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Reactions of some Free Radicals Derived from Uracil with Nickel(II) Compounds

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Reactions of Ni^{II} compounds with the transient adducts of uracil, *viz.* U^- and UOH, have been studied in the steady-state radiolysis of uracil in the presence of different Ni^{II} species, *e.g.* $NiSO_4$, $Ni^{II}EDTA$, $Ni^{II}NTA$, $Ni^{II}IDA$ and $Ni^{II}(IDA)_2$. The U^- radicals formed by the reaction of uracil with e^-_{aq} transfer an electron to the Ni^{II} species. The redox behaviour of UOH radicals has been investigated by following the ligand-degradation products of the Ni^{II} complexes and the degradation of the base. The ligand-degradation products, *e.g.* formaldehyde and glyoxalic acid, arise from the degradation of the metal complex through its oxidation to Ni^{III} by C_6–UOH radical species. Unlike Cu^{II} or Fe^{III} ions, Ni^{II} ions have very little effect on the radiosensitivity of uracil. The radiosensitising ability of the metal ions, which is dependent on electron transfer from UOH to the metal ion, is correlated with the redox potential of the metal ion couple $M^{n+}/M^{(n-1)+}$.

The effect of water-derived free radicals on the radiolysis of uracil is to form radical species,[1] *viz.* UOH, U^- and UH. Reactions between such radical species and transition metal ions have become important because of their relevance in determining the radiosensitivities of biological molecules. Our studies on the effect of Fe^{III} and Cu^{II} ions on the radiolysis of uracil revealed that these ions are capable of inducing enhanced degradation of the pyrimidine base in deaerated media.[2,3] The pyrimidine base, *i.e.* uracil, has been chosen to represent biomolecules because it is the most sensitive of the various constituents of nucleic acid to radiation.[4] Ni^{II} is an important transition-metal ion, and in extending our study to the role of various metal ions in inducing radiosensitisation attempts were made in this investigation to study the reactions of Ni^{II} with the transient radical species derived from uracil.

EXPERIMENTAL

MATERIALS

Uracil (E. Merck) was recrystallised three times from triply distilled water. $[^{14}C_2]$Uracil (14 mCi dm^3 $mmol^{-1}$) was obtained from BARC, Bombay. The Ni^{II} complexes, $Ni^{II}EDTA$, $Ni^{II}NTA$, $Ni^{II}IDA$ and $Ni^{II}(IDA)_2$ were prepared by the usual methods;[5-7] EDTA, NTA and IDA represent ethylenediamine tetra-acetate, nitrilotriacetate and iminodiacetate, respectively. All chemicals and solvents were of analytical reagent grade, deaeration was carried out by argon saturation and pure N_2O was used. Irradiation was carried out with ^{60}Co γ-rays and the dose rate was determined using a Fricke dosimeter.

ANALYSIS

The products of the radiolysis were separated by paper chromatography using butan-1-ol + water (86:14) as solvent and they were identified as described earlier.[2,3] The base-degradation yield and the yields of the radiolytic products were determined from the relative activity in the area of the respective peaks in the active chromatogram. The degradation of the base was also determined spectrophotometrically by measuring the loss of absorbance at 260 nm. H_2O_2 was determined spectrophotometrically using titanium(III) sulphate reagent.[8] Attempts to measure H_2O_2 by iodometry,[9] however, gave higher results, the implications of which are discussed below. Formaldehyde was determined using chromotrophic acid[10] and glyoxalic acid was determined using DNPH.[11]

RESULTS AND DISCUSSION

In γ-irradiated dilute aqueous solutions the reactions are initiated by the water-derived active species, *e.g.* e^-_{aq}, H and OH ($H_2O \rightsquigarrow e^-_{aq}$, H, OH), which are known to react with uracil[1] to form U^-, UH and UOH:

$$U + e^-_{aq} \rightarrow U^- \quad (1)$$

$$U^- + H^+ \rightleftharpoons UH \quad (2)$$

$$U + H \rightarrow UH \quad (3)$$

$$U + OH \rightarrow UOH. \quad (4)$$

In the absence of any additive, the transients derived from uracil in reactions (1)–(4) undergo various transformations giving different products and as a result the base is degraded. $G(-U)$ values* in deaerated and N_2O-saturated solutions of uracil were found to be *ca.* 2.8 and *ca.* 3.3, respectively, as shown in table 1. However, when Ni^{II} ions are present, the primary radicals compete for reactions with uracil and Ni^{II} ions. The rate constants for the reactions of e^-_{aq} with $NiSO_4$ and uracil are 2.9×10^{10} dm^3 mol^{-1} s^{-1} and 1.1×10^{10} dm^3 mol^{-1} s^{-1}, respectively.[1, 12] Hence when the concentration of Ni^{II} is low compared with that of uracil, almost all the e^-_{aq} is expected to react with uracil to give U^- [reaction (1)]. However, the OH radicals will in general react with uracil since their reaction with uracil is much faster than that with Ni^{II}. If the Ni^{II} ions are reactive towards the transient adducts of uracil, *i.e.* U^-, UH and UOH, the course of the reactions of these transients will be modified because of the presence of the Ni^{II} ions, and hence $G(-U)$ values are expected to be influenced by the addition of Ni^{II} ions to the aqueous solutions of uracil before irradiation.

