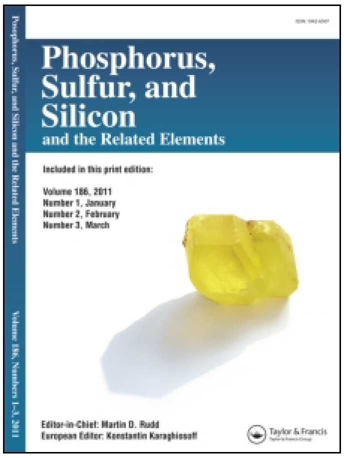

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FREE RADICAL CHEMISTRY OF SELENIUM CONTAINING COMPOUNDS

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FREE RADICAL CHEMISTRY OF SELENIUM CONTAINING COMPOUNDS

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Abstract The nature and the reactivity of selenium-containing free radicals produced directly or indirectly by irradiation of aqueous solutions have been studied. Fast reaction techniques, primarily pulse radiolysis, have provided information concerning the chemical reactions involving free radicals of potential significance in chemistry and biology and have contributed to the elucidation of some mechanisms.

INTRODUCTION

Selenium, although toxic at high concentrations, may function as an antioxidant in many biochemical processes. It may reduce free radical reactions which contribute to the decline of the immune response with age and may exert an inhibitory effect on the development of mutagenicity, certain types of cancer, other pathologies and on the toxic effects of some heavy metals as well as ionizing radiation[1]. Endogenous peroxidic substrates as well as exogenous agents (i.e., radiation, chemical pollution, drugs etc.) may cause cellular-free radical damage. The formation of free radicals can be prevented "in vivo" by the activity of enzymes such as superoxide dismutase, catalase and glutathione peroxidase. A selenium atom is present at the active site of glutathione peroxidase[2]. The function of selenium is to reduce the peroxidic substrates before the production of high concentrations of OH radicals. These are powerful oxidant agents capable of initiating severe oxidative degradation of cellular components.

As an antioxidant, alone or in combination with vitamin E, selenium has proved successful in counteracting the toxic effects of some heavy metals (mercury, cadmium, lead, silver, arsenic etc.) and therefore it may offer a workable antidote for humans exposed to these environmental hazards. The inhibitory effect of selenium on the development of certain types of cancer may be linked to the free-radical theory of carcinogenesis. Antioxidants have been postulated to exert an anticancer effect acting as scavengers of genotoxic free radicals. Selenium-containing compounds generally show radioprotective properties in a variety of biological and chemical systems.

In all these processes (aging, metal toxicity, carcinogenesis, radiation damage) and probably in other pathological events, the role of selenium-containing compounds may be to quench radicals and therefore to act as an antagonist of damaging processes.

In this communication, data are presented on the reactivity of selenium compounds with simple free radicals and on the nature of selenium-containing free radicals.

PULSE RADIOLYSIS TECHNIQUE

The majority of the data on free radicals reported in this paper derive from radiation chemical experiments and in particular from pulse radiolysis technique[3].

Pulse radiolysis uses a short intense pulse of radiation to induce the initial physical-chemical damage and fast recording techniques (i.e., absorption kinetic spectrophotometry with oscillographic output) are used to investigate the short-lived chemical species produced and to follow their subsequent reaction pathways. Unlike photochemistry, where the incident energy is a particular chromophore, the absorption of ionizing radiation occurs non-selectively and, in dilute solution, exclusively by the solvent. The redox nature of irradiated water is well known and is due to the powerful oxidative capacity of the $OH\cdot$ radical and the powerful reductive capacity of the hydrogen atom $H\cdot$ and of the hydrated electron e^-_{aq}.

REACTIVITY OF SELENIUM ORGANICS WITH FREE RADICALS

The rate constant for the reaction of water radicals with some selenium organics, selenourea and selenoamino acids, are shown in Table I.

Organic selenium compounds react with the hydrated electron and $OH\cdot$ radicals at, or near, diffusion controlled rates. The rate constants of selenoamino acids are higher than for other aliphatic aminoacids and are of the same order of magnitude of those of thioamino acids[9]. Also, selenourea shows high reactivity towards the primary radicals of water and the rate constants are higher than those reported for urea and thiourea[9].

