



Evaluation of the Effect of Insulin towards the Activity of Drug-Metabolizing Enzymes (DMEs)

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SUMMARY. Insulin, a peptide hormone produced by beta cells in the pancreas, is a hormone playing an important role in the regulation of the level of glucose in the blood. The injection of insulin is an efficient therapeutic method to treat diabetes. The adverse effects of overdosing of insulin were evaluated in this study through investigating the inhibition potential of insulin towards various isoforms of UDP-glucuronosyltransferases (UGTs). Recombinant UGTs-catalyzed glucuronidation of 4-methylumbelliferone (4-MU) was employed as the probe reaction, and 50 µg/mL of insulin was added to investigate the inhibition potential; 50 µg/mL of insulin was selected as the initial screening concentration to determine the inhibition of insulin towards the activity of UGT isoforms. Fifty µg/mL of insulin did not show significant inhibition towards UGT1A1, UGT1A3, UGT1A8, and UGT2B7. However, 50 µg/mL of insulin has been demonstrated to exert significant inhibition towards UGT1A7 ($p < 0.001$) and UGT1A9 ($p < 0.001$). In conclusion, the risk of overdosing of insulin was indicated in this study due to the inhibition of insulin towards the activity of UGT1A7 and UGT1A9.

RESUMEN. La insulina, una hormona peptídica producida por las células beta en el páncreas, es una hormona que juega un papel importante en la regulación del nivel de glucosa en la sangre. La inyección de insulina es un método terapéutico efectivo para tratar la diabetes. Los efectos adversos de la sobredosis de insulina se evaluaron en este estudio investigando el potencial de inhibición de la insulina hacia varias isoformas de UDP-glucuronosiltransferasas (UGT). / Se añadió UGTs catalizada recombinantes glucuronidación de 4-metilumbeliferona (4-MU) fue empleado como la reacción de la sonda, y 50 µg/mL de insulina para investigar la inhibición potencial; 50 µg/mL de insulina se seleccionó como la concentración de selección inicial para determinar la inhibición de la insulina hacia la actividad de las isoformas UGT. Cincuenta µg/mL de insulina no mostraron una inhibición significativa hacia UGT1A1, UGT1A3, UGT1A8 y UGT2B7. Sin embargo, se ha demostrado que 50 µg/mL de insulina ejercen una inhibición significativa hacia UGT1A7 ($p < 0,001$) y UGT1A9 ($p < 0,001$). En conclusión, el riesgo de sobredosis de insulina se indicó en este estudio debido a la inhibición de la insulina hacia la actividad de UGT1A7 y UGT1A9.

KEY WORDS: Insulin, drug-metabolizing enzymes (DMEs), UDP-glucuronosyltransferases (UGTs), therapeutic risk.

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