



Chemoprevention with the Combination of Ginsenoside Rd, Vitamin D3 and Metformin on Colitis-Associated Colon Neoplasia in Mice

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SUMMARY. Ginsenoside Rd (GRd) is a protopanaxadiol-type ginsenoside found in ginseng whose antitumor activities have been reported. We previously reported the chemoprevention of vitamin D3 (VD3) and metformin (Met) in mice and rat models of colorectal carcinogenesis. Here we investigated the potential synergistic chemoprevention of GRd, VD3, and Met on colitis-associated colon neoplasia induced with 1,2-dimethylhydrazine dihydrochloride (DMH) via intraperitoneal injection, and dextran sodium sulfate (DSS) in the drinking water. Our results showed that combination of GRd, VD3, and Met treatment exhibit synergistic effects against the early colon cancer, as evidenced by reduced the numbers of aberrant crypt foci (ACF) and tumor in the colon of mice. The possible mechanism of their action was associated with downregulation S6P expression via the AMPK/mTOR pathway. These results suggest that the combination of GRd, VD3, and Met may prevent colon cancer associated with colitis.

RESUMEN. Ginsenoside Rd (GRd) es un ginsenosido de tipo protopanaxadiol que se encuentra en el ginseng cuyas actividades antitumorales han sido reportadas. Anteriormente informamos la quimiopreención de la vitamina D3 (VD3) y metformina (Met) en ratones y ratas modelos de carcinogénesis colorrectal. Aquí investigamos la posible quimiopreención sinérgica de GRd, VD3 y Met en la neoplasia de colon asociada a colitis inducida con diclorhidrato de 1,2-dimetilhidrazina (DMH) mediante inyección intraperitoneal y sulfato de sodio de dextrano (DSS) en el agua potable. Nuestros resultados mostraron que la combinación del tratamiento con GRd, VD3 y Met exhibe efectos sinérgicos contra el cáncer de colon temprano, como lo demuestra la reducción de la cantidad de focos de criptas aberrantes (ACF) y tumores en el colon de ratones. El posible mecanismo de su acción se asoció con la expresión de S6P de regulación negativa a través de la vía AMPK/mTOR. Estos resultados sugieren que la combinación de GRd, VD3 y Met puede prevenir el cáncer de colon asociado con la colitis.

KEY WORDS: chemoprevention, colitis-associated colon neoplasia, ginsenoside Rd, metformin, vitamin D3.

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