Background

Fucoidans are a group of sulfated polysaccharides derived from brown seaweed. They are commonly used as dietary supplements due to their reported medicinal properties, including anti-cancer activity. The effect of dietary administration of fucoidan in rodent models of colitis was investigated here, as well as the effect of fucoidan treatment on human colon cancer patients. Patients with ulcerative colitis and Crohn’s disease are at increased risk for developing colorectal cancer, whilst chronic inflammation is believed to promote carcinogenesis. The development of safe treatments that target gut health is therefore a priority.

What are fucoidans?

Fucoidans are non-gelling sulfated polysaccharides that occur naturally in brown seaweeds and echinoderms. They contain primarily fucose as a backbone sugar and are large, heterodisperse molecules. The physicochemical properties and bioactivities of fucoidan are structure dependent, differing according to the seaweed species they are extracted from.

Collitis study model

Fucoidan from Fucus vesiculosus was administered in the diet and evaluated in the dextran sulfate sodium (DSS) mouse model of acute colitis*. Healthy mice, DSS-treated mice and DSS/fucoidan-treated mice were monitored for clinical signs of colitis. At the end of the experiment, sections of the colon were prepared for microscopy. Tissue from the distal colon was cultured for 24 hours, after which supernatants were collected and analysed for cytokines.

RESULTS: Fucoidan administered in the diet significantly lessened clinical symptoms, pathology and cytokine elevations compared to the control colitis group (Table 1). In addition, histology demonstrated fucoidan induced a profound reduction in structural changes to the gut (Figure 1).

Table 1: Effect of oral fucoidan on colon-derived cytokine levels.

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>% change (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-1α</td>
<td>-51.9 (0.0002)</td>
</tr>
<tr>
<td>IL-1β</td>
<td>-52.0 (0.0001)</td>
</tr>
<tr>
<td>TNF-α</td>
<td>-52.1 (0.0001)</td>
</tr>
<tr>
<td>MIP-1α</td>
<td>-61.6 (0.0004)</td>
</tr>
<tr>
<td>MIP-1β</td>
<td>-60.8 (0.0007)</td>
</tr>
<tr>
<td>GM-CSF</td>
<td>-61.6 (0.0001)</td>
</tr>
</tbody>
</table>

TABLE 1: Effect of oral fucoidan on colon-derived cytokine levels.

HCT116 study model

a) Flow cytometry

Human colon cancer cells (HCT116) were treated with fucoidan and monitored for cell cycle arrest using colony formation and flow cytometry techniques. Fucoidan caused a great decrease in colon cancer cell colony formation, but supported normal fibroblast colony formation (data not shown).

RESULTS: Fucoidan induced a significant (p<0.01) G1 arrest in HCT116 cells at 72 hours.

b) DNA damage

Cellular γH2AX induction is usually seen as a marker of DNA damage-induced repair activity. Normal cells and human colon cancer cells (HCT116) were treated with fucoidan and tested for DNA damage.

RESULTS: Fucoidan caused DNA damage in HCT116 cells, but not in normal cells, as displayed in Figures 4 and 5.

Conclusions

Dietary administration of fucoidan in the rodent colitis model was highly successful in inhibiting clinical signs, histology and cytokine markers of disease. In vitro, fucoidan was able to mediate cell cycle arrest of human colon cancer cells and cause DNA damage. In contrast, colitis DNA damage was not observed in healthy cells treated with fucoidan. These results show fucoidan has potential as a dietary intervention for inflammation and prevention of cancer in the gut.

REFERENCES: