분류번호	IV-P-2

The Acute Toxicity of Novel Platinum(II) Complexes

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This study was conducted to examine novel Pt(II) complexes, (KHPC-002: [Pt(trans-1-dach) (DPPE)].$2NO_3$, KHPC-005:[Pt(cis-1-dach)(DPPP)].$2NO_3$ and KHPC-006:[Pt(cis-1-dach) (DPPE)]. $2NO_3$) for their acute toxicities and toxicological profiles in preclinical studies.

In male and female mice given a single intraperitoneal administration of KHPC-002, KHPC-005 and LHPC-006, we determined that LD_{50} values of pt(II) complexes were 295.5mg/kg(M), 350.4mg/Kg(F):KHPC-002, 158.7mg/Kg(M), 157.7mg/Kg(F); KHPC-005, 574.8mg/Kg(M), 596.5 mg/Kg (F); KHPC-006, respectively. In gross and histopathological examination on dead animals, no abnormal changes were observed in any organs.

In the acute toxicity study in rats, three dosing groups of Sprague-Dawley male rats in each compounds were given a single intraperitoneal injection of KHPC-002, KHPC-005 and KHPC-006. In order to compare the toxic effects of these novel Pt(II) complexes with those of cisplatin, one group Sprague-Dawley male rats were given 7mg/kg i.p injection of cisplatin. Body weights showed dose-related decrease in all treatment groups when compared with the control group.

From the results of hematological examination, KHPC-002 (60mg/kg) and KHPC-005(120mg/kg) reduced white blood cells and platelet counts in contrast to the increase of those in KHPC-006 (120mg/kg).

Serum biochemical values of KHPC-002 and KHPC-005 showed a normal range of BUN and slightly increase in the creatinine values. However, KHPC-006 (120mg/Kg) showed 1.5 fold increase the BUN and creatinine values, indicating nephrotoxicity. The decreae of ALP values were observed in high dose administration group of KHPC-005 and KHPC-006. No changes were detected in serum hepatotoxicological values (such as ALT, AST, glucose and total bilirubin) of KHPC-002, KHPC-005 and KHPC-006. Considering the results of this study, the toxic profiles of these new Pt(II) complexes were considerably lower than those of cisplatin.