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Pharmacokinetic Interaction between Lapatinib and Sorafenib Following Single and Co-Oral Administration in Rats

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***SUMMARY*. This study examined whether oral administration of sorafenib to the rats with lapatinib led to any pharmacokinetic interactions. Twenty-four rats were divided randomly into 3 groups, lapatinib group (lapatinib 25 mg/kg, n = 8), sorafenib group (sorafenib 15 mg/kg, n = 8) and co-administration group (sorafenib 15 mg/kg and lapatinib 25 mg/kg, n = 8). The concentration of lapatinib and sorafenib in rat plasma was determined by a sensitive and simple UPLC-MS-MS method. There was no statistical pharmacokinetics difference for lapatinib in the lapatinib group and co-administration group, the sorafenib could not influence the pharmacokinetic profile of lapatinib in rats. There was statistical pharmacokinetics difference for sorafenib in the sorafenib group and co-administration group, when co-oral administration lapatinib with sorafenib, $MRT_{(0-t)}$ increased from 10.7 to 13.3 h ($p < 0.05$), $t_{1/2}$ increased from 7.6 to 9.5 h ($p < 0.01$). These data indicate lapatinib could slightly influence the pharmacokinetic profile of sorafenib in rats, which might cause drug-drug interactions when using lapatinib with sorafenib.**

RESUMEN. En el presente estudio se examinó si la administración oral de sorafenib con lapatinib a ratas produjo alguna interacción farmacocinética. Veinticuatro ratas se dividieron aleatoriamente en 3 grupos, el grupo lapatinib (lapatinib 25 mg/kg, n = 8), el grupo de sorafenib (sorafenib 15 mg/kg, n = 8) y el grupo co-administración (sorafenib 15 mg/kg y lapatinib 25 mg/kg, n = 8). La concentración de lapatinib y sorafenib en plasma de rata se determinó por un método de UPLC-MS-MS sensible y simple. No hubo diferencia estadística para la farmacocinética de lapatinib en el grupo de lapatinib ni en el grupo de co-administración, demostrando que el sorafenib no influía en el perfil farmacocinético de lapatinib en ratas. No hubo diferencia estadística farmacocinética de sorafenib en el grupo de grupo de sorafenib ni en el grupo de co-administración; en la co-administración oral de lapatinib con sorafenib, $MRT_{(0-t)}$ aumentó desde 10,7 hasta 13,3 h ($p < 0,05$), $t_{1/2}$ aumentó de 7.6 a 9,5 h ($p < 0,01$). Estos datos indican que lapatinib podría influir ligeramente en el perfil farmacocinético de sorafenib en ratas, lo que podría causar interacciones fármaco-fármaco cuando se utiliza lapatinib conjuntamente con sorafenib.

KEY WORDS: Interaction, Lapatinib, Pharmacokinetic, Rat, Sorafenib.

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