



The Absolute Bioavailability and Food Effects on Pharmacokinetics of L-3-n-Butylphthalide Tablet in Healthy Chinese Subjects

Meng WANG¹, Kun LOU², Quan-ying ZHANG^{1*},
Yue-yin PENG², Wen-yuan HUA¹ & Ming HUANG¹

¹ Clinical pharmacology laboratory, The Second Affiliated Hospital of Soochow University, Suzhou, China

² Department of clinical medicine, CSPC Zhongqi Pharmaceutical Technology (Sjz) Co., Ltd., Shijiazhuang, China

SUMMARY. L-3-n-butylphthalide (L-NBP) is a potential drug for treatment of Alzheimer's disease. This study evaluated the absolute bioavailability and food effects on pharmacokinetics of L-NBP tablet in healthy Chinese subjects. This was a single-center, randomized, single-dose, open-label, three-period, and cross-over study. Twelve healthy subjects were randomly assigned to receive single oral dose of 240 mg L-NBP tablet in fasted state or fed state or intravenous infusion of 70 mg L-NBP sodium chloride injection in fed state on 3 separate visits. Plasma samples were analyzed with LC-MS/MS. Pharmacokinetic parameters were calculated with WinNonlin software. In fasted and fed state, the main pharmacokinetic parameters of L-NBP tablet were as follows: C_{max} were 303.92 ± 126.39 and 273.23 ± 144.51 ng/mL, $t_{1/2}$ were 7.54 ± 1.31 and 8.94 ± 3.47 h, t_{max} were 1.31 ± 0.56 and 2.96 ± 1.09 h, $AUC_{0-48 h}$ were 647.59 ± 225.20 and 743.05 ± 305.10 ng/mL·h, and $AUC_{0-\infty}$ were 659.82 ± 229.07 and 758.77 ± 311.86 ng/mL·h, respectively. The absorption rate of L-NBP tablet was delayed by food intake but the absorption degree was not affected. The absolute bioavailability of L-NBP tablet was $19.02 \pm 6.45\%$.

RESUMEN. L-3-n-butylphthalida (L-NBP) es un fármaco potencial para el tratamiento de la enfermedad de Alzheimer. Este estudio evaluó los efectos de biodisponibilidad y de los alimentos sobre la farmacocinética de la tableta de L-NBP en sujetos sanos chinos, utilizando un estudio. monocéntrico, aleatorizado, de dosis única, abierto, de tres períodos y cruzado. Doce sujetos sanos fueron asignados al azar para recibir una sola dosis oral de tabletas de 240 mg de L-NBP o una inyección intravenosa en ayunas o estado alimentado de una infusión de 70 mg L-NBP en cloruro de sodio en estado alimentado en 3 visitas separadas. Las muestras de plasma se analizaron con LC-MS/MS. Los parámetros farmacocinéticos se calcularon con el software WinNonlin. En estado de ayuno y alimentados, los principales parámetros farmacocinéticos de la tableta L-NBP fueron los siguientes: C_{max} 303.92 ± 126.39 y 273.23 ± 144.51 ng/mL, $t_{1/2}$ 7.54 ± 1.31 y 8.94 ± 3.47 h, t_{max} 1.31 ± 0.56 y 2.96 ± 1.09 h, $AUC_{0-48 h}$ 647.59 ± 225.20 y 743.05 ± 305.10 ng/mL·h, y $AUC_{0-\infty}$ 659.82 ± 229.07 y 758.77 ± 311.86 ng/mL·h, respectivamente. La tasa de absorción de la tableta L-NBP se retrasó por la ingesta de comida, pero el grado de absorción no se vio afectada. La biodisponibilidad absoluta de la tableta L-NBP fue $19.02 \pm 6.45\%$.

KEY WORDS: high fat and calories diet, HPLC-MS/MS, L-3-n-butylphthalide tablet, pharmacokinetics.

* Author to whom correspondence should be addressed. E-mail: enigmatz@163.com