분류번호	IV-P-6

New platinum-complex compounds with reduced nephrotoxicity discovered in long term histoculture of human renal cortex

Chang, S-G[1], Jung, J.C.[1], Rho,Y.S[1].,Kwon, D.U[1].,and Hoffman, R.M[2].

The Kyung Hee University, Seoul Korea[1], Anticancer Inc. 7917 Ostrow St. San Diego, CA 92111 U.S.A.[2], Lab. of Cancer Biology, University of California, San Diego, La Jolla, CA, 92093-0609 U.S.A.[2]

Cisplatinum is often effective in cancer treatment, but potent nephrotoxicity limits its clinical use. We have, therefore, developed new anticancer drugs that contain platinum. We have synthesized six new platinum compounds based on Figure 1.

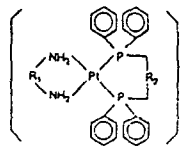

Fig.1

R_1 : trans-l-cyclohexane-, R_2 : $-CH_2-CH_2-$(drug B),
R_1 : trans-d-cyclohexane-,R_2 : $-CH_2-CH_2-$(drug D),
R_1 : cis-cyclohexane-, R_2 : $-CH_2-CH_2-CH_2-$(drug E),
R_1 : cis-cyclohexane-, R_2 :$-CH_2-CH_2-$ (drug F),
R_1 : $-CH_2-CH_2-$, R_2 : $-CH_2-CH_2-CH_2-$ (drug H)
R_1 : $-CH_2-CH_2-$, R_2 : $-CH_2-CH_2-$ (drug I)

Drugs were initially administrated at 5 x 10^{-4}M with 48 hours exposure in monolayer cultures of primary rabbit proximal tubular cells and human renal cortical cells with the M.T.T. endpoint to measure toxicity.

Drug concentrations of 10^{-3}M, 10^{-4}M, and 10^{-5}M with 72 hours exposure were used for human renal cortical tissues in 7 weeks histoculture with toxicity measured by the glucose-consumption endpoint.

From these studies, we determined that the new platinum drugs have lower nephrotoxicity than cisplatinum.

Drugs D, E, and H. have lower nephrotoxicity than the other new drugs.

We are currently measuring the anticancer efficacy of drugs D, E, and H.