EPR spin-trapping investigation into the mechanism of *tert*-butylhydroperoxide decomposition by CU^{2+} ions: evidence for single-electron reduction with initial generation of $^{\bullet}OC(CH_3)_3$and CU^{3+}

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Lipid peroxidation (e.g., in low density lipoprotein) is often initiated *in vitro* by CU^{2+} ions, which are widely assumed to oxidise lipid hydroperoxides (LOOH) to peroxyl radicals (Reaction 1). The Cu^{+} generated may then react with LOOH to generate alkoxyl radicals (Reaction 2).

$$CU^{2+} + LOOH \longrightarrow Cu^{+} + LOO^{\bullet} + H^{+} \quad (1)$$

$$Cu^{+} + LOOH \longrightarrow CU^{2+} + LO^{\bullet} + OH^{-} \quad (2)$$

However, Reaction 1 is thermodynamically unfavourable. An alternative mechanism has been proposed in which LOOH undergoes single-electron *reduction* by CU^{2+} (Reaction 3).

$$CU^{2+} + LOOH \longrightarrow CU^{3+} + LO^{\bullet} + H^{+} \quad (3)$$

We have studied the reaction between CU^{2+} (complexed to simple peptides) and *tert*-buty1hydroperoxide in the presence of 5,5-dimethyl-1-pyrroline-*N*-oxide (DMPO). Spectra contained signals from the $^{\bullet}OC(CH_3)_3$ and $^{\bullet}CH_3$ adducts of IDMPO. Prominent signals from the $^{\bullet}OCH_3$ adduct were also often present. In some earlier studies, this signal has been assigned incorrectly to the $^{\bullet}OOC(CH_3)_3$ adduct, which is now known to be unstable. In order to determine whether generation of these radicals involves oxidation or reduction of ^{t}BuOOH by CU^{2+} complementary reactions were conducted using metal complexes of well-characterised redox behaviour. Based on the findings from experiments involving the CU^{2+} complex of bathocuproine disulfonate and the Fe^{2+} complex of diethylenetriaminepentaacetate, we propose that ^{t}BuOOH undergoes a single-electron reduction by CU^{2+}, forming CU^{3+} and the *tert*-butoxyl radical, which undergoes rapid β-scission to $^{\bullet}CH_3$ (forming $^{\bullet}OCH_3$ upon oxygen addition). These findings have important implications for the mechanisms by which CU^{2+} initiates lipid peroxidation.

Supported by the Cancer Research Campaign