Fig. 1 shows the change in absorbance of uracil in the presence of $NiSO_4$ in an N_2O-saturated solution after γ-irradiation. $NiSO_4$ or its radiolysed products do not absorb in the range where uracil absorbs. Hence the decomposition of uracil is determined from the loss of absorbance at its absorption maximum, 260 nm. The decomposition of uracil is found to be linear with dose in the range $(3\text{–}80) \times 10^{17}$ eV cm^{-3}, *i.e.* 48–1280 Gy, and $G(-U)$ was determined from the slope of the plot of yield against dose. Fig. 2 shows the effect of initial concentration of $NiSO_4$ on the decomposition yield of uracil in both argon-saturated and N_2O-saturated solutions. In N_2O-saturated solution, $[NiSO_4]$ has no influence on $G(-U)$. However, in argon-saturated solution the base-decomposition yield, $G(-U)$, decreases with increasing $[NiSO_4]$, but when $[NiSO_4]$ is $\gtrsim 5 \times 10^{-4}$ mol dm^{-3}, $G(-U)$ reaches a steady value of *ca.* 1.8. Hence the effect of Ni^{II} ions on the reactivity of uracil-derived radicals was studied at $[NiSO_4] \approx 5 \times 10^{-4}$ mol dm^{-3}. $G(-U)$ values determined under such conditions are shown in table 1. From table 1 and fig. 2 it is found that although in N_2O-saturated solutions the Ni^{II} ion has no influence on the radiosensitivity of uracil, in argon-saturated solutions it has some protecting effect. Furthermore, in aerated

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* 1 *G* unit = 1.04×10^{-1} μmol J^{-1}.

Table 1. Observed yields in the radiolysis of uracil[a] in the presence of different $\mathrm{Ni^{II}}$ compounds[b] at neutral pH

$\mathrm{Ni^{II}}$ compound	conditions	$G(-\mathrm{U})$	$G(\mathrm{HCHO})$	$G(\mathrm{OHC{\cdot}CO_2H})$	$G(\mathrm{>C{=}O})^c$
	argon satd	2.8			
	$\mathrm{N_2O}$ satd[d]	3.3			
	aerated[e]	2.7			
$\mathrm{NiSO_4}$	argon satd	1.8			
$\mathrm{NiSO_4}$	$\mathrm{N_2O}$ satd[d]	2.9			
$\mathrm{NiSO_4}$	aerated[e]	3.0			
$\mathrm{NiSO_4}$	0.4 mol $\mathrm{dm^{-3}}$ 2-methylpropan-2-ol, argon satd	0.4			
$\mathrm{Ni^{II}EDTA}$	argon satd	1.7	0.8	0.2	1.0
$\mathrm{Ni^{II}EDTA}$	$\mathrm{N_2O}$ satd[d]	2.8	0.9	0.5	1.4
$\mathrm{Ni^{II}EDTA}$	aerated[e]	2.3	0	0	0
$\mathrm{Ni^{II}EDTA}$	0.4 mol $\mathrm{dm^{-3}}$ 2-methylpropan-2-ol, argon satd	0.2	0	0	0
$\mathrm{Ni^{II}NTA}$	argon satd	1.6	0	0.4	0.4
$\mathrm{Ni^{II}NTA}$	$\mathrm{N_2O}$ satd[d]	3.1	0.6	0	0.6
$\mathrm{Ni^{II}NTA}$	aerated[e]	2.7	0	0.1	0.1
$\mathrm{Ni^{II}NTA}$	0.4 mol $\mathrm{dm^{-3}}$ 2-methylpropan-2-ol, argon satd	0.4	0	0	0
$\mathrm{Ni^{II}IDA}$	argon satd	1.4	0.3	0.1	0.4
$\mathrm{Ni^{II}IDA}$	$\mathrm{N_2O}$ satd[d]	2.9	0	0.7	0.7
$\mathrm{Ni^{II}IDA}$	aerated[e]	2.4	0	0	0
$\mathrm{Ni^{II}IDA}$	0.4 mol $\mathrm{dm^{-3}}$ 2-methylpropan-2-ol, argon satd	0.4	0	0	0
$\mathrm{Ni^{II}(IDA)_2}$	argon satd	1.7	0	0.4	0.4
$\mathrm{Ni^{II}(IDA)_2}$	$\mathrm{N_2O}$ satd[d]	3.3	0	0.8	0.8
$\mathrm{Ni^{II}(IDA)_2}$	aerated[e]	2.6	0	0	0
$\mathrm{Ni^{II}(IDA)_2}$	0.4 mol $\mathrm{dm^{-3}}$ 2-methylpropan-2-ol, argon satd	0.4	0	0	0

