Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense)*
Lat. Am. J. Pharm. **36** (6): 1204-9 (2017)

Received: March 13, 2017
Accepted: March 17, 2017

Determination and Pharmacokinetic Study of Daurisoline in Rat Plasma by UPLC-MS/MS

Yongxi JIN [1] #, Chengcheng SONG [2] #, Lingjiu SHAO [3] #, Lingtian WANG [4], Xiaoting TU [5], Bingbao CHEN [5], Junyan CHEN [5], Yinghao ZHI [1], Congcong WEN [5] & Wenzong ZHU [1] *

[1] *Department of Rehabilitation, Wenzhou Municipal Hospital of Traditional Chinese Medicine,Wenzhou 325005, China*
[2] *Zhejiang Chinese Medical University, Hangzhou 310053, China*
[3] *Department of Nephrology, Wenzhou Central Hospital, Wenzhou 325000, China*
[4] *School of Medicine, Shandong University, Jinan 250012, China*
[5] *Laboratory Animal Centre, Wenzhou Medical University, Wenzhou 325035, China*

SUMMARY*. Daurisoline is a bis-benzylisoquinoline alkaloid isolated from the rhizomes of *Menispermum dauricum* (Menispermaceae). In this work, a sensitive and selective UPLC-MS/MS method for determination of daurisoline in rat plasma was developed and applied to a pharmacokinetic study. An UPLC-MS/MS with an electrospray ionization (ESI) interface, and multiple reactions monitoring (MRM) mode was used for determination of daurisoline in rat plasma. Chromatographic separation was achieved on a C18 column (2.1 × 50 mm, 1.7 μm). Twelve rats were used to study the pharmacokinetics of daurisoline, blood samples (0.3 mL) were collected from the tail vein between 0.0333 and 24 h after intravenous (2 mg/kg) administration, and between 0.0833 and 8 h after oral (5 mg/kg) administration. Protein precipitation by acetonitrile was used to prepare samples. Calibration plots were linear throughout the range 3-1000 ng/mL with an LLOQ of 3 ng/mL. Mean recoveries ranged from 77.4 to 86.9%. RSD of intra-day and inter-day precision were less than 13%, and the accuracy was between 91.0 and 105.3%. The primary pharmacokinetic parameters, $AUC_{(0-t)}$ were 497.8 ± 81.4 and 184.5 ± 62.9 ng/mL.h, $t_{1/2}$ were 6.3 ± 5.1 and 1.4 ± 0.3 h, CL were 3.9 ± 0.8 and 29.4 ± 11.4 L/h/kg for daurisoline after intravenous and oral administration, respectively. The bioavailability was found to be 14.8%. The UPLC-MS/MS method was successfully applied to pharmacokinetic study of daurisoline after intravenous and oral administration in rats; the bioavailability was reported for the first time.

RESUMEN. Daurisolina es un alcaloide de bis-bencilisoquinolina aislado de los rizomas de *Menispermum dauricum* (Menispermaceae). En este trabajo se desarrolló un método sensible y selectivo de UPLC-MS/MS para la determinación de daurisolina en plasma de rata y se aplicó a un estudio farmacocinético. Para la determinación de daurisolina en plasma de rata se utilizó UPLC-MS/MS con interfaz de ionización por electrospray (ESI) y modo de monitorización de reacciones múltiples (MRM). La separación cromatográfica se consiguió en una columna C18 (2,1 × 50 mm, 1,7 μm). Se usaron doce ratas para estudiar la farmacocinética de daurisolina, se recogieron muestras de sangre de la vena de la cola entre 0,0333 y 24 h después de la administración intravenosa (2 mg/kg) y entre 0,0833 y 8 h después de la administración oral (5 mg/Kg). La precipitación de proteínas por acetonitrilo se utilizó para preparar las muestras. Las parcelas de calibración fueron lineales en el intervalo de 3-1000 ng/mL con un LLOQ de 3 ng/mL. Las recuperaciones medias oscilaron entre 77,4 y 86,9%. RSD de intra-día e inter-día de precisión fueron menores al 13%, y la precisión estuvo entre 91,0 y 105,3%. Los parámetros farmacocinéticos primarios fueron los siguientes: $AUC_{(0-t)}$ 497,8 ± 81,4 y 184,5 ± 62,9 ng/mL.h, $t_{1/2}$ 6,3 ± 5,1 y 1,4 ± 0,3 h, CL 3,9 ± 0,8 y 29,4 ± 11,4 L/h/Kg para daurisolina después de la administración intravenosa y oral, respectivamente. Se encontró que la biodisponibilidad era del 14,8%. El método UPLC-MS/MS se aplicó con éxito al estudio farmacocinético de daurisolina después de la administración intravenosa y oral en ratas; la biodisponibilidad se informó por primera vez.

KEY WORDS: bioavailability, mass spectrometry, *Menispermum dauricum,* quantitative, ultra-performance liquid chromatography.

# These authors contributed equally to this work.
* Author to whom correspondence should be addressed. *E-mail:* zhuwenzongwz@163.com

ISSN 0326 2383 (printed ed.)
ISSN 2362-3853 (on line ed.)