[PD1-48] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Inhibition of prostaglandin E2 production by hydroxychalcone derivatives and the mechanism of action

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Effects of fifteen chalcone derivatives synthesized on prostaglandin E_2 production in rat peritoneal macrophages stimulated by 12-O-tetradecanoylphorbol-13-acetate (TPA), were examined to clarify the structure-activity relationship. Among chalcone derivatives tested, 2',4-dihydroxy-4'-methoxychalcone (compound 3), 2',4-dihydroxy-6'-methoxychalcone(compound 8) and 2'-hydroxy-4'-methoxychalcone (compound 9) were found to suppress significantly prostaglandin E_2 production, even at the concentration as low as 3 μM. Cyclooxygenase (COX)-1 isolated from sheep seminal vesicle was slightly inhibited by compound 9, although it showed no inhibition of COX-2 isolated from sheep placenta. At concentrations to inhibit prostaglandin E_2 production, compound 9 showed no effect on the release of radioactivity from [^{3}H]arachidonic acid-labeled macrophages stimulated by TPA. Western blot analysis revealed that the induction of COX-2 protein by TPA was inhibited by these three compounds in parallel with the inhibition of prostaglandin E_2 production. These findings suggest that the inhibition of prostaglandin E_2 production by these chalcone derivatives is due to the inhibition of TPA-induced COX-2 protein expression and 2-hydroxy, 4- or 6-methoxy and 4'-hydroxy or 4'-hydrogen groups are required for the expression of the inhibitory activity of prostaglandin E_2 production.

[PD1-49] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Novel Platinum(IV) compound, K101, having octahedral structure as Anticancer agent I - Synthesis and Evaluation of Anticancer activity

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Novel Pt(IV) compound, trans,cis-[Pt(acetato)2Cl2(1,4-butanediamine)] (K101) was synthesized for the purpose of development as new anticancer drug. The octahedal structure of trans,cis-[Pt(acetato)2Cl2 (1,4-butanediamine)] was determined by X-ray crystal diffraction method. Anticancer activity was examed using murine and human 12 cancer cell lines. Among them, K101 has shown excellent anticancer activity in human colon and breast cancer cell line realtive to cisplatin in vitro. In IC50 values, K101 is 1.95, 1.23μmol/mℓ and cisplatin is 7.89, 14.67μmol/mℓ in HCT116, HCT15 cell lines, K101 is 1.86, 1.25, 2.89μmol/mℓ and cisplatin is 10.33, 12.23, 17.51μmol/mℓ in SK-BR3, MCF7, MDA-MB231, respectively. In vivo activity against mouse B16 melanoma, antitumor activity of K101 is similar to cisplatin.

[PD1-50] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Selective cytotoxicity of a new platinum(II) complex on human ovarian cancer cell-lines and normal kidney cells

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