dose in r. Here again the average values and the standard errors are given. The dashed line indicates the average values and the standard errors in the control animals.

A significant increase in the density of the blood serum was observed 6 h after the application of 0·2 mg *tris*-(β-chlorethyl amine hydrochloride) and 24 h after intravenous application of colloidal chromium phosphate labelled with phosphorus-32 in a quantity corresponding to an absorbed dose of 7,000 rads in the liver.

From the results achieved, it follows that the changes in the density of the blood serum depend on the extent of the whole-body irradiation dose and on the period of irradiation. Maximum changes were observed 6 h after the application of a 500 r. irradiation dose. Knowing that the changes in the blood serum density are subjected to a series of factors, we presume, however, that the disturbance in proteosynthesis and the disturbance in DNA creation leads to the accumulation of catabolites in the blood. These catabolites, in the same way as the decay products, especially those of the white blood elements can take part in the changes affecting the serum density. It is also possible that a change in the space configuration of the protein macromolecules and the altered conditions in the water quantity bound on proteins may play here an important part. In doses greater than LD_{100} it is necessary to take into consideration the disturbed renal function. These factors are being examined at present, and we are investigating the correlation between the changes in blood serum density and other changes in the physico-chemical properties of blood.

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Complex Amine Oxides with Radioprotectant Properties

Previous reports[1–3] have shown that certain amine oxides can increase total survival after lethal whole-body X-irradiation. Recently it was found that the complex compounds in Table 1 were active radioprotectants.

Groups of 20 *CF*-1 male mice were given orally 250 mg/kg of the compounds 24 h prior to exposure to 600 r. X-irradiation under our usual conditions[3]. The degree of radioprotection based on total survival varied from 15 to 40 per cent, although the —N=C— structure required for activity was present in all compounds. These differences in activity may be related to substituent groups exerting directing influences on the molecules and forcing the radiation-induced oxidizing radicals to attack substituent groups which are less readily oxidizable. Both isoimidazole derivatives present two methyl groups where such oxidations could occur, but directing influences could cause the oxidation to occur in the 4 position of the benzene ring. Under such conditions one would expect the compound containing the phenyl group to be more potent because hydroxylation is a one-step process whereas the tolyl group usually is converted to the corresponding acid by a three-step process. The results in Table 1 support this explanation.

Table 1. Effect of Complex Amine Oxides on Survival after X-Irradiation

Medication	ST_{50} and range	Slope and range	Mortality Final (%)	Day
Saline control	13·1 (10·8–5·9)	1·54 (1·34–1·78)	90	30
4,5-dimethyl-2-(*p*-tolyl)-1,3-isoimidazole-1,3-dioxide	15·5*(12·8–18·8)	1·52 (1·30–1·78)	75	30
4,5-dimethyl-2-phenyl-2-isoimidazole-1,3-dioxide	—	—	65	30
3,4-diphenyl furazan-1-oxide	—	—	60	30
Saline control	8·0 (6·6–9·7)	1·55 (1·35–1·78)	95	17
5-Quinazolinol,3-oxide	—	—	55	30

ST_{50}, day on which 50 per cent of animals are expected to be still alive. Confidence limits are calculated at $P=0·05$ (ref. 4). All drugs 250 mg/kg orally 24 h pre-irradiation.
*Not significant at $P=0·05$.

Similarly, radiation-induced hydroxylation of the phenyl group could explain its radioprotectant activity. The quinazolinol compound can exist *in vivo* in the keto or lactam form and should behave analogously to a hydroxyquinoline. This would form the —N=C— structure, and the substituent group in position 4 could direct the oxidation to the 2 position. Previous work[1,2], as well as these results, would support the foregoing radical trapping mechanism as an explanation for the radioprotectant activity of the compounds in Table 1. Furthermore, such results indicate a direction for further research in the development of new and better radioprotectant drugs.

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Indirect Action of X-Radiation on Mammalian Cells

Ionizing radiations may impair the reproductive capacity of cells either by directly altering specific biochemical sites or indirectly by giving rise to free radicals in water which then react chemically with specific sites. In the frozen state the mobility of free radicals is hindered, and consequently the radiosensitivity of cells reduced to an extent that depends on the degree to which the indirect mechanism is involved.

Although the demonstration that radiosensitivity of a system is reduced in the frozen state does not by itself constitute proof that the indirect mechanism is involved, since a number of physico-chemical factors (oxygen sensitization[1]; temperature dependence of radiosensitivity independently of change in state[2,3])