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

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***SUMMARY*. This study investigates the pharmacokinetic interactions between quercetin and amlodipine in rats. Twelve male Sprague-Dawley rats were randomly assigned into twogroups: amlodipinegroup (1 mg/kg of amlodipine) and quercetin (20 mg/kg/day for 7 days) + amlodipine (1 mg/kg) group. Plasma concentrations of amlodipine were determined by using a sensitive and reliable LC-MS/MS method. The effects of quercetin 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 quercetin, the C_{max} of amlodipine increased from 13.78 ± 3.57 to 19.96 ± 4.56 μg/L ($p < 0.05$), 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 quercetin. 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 quercetin. It can be speculated that the drug-drug interaction between quercetin and amlodipine might occur, which might have resulted from inhibiting the metabolism of amlodipine by quercetin when they were co-administered.**

RESUMEN. Este estudio investiga las interacciones farmacocinéticas entre quercetina y amlodipina en ratas. Doce ratas macho Sprague-Dawley fueron asignadas aleatoriamente en dos grupos: grupo amlodipina (1 mg/kg de amlodipina) y grupo quercetina (20 mg/kg/día durante 7 días) + 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 la quercetina en la estabilidad metabólica de la amlodipina se investigaron mediante el uso de sistemas de incubación de microsomas de hígado de rata. Los resultados indicaron que cuando las ratas fueron pretratadas con quercetina, la $C_{máx}$ de amlodipina aumentó de 13,78 ± 3,57 a 19,96 ± 4,56 μg/L ($p < 0.05$), la $T_{máx}$ aumentó de 4.04 ± 1.15 a 5.89 ± 1.64 h ($p < 0.05$), y el AUC_{0-t} aumentó aproximadamente 104% ($p < 0.05$), lo que sugiere que el comportamiento farmacocinético de amlodipina se vio afectado después de la coadministración oral de quercetina. Además, la semivida metabólica se prolongó de 35,2 ± 6,5 a 56,8 ± 11,7 min ($p < 0,05$) con el pretratamiento de la quercetina. Se puede especular que la interacción fármaco-fármaco entre la quercetina y la amlodipina podría ocurrir, lo que podría resultar de la inhibición del metabolismo de la amlodipina por la quercetina cuando se administraron conjuntamente.

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

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