[a] $[\mathrm{U}] = 2 \times 10^{-3}$ mol $\mathrm{dm^{-3}}$; [b] $[\mathrm{Ni^{II}}] = 5 \times 10^{-4}$ mol $\mathrm{dm^{-3}}$; [c] total carbonyl yield; [d] $[\mathrm{N_2O}] \approx 2.5 \times 10^{-2}$ mol $\mathrm{dm^{-3}}$, ref. (20); [e] $[\mathrm{O_2}] \approx 2.7 \times 10^{-4}$ mol $\mathrm{dm^{-3}}$, ref. (21).

solution $G(-\mathrm{U})$ values were unaffected by the presence of $\mathrm{Ni^{II}}$ ions. Whether the role of $\mathrm{Ni^{II}}$ ions is modified because of complexation or not, the radiolysis of uracil was also carried out in the presence of various $\mathrm{Ni^{II}}$ complexes of aminopolycarboxylic acids. The measured $G(-\mathrm{U})$ values are also shown in table 1. From the comparison of $G(-\mathrm{U})$ values observed in the radiolysis of uracil in the presence of $\mathrm{Ni^{II}}$ ions under different conditions very little can be said regarding the effect of $\mathrm{Ni^{II}}$ ions on the degradation of the base. However, a complete analysis of the products arising from the base degradation may shed some light on this, and hence the products of radiolysis arising from the degradation of the base were separated by paper chromatography using butan-1-ol + water (86 : 14) as solvent. The pattern of radioactivity on the paper

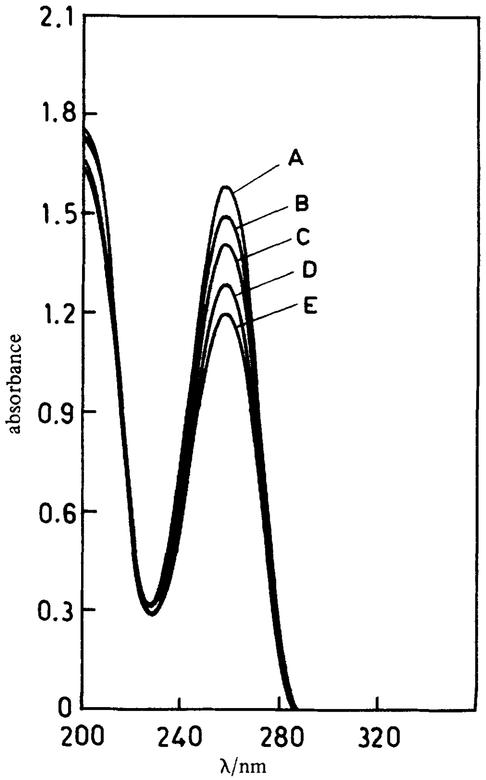

Fig. 1. Absorption spectra of γ-radiolysed uracil solution in the presence of $NiSO_4$ in N_2O-saturated solution. A, Unirradiated 2×10^{-3} mol dm^{-3} uracil or 2×10^{-3} mol dm^{-3} uracil and 5×10^{-4} mol dm^{-3} $NiSO_4$; irradiated to doses of B, 1.9×10^{18} eV cm^{-3} (304 Gy); C, 3.8×10^{18} eV cm^{-3} (608 Gy); D, 5.8×10^{18} eV cm^{-3} (928 Gy); E, 7.7×10^{18} eV cm^{-3} (1232 Gy). The spectra were recorded after 10 times dilution, path length 1 cm.

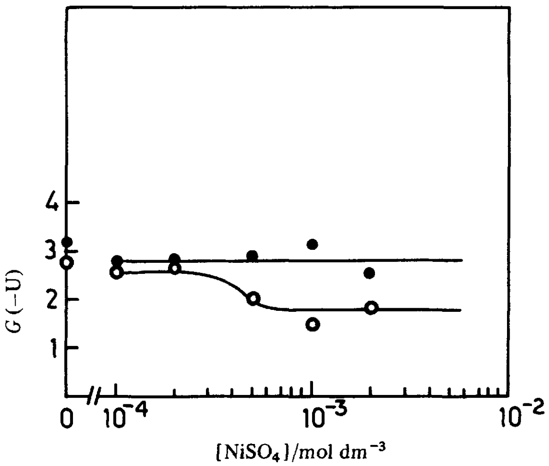

Fig. 2. Effect of initial concentration of $NiSO_4$ on the base degradation yield, $G(-U)$; [U] = 2×10^{-3} mol dm^{-3}: ○, argon-saturated solution; ●, N_2O-saturated solution.

