Highly Sensitive Determination Method for Orally Active Antitumor Platinum Complexes of Next Generation and Their Active Metabolites

1996 Fiscal Year Final Research Report Summary

Highly Sensitive Determination Method for Orally Active Antitumor Platinum Complexes of Next Generation and Their Active Metabolites

Research Project

Project/Area Number

07672312

Research Category

Grant-in-Aid for Scientific Research (C)

Allocation Type

Single-year Grants

Section

一般

Research Field

Physical pharmacy

Research Institution

Kanazawa University

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1995 – 1996

Keywords

antitumor agent / platinum complex / oral agent / pro-drug / active metabolite / HPLC / biological sample / highly sensitive determination method

Research Abstract

This study was conducted to develop highly sensitive method for determining orally active antitumor platinum complexes of the next generation and their active metabolites. The complexes used were trans, cis, cis-bis (n-butyrato) (1R,2R-cyclohexanediamine) (oxalato) platinum (IV) (C4-OHP) and trans, cis, cis-bis (n-valerato) (1R,2R-cyclohexanediamine) (oxalato) platinum (IV) (C5-OHP), which are expected as promising oral agents because of their high antitumor activities in screening tests. Oral antitumor activities of C4-OHP and C5-OHP were first evaluated in mice bearing mouse leukemia L 1210. Significant increase in life span was observed with C5-OHP-treated group but not with C4-OHP-treated group. Therefore, subsequent study was made mainly on C5-OHP.Then, HPLC method for determining C5-OHP in biological samples was developed. C5-OHP was extracted with ethyl acetate and then subjected to reversed-phase HPLC.C5-OHP was chromatographed on an ODS column with water/methanol eluent and spectrophotometrically detected by at 210 nm. This method was found to be highly sensitive, giving the detection limit of 50 nM.C5-OHP in plasma, urine and cultured cell samples could be determined. Next, examination of active metabolites of C5-OHP was made by means of HPLC,revealing that (1R,2R-cyclohexanediamine) (oxalato) platinum (II) (OHP) was yielded from C5-OHP and the production was almost quantitative. Therefore, HPLC method for determining OHP in biological samples was developed. OHP was chromatographed in reversed-phase mode followed by post-column derivatization by sodium bisulfite and spectrophotometric detection at 290 nm. This method was also sensitive, giving the detection limit of 50 nM.The method required no pretreatment of samples but deproteinization by ultrafiltration and applicable to plasma, urine and cultured cell samples.

Research Products (10 results)

All | Other

All | Publications (10 results)

[Publications] Ryoichi Kizu: "Development of New Oral Antitumor 1R, 2R-Cyclohexanediamine-Platinum (IV) Complex : trans- (n-Valerato) chloro (1R, 2R-cyclohexanediamine) (oxalato) platinum (IV)" Cancer Chemotherapy and Pharmacology. (1997)

[Publications] Masazumi Eriguchi: "Development of Orally Active Antitumor 1R, 2R-cyclohexanediamine-Pt (IV) Complexes : trans-Bis (carboxylato) (oxalato) (1R, 2R-cyclohexanediamine) platinum (IV)" Metal-Based Drugs. (1997)

[Publications] Ryoichi Kizu: "An Orally Active Antitumor Cyclohexanediamine-Pt (IV) Complexes : trans, cis, cis-Bis (n-valerato) (oxalato) (1R, 2R-cyclohexanediamine) Pt (IV)" Anti-Cancer Drugs. 7. 248-256 (1996)

[Publications] Ryoichi Kizu: "A Sensitive Postcolumn Derivatization/UV Detection System for HPLC Determination of Antitumor Divalent and Quadrivalent Platinum Complexes" Chemical & Pharmaceutical Bulletin. 43. 108-114 (1995)

[Publications] Yoshinori Kidani: "Platinum and Other Metal Coordination Compounds in Cancer Chemotherapy 2" H. M. Pinedo and J. H. Shornagel, 357 (1996)

[Publications] Motoichi Miyazaki: "Strategy for Air Pollution Control in East Asia" E. Hirai, 152 (1996)

[Publications] R.Kizu, T.Nakanishi, T.Tashiro, M.Noji, A.Matsuzawa, M.Eriguchi, Y.Takeda, N.Akiyama and Y.Kidani: "Development of New Oral Antitumor 1R,2R-Cyclohexanediamine-Platihum (IV) Complex : trans- (n-Valerato) chloro (1R,2R-cyclohexanediamine) (oxalato) platinum (IV)" Cancer Chemotherapy and Pharmacology. (accepted).

[Publications] M.Eriguchi, A.Matsuzawa, Y.Takeda, N.Akiyama, T.Tashiro, R.Kizu and Y.Kidani: "Development of Orally Active Antitumor 1R,2R-cyclohexanediamine-Pt (IV) Complexes : trans-Bis (carboxylato) (oxalato) (1R,2R-cyclohexane-diamine) platinum (IV)" Metal-Based Drugs. (accepted).

[Publications] R.Kizu, T.Nakanishi, T.Tashiro, M.Noji, A.Matsuzawa, M.Eriguchi, Y.Takeda, N.Akiyama and Y.Kidani: "An Orally Active Antitumor Cyclohexanediamine-Pt (IV) Complexes : trans, cis, cis-Bis (n-valerato) (oxalato) (1R,2R-cyclohexanediamine) Pt (IV)" Anti-Cancer Drugs. 7. 248-256 (1996)

[Publications] R.Kizu, T.Yamamoto, T.Yokoyama, M.Tanaka and M.Miyazaki: "A Sensitive Postcolumn Derivatization/UV Detection System for HPLC Determination of Antitumor Divalent and Quadrivalent Platinum Complexes" Chemical & Pharmaceutical Bulletin. 43. 108-114 (1995)

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