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Inhibitory Effect of Myricetin on the Pharmacokinetics of Aripiprazole *In Vivo* and *In Vitro*

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SUMMARY. **The aim of this study was to explore the impact of myricetin on the metabolism of aripiprazole both *in vivo* and *in vitro*. Fourteen healthy male SD rats were randomly divided into two groups: A group (control group) and B group (a single dose of 80 mg/kg myricetin). A single dose of 3 mg/kg aripiprazole wasadministered orally 30 min after administration of myricetin. Aripiprazole plasma levels were measured by UPLC-MS/MS, and pharmacokinetic parameters were calculated by DAS 3.0 software. The single dose of 80 mg/kg myricetin significantly ($p < 0.05$) increased the AUC, $t_{1/2}$ and C_{max} of aripiprazole and decreased the T_{max} and CL. Also, different concentrations of myricetin together incubation with aripiprazole in CYP3A4*1, CYP2D6*1, human and rat microsomes, the IC50 values was 20.25, 95.54, 25.33, and 73.65 μmol/L, respectively. This result indicated that myricetin could significantly inhibit the metabolism of aripiprazole both *in vivo* and *in vitro*.**

RESUMEN. El objetivo de este estudio fue explorar el impacto de la miricetina en el metabolismo del aripiprazol tanto *in vivo* como *in vitro*. Catorce ratas SD sanas machos se dividieron aleatoriamente en dos grupos: grupo A (grupo control) y grupo B (una dosis única de 80 mg/kg de miricetina). Se administró una dosis única de 3 mg/kg de aripiprazol por vía oral 30 min después de la administración de miricetina. Los niveles plasmáticos de aripiprazol se midieron mediante UPLC-MS/MS y los parámetros farmacocinéticos se calcularon mediante el software DAS 3.0. La dosis única de 80 mg/kg de miricetina significativamente ($p < 0.05$) aumentó el AUC, $t_{1/2}$ y C_{max} de aripiprazol y disminuyó el T_{max} y CL. Además, las diferentes concentraciones de miricetina junto con la incubación con aripiprazol en CYP3A4*1, CYP2D6*1, microsomas humanos y de rata, los valores de CI50 fueron 20.25, 95.54, 25.33 y 73.65 μmol/L, respectivamente. Este resultado indicó que la miricetina podría inhibir significativamente el metabolismo del aripiprazol tanto *in vivo* como *in vitro*.

KEY WORDS: aripiprazole, drug metabolism, inhibitory effect, liver microsomes, myricetin.

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