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In Vivo Evaluation of Fixed Dose Combination Tablets of Aripiprazole and Divalproex Sodium; A Pilot Pharmacokinetic Assay

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***SUMMARY*. By reducing the medication burden, compliance of psychiatric patients can be improved. In view of the massive challenges in the treatment compliance of the psychiatric patients, the current pharmacokinetic study assesses the feasibility of co-administration of aripiprazole and divalproex sodium in the form of fixed dose combinations (FDC) in healthy rabbits. Animals were categorized in four groups having six animals each. Relevant tablets of aripiprazole 5 mg (group A), divalproex sodium 500 mg (group D) and aripiprazole 5 mg plus divalproex sodium 500 mg (group FDC) were orally administered. Blood samples, collected at specified time intervals were analyzed using HPLC-UV after simple liquid-liquid extraction. Valproate when co-administered with aripiprazole in FDC, increased the C_{max}, T_{max} and AUC of aripiprazole by 9.5, 35.5, 20.5, and 5.9%, respectively, while t1/2, Vd and Cl of aripiprazole decreased by 12.8, 16, and 6%, respectively. Oppositely, C_{max} of valproate increased by 11% whereas T_{max}, $t_{1/2}$, AUC, Vd and Cl of valproate decreased by 9.8, 4.3, 1.8, and 0.7%, respectively, when used with aripiprazole in the form of FDC. The fixed combination of aripiprazole and divalproex sodium could be an economical and result oriented substitute to conventional individual tablets in terms of patient compliance, which needs to be further evaluated with positive control.**

RESUMEN. Al reducir la carga del tratamiento se puede mejorar el cumplimiento de los pacientes psiquiátricos. En vista de los enormes desafíos en el cumplimiento del tratamiento de los pacientes psiquiátricos, el estudio farmacocinético actual evalúa la viabilidad de la administración conjunta de aripiprazol y divalproex sódico en la forma de dosis combinada fija (FDC) en conejos sanos. Los animales se clasificaron en cuatro grupos con seis animales cada uno. Comprimidos relevantes de aripiprazol 5 mg (grupo A), divalproex sódico 500 mg (grupo D) y aripiprazol 5 mg más divalproex sodio 500 mg (grupo FDC). Las muestras de sangre, recolectadas a intervalos de tiempo especificados, se analizaron mediante HPLC-UV después de una simple extracción líquido-líquido. El valproato, cuando se administró junto con aripiprazol en FDC, aumentó la C_{max}, T_{max} y el AUC de aripiprazol en un 9,5%, 35,5%, 20,5% y 5,9%, respectivamente, mientras que t1/2, Vd y Cl de aripiprazol disminuyeron en 12,8%, 16% y 6%, respectivamente. Opuestamente, la C_{max} de valproato aumentó en 11% Cuando T_{max}, $t_{1/2}$, AUC, Vd y Cl de valproato disminuyeron un 9.8%, 4,3%, 1,8% y 0,7%, respectivamente, cuando se usaron con aripiprazol en forma de FDC. La combinación fija de aripiprazol y divalproex sódico podría ser un sustituto económico y orientado a resultados respecto a los comprimidos individuales convencionales en términos de cumplimiento del paciente, que debe evaluarse más a fondo con un control positivo.

KEY WORDS: aripiprazole, compliance, divalproex sodium, fixed dose combination.

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