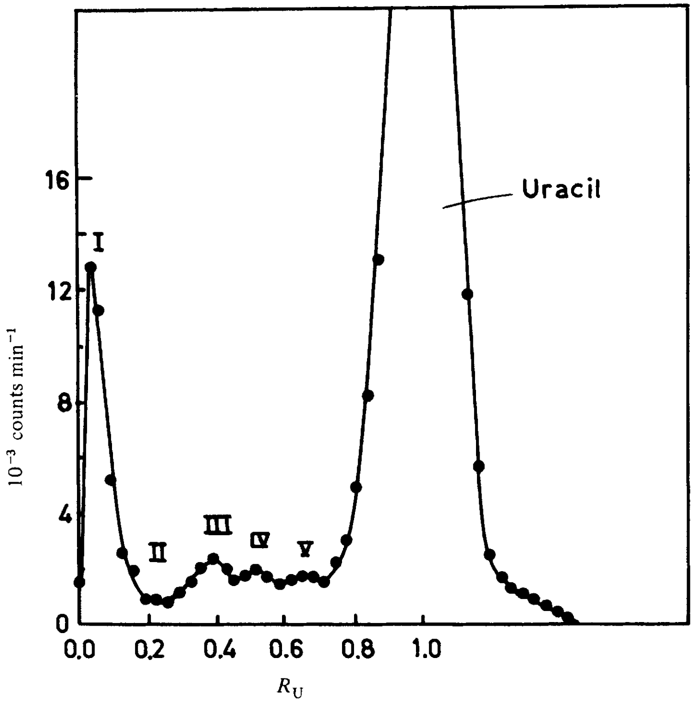

Fig. 3. Pattern of radioactivity on chromatogram of γ-irradiated 2×10^{-3} mol dm^{-3} .uracil solution in presence of 5×10^{-4} mol dm^{-3} $NiSO_4$ under N_2O-saturated conditions at neutral pH. Absorbed dose = 7.7×10^{18} eV cm^{-3} (1232 Gy). R_U denotes the distance travelled by each product with respect to that of uracil.

chromatogram is shown in fig. 3. The nature of the products formed is identical to that obtained in the radiolysis of uracil in the presence of other metal ions,[2, 3] *e.g.* Cu^{II} and Fe^{III}. The products corresponding to peaks (I)–(V) have been assigned as dimer(I), *cis*-uracil glycol(II), *trans*-uracil glycol(III), hydroxydihydrouracil(IV) and isobarbituric acid + dihydrouracil(V). The large peak is due to undecomposed uracil. Although $G(-U)$ values were followed from very low to high doses, because of the experimental difficulty in determining the very small concentration of the products formed during radiolysis at very low doses the product analysis was performed only for the higher doses, *e.g.* $(2\text{–}8) \times 10^{18}$ eV cm^{-3}, *i.e.* 320–1280 Gy. A typical plot for the formation of different products at various absorbed doses is shown in fig. 4. It is evident from fig. 4 that the formation of the products is linear with dose in the range $(2\text{–}8) \times 10^{18}$ eV cm^{-3}, *i.e.* 320–1280 Gy, and hence the yields were calculated from the slopes of the respective straight lines. The yields of different radiolytic products arising from the degradation of uracil at neutral pH in the presence of various Ni^{II} species, *e.g.* $NiSO_4$ and Ni^{II}EDTA, under different conditions of radiolysis are shown in table 2. It is evident from table 2 that Ni^{II} ions, whether present as $NiSO_4$ or as Ni^{II}EDTA, behave similarly in the degradation of uracil.

It is evident from table 1 that $G(-U)$ values observed in the deaerated solutions of uracil are decreased by the addition of Ni^{II} ions. This may be due to the partial scavenging of e^-_{aq} by Ni^{II} ions:

