

¹⁸O-LABELED LINOLEIC ACID HYDROPEROXIDE INDUCES THE FORMATION OF ¹⁸O-LABELED 7,8-DIHYDRO-8-OXO-2'-DEOXYGUANOSINE

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Lipid hydroperoxides are potentially toxic compounds generated as primary products of lipid peroxidation. Despite their relative stability, these hydroperoxides are easily decomposed by metal ions, generating oxyl radicals, reactive breakdown products and singlet oxygen. These reactive species are capable to induce potentially mutagenic DNA base modifications, such as 7,8-dihydro-8-oxo-2'-deoxyguanosine (8-oxodGuo). The aim of this study was to characterize the mechanism involved in LOOH mediated oxidation of 2'-deoxyguanosine (dGuo). For this purpose we used ¹⁸O-labeled linoleic acid hydroperoxide (LA¹⁸O¹⁸OH) and detected the products by HPLC-MS/MS. Incubations of dGuo with LA¹⁸O¹⁸OH and Cu(II) in 50 % acetonitrile at 37°C for 5 min yielded [¹⁸O]-8-oxodGuo as well as [¹⁶O]-8-oxodGuo at a ratio of 86:14. The level of [¹⁸O]-8-oxodGuo was not changed in the presence 78% H₂¹⁸O. Interestingly, the total amount of 8-oxodGuo was 30 % higher in the reaction conducted in D₂O. The increase in 8-oxodGuo in the presence of D₂O and the detection of [¹⁸O]-8-oxodGuo strongly points to the involvement of ¹⁸O-labeled singlet oxygen as the intermediate responsible for the oxidation of dGuo.

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