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In Silico Prediction of CYP3A4-mediated Drug-drug Interactions by Time-dependent Inhibitors Using Therapeutic Plasma Concentrations and Enzyme Inhibition Constants

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SUMMARY. Time-dependent inhibitors (TDI) of cytochrome P450 enzymes, particularly CYP3A4, are critical in pharmacokinetic drug-drug interactions (DDIs). We evaluated an empirical model relating ln(AUCRavg) to ln(TRavg/KI) in 11 TDIs with available clinical data. The model demonstrated a statistically significant, moderately strong relationship (R = 0.68, *p* = 0.031). These findings support its utility in early DDI risk assessment and screening strategies.

RESUMEN. Los inhibidores dependientes del tiempo (IDT) de las enzimas del citocromo P450, en particular el CYP3A4, son cruciales en las interacciones farmacocinéticas fármaco-fármaco (IDF). Evaluamos un modelo empírico que relaciona ln(AUCRavg) con ln(TRavg/KI) en 11 IDT con datos clínicos disponibles. El modelo demostró una relación estadísticamente significativa y moderadamente fuerte (R = 0,68; *p* = 0,031). Estos hallazgos respaldan su utilidad en la evaluación temprana del riesgo de IDT y en las estrategias de cribado.

KEY WORDS: cytochrome p-450, drug-drug interactions, inhibition constant

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