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A comparative study of genoprotective activity of phenolic catabolites between normal and adenocarcinoma colonic cells in vitro

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(Poly)phenols are plant-derived bioactive compounds abundant in human diet,[1,2] that are largely metabolised to simpler phenolic catabolites upon ingestion[3–5]. These compounds have been attributed with several beneficial effects on human health,[4,6,7] but further analyses on the properties of these bioavailable catabolites is needed. To this end, four previously identified microbiota mediated phenolic catabolites were assessed for their anti- genotoxicity and ability to activate the Nrf2-pathway, which provides protection against oxidative stress.

Normal and adenocarcinoma colonocyte cell lines were cultured with either 4-hydroxybenzoic acid (HBA), benzoic acid (BA), 3-(3-hydroxyphenyl) propionic acid (3'HPPA), or 3- phenylpropionic acid (3PPA) at 10 μM, 50 μM, and 100 μM for 24 hours. The phenolic catabolites were determined to be non-cytotoxic in both cell lines up to 100 μM.

Each phenolic catabolite exhibited significant ($p < 0.001$) genoprotective activity (COMET assay) in both cell lines but with varying potency. Furthermore, gene expression (qPCR) studies showed that exposure to the phenolics altered the expression of key genes in the nuclear factor erythroid-derived 2-like 2 (Nrf2)-antioxidant response pathway, namely Nrf2, heme oxygenase 1 (HO-1), and NAD (P)H dehydrogenase quinone 1 (NQO1). Specifically, treatment of either cell line with the phenolics at 50 μM and 100 μM resulted in significant increases (ranging from 1.46-fold to 3.17-fold, $p < 0.001$) in gene expression for most genes of interest, and there appears to be some correlation between the degree of genotoxic protection offered and the elevation of expression of specific genes.

To conclude, microbiota mediated phenolic metabolites at physiologically relevant concentrations can reduce DNA damage in both normal and adenocarcinoma colonic cells and may be in part mediated by an upregulation of the Nrf2-ARE pathway.

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