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Evaluation of transport mechanism and pharmacokinetics of kaurenoic acid derived from *Aralia continentalis* Kitagawa in Korean subjects

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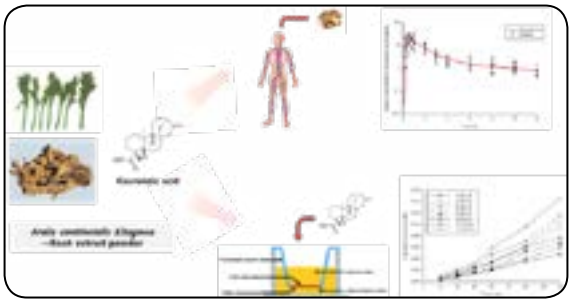
Kaurenoic acid is a representative diterpene of *Aralia continetalis* Kitagawa root which has been widely used as a tradition herbal medicine in Asia. It has effective for anticonvulsant, tumor suppression, and anti-inflammatory. The purposes of this study is to evaluate pharmacokinetics after oral administration of *Aralia Continetalis* Radix extract powder in Korean subjects and to estimate the transport mechanism of kaurenoic acid in Caco-2 cell. Ten healthy Korean subjects were employed by randomized, open labeled for phase I study and received the clinical oral dose of *Aralia continentalis* Radix extract powder. Blood samples were collected at predetermined time after administration. The concentration of kaurenoic acid was determined by UPLC-MS/MS method after liquid-liquid extraction. The PK parameters were calculated by compartment model using WinNonlin® software (Ver 6.4, Pharsight®, a Certara™ Company). Transport assay was conducted on Caco-2 cell monolayer with various concentrations (4, 6, 8, and 10 μM). Cell cytotoxicity was tested at 1-100 μM using cell counting Kit-8 reagent. The PK model of kaurenoic acid was described well by the two-compartment model with first-order absorption. The mean parameters were 53.35 ng*h/mL for the area under the time-concentration curve ($AUC_{0-\infty}$), 21.50 L/h for the total body clearance (CL/F), and 1.34 h for the elimination half-life ($t_{1/2}$). Cell cytotoxicity was not obserbed at 1, 10, 50 μM, whereas only 3.6% of cells died at 100 μM after adding of kourenoic acid at 24 h. In the bidirectional transport study, efflux ratio was ranged from 1.35 to 1.82. Therefore, kaurenoic acid was not a substrate for active efflux transporters. We successfully characterized the PK profile of kaurenoic acid in the Korean subjects and identified the transportation route in Caco-2 cell monolayer.



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Biography

Hea Young Cho is an Associate Professor of College of Pharmacy at CHA University, Republic of South Korea. She received her PhD Degree in Biopharmaceutical Science from Chonnam National University, Republic of South Korea. She has served as Postdoctoral Fellow at the State University of New York, Buffalo (USA), and Deputy Director of Clinical Trials Management Division at Korea Food and Drug Administration (KFDA). Her research interest involves the investigation about PK/PD modeling and ADMET. She has been a Member of the International Society for the Study of Xenobiotics (ISSX) and American Association of Pharmaceutical Scientists (AAPS). She currently serves as an Expert Committee Member for Health Technology Policy Review of the Ministry of Health and Welfare, and Committee Member for Central Pharmaceutical Affairs Council, Ministry of Food and Drug Safety (MFDS). Her research interest include: PK/PD modeling, PBPK modeling and ADMET.

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