The order of reactivity with radicals of ureas and sulfur (or selenium) containing amino acids seems to parallel the better radioprotective ability of selenium organics in biological and chemical systems[10,11].

The suggestion that selenium organics are able to react with free radicals and to stabilize them is supported by irradiation of organic compounds in the solid state, where the presence of selenourea suppresses the formation of free radicals by an amount proportional to its concentration[12].

TABLE I - Rate constants for the reaction of water radicals with selenium organics.

Reaction	pH	k(dm^3 mol^{-1} s^{-1})	Reference
selenourea + e^-_{aq}	6-11	4.0×10^9	4
selenocystine + e^-_{aq}	6	7.6×10^9	5
selenocystine + e^-_{aq}	11	3.9×10^9	5
selenomethionine + e^-_{aq}	7	1.8×10^9	6
selenoethionine + e^-_{aq}	7	2.0×10^9	7
selenourea + OH°	7	$5.5\text{-}7.2 \times 10^9$	4
selenocystine + OH°	7	$1.0\text{-}1.7 \times 10^9$	5
selenomethionine + OH°	7	1.3×10^{10}	6
selenoethionine + OH°	7	1.2×10^{10}	7
selenodicysteine + OH°	7	8.1×10^9	8
selenourea + H°	7	$6.3\text{-}7.5 \times 10^8$	4

Also, the evidence that neutron activation has proved to be a good method for labelling selenourea with ^{75}Se in high yield[13], although the recoil of the (n,γ)

