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Inhibitory Effects of 17 Steroids Towards 6 Major Cytochrome P450 Isoforms

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***SUMMARY*. The aim of present study was to investigate drug-drug interaction (DDI) potential of 17 steroids by examining their inhibitory effects towards 6 major cytochrome P450 (CYP) isoforms. Inhibitory effects of 17 steroids (aldosterone, androstenedione, corticosterone, cortisol, dehydroepiandrosterone, 11-deoxycortisol, dexamethasone, estrone, 17α-hydroxyprogesterone, medroxyprogesterone, megestrol acetate, methylprednisolone, methyltestosterone, prednisolone, prednisone, pregnenolone, and testosterone) at 100 μM (25 μM for estrone) were tested towards 6 major P450 isoforms including CYP1A2, CYP2A6, CYP2C9, CYP2D6, CYP2E1, and CYP3A4 in human liver microsomes. The results demonstrated that CYP3A4 was mostly sensitive to the inhibitory effect of the steroids. CYP2C9 and CYP1A2 were moderately affected. CYP2A6 and CYP2D6 were the least inhibited. Instead of inhibition, activation was observed towards CYP2E1 by some steroids. Given the limited inhibition and the potential maximal physiological concentrations, these steroids were considered less likely to lead to serious DDI via the inhibition of P450 *in vivo*.**

RESUMEN. El objetivo del presente estudio fue investigar la interacción potencial fármaco-fármaco (DDI) de 17 esteroides mediante el examen de sus efectos inhibitorios hacia 6 isoformas principales del citocromo P450 (CYP). Los efectos inhibidores de 17 esteroides (aldosterona, androstenediona, corticosterona, cortisol, dehidroepiandrosterona, 11-desoxicortisol, dexametasona, estrona, 17α-hidroxiprogesterona, medroxiprogesterona, acetato de megestrol, metilprednisolona, metiltestosterona, prednisolona, prednisona, pregnenolona y testosterona) en concentración 100 μM (25 μM para la estrona) se pusieron a prueba en microsomas hepáticos humanos frente a las 6 principales isoformas del citocromo P450, incluyendo CYP1A2, CYP2A6, CYP2C9, CYP2D6, CYP2E1 y CYP3A4. Los resultados demostraron que CYP3A4 era sensible al efecto inhibidor de la mayoría los esteroides. CYP2C9 y CYP1A2 fueron moderadamente afectados. CYP2A6 y CYP2D6 fueron los menos inhibidos. En lugar de la inhibición, se observó activación hacia CYP2E1 por algunos esteroides. Dada la limitada inhibición y las posibles concentraciones fisiológicas máximas, se considera poco probable que estos esteroides conduzcan a graves DDI a través de la inhibición del P450 *in vivo*.

KEY WORDS: Cytochrome P450 (CYP), *In vivo* drug-drug interaction (DDI), Steroids.

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