P-29

Characterization of the products from UVA irradiated N-nitrosoproline with deoxyguanosine

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N-Nitrosoproline (NPRO) is known to formed from N-proline with nitrite in vivo. Previously we reported that UVA-irradiated NPRO induced single strand DNA breaks, photo-mutagenicities in the Ames test and micronucleous formation in the human derived cultured cell (WTK-1). In this study, we investigate the photoreaction of 2'-deoxyguanosine (dGuo) with NPRO plus UVA.

1 mM of dGuo and 10 mM of NPRO were dissolved in Na phosphate buffer (10 mM at pH 7.4) or Na acetate buffer (10 mM at pH 4.3, or 3 M at pH 3.7), and then irradiated with UVA (320-400 nm, 0.98 mW/cm\textsuperscript{2}) at 4\textdegree{}C with continuous shaking. Irradiation was also performed with monochromatic light at 320, 340 and 360 nm. The reaction mixture was analyzed by HPLC-UV and -ECD.

Irradiation time-dependent decrease of NPRO and formation of 8-oxo-deoxyguanosine (8-oxodG) were observed in the neutral condition. The formation of 8-oxodG was highest at 340 nm, the absorption maximum of NPRO. In the acidic condition, formations of 8-oxodG and two other product-peaks were observed. These observation suggests formation of 8-oxodG and other photoprodut might play a role in the photomutagenesis caused by NPRO + UVA.

N-ニトロソプロリンのUVA光反応によるデオキシグアノシン付加体形成
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P-30

Site-specific DNA damage induced by purpurin, a natural pigment, with reference to carcinogenesis

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Key Words: Purpurin, DNA damage, Carcinogenesis

Purpurin (1,2,4-trihydroxy-9,10-anthraquinone) is a natural pigment isolated from madder root (Rubia tinctorum). It has been reported that purpurin is carcinogenic to male rats. To clarify the mechanism of carcinogenesis by purpurin, we investigated the ability of DNA damage induced by purpurin using \textsuperscript{32}P-5'-end-labeled DNA fragments obtained from the c-Ha-ras-1 protooncogene and the p16 and p53 tumor suppressor genes. Purpurin caused DNA damage in the presence of Cu(II). Piperidine treatment led to DNA damage, suggesting that purpurin caused base modification without breakage of deoxyribose phosphate backbone. Purpurin frequently induced piperidine-labile sites at continuous guanine and thymine residues in DNA fragments. Typical free hydroxyl radical (•OH) scavengers and H\textsubscript{2}O\textsubscript{2} scavengers did not inhibit the DNA damage. Bathocuproine, a Cu(I) chelator, and SOD inhibited Cu(II)-mediated DNA damage induced by purpurin, suggesting that Cu(I) and O\textsubscript{2}\textsuperscript{−} required for the DNA damage. Finally, it is concluded that clustered DNA damage induced by purpurin appears to play an important role in purpurin induced-carcinogenesis.

天然色素purpurinによる塩基特異的DNA損傷：発がんとの関連
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