]. Although selenourea is not exempt of some toxicity [13], these data seem to be of interest both in radiobiology and in clinical radiotherapy.

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