Rhamnogalacturonan protects against DSS-induced colitis

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Ulcerative colitis is a chronic disorder that affects the colon with unknown etiology and the currently therapy has low effectiveness with numerous adverse effects.¹ Recently, it has been observed that polysaccharides purified from plants protect the stomach against lesions.² Here, we aimed to investigate the therapeutic effects of a rhamnogalacturonan (RGal, 1), a polysaccharide isolated from leaves of Acmella oleracea (L.) R.K. Jansen, Asteraceae, in an experimental colitis model induced by dextran sulfate sodium (DSS) in mice (CEUA-BIO: 721). DSS was administrated for 5 days followed by 2 days of water. The animals were orally treated with vehicle (water, 1 ml/kg) or RGal (10 mg/kg) daily. Colitis score (body weight and fecal consistency) were monitored daily. After 7 days, the colons were collected, measured and weighed and used for histological and immunohistochemistry evaluation. Wound healing and permeability assay were carried out with heterogeneous human epithelial colorectal adenocarcinoma cells (Caco-2). IL-8 levels, expression and distribution of tight junction proteins claudin-1 and occludin were analyzed by ELISA, immunoblot or immunofluorescence. At day 8, RGal reduced the colitis score ~46%, protected mice from weight loss ~51% and reduced the macroscopic damage when compared to the DSS group. RGal also prevents the reduction of colon length (RGal: 9.1 ± 0.2 cm; DSS: 7.1 ± 0.2 cm), and protected the colonic ganglion cells. When compared to the DSS group, RGal increased mucosal and submucosal thickness in 22 and 54% and decreased the thickness of the muscular layer and total wall in 38 and 18%. Furthermore, RGal promoted the maintenance of mucosal enterocytes and mucus secreting goblet cells in addition to conserving collagen homeostasis and increasing cell proliferation. Besides to promote wound healing in Caco-2 cells, RGal (1000 µg/ml) prevented the cellular permeability in 65%, when compared to IL-1β group. Also, RGal reduced IL-8 secretion (RGal: 807 ± 49.7 pg/ml) and a diminished claudin-1 expression (40%) when compared to IL-1β group.³ Collectively, we demonstrated that RGal reduces the severity of DSS colitis in mice through protecting colon epithelium and neurons of the myenteric plexus, reducing epithelial permeability and cytokine secretion and maintaining the integrity of junction complexes. Thus, RGal may represent a promising molecule for drug development to the treatment of ulcerative colitis.
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References


