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The Glucuronidation of Arctigenin Decreases Arctigenin-Propofol Interaction Risk

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***SUMMARY*. Propofol, also named as 2,6-diisopropylphenol, is a common agent used to induce and maintain anesthesia. The present study aims to evaluate the effect of glucuronidation metabolism towards the UGT1A9-mediated arctigenin-propofol interaction. *In silico* docking method was employed. Homology modeling was used to get the crystal structure of UGT1A9, and autodock software was used to dock arctigenin and its glucuronide into the activity cavity of UGT1A9. Through homology modeling, the crystal structure of UGT1A9 was obtained, and the active cavity was consisted of amino acids residues Ser5, Leu31, Val35, Arg57, Leu62, Ala61, and Asp228. Both arctigenin and its glucuronide can be well docked into the activity cavity of UGT1A9, and the binding free energy was calculated to be -8.87 kcal/mol and -7.74 kcal/mol, respectively, indicating stronger binding capability of arctigenin than its glucuronide. In conclusion, the glucuronidation of arctigenin weakens the clinical drug-drug interaction between arctigenin and propofol.**

RESUMEN. Propofol (2,6-diisopropilfenol) es un agente comunmente utilizado para inducir y mantener la anestesia. El presente estudio tiene como objetivo evaluar el efecto del metabolismo de la glucuronidación hacia la interacción arctigenina-propofol mediada por UGT1A9. Se empleó el método de acoplamiento *in silico*. La homología de modelado se utilizó para obtener la estructura cristalina de UGT1A9 y el software AutoDock para anclar arctigenina y su glucurónido en la cavidad activa de UGT1A9. A través del modelado de homología se obtuvo la estructura cristalina de UGT1A9; la cavidad activa consiste en residuos de los aminoácidos Ser5, Leu 31, Val 35, Arg57, Leu62, Ala61 y Asp228. Tanto arctigenina como su glucurónido pueden ser bien anclados en la cavidad activa de UGT1A9 y la energía libre de unión se calculó en -8,87 kcal/mol y -7,74 kcal/mol, respectivamente, lo que indica una mayor capacidad de unión de arctigenina que de su glucurónido. En conclusión, la glucuronidación de arctigenina debilita la interacción fármaco-fármaco clínica entre arctigenina y propofol.

KEY WORDS: arctigenin, drug-drug interaction, glucuronidation, in silico, UDP-glucuronosyltransferases (UGTs).

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