$$Ni^{II} + e^-_{aq} \rightarrow Ni^{I}. \qquad (5)$$

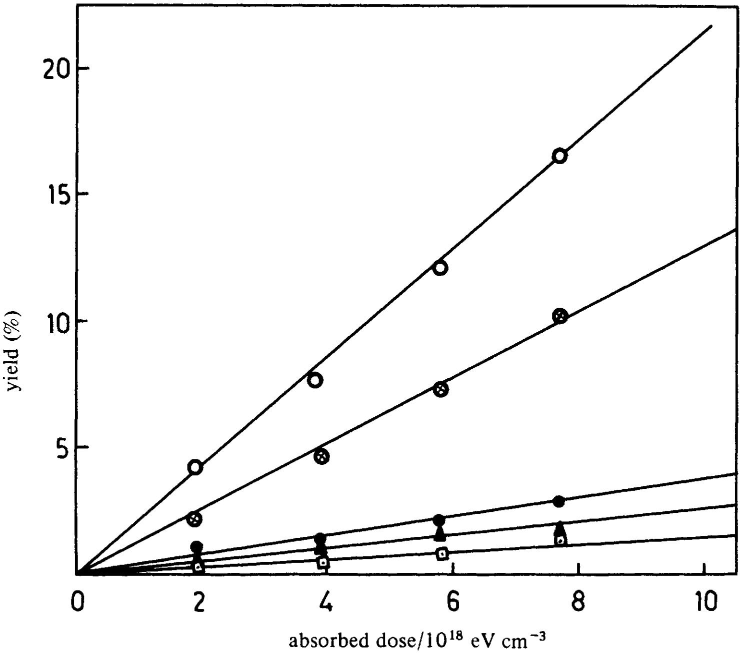

Fig. 4. Effect of absorbed dose on the degradation of uracil and the formation of different products during radiolysis of 2×10^{-3} mol dm^{-3} uracil in the presence of 5×10^{-4} mol dm^{-3} $NiSO_4$ in N_2O-saturated solution at neutral pH. Absorbed dose $(2-8) \times 10^{18}$ eV cm^{-3} (320–1280 Gy). ○, Loss of uracil; ⊗, dimer, ●, *trans*-uracil glycol; ▲, isobarbituric acid + dihydrouracil; □, hydroxydihydrouracil.

Table 2. Radiolytic yields of different products in the γ-radiolysis of uracil[a] in the presence of Ni^{II} compounds[b] at neutral pH

	condition					
G (products)	A	B	C	D	E	F
G (dimer)	0.8	1.5	0.1	0.5	1.4	0.1
G (*cis*-uracil glycol)	0.2	0.2	0.1	0.2	0.3	0.1
G (*trans*-uracil glycol)	0.3	0.5	0.3	0.5	0.6	0.8
G (hydroxydihydrouracil)	0.2	0.2	0.2	0.2	0.2	0.3
G (isobarbituric acid	0.3	0.3	0.3	0.3	0.3	0.3
G (dialuric acid)	—	—	1.6	—	—	0.7
G (−uracil)	1.8	2.9	2.8 (3.0)[c]	1.7	2.8	2.3

[a] [U] = 2×10^{-3} mol dm^{-3}; [b] [Ni^{II}] = 5×10^{-4} mol dm^{-3}; [c] determined spectrophotometrically from the loss of absorbance at 260 nm.

Conditions: A, $NiSO_4$ in argon-saturated solution; B, $NiSO_4$ in N_2O-saturated solution; C, $NiSO_4$ in aerated solution; D, Ni^{II}EDTA in argon-saturated solution; E, Ni^{II}EDTA in N_2O-saturated solution; F, Ni^{II}EDTA in aerated solution.

However, a consideration of the rate constant data (k_5 for $NiSO_4$ is *ca.* 2.9×10^{10} dm^3 mol^{-1} s^{-1}[12] and $k_1 \approx 1.1 \times 10^{10}$ dm^3 mol^{-1} s^{-1})[1] it is evident that under our experimental conditions where $[U] = 2 \times 10^{-3}$ mol dm^3 and $[Ni^{II}] = 5 \times 10^{-4}$ mol dm^{-3} only *ca.* 40% of e^-_{aq} will undergo reaction (5) and the rest will react with uracil *via* reaction (1) to give U^-. Again, as the k_5 values for Ni^{II}EDTA and Ni^{II}NTA are much lower[6,12] compared with that for $NiSO_4$, it is expected that in their presence almost all the e^-_{aq} will react with uracil to give U^-. Hence the identical $G(-U)$ values observed in the deaerated solution of uracil in the presence of both $NiSO_4$ and different Ni^{II} complexes are due to the fact that under these conditions the U^- radical transfers an electron to Ni^{II} and uracil is regenerated:

$$U^- + Ni^{II} \rightarrow Ni^{I} + U. \tag{6}$$

This type of electron transfer from U^- to a metal ion at a higher oxidation state has been shown previously[2,3] in the radiolysis of uracil in the presence of Fe^{III} and Cu^{II} ions. In N_2O-saturated solution where e^-_{aq} is converted to an equivalent amount of OH

