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Poster Presentation
SCOPE; Radioisotopes in Nuclear medicine

SYNTHESIS AND EVALUATION OF A NOVEL SUGAR CONJUGATED PLATINUM COMPLEX LABELED WITH ^{191}Pt

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Platinum antitumor agents such as cisplatin are widely used in the clinical treatments even now and adopted in many regimens of chemotherapy for various cancer. Although they have very potent antitumor activities, serious side effects are often caused by the strong cytotoxicity against normal cells due to their lack of tumor specificity. Therefore, it is necessary to develop novel platinum complex having high tumor selectivity. In this study, we decided to design and evaluate a novel sugar conjugated platinum complex (FDG-Pt) for improved tumor uptake and reduced side effects by using the drug properties of 2-deoxy-2-[^{18}F]fluoroglucose ([^{18}F]FDG) for PET diagnosis, namely cellular uptake via the glucose transporter and intracellular metabolic trapping. In order to clarify the pharmacokinetic properties of FDG-Pt, we also decided to develop FDG-Pt labeled with^{191}Pt ([^{191}Pt]FDG-Pt).

FDG-Pt was synthesized by complex formation through the introduction of Pt into the 1,3-diamine moiety. The cytotoxicity of FDG-Pt was evaluated in cultured Hela cells by the MTS assay. [^{191}Pt]FDG-Pt was synthesized using [^{191}Pt]K_2PtCl_4 produced by accelerator neutron activation method（Nagai, et al. *J.Phys. Soc. Jpn*, 2013, 82, 064201）, and the progress of ^{191}Pt labeling reaction was investigated by HPLC analysis and TLC-autoradiography. We injected [^{191}Pt]FDG-Pt intravenously via the tail vein to healthy mice and tumor-bearing mice (Hela cells), and evaluated its biodistribution of [^{191}Pt]FDG-Pt by calculating the radioactivity concentration (%ID/g) in each organ after dissection.

FDG-Pt was synthesized from 1,3,4,6-tetra-*O*-acetyl -*β*- D –mannopyranose in a total of 8 steps with a total yield of 11.3%. From the results of MTS assay, it was found that FDG-Pt exhibits cell- killing activity in a concentration-dependent manner. [^{191}Pt]FDG-Pt was obtained as a radiochemical yield of 14.5 ± 8.0% (n=6). Although preliminary, [^{191}Pt]FDG-Pt was found to accumulate in tumor: 0.74 %ID/g, liver: 1.00 %ID/g, and kidney: 1.86 %ID/g at 24 hours after administration, with the highest accumulation in the thyroid at 47.3%ID/g. High accumulation in the thyroid was observed even in healthy mice.

Since FDG-Pt has cell-killing activity and [^{191}Pt]FDG-Pt showed accumulation in tumor, FDG-Pt meet the basic requirements for a novel platinum complex.