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Effects of Berberine on Pharmacokinetics of Amlodipine in Rats and its Potential Mechanism

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SUMMARY. **This study investigates the pharmacokinetic interactions between berberine and amlodipine in rats. Twelve male Sprague-Dawley rats were randomly assigned into two groups: amlodipine group (1 mg/kg of amlodipine) and berberine (20 mg/kg) + amlodipine (1 mg/kg) group. Plasma concentrations of amlodipine were determined by using a sensitive and reliable LC-MS/MS method. The effects of berberine on the metabolic stability of amlodipine were investigated by using rat liver microsome incubation systems. The results indicated that when the rats were pretreated with berberine, the C_{max} of amlodipine increased from 13.78 ± 3.57 to 19.96 ± 4.56 ng/mL ($p < 0.05$), the T_{max} increased from 4.04 ± 1.15 to 5.89 ± 1.64 h ($p < 0.05$), and the AUC_{0-t} increased by approximately 104% ($p < 0.05$), which suggested that the pharmacokinetic behavior of amlodipine was affected after oral co-administration of berberine. Additionally, the metabolic half-life was prolonged from 35.2 ± 6.5 to 56.8 ± 11.7 min ($p < 0.05$) with the pretreatment of berberine. It can be speculated that the drug-drug interaction between berberine and amlodipine might occur, which might have resulted from inhibiting the metabolism of amlodipine by berberine when they were co-administered.**

RESUMEN. Este estudio investiga las interacciones farmacocinéticas entre berberina y amlodipina en ratas. Doce ratas macho Sprague-Dawley fueron distribuidas aleatoriamente en dos grupos: grupo amlodipina (1 mg/kg de amlodipina) y grupo berberina (20 mg/kg) + grupo amlodipina (1 mg kg). Las concentraciones plasmáticas de amlodipina se determinaron mediante el uso de un método LC-MS/MS sensible y confiable. Los efectos de berberina sobre la estabilidad metabólica de la amlodipina se investigaron mediante el uso de sistemas de incubación con microsomas de hígado de rata. Los resultados indicaron que cuando las ratas fueron tratadas previamente con berberina, la C_{max} de amlodipina aumentó de 13.78 ± 3.57 a 19.96 ± 4.56 ng/mL ($p < 0.05$), T_{max} aumentó de 4.04 ± 1.15 a 5.89 ± 1.64 h ($p < 0.05$), y la AUC_{0-t} aumentó en aproximadamente un 104% ($p < 0.05$), lo que sugiere que el comportamiento farmacocinético de amlodipina se vio afectado después de la administración conjunta de berberina por vía oral. Además, la semivida metabólica se prolongó desde 35.2 ± 6.5 a 56.8 ± 11.7 min ($p <0.05$) con el pretratamiento de berberina. Se puede especular que la interacción fármaco-fármaco entre berberina y amlodipina podría ocurrir, lo que podría ser el resultado de la inhibición del metabolismo de amlodipina por berberina cuando se administraron conjuntamente.

KEY WORDS: amlodipine, berberine, drug-drug interaction, LC-MS/MS, pharmacokinetics.

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