

METABOLISM OF IBUPROFEN IN CHIMERIC MICE WITH HUMANIZED LIVER

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[Purpose] Ibuprofen (IBP), which is a widely used nonsteroidal anti-inflammatory drug (NSAID), is a 2-arylpropionic acid derivative. Remarkable species and strain differences in the metabolic pathways of IBP have been reported. In humans, a major metabolite of IBP is acyl glucuronide, whereas in rats the main metabolite is 2'-hydroxy IBP. In this study, we examined whether chimeric mice with human hepatocytes (human-chimeric mice), which have more than 70% human hepatocytes in their liver, are useful for the prediction of human metabolism of IBP.

[Methods] IBP was orally administered to human-chimeric mice and Slc:Wistar/ST rats, and 24 hour urine was collected. The urine samples were subjected to solid phase extraction, and IBP and its metabolites were quantitated by means of LC/MS/MS.

[Results and Discussion] In Slc:Wistar/ST rats, the main metabolite of IBP was hydroxy-IBP and no unchanged IBP was detected in urine. The glucuronide and the taurine-conjugate of hydroxy-IBP were observed. In human-chimeric mice, the glucuronide of IBP was detected as the main metabolite. IBP and the taurine conjugate of IBP were also formed. The metabolic profile of IBP in human-chimeric mice was similar to reported data in humans.

[Conclusion] Human-chimeric mice showed human-type metabolism of IBP.