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Serum Albumin Addition Affects the Inhibition of Glimepiride Towards UDP-Glucuronosyltransferases (UGTs)

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***SUMMARY*. Diabetes remains to be one of the top reasons threatening the human health, and glimepiride is a medium- to long-acting sulfonylurea antidiabetic drug clinically used to treat type 2 diabetes. The present study aims to compare the inhibition ability of glimepiride towards UDP-glucuronosyltransferase (UGT) 1A6 in the incubation system with and without albumin. In the incubation system without bovine serum albumin (BSA), 100 μM of glimepiride completely inhibited the metabolism of recombinant UGT1A6-catalyzed glucuronidation of 4-methylumbelliferone (4-MU). The addition of BSA in the incubation system significantly weakened the inhibition potential of glimepiride towards recombinant UGT1A6-catalyzed glucuronidation of 4-MU. Furthermore, the influence of BSA towards the inhibition kinetic type of glimepiride towards UGT1A6 was investigated. The intersection point was located in the horizontal axis of Lineweaver-Burk plot in the incubation system without BSA, indicating the noncompetitive inhibition towards UGT1A6. In the incubation mixture with BSA, the intersection point was located in the verticle axis of Lineweaver-Burk plot, indicating the competitive inhibition of glimepiride towards UGT1A6. Therefore, much caution should be given for the *in vitro-in vivo* extrapolation (IVIVE) to predict *in vivo* interaction between glimepiride and drugs mainly undergoing UGT1A6-catalyzed metabolism.**

RESUMEN. La diabetes sigue siendo una de las principales amenazas de la salud humana; glimepirida es una sulfonilurea antidiabética de acción prolongada, clínicamente utilizada para tratar la diabetes tipo 2. El presente estudio tiene como objetivo comparar la capacidad de inhibición de la glimepirida hacia UDP-glucuronosiltransferasa (UGT) 1A6 en el sistema de incubación con y sin albúmina. En el sistema de incubación sin albúmina de suero bovino (BSA), 100 μM de glimepirida inhibió completamente el metabolismo de la glucuronidación de 4-metilumbeliferona (4-MU) catalizada de UGT1A6 recombinante. La adición de BSA en el sistema de incubación debilita significativamente el potencial de inhibición de la glimepirida hacia la glucuronidación de 4-MU catalizada por UGT1A6 recombinante. Además, se investigó la influencia de BSA sobre el tipo cinética de inhibición de la glimepirida hacia UGT1A6. El punto de intersección se encuentra en el eje horizontal de Lineweaver-Burk en el sistema de incubación sin BSA, lo que indica la inhibición no competitiva hacia UGT1A6. En la mezcla de incubación con BSA, el punto de intersección se encuentra en el eje vertical de Lineweaver-Burk, indicando la inhibición competitiva de la glimepirida hacia UGT1A6. Por lo tanto, se debe tener mucho cuidado en la extrapolación *in vitro-in vivo* (IVIVE) para predecir la interacción *in vivo* entre glimepirida y drogas sometidas principalmente a metabolismo catalizado por UGT1A6.

KEY WORDS: bovine serum albumin, diabetes, glimepiride, UDP-glucuronosyltransferase (UGT) 1A6.

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