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Co-administration with Tetrandrine Alters the Pharmacokinetic Profile of Four Probe Drugs of Cytochrome P450 Enzymes in Rats

Lianguo CHEN [1] #, Xiaomin GAO [2] #, Yichuan CHEN [1], Jianhua XIONG [1], Jinzhao YANG [1], Yanli WEI [3], Yiping LIN [3], Xiaoqian YING [3], Youyan ZHONG [1] * & Meiling WU [3] *

[1] *Wenzhou People's Hospital Wenzhou 325000, China.*
[2] *Department of Urology, Changhai Hospital, Second Military Medical University, Shanghai 200433, P.R. China.*
[3] *Jinhua Polytechnic, Jinhua 321000, China.*

***SUMMARY*. The present study aimed to investigate the effects of tetrandrine (Tet) on cytochrome P450 (CYP450) enzymes (CYP1A2, CYP2C9, CYP2D6 and CYP3A4) of rats by using four cocktail probe drugs (phenacetin, tolbutamide, metoprolol, and midazolam). After pretreatment for 14 consecutive days with Tet (treatment group) or saline (control group) by oral administration, probes were given to rats by oral administration. Blood samples were obtained at a series of time-points and the concentrations of four probe drugs in plasma were determined by a UPLC-MS/MS method. The results showed that treatment with Tet had a significant inductive effect on CYP1A2, CYP2C9, CYP2D6, and CYP3A4. Therefore, caution must be needed during the concomitant use of Tet with other drugs metabolized by the corresponding enzymes because of potential drug-Tet interactions. In addition, we found that Tet may be effective in reducing serum uric acid.**

RESUMEN. El presente estudio tuvo como objetivo investigar los efectos de la tetrandrina (Tet) en las enzimas del citocromo P450 (CYP450) CYP1A2, CYP2C9, CYP2D6 y CYP3A4 en ratas mediante el uso de cuatro fármacos de sonda de cóctel (fenacetina, tolbutamida, metoprolol y midazolam). Después del tratamiento previo durante 14 días consecutivos con Tet (grupo de tratamiento) o solución salina (grupo de control) mediante administración oral, se administraron sondas a ratas por vía oral. Las muestras de sangre se obtuvieron en una serie de puntos temporales y las concentraciones de cuatro fármacos de sonda en plasma se determinaron mediante un método de UPLC-MS/MS. Los resultados mostraron que el tratamiento con Tet tuvo un efecto inductivo significativo en CYP1A2, CYP2C9, CYP2D6 y CYP3A4. Por lo tanto, es posible que se necesite precaución durante el uso concomitante de Tet con otros fármacos metabolizados por las enzimas correspondientes debido a las posibles interacciones entre el fármaco y el Tet. Además, encontramos que el Tet puede ser eficaz para reducir el ácido úrico en suero.

KEY WORDS: cocktail, CYP450, pharmacokinetics, tetrandrine, UPLC-MS/MS.

# These authors contributed equally to the manuscript.
* Authors to whom correspondence should be addressed. *E-mails:* meilingwujh@126.com (Meiling Wu), 82420849 @qq.com (Youyan Zhong).

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