$$e^-_{aq} + N_2O \rightarrow OH + OH^- + N_2 \tag{7}$$

the yield of the base degradation, $G(-U)$, when the radiolysis of uracil (2×10^{-3} mol dm^{-3}) is carried out in the presence of 5×10^{-4} mol dm^{-3} Ni^{II} ions, is double that obtained in deaerated solution. Hence, we conclude that under these conditions the intermediate UOH species formed through the reaction of OH radicals are responsible for the base degradation. This has been verified by irradiating 2×10^{-3} mol dm^{-3} uracil in the presence of the same concentration of Ni^{II} ions and 0.4 mol dm^{-3} 2-methylpropan-2-ol where $G(-U)$ values were found to be negligibly small (table 1). This is because 2-methylpropan-2-ol is a very good scavenger[12] of OH radicals and hence only e^-_{aq} is left behind to react with uracil to give U^-, which may then disappear *via* reaction (6). The question now arises as to whether the UOH radicals undergo reaction with Ni^{II} ions by electron transfer, as was observed in the case of Fe^{III} and Cu^{II} ions, or whether they undergo reactions between themselves, as was observed in the absence of any metal ion.[13] However, since the observed $G(-U)$ values (table 2) are the same regardless of whether Ni^{II} ions are present, it may be assumed that Ni^{II} ions have no influence on the reactivity of UOH radicals. Thus, when 2×10^{-3} mol dm^{-3} uracil is irradiated in the presence of 5×10^{-4} mol dm^{-3} $NiSO_4$ or Ni^{II}EDTA in N_2O-saturated solutions, the product distribution was found to be the same as that obtained in the absence of any metal ion. However, when the Ni^{II} ions are complexed with NTA or IDA the yields of dimer were found to decrease, with a simultaneous increase in the yield of *trans*-glycol. Furthermore, appreciable amounts of carbonyl compounds, *e.g.* formaldehyde and glyoxalic acid, were detected among the products. Note that these carbonyl compounds have been found to constitute the products of radiolysis when Ni^{II} complexes of EDTA, NTA and IDA are radiolysed[5-7] in aerated or in deaerated solution. The formation of these products may arise from oxidation of the corresponding complexes by OH and H radicals. However, a consideration of the rate constant data[1,5-7,12] for the reactions of OH with the Ni^{II} complexes and uracil shows that under the experimental conditions (table 1) the OH radicals will preferentially react with uracil rather than with the Ni^{II} complexes to form UOH *via* reaction (4). Hence the carbonyl compounds formed in the radiolysis of uracil and Ni^{II} complexes must result from the reaction of UOH with the complexes. In fact, the C_6–OH adduct of uracil has been reported to be oxidising and may oxidise Ni^{II} complexes by either of the two processes: (1) the C_6–UOH radical may oxidise Ni^{II} to Ni^{III}

$$Ni^{II}(R_2NCH_2COO^-) + UOH \rightarrow Ni^{III}(R_2NCH_2COO^-) + UOH^- \tag{8}$$

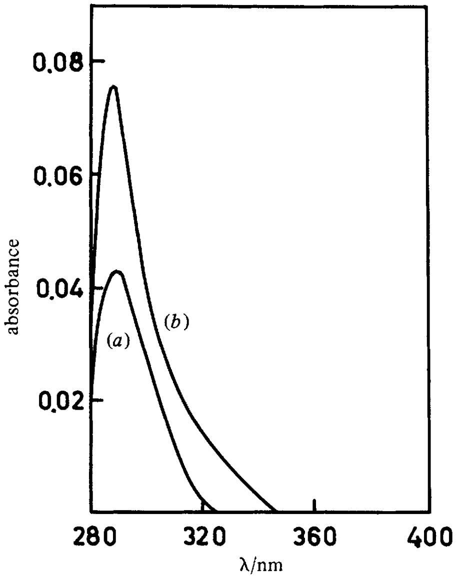

Fig. 5. Difference spectra of 2×10^{-3} mol dm^{-3} uracil in the presence of 5×10^{-4} mol dm^{-3} Ni^{II}EDTA in N_2O-saturated solution irradiated to a dose of (*a*) 1.7×10^{18} eV cm^{-3} (272 Gy) and (*b*) 3.4×10^{18} eV cm^{-3} (544 Gy).

or (2) it may abstract hydrogen from the ligand to form a dehydrogenated radical

$$\mathrm{Ni^{II}(R_2NCH_2COO^-) + UOH \rightarrow Ni^{II}(R_2NCHCOO^-) + UHOH.} \qquad (9)$$

However, if reaction (9) occurs, then the products of degradation should be mostly hydroxydihydrouracil, but the yield of this product is not large enough. Hence we presume that the other alternative, reaction (8), determines the fate of the UOH radicals. Thus Ni^{II} will be oxidised to Ni^{III} and the Ni^{III} complex species[7] may then give rise to carbonyl compounds:

$$\mathrm{Ni^{III}(R_2NCH_2COO^-) \longrightarrow Ni^{II}(R_2NCH_2COO)}$$
$$\xrightarrow{-\mathrm{CO_2}} \mathrm{Ni^{II}(R_2NCH_2)} \xrightarrow{\mathrm{H_2O}} \mathrm{Ni^{I}R_2NH + CH_2O + H^+} \qquad (10)$$

