P-43

Analysis of DNA adducts formed from chloropropyl nitrosamine

S Ishikawa, M Hatanaka, R Odamaki and M Mochizuki (Kyoritsu Univ Pharm) ishikawa-st@kyoritsu-ph.ac.jp

Keywords: Nitrosamines; DNA adducts; DNA Cross-link

N-Nitroso-N-(acetoxymethyl)-3-chloropropylamine (CP) is one of the chlorinated nitrosamines designed for new candidates as mimics of antitumor chloroethyl nitrosoureas. CP showed direct mutagenicity not only in Salmonella typhimurium TA1535, but also in TA92, suggesting that it acted as bifunctional alkylating agent. Furthermore, CP formed DNA interstrand cross-links in plasmid DNA. To elucidate the detail mechanism of bifunctional behaviour of CP, we investigated CP-derived DNA adducts.

CP reacted with 2'-deoxyguanosine (dG) in phosphate buffer (pH 7.4), 37 °C, in the presence of esterase. When the reaction solution was analyzed by HPLC, four peaks were detected in addition to dG. Because the peak area of new peaks increased time- and CP dose-dependently, these peaks were thought to be formed from CP. Preparative HPLC was performed and one of the isolated fractions was analyzed by 1H-NMR. The NMR showed the signals for protons derived from deoxyribose, and three methylene signals were equimolar to deoxyribose. Furthermore, in MALDI-TOF-MS analysis, the mass ion detected was matched for chloropropylated guanine, showing that CP adducted dG. Studies using double stranded DNA is in progress to detect cross-linked adducts.

P-44

キャンセルになりました