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Pharmacokinetic Interaction Study of Combining Cabozantinib with Erlotinib in Rats by UPLC-MS/MS

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***SUMMARY*. This study examined whether oral administration of erlotinib to rats with cabozantinib led to any pharmacokinetic interactions or not. Twenty four rats were randomly divided into 3 groups, cabozantinib group (cabozantinib 30 mg/kg, n = 8), erlotinib group (erlotinib 25 mg/kg, n = 8) and co-administration group (erlotinib 25 mg/kg and cabozantinib 30 mg/kg, n = 8). The concentration of cabozantinib and erlotinib in rat plasma was determined by a sensitive and simple UPLC-MS/MS method. There was statistical pharmacokinetics difference for cabozantinib in the cabozantinib group and co-administration group, when co-oral administration cabozantinib with erlotinib, the $AUC_{(0-t)}$ and C_{max} increased ($p < 0.01$). There was statistical pharmacokinetics difference for erlotinib in the erlotinib group and co-administration group, when co-oral administration erlotinib with cabozantinib, the $AUC_{(0-t)}$ increased and CL decreased ($p < 0.05$). These data indicate erlotinib could influence the pharmacokinetic profile of cabozantinib in rats, and vice versa, which might cause drug–drug interactions when using cabozantinib with erlotinib.**

RESUMEN. Este estudio examinó si la administración oral de erlotinib a ratas con cabozantinib condujo a ninguna interacción farmacocinética o no. Veinticuatro ratas se dividieron aleatoriamente en 3 grupos, el grupo cabozantinib (cabozantinib 30 mg/kg, n = 8), el grupo de erlotinib (erlotinib 25 mg/kg, n = 8) y el grupo co-administración (erlotinib 25 mg/kg y cabozantinib 30 mg/kg, n = 8). La concentración de cabozantinib y erlotinib en plasma de rata se determinó por un método UPLC-MS/MS sensible y simple. No hubo diferencia farmacocinética estadística para cabozantinib en el grupo grupo cabozantinib y co-administración; cuando se co-administrópor vía oral cabozantinib con erlotinib, la $AUC_{(0-t)}$ y la $C_{máx}$ aumentaron ($p < 0,01$). No hubo diferencia estadística farmacocinética de erlotinib en el grupo de grupo de erlotinib y co-administración, cuando co-administración oral de erlotinib con cabozantinib, el $AUC_{(0-t)}$ aumentó y CL disminuyó ($p < 0,05$). Estos datos indican que erlotinib podría influir en el perfil farmacocinético de cabozantinib en ratas y viceversa, que puede provocar interacciones fármaco-fármaco cuando se utiliza cabozantinib con erlotinib.

KEY WORDS: Erlotinib, Cabozantinib, Pharmacokinetic, Rat, Interaction.

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\# These two author contribute equal to the work.

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