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Synthesis, Characterization and Pharmacodynamics Studies of a Co-Drug Containing Paracetamol and Ibuprofen

Chao JIN [1], Jianyu ZHOU [1] #, Hualin FU [1] *, Ping ZOU [2], Gang SHU [1], Wei ZHANG [1], Wenfeng LI [1] & Guangneng PENG [1]

[1] *College of Veterinary Medicine, Sichuan Agricultural University, Chengdu City, 611130, Sichuan Province, China*

[2] *College of Science, Sichuan Agriculture University, Ya'an city, 625014, Sichuan Province, China*

***SUMMARY*. A co-drug containing paracetamol (PCM) and ibuprofen (IPF), 4-(acetylamino) phenolic hydroxyl-ibuprofen (PHI), was synthesized and investigated as a topical co-drug with the aim of reducing gastric mucosal injuries of the two parent drugs. Some physicochemical parameters were ascertained, and the hydrolysis and pharmacodynamic studies were examined as well. The hydrolysis of PHI was accorded with first-order kinetic equation at 37 and 60 °C in different pH phosphate buffer solution, and relative stability of pH value for PHI was from 4.0 to 6.0. In mice ear edema test, PHI had evidently superior analgesic effect than control group ($P < 0.01$) and there was no significant difference both the co-drug and the equivalent of the physical mixture ($P > 0.05$). The toxicology experiments showed that there were no obvious pathological changes in stomach, liver and kidney in the PHI group, while the damage of the liver and stomach mucosal layer from the physical mixture group was greater compared to the IPF and PCM group. These results confirmed the promising potential of the co-drug in the management of analgesia and less side effects.**

RESUMEN. Un co-fármaco que contiene paracetamol (PCM) e ibuprofeno (IPF), 4-(acetilamino) fenólico hidroxilo ibuprofeno (PHI), fue sintetizado e investigado como un co-fármaco tópico con el objetivo de reducir las lesiones de la mucosa gástrica de los dos fármacos originales. Fueron determinados algunos parámetros físico-químicos y también se examinaron la hidrólisis y los estudios farmacodinámicos. La hidrólisis de PHI corresponde a una ecuación cinética de primer orden a 37 y 60 °C en solución tampón de fosfato de pH diferente, y la estabilidad relativa del valor de pH para PHI es de 4,0 a 6,0. En prueba de edema de la orejade ratón, PHI tuvo efecto analgésico evidentemente superior a la del grupo control ($P < 0,01$) y no hubo diferencia significativa entre el co-fármaco y el equivalente de la mezcla física ($P > 0,05$). Los experimentos de toxicología mostraron que no hubo cambios patológicos obvios en estómago, hígado y riñón en el grupo PHI, mientras que el daño de la capa de hígado y el estómago de la mucosa del grupo mezcla física fue mayor en comparación con el grupo de IPF y PCM. Estos resultados confirmaron el potencial prometedor de la co-fármaco en la gestión de la analgesia, con menos efectos secundarios.

KEY WORDS: analgesic effect, co-drug, ibuprofen, paracetamol, prodrug.

* Author to whom correspondence should be addressed. *E-mail:* fuhl2005@sohu.com

\# Author contributed equally to this work and should be considered co-first author.

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