

Comparison of *in vivo* and *in vitro* digestion of polyphenol composition in lingonberries: potential impact on colonic health

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Evidence from epidemiological studies suggests that diets rich in fruit and vegetables may contribute to a reduced risk of colorectal cancer (CRC). A recent meta-analysis of risk factors associated with colorectal cancer reported a decreased risk associated with fruit consumption (RR = 0.85, 95% CI = 0.75–0.96 for 3 servings/day) and also emphasized that low fruit and vegetable consumption was associated with a moderately increased risk of CRC⁽¹⁾. Lingonberry (*Vaccinium vitis-idaea* L) is a popular edible berry in Scandinavian countries and is increasing in popularity across Europe. Lingonberry possesses a complex (poly)phenolic profile, which may contribute to its putative anticancer activity. Following consumption and digestion, limited uptake from the small intestine results in berry (poly)phenolic compounds entering the colon, where they are subject to microbiota-mediated metabolism⁽²⁾. Therefore, it is likely that the colonic epithelium is exposed to phenolic metabolites as well as the original parent compounds.

The aim of this study was to evaluate the impact of *in vivo* and *in vitro* digestion on phenolic composition and bioactivity of lingonberries. Lingonberry extracts obtained after simulated *in vitro* digestion (IVDL) and subsequent faecal fermentation (IVFL) were compared to samples of ileal fluid (IF) obtained from an ileostomist⁽³⁾ pre & post lingonberry consumption 150 g (ID 12/WS/0192). Bioactivity of the extracts was tested using a physiologically-relevant dose range (0–50 µg/ml gallic acid equivalents) over a 24 hour exposure period using *in vitro* colonocyte models of colorectal carcinogenesis (Comet assay HT29, mutagenicity assay HT29G¹⁷neo, Matrigel invasion assay HT115)⁽⁴⁾. LC-MS analysis confirmed that *in vitro* digestion altered the (poly)phenol composition relative to the original lingonberry and similar patterns were observed for the ileal fluid. On the other hand, the IVFL sample had high levels of simple aromatic components. Digested and fermented extracts exhibited significant ($p < 0.05$) anti-genotoxic, anti-mutagenic and anti-invasive effects compared to the appropriate controls (ANOVA, Post Hoc Dunnett T test) in all *in vitro* models. The ileal fluid demonstrated a significant reduction in DNA damage ($p < 0.05$), but at a higher total polyphenol concentration (µg/ml GAE/ml) than the IVDL. Despite extensive structural modification following digestion and fermentation, lingonberry extracts retained their bioactivity. These data reinforce the need for screening studies to consider the impact of digestion when investigating bioactivity of dietary phytochemicals.

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