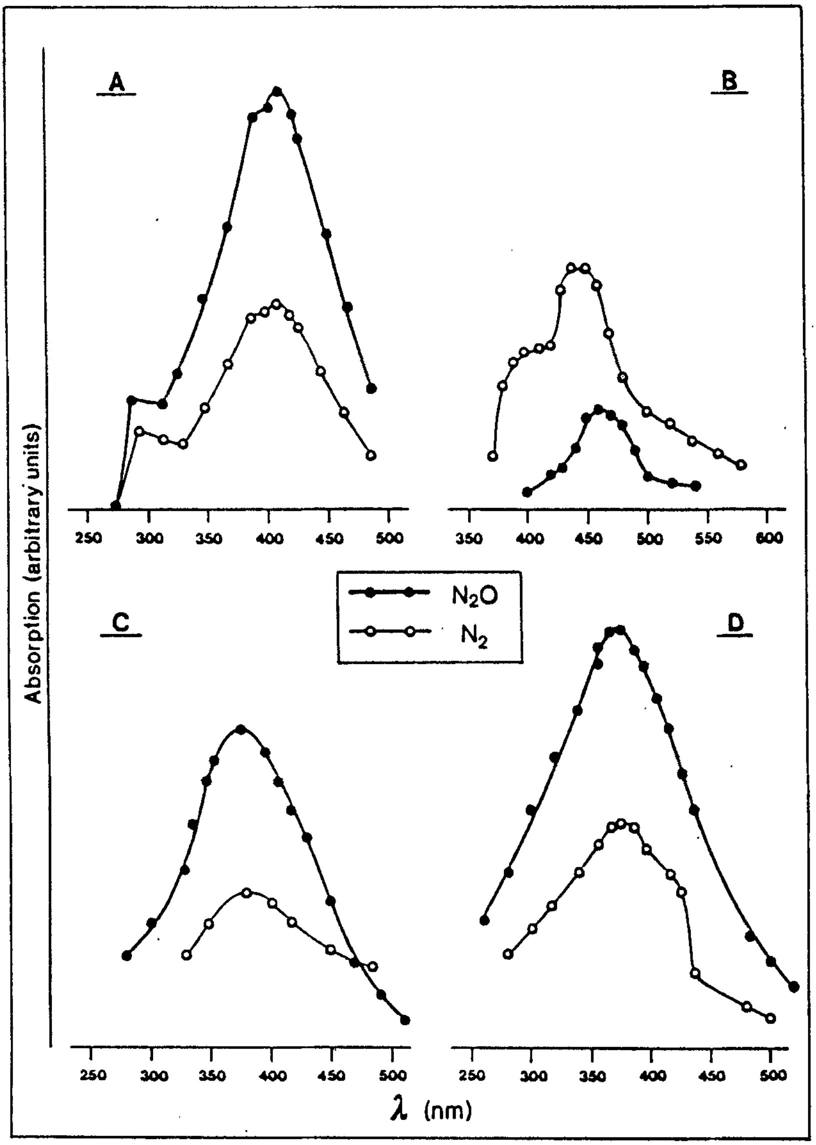

FIGURE 1 Transient absorption from pulse irradiated aqueous solutions containing selenium organics: A) selenourea (from Badiello and Fielden[4]); B) selenocystine (from Tamba and Badiello[5]); C) selenomethionine (from Tamba and al.[6]); D) selenoethionine (from Badiello and Tamba[7]).

reaction has sufficient energy to break the Se-C bond, reflects the efficiency of selenium as a radical scavenger.

ORGANOSELENIUM RADICALS

When aqueous solutions of selenium organics are pulse-irradiated, an intense transient absorption with a maxium from 380 to 450 nm is produced (Figure 1). In Fig. 1, the transient absorption is increased by a factor of two by saturating the solution with N_2O in order to convert all e^-_{aq} to OH· radicals. This means that the electron adduct has no significant absorption in this spectral region and that the bulk of the transient absorption is due to OH· attack on the compounds.

In all cases this absorption is attributed to the formation of radicals in which selenium atom (or atoms) is (or are) involved. Sulphur organics, when irradiated, show transient absorption in a similar spectral region [13].

In the case of selenourea both the OH· radical and the H· atom give rise to the same radical species when they react with the solute. The radical formed by this reaction with a strong absorption band at 410 nm is shown to be a charged complex involving two selenourea molecules.

In the case of selenocystine, e^-_{aq} reacts with the -Se-Se-group and gives rise to a transient absorption peaking at 400 nm. The electron adduct decays in an equilibrium reaction to the radical RSe· responsible for the 460 nm absorption shown in Figure 2 (B). The same radical absorbing at 460 nm is formed by OH· radicals.

The product of the reaction of e^-_{aq} with selenomethionine and selenoethionine does not give rise to significant absorption while the OH· attack occurs at the Se atom with the formation of transient absorption at around 380 nm.

These pulse radiolysis results may be linked to the steady state radiolysis data and indicate that the decomposition of selenourea and selenoamino acids is due mainly to OH· attack. Meanwhile, hydrated electrons are partially scavenged by selenium atoms resulting in less damage to the molecule.

RADICALS DERIVED FROM INORGANIC SELENIUM COMPOUNDS

In the case of pulse radiolysis of inorganic selenium compounds, intense spectra peaking from 350 to 450 nm were obtained. Figure 2 shows the transient spectra for hydrogen selenide[14], selenocyanate[15] and selenium dioxide[16].

