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Short communication

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In Vitro-In Silico Determination of the Inhibition of 6-Shogaol Towards Phase II Drug-Metabolizing Enzymes (DMEs)

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***SUMMARY*. 6-shogaol is an important ingredient isolated from ginger, and has been reported to exert therapeutic potential towards lung cancer. To indicate the potential drug-drug interaction, the inhibition potential of 6-shogaol towards important phase II drug-metabolizing enzyme UDP-glucuronosyltransferases (UGTs) was evaluated. Among the tested UGT isoforms, 6-shogaol exhibited strong inhibition towards UGT1A7, 1A8, 1A9 and 2B7, with negligible influence towards the activity of other UGT isoforms. Noncompetitive inhibition of 6-shogaol towards UGT1A7 was demonstrated, and the inhibition kinetic parameters (K_i) were calculated to be 0.05 μM for 6-shogaol's inhibition towards UGT1A7. Competitive inhibition of 6-shogaol towards the activity of UGT2B7 was demonstrated, and the inhibition kinetic parameters (K_i) was calculated to be 3.4 μM for 6-shogaol, respectively. *In silico* docking method was used to explain the inhibition of 6-shogaol towards the activity of UGT2B7, and the results showed that hydrophobic interactions contributed to the strong interaction between 6-shogaol and the activity cavity of UGT2B7. In conclusion, the data showed that close monitoring was needed for the interaction between 6-shogaol and the drugs mainly undergoing UGT1A7, 1A8, 1A9, and 2B7-catalyzed metabolism.**

RESUMEN. El 6-shogaol es un ingrediente importante aislado de jengibre y se ha informado que posee potencial terapéutico para el tratamiento del cáncer de pulmón. Para indicar el potencial de interacción fármaco-fármaco, fue evaluado el potencial de inhibición de 6-shogaol hacia la UDP-glucuronosiltransferasa (UGT), enzima metabolizadora de drogas en fase II. Frente a las isoformas de UGT ensayadas, 6-shogaol exhibió fuerte inhibición hacia UGT1A7, 1A8, 1A9 y 2B7, con influencia insignificante hacia la actividad de otras isoformas de UGT. Se demostró inhibición no competitiva de 6-shogaol hacia UGT1A7 y el parámetro cinético de inhibición (K_i) calculado para la inhibición 6-shogaol hacia UGT1A7 fue 0,05 μM. La inhibición competitiva de 6-shogaol hacia la actividad de UGT2B7 se demostró y el parámetro cinético de inhibición (K_i) se calculó que era 3,4 μM para 6-shogaol. El método *in silico* de acoplamiento se utilizó para explicar la inhibición de 6-shogaol hacia la actividad de UGT2B7; los resultados mostraron que las interacciones hidrófobas contribuyen a la fuerte interacción entre 6-shogaol y la cavidad activa de UGT2B7. En conclusión, los datos mostraron que es necesaria una estrecha vigilancia para la interacción entre 6 shogaol y los medicamentos sometidos al metabolismo catalizado principalmente por UGT1A7, 1A8, 1A9 y 2B7.

KEY WORDS: drug-drug interaction, 6-shogaol, UDP-glucuronosyltransferases (UGTs).

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