## Brewers's rice modulates oxidative stress in azoxymethane-mediated colon carcinogenesis in rats

## ABSTRACT

Aim: To investigate the mechanistic action of brewers' rice in regulating the Wnt/nuclear factor-kappa B (NF-kB)/Nrf2-signaling pathways during colon carcinogenesis in male Sprague-Dawley rats. Methods: Male Sprague-Dawley rats were randomly divided into the following five groups (six rats in each group): (G1) normal, (G2) azoxymethane (AOM) alone, (G3) AOM + 10% (weight (w)/weight (w)) brewers' rice, (G4) AOM + 20% (w/w) brewers' rice, and (G5) AOM + 40% (w/w) brewers' rice. They were intraperitoneally administered 15 mg/kg body weight of AOM in saline once weekly over a two-week period and treated with an American Institute of Nutrition (AIN)-93G diet containing 10%, 20%, and 40% (w/w) brewers' rice. The mRNA levels of glycogen synthase kinase  $3\beta$  (GSK3 $\beta$ ),  $\beta$ catenin, key inflammation markers, nuclear factor E2-related factor 2 (Nrf2), and heme oxygenase-1 (HO-1)-dependent transcriptional activity were assessed by quantitative realtime polymerase chain reaction analyses. The colon superoxide dismutase, malondialdehyde, and nitric oxide levels were also analyzed to assess the antioxidant effect of these treatments. The results were analyzed using one-way analysis of variance (ANOVA), and a P value of <0.05 was considered significant. Results: The overall analyses demonstrated that the dietary administration of brewers' rice in AOM-induced rat colon carcinogenesis resulted in the transcriptional upregulation of GSK3β, inducible nitric oxide synthase (iNOS), Nrf2, and HO-1. We discovered that the dietary administration of brewers' rice downregulated the  $\beta$ catenin and NF-κB mRNA levels. A significant reduction in β-catenin expression was found in the groups administered with 20% (0.611  $\pm$  0.034) and 40% (0.436  $\pm$  0.045) (w/w) brewers' rice compared with that of the group treated with AOM alone (1.000  $\pm$  0.064) (P < 0.05). The NF-kB expression was significantly lower between the AOM-alone group (1.000  $\pm$  0.048) and those groups fed with diets containing 10% (w/w) brewers' rice (0.255  $\pm$  0.022), 20% (w/w) brewers' rice (0.450  $\pm$  0.045), or 40% (w/w) brewers' rice (0.541  $\pm$  0.027) (P < 0.05). Brewers' rice improved the antioxidant levels, indicating that brewers' rice can enhance effective recovery from oxidative stress induced by AOM. Conclusion: Our results provide evidence that brewers' rice can suppress colon cancer via the regulation of Nrf2 expression and the inhibition of the Wnt/NF-kB signaling pathways.

**Keyword:** Brewers' rice; Colon cancer; Nuclear factor E2-related factor 2; Nuclear factorkappa B; β-catenin