$$\mathrm{Ni^{III}(R_2NCH_2COO^-) + Ni^{II}(R_2NCH_2COO^-)}$$
$$\longrightarrow \mathrm{Ni^{II}(R_2NCH_2COO^-) + Ni^{II}(R_2NCHCOO^-) + H^+} \qquad (11)$$

$$\mathrm{2Ni^{II}(R_2NCHCOO^-) \longrightarrow Ni^{II}(R_2NCH_2COO^-) + Ni^{II}R_2NH + CHO \cdot COOH}$$
$$\longrightarrow \mathrm{Ni^{II}(R_2NCH_2COO^-) + Ni^{II}R_2NH + CO_2 + CH_2O.} \qquad (12)$$

Evidence for the formation of Ni^{III} species has been put forward by Lati and Meyerstein[15] in the radiolysis of Ni^{II}EDTA in N_2O-saturated solution. They found that the species is stable even after 10 min irradiation. Formation of Ni^{III} species was also followed in the present investigation during the radiolysis of uracil in the presence of Ni^{II} complexes. Fig. 5 shows the difference spectrum of the products formed during the radiolysis of uracil in the presence of Ni^{II} EDTA in N_2O-saturated solution for different absorbed doses. The product is stable and has an absorption maximum at 295 nm, which agrees with that reported by Lati and Meyerstein.[15] We then infer that

Table 3. Yields of H_2O_2 in the γ-radiolysis of uracil[a] in the presence of different Ni^{II} compounds[b]

Ni^{II} compound	conditions	$G(H_2O_2)^e$	$G(H_2O_2)+G(Ni^{III})^f$
$NiSO_4$	argon satd	0.6	0.5
$NiSO_4$	N_2O satd[c]	0.8	1.1
$NiSO_4$	aerated[d]	2.0	5.0
Ni^{II}EDTA	argon satd	0.5	0.8
Ni^{II}EDTA	N_2O satd[c]	0.5	1.2
Ni^{II}EDTA	aerated[d]	2.4	5.4
Ni^{II}NTA	argon satd	0.3	1.0
Ni^{II}NTA	N_2O satd[c]	0.8	1.4
Ni^{II}NTA	aerated[d]	2.1	3.6
Ni^{II}IDA	argon satd	0.3	1.2
Ni^{II}IDA	N_2O satd[c]	0.9	1.8
Ni^{II}IDA	aerated[d]	2.8	3.6

[a] $[U] = 2\times10^{-3}$ mol dm^{-3}; [b] $[Ni^{II}] = 5\times10^{-4}$ mol dm^{-3}; [c] $[N_2O] \approx 2.5\times10^{-2}$ mol dm^{-3}, ref. (20); [d] $[O_2] \approx 2.7\times10^{-4}$ mol dm^{-3}, ref. (21); [e] measured by Ti^{III} sulphate method; [f] measurement of I^- oxidation.

the observed absorption is due to Ni^{III} EDTA. This is supported by the fact that it oxidises KI solution liberating iodine. Thus the yield of H_2O_2 was measured both by the $Ti_2(SO_4)_3$ method[8] and using KI.[9] The results are shown in table 3, from which it is evident that when the Ni^{II} ions are complexed, the amount of I^- oxidised does not agree with what is expected from H_2O_2, as measured by the $Ti_2(SO_4)_3$ method. The enhanced oxidation of I^- may reasonably be thought to be formed by the intermediate formation of Ni^{III} complexes.

It is evident from the above discussion that the extent of base degradation will be determined by the subsequent transformation of the UOH^- which is formed in reaction (8). However, a major portion of the UOH^- is known to revert back to uracil

$$UOH^- \xrightarrow{H_2O} U + OH^- \tag{13}$$

and only a small portion of it undergoes reaction with water to form hydroxydihydrouracil[3, 13]

$$UOH^- \xrightarrow{H_2O} UHOH + OH^-. \tag{14}$$

In fact the observed small yields of hydroxydihydrouracil as shown in table 2 are in good agreement with this. The proposed mechanism, however, requires that the base-degradation yield (table 2) should be equal to the yield of hydroxydihydrouracil. However, the base-degradation yield is much higher (table 2). Besides hydroxydihydrouracil, the products comprise dimer, glycols and isobarbituric acid. Hence there must be other pathways for the disappearance of UOH leading to the formation of these products.

