분류번호	III-1

제 목	제 3세대 백금착체 항암제 신약개발 1. Design, synthesis and antitumor activity of 3rd generation platinum complexes.
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As part of a research program to develope 3rd generation antitumor platinum complexes, a series of platinum complexes which have 4,5-bis-(aminomethyl)-1,3-dioxolane derivatives as bidenate amine ligands, represented by the general structual formula was prepared.

The R_1 and/or R_2 substituents in this series of platinum complexes can be hydrogen, alkyl, or jointly formed cyclohexane. Two X_s can be a bidenate leaving ligand such as 1,1-cyclobutanedicarboxylate, malonate, dimethylmalonate, ethylmalonate, glycolate, L-lactate, or N-methyliminodiacetate. From based on the pharmacological and toxicological studies, we have chosen SKI 2053R, *cis*-malonato[(4R,5R)-4,5-bis(aminomethyl)-2-isopropyl-1,3-dioxolane] platinum(Ⅱ) complex (NSC D644591) as a candidate for clinical evaluation.

The antitumor activity of a new antitumor platinum complex, *cis*-malonato [(4R,5R)-4,5-bis(aminomethyl)-2-isopropyl-1,3-dioxolane]platinum(Ⅱ) (SKI 2053R, NSC D644591), was compared with those of cisplatin and carboplatin using murine tumors. We evaluated three platinum complexes against L1210/CPR, a subline of L1210 leukemia resistant to cisplatin for their abilities to overcome tumor resistance to cisplatin. The *in vitro* cytotoxicity of SKI 2053R to L1210 cell line was 2.5-fold less potent than that of cisplatin, and was 10-fold more cytotoxic than that of carboplatin. SKI 2053R retained similar cytotoxic effect and antitumor activity to L1210/CPR cell line, like the cytotoxicity of SKI 2053R to L1210 cell line, while either cisplatin or carboplatin had not property to overcome the acquired cisplatin-resistance. SKI 2053R exhibited greater or comparable antitumor activity than cisplatin or carboplatin in murine tumor models.