

ビタミンD₃新規代謝経路の解明と骨粗鬆症薬開発への展開

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2004 Fiscal Year Final Research Report Summary

Analysis of C-3 epimerization mechanism in vitamin D₃ to develop a new osteoporosis drug

Research Project

Project/Area Number

14572030

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

Principal Investigator

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Project Period (FY)

2002 - 2004

Keywords

vitamin D₃ / osteoporosis / C-3 epimerization / LC / MS / derivatization / hydroxysteroid dehydrogenase / in vitro assay for bone metabolism / ultramicro analysis

Research Abstract

First, highly sensitive LC/MS methods for analysis of vitamin D₃ drug and metabolites were developed. Cookson-type reagents, which quantitatively react with vitamin D₃ compounds to form the Diels-Alder adducts, were employed to enhance their detection responses in APCI-MS. Pharmacokinetic study of 1 α -hydroxyvitamin D₃ in humans was carried out by the LC/MS method combined with derivatization with a proton-affinitive Cookson-type reagent, DMEQTAD. Using this method, urinary vitamin D₃ metabolites in human under physiological conditions were also detected and characterized. Next, an electron-affinitive Cookson-type reagent, NPTAD, was applied to the assay of 25-hydroxyvitamin D₃ in human plasma using LC/electron capture APCI-MS. This method was superior to the commercially available RIA in sensitivity and sample throughput. Furthermore, a new derivatization reagent having the boronic acid as the reacting group was developed for the assay of 24,25-dihydroxyvitamin D₃ [24,25(OH)₂D₃].

Second, studies on the C-3 epimerization in 24,25(OH)₂D₃ were performed. In consequence, we found the 3-epimer[3-epi-24,25(OH)₂D₃] is formed from 24,25(OH)₂D₃ by the catalysis of 3 α - and β -hydroxysteroid dehydrogenase (HSD) and the HSD-catalyzed epimerization is reversible. In addition, 3-oxo-form was also isolated from the reaction mixture, which strongly suggested that the formation of the 3-epimer by HSD involves a dehydrogenation and reduction processes.

In third study, osteoclastic and osteoblastic activities of some vitamin D₃ compounds were examined using a culture system of the goldfish scale. It was observed that 3-

Research Products (16 results)

All 2004 2003 2002

All Journal Article

- [Journal Article] 電子捕獲大気圧化学イオン化を利用する生理活性ステロイドの高速液体クロマトグラフィー/質量分析 2004 ▾
- [Journal Article] Analysis of C-3 epimerization in (24R)-24,25-dihydroxyvitamin D₃ catalyzed by hydroxysteroid dehydrogenase 2004 ▾
- [Journal Article] High-performance liquid chromatography/electron capture atmospheric pressure chemical ionization-mass spectrometric determination of biologically active steroids 2004 ▾
- [Journal Article] Analysis of C-3 epimerization in (24R)-24,25-dihydroxyvitamin D₃ catalyzed by hydroxysteroid dehydrogenase 2004 ▾
- [Journal Article] Development of analyses of biological steroids using chromatography -special reference to vitamin D compounds and neurosteroids- 2003 ▾
- [Journal Article] Application of 4-(4-nitrophenyl)-1,2,4-triazoline-3,5-dione to analysis of 25-hydroxyvitamin D₃ in human plasma by liquid chromatography/electron capture atmospheric pressure chemical ionization-mass spectrometry 2003 ▾
- [Journal Article] Development of analyses of biological steroids using chromatography -special reference to vitamin D compounds and neurosteroids- 2003 ▾
- [Journal Article] Application of 4-(4-nitrophenyl)-1,2,4-triazoline-3,5-dione to analysis of 25-hydroxyvitamin D₃ in human plasma by liquid chromatography/electron capture atmospheric pressure chemical ionization-mass spectrometry 2003 ▾
- [Journal Article] Liquid chromatography-mass spectrometric method combined with derivatization for determination of 1α-hydroxyvitamin D₃ in human plasma 2002 ▾
- [Journal Article] Characterization of urinary metabolites of vitamin D₃ in man under physiological conditions using liquid chromatography-tandem mass spectrometry 2002 ▾
- [Journal Article] Cookson型誘導体化試薬を用いるビタミンDの高速液体クロマトグラフィー/質量分析 2002 ▾
- [Journal Article] Electron-capturing derivatization of neutral steroids for increasing sensitivity in liquid chromatography/negative atmospheric pressure chemical ionization-mass spectrometry 2002 ▾
- [Journal Article] Liquid chromatography-mass spectrometric method combined with derivatization for determination of 1α-hydroxyvitamin D₃ in human plasma 2002 ▾
- [Journal Article] Characterization of urinary metabolites of vitamin D₃ in man under physiological conditions using liquid chromatography-tandem mass spectrometry 2002 ▾
- [Journal Article] High-performance liquid chromatography/mass spectrometry of vitamin D compounds employing derivatization with Cookson-type reagents 2002 ▾
- [Journal Article] Electron-capturing derivatization of neutral steroids for increasing sensitivity in liquid chromatography/negative atmospheric pressure chemical ionization-mass spectrometry 2002 ▾

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