In connection with this it is instructive to consider the redox behaviour of the UOH adduct. Although the C_6–OH adduct is oxidising, the other form of the adduct, *i.e.* C_5–UOH, is known to be reducing[14] and hence it may be assumed that a part of the adduct undergoes electron transfer to Ni^{II}, as was observed with other metal ions,[2,3] *e.g.* Cu^{II} and Fe^{II}:

$$UOH + Ni^{II}(R_2NCH_2COO^-) \rightarrow UOH^+ + Ni^{I}(R_2NCH_2COO^-). \quad (15)$$

The UOH^+ formed in reaction (15) then undergoes various reactions to give different products[2,3]

$$\begin{tikzcd} & U(OH)_2(glycol) \\ UOH^+ \arrow[ur, "a"] \arrow[dr, "b"'] & \\ & UO\ (isobarbituric\ acid) \end{tikzcd} \quad (16)$$

$$UOH^+ + UOH^- \rightarrow dimer. \quad (17)$$

Evidence for the occurrence of reaction (15) cannot be put forward unless the formation of Ni^{I} species is followed. However, it is not possible to follow the formation of Ni^{I} species in steady-state radiolysis and hence the occurrence of reaction (15) is uncertain, although a comparison of the electron-transfer rate of other reducing agents with Ni^{II} may provide an explanation. It has been shown by Buxton *et al.*[16,17] that strong reducing agents such as $CO_2^{\cdot -}$ do not reduce Ni^{II} to Ni^{I} efficiently. Furthermore, if reaction (15) is followed by reactions (16) and (17), then the UOH radicals could not revert back to uracil and hence radiosensitisation of uracil by Ni^{II} ions would have been observed. Hence the possibility of the occurrence of reaction (15) is questionable.

The alternative is that the UOH radicals undergo the reactions that were observed[13] in the absence of any metal ion to give rise to different products:

$$2\ UOH \longrightarrow dimer \quad (18)$$

$$2\ UOH \longrightarrow UOH^+ + UOH^-. \quad (19)$$

$$UOH^- \xrightarrow{H_2O} U + OH^- \quad (13)$$

$$UOH^+ \xrightarrow{H_2O} U(OH)_2 + UO \quad (16)$$

$$UOH^+ + UOH^- \longrightarrow dimer \quad (17)$$

AERATED SOLUTIONS

When uracil solutions are radiolysed in the presence of different Ni^{II} compounds in aerated solutions, the base-degradation yields were found to be equivalent to G_{OH} (table 1). Under the experimental conditions, where $[uracil] = 2 \times 10^{-3}$ mol dm^{-3} and $[Ni^{II}] = 5 \times 10^{-4}$ mol dm^{-3}, the OH radical and the major portion of e_{aq}^- will react with uracil giving UOH and U^-, respectively,[1,12] but the H atoms will be scavenged to give HO_2 which will subsequently give rise to H_2O_2:

$$H + O_2 \rightarrow HO_2 \quad (20)$$

$$2\ HO_2 \rightarrow H_2O_2 + O_2. \quad (21)$$

It was observed previously that the U^- radicals readily transfer electrons to electron-affinic compounds.[18] Two possibilities may arise: either it reduces oxygen to O_2^- or it reduces Ni^{II} to Ni^{I}. If O_2^- is formed, it will give rise to the formation of hydrogen peroxide:

$$2O_2^- + 2H^+ \rightarrow H_2O_2 + O_2. \quad (22)$$

Hence if the U^- transfers an electron to O_2, the yield of hydrogen peroxide would be $\frac{1}{2}[G(\text{H})+G(e^-_{aq})]+G(\text{H}_2\text{O}_2) = 2.4$, and the observed yield of H_2O_2 is close to this value (table 3). Hence it may be argued that the U^- radicals do not reduce Ni^{II} in aerated solution, but react with O_2 and regenerate uracil. As UOH is less reducing[18] than U^- or UH, it is expected that it will react with oxygen to give peroxy compounds which will subsequently give rise to different products:[1, 14, 19]

$$\text{UOH}+\text{O}_2 \rightarrow \text{U(O}_2\text{)OH} \rightarrow \text{U(OH)}_2+\text{UO}. \tag{23}$$

Note that in the radiolysis of uracil in presence of Cu^{II}, some Cu^{I} was observed, even in the aerated solutions.[3] This small reduction of Cu^{II} to Cu^{I} was attributed to the U^- radicals transferring electrons to Cu^{II}. Furthermore, when uracil is radiolysed in the presence of Fe^{III} ions[2] at pH *ca.* 1 in an aerated medium, a small fraction of Fe^{II} was formed because of the partial reduction of Fe^{III} to Fe^{II} by UOH radicals. These differences in the behaviour of U^- or UOH in reducing the metal ions may be because of the different redox behaviour of the $\text{Fe}^{\text{III}}/\text{Fe}^{\text{II}}$, $\text{Cu}^{\text{II}}/\text{Cu}^{\text{I}}$ and $\text{Ni}^{\text{II}}/\text{Ni}^{\text{I}}$ systems.[5] The redox potential for the last is comparatively low in comparison with the former two and hence no reduction of Ni^{II} because of U^- or UOH was observed in aerated solutions in the present investigation.

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