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Short communication

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Amplication Influence of Deoxyschizandrin Towards Adverse Effect of Glioma Therapeutic Drug Irinotecan

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***SUMMARY*. Irinotecan is an effective drug for glioma treatment. Irinotecan-induced toxicity strongly limits its clinical utilization, and the glucuronidation of its active metabolite SN-38 is the key inducer for irinotecan-induced toxicity. The present study aims to investigate the influence of deoxyschizandrin towards the toxicity of irinotecan, and the potential mechanism was initially discussed. The pre-treatment of deoxyschizandrin significantly strengthened irinotecan-induced toxicity, indicated by the strengthened damage towards ileum tissue and increased body weight loss. Potential mechanism was investigated through determining the inhibition potential of deoxyschizandrin towards SN-38 glucuronidation. Concentration-dependent inhibition of deoxyschizandrin towards the metabolism of SN-38 was demonstrated. The inhibition type belonged to the competitive inhibition. Through nonlinear fitting using competitive equation, the inhibition kinetic parameter was calculated to be 43.6 μM. In conclusion, the amplication influence of deoxyschizandrin towards adverse effect of glioma therapeutic drug irinotecan was demonstrated, and the inhibition of deoxyschizandrin towards SN-38 glucuronidation was indicated as the potential mechanism.**

RESUMEN. El irinotecán es un fármaco eficaz para el tratamiento del glioma. La toxicidad inducida por el irinotecan limita fuertemente su utilización clínica y la glucuronidación de su metabolito activo SN-38 es el inductor clave de la toxicidad inducida por irinotecán. El presente estudio tiene como objetivo investigar la influencia de deoxischizandrina sobre la toxicidad de irinotecan, y el mecanismo potencial fue discutido inicialmente. El pretratamiento de deoxischizandrina reforzó significativamente la toxicidad inducida por irinotecán, indicado por el daño de tejido reforzado del íleon y el aumento de la pérdida de peso corporal. El mecanismo fue investigado a través de la determinación del potencial de la inhibición de la deoxyschizandrina hacia la glucuronidación de SN-38. Se demostró la inhibición dependiente de la concentración de deoxischizandrina sobre el metabolismo de SN-38. El tipo de inhibición es competitiva. A través de ajuste no lineal utilizando la ecuación competitiva, el parámetro cinético de inhibición se calculó en 43,6 μM. En conclusión se demostró la influencia de deoxischizandrina sobre el efecto adverso de irinotecán en el glioma, pudiendo ser el mecanismo potencial la inhibición de la deoxischizandrina sobre la glucuronidación de SN-38.

KEY WORDS: Deoxyschizandrin, Irinotecan, Toxicity.

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