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Quantification of Rebamipide in Human Plasma by HPLC-MS/MS and Application to A Pharmacokinetic Study in Chinese Healthy Volunteers

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***SUMMARY*. The aim of this study was to investigate the pharmacokinetic of rebamipide in healthy Chinese volunteers, which is critical to the safety and efficacy. A selective and sensitive method was developed and validated for the determination of rebamipide in human plasma. The separation was carried out on Inertsil®ODS-3 column, with a mobile phase constituted by methanol and 1% formic acid (70:30, V/V). The Agilent 6410 Triple Quadrupole mass spectrometer was used for the detection. Under positive-ion multiple reaction monitoring mode, the respective mass transitions for quantification of rebamipide and carbamazepine (internal standard, IS) were m/z 371.3→216.4 and m/z 237.2→194.2, respectively. After validation, this method was successfully applied in a pharmacokinetic study of rebamipide in Chinese healthy volunteers under fasted condition. After single oral dose of 100 mg, the main pharmacokinetic parameters of rebamipide were as follows: C_{max} = 165.11 ± 50.53 ng/mL, AUC_{0-t} = 637.30 ± 208.67 ng·h/mL), T_{max} = 2.71 ± 1.18 h, and $t_{1/2}$ = 1.63 ± 0.51 h. Double peak phenomenon was observed in mean plasma concentration curves.**

RESUMEN. El objetivo de este estudio fue investigar la farmacocinética de rebamipida en voluntarios chinos sanos, que es fundamental para la seguridad y la eficacia. Se desarrolló y validó un método selectivo y sensible para la determinación de rebamipida en plasma humano. La separación se realizó en una columna Inertsil®ODS-3, con una fase móvil constituida por metanol y ácido fórmico al 1% (70:30, V / V). Se usó el espectrómetro de masas Agilent 6410 Triple Quadrupole para la detección. En el modo de monitoreo de reacción múltiple de iones positivos, las respectivas transiciones de masa para la cuantificación de rebamipida y carbamazepina (estándar interno, IS) fueron m/z 371.3→216.4 y m/z 237.2→194.2, respectivamente. Después de la validación, este método se aplicó con éxito en un estudio farmacocinético de rebamipida en voluntarios sanos chinos en ayunas. Después de una dosis oral única de 100 mg, los principales parámetros farmacocinéticos de rebamipida fueron los siguientes: C_{max} = 165.11 ± 50.53 ng/mL, AUC_{0-t} = 637.30 ± 208.67 ng h/mL), T_{max} = 2.71 ± 1.18 h, y $t_{1/2}$ = 1.63 ± 0.51 h. Se observó un fenómeno de doble pico en las curvas de concentración plasmática media.

KEY WORDS: Chinese healthy volunteers, double peak, HPLC-MS/MS, pharmacokinetic, rebamipide.

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