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Short communication

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The Risk of Flavonoids Utilization in the Anti-Tumor Therapy

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***SUMMARY*. Food and Drug Administration (FDA) remains to pay much caution to approve flavonoids as clinical drugs. The present study aims to investigate the potential influence of flavonoids apigenin and kaempferol towards the toxicity of irinotecan. For irinotecan-induced diarrhea model, intraperitoneal injection (i.p.) of 50 mg/kg body weight of irinotecan was performed for 3 days. For the protection role of apigenin and kaempferol, 500 mg/kg body weight of apigenin or kaempferol was given through intraperitoneal injection (i.p.) for 30 days before the administration of irinotecan. The body weight was monitored daily during the treatment of irinotecan. The treatment with irinotecan (50 mg/kg, i.p.) for 3 days did not induce the significant decrease of body weight. The pre-treatment of apigenin or kaempferol (500 mg/kg, i.p.) can significantly strengthen irinotecan-induced toxicity, as indicated by the increased body weight loss in comparison with irinotecan-treatment group. Furthermore, the mechanisms were elucidated from the following reasons: 1) The pre-treatment of apigenin or kaempferol significantly inhibited the expression of UGT1A1, indicated by the decreased level of ugt1a1 mRNA. 2) Apigenin or kaempferol significantly inhibited glucuronidation metabolism of SN-38 which is the active metabolite of irinotecan. In conclusion, the utilization risk of flavonoids in the anti-tumor utilization was demonstrated in the present study. All these results provide a caution for approving the flavonoids as the clinical drugs.**

RESUMEN. La Food and Drug Administration (FDA) de EE.UU. mantiene mucha precaución para aprobar los flavonoides como fármacos clínicos. El presente estudio tiene como objetivo investigar la posible influencia de los flavonoides apigenina y kaempferol sobre la toxicidad de irinotecan. Para el modelo de diarrea inducida por irinotecán, se realizó una inyección intraperitoneal (ip) de 50 mg/kg de peso corporal de irinotecán durante 3 días. Para estudiar el rol de protección de la apigenina y kaempferol, se administraron 500 mg/kg de peso corporal de apigenina o kaempferol por medio de inyección intraperitoneal (ip) durante 30 días antes de la administración de irinotecán. El peso corporal se controló diariamente durante el tratamiento de irinotecan. El tratamiento con irinotecan (50 mg/kg, ip) durante 3 días no indujo una disminución significativa del peso corporal. El pre-tratamiento de apigenina o kaempferol (500 mg/kg, ip) puede fortalecer significativamente la toxicidad inducida por irinotecán, como se indica por el aumento de la pérdida de peso corporal en comparación con el grupo de tratamiento con irinotecan. Además, los mecanismos responderían a alguna de las siguientes razones: 1) El pre-tratamiento de apigenina o kaempferol inhibe significativamente la expresión de UGT1A1, indicado por la disminución del nivel de ARNm de UGT1A1; 2) La apigenina o kaempferol inhibió significativamente el metabolismo de la glucuronidación de SN-38, que es el metabolito activo de irinotecan. En conclusión, el riesgo de utilización de flavonoides en la utilización anti-tumor se demostró en el presente estudio. Estos resultados proporcionan una advertencia para la aprobación de los flavonoides como fármacos clínicos.

KEY WORDS: flavonoids, irinotecan, toxicity, drug-drug interaction

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