The Utilization of Benzbromarone in Old People Disrupts the Intestinal Drug-Metabolizing Enzymes

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SUMMARY. Gout, frequently diagnosed in men and old people, has been reported to be induced by the elevated uric acid in the blood. Benzbromazone has been clinically utilized as an uricosuric agent to control hyperuricemia through suppressing the reabsorption of uric acid. The present study aims to analyze whether benzbromarone has other adverse effects besides benzbromarone-induced hepatotoxicity. The risk of benzbromarone-induced colon cancer was predicted through investigating the inhibition of benzbromarone on the activity of intestinal UDP-glucuronosyltransferase (UGT) isoforms which play important roles in the pathogenesis of colon cancer. In vitro intestinal UGTs-catalyzed glucuronidation of 4-methylumbelliferone (4-MU) was employed as the probe reaction. Benzbromarone 100 μM was used to perform the initial screening for the inhibition of benzbromarone on the intestinal UGT isoforms, which inhibited 92.7% activity of UGT1A7 (p < 0.001), and 94.1% activity of UGT1A8 (p < 0.001). For UGT1A10, 100 μM of benzbromarone can completely inhibit its activity (p < 0.001). In summary, benzbromarone showed strong inhibition towards the activity of intestinal UGT isoforms (UGT1A7, -1A8, -1A10), predicting a possible risk of benzbromarone-induced colon cancer.

KEY WORDS: benzbromarone, colon cancer, intestinal UDP-glucuronosyltransferases (UGTs), gout.

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