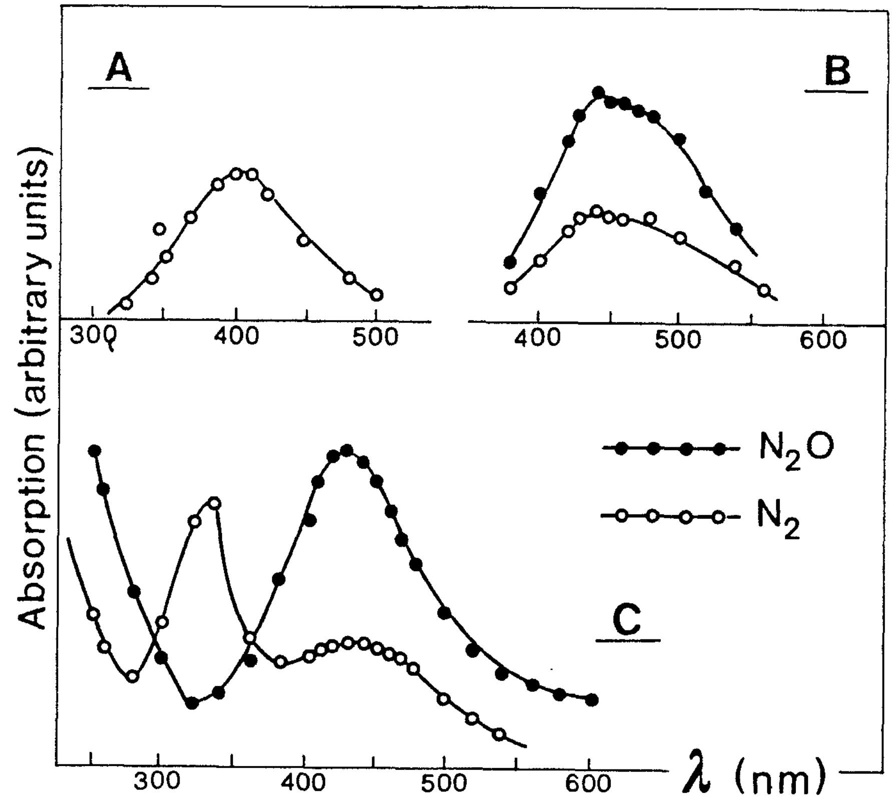

FIGURE 2 Transient absorption from pulse irradiated aqueous solutions containing inorganic selenium compounds. A) selenidric acid (from Shoneshofer and al.[14]); B) selenocyanate (from Badiello and Tamba[15]); C) selenium dioxide (from Tamba and Badiello[16]).

Of particular importance are the application of some Se-containing free radicals in problems of biological interest. A good example of the application of radiation-chemical techniques to biochemistry and biology is the use of selectively oxidizing secondary radicals, including selenocyanate and selenite to investigate the amino acid composition of the active site of biomacromolecules[17,18].

These secondary free radical reagents show some selectivity in their reactions with amino acids and can be used, in combined pulse radiolysis and inactivation experiments, as probes to study the role of the crucial amino acids involved directly in enzyme function.

Table II shows the absorption maximum for each radical and the bimolecular rate constant value with some amino acids.

One can observe that both secondary radicals react rapidly with amino acids which are residues of probable importance in the composition of the active site of the macromolecule. Moreover, both radicals present strong absorption spectra (Figure 2), so their reactions can be observed directly.

TABLE II - Physical chemical data for Se-containing inorganic radicals.

Radical	λ_{max} (nm)	reactivity with amino acids $k(dm^3mol^{-1}s^{-1})$					Ref.
		Tyr	Try	His	Cys	Meth	
$(CNSe)_2^{\bullet -}$	440	1.0×10^7	1.0×10^7	$<1 \times 10^7$	6.8×10^7	$<1 \times 10^7$	15
$SeO_3^{\bullet -}$	430	1.1×10^9	3.3×10^9	4.3×10^7		1.2×10^8	19

The studies on the effect of selenocyanate and selenite radicals on the inactivation of some enzymes (ribonuclease, lysozime, *a*-chymotrypsin, alcohol dehydrogenases etc.) have confirmed and/or identified the crucial residues involved in the catalytic site of the enzyme.

CONCLUSION

Pulse radiolysis studies have emphasized the great reactivity of selenium-containing compounds with free radicals and their tendency to form stable radical intermediates which can restore the original molecule by means of self-repair or back-reactions mechanisms.

Of particular interest in this context are the comparative E.S.R. studies by Colombetti and Monti[20] on the formation and stabilization of free radicals in X-irradiated thio and selenoamino acids. A low free radical yield was found in irradiated selenoamino acids indicating the presence of repair mechanisms.

In conclusion, the ability of selenium-containing compounds to protect against ionizing radiation, by means of free radical mechanism, may be a clue to the biological antioxidant role of selenium and to the other interesting properties of the element (anticarcinogen, antitoxicant, etc.).

If the pulse radiolysis studies on selenium compounds have elucidated the reactivity of these molecules with free radicals and the nature of selenium containing radicals, our knowledge on this subject is incomplete. The subject of neutral selenium-free radicals is much less well documented by ESR experiments than that of selenium-containing anions and cations, therefore the field is open to further investigation.

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