

A COMPARISON BETWEEN A CANNABIS EXTRACT WITH HIGH CONTENT IN CANNABIDIOL AND PURE CANNABIDIOL ON EXPERIMENTAL INTESTINAL INFLAMMATION AND HYPERMOTILITY

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Cannabis sativa has been historically used to relieve the symptoms of inflammatory and functional gastrointestinal disorders (Izzo et al., 2015). Anecdotal evidence about the beneficial effect of Cannabis in the gastrointestinal tract has been recently supported by studies in patients with inflammatory bowel disease (IBD) (Naftali et al., 2014). In this study, we investigated the effect of a standardized Cannabis sativa extract with high content of cannabidiol (CBD), named CBD BDS (i.e., CBD botanical drug substance), as well as of the pure major component CBD on mucosal inflammation and hypermotility in experimental models of intestinal inflammation.

Colitis and intestinal hypermotility were induced in mice by administration of dinitrobenzenesulfonic acid (DNBS) and croton oil, respectively (Borrelli et al., 2015; Izzo et al., 2012). CBD BDS and pure CBD were given - either intraperitoneally (1-30 mg/kg) or by oral gavage (5-60 mg/kg) - after the inflammatory insults (curative protocol). CBD levels were detected in the colon, liver and brain (after the oral treatment of CBD BDS or pure CBD) by HPLC coupled to ion trap-time of flight mass spectrometry.

Oral and intraperitoneal administration of CBD BDS attenuated DNBS-induced colon shortening (a gross marker of intestinal damage/inflammation) and infiltrating neutrophils. CBD BDS also reduced intestinal transit in a model of inflammation-induced dysmotility, at doses lower than those required to affect transit in healthy mice. Under the same experimental conditions, pure CBD did not ameliorate colitis, although it normalized transit in the croton oil model of intestinal dysfunction.

In conclusion, oral administration of a Cannabis extract with high content in CBD, given in a curative protocol, attenuates inflammation and dysmotility in intestinal models of inflammation. Pure CBD did not display a similar pattern of protective effects. Ultimately, our data support the rationale of combining CBD with other minor constituents present in Cannabis sativa for the clinical development of Cannabis-derived medicines in IBD.

Izzo et al. (2015). *Handb Exp Pharmacol.* 231, 423-447.

Naftali et al. (2014) *Dig Dis.* 32, 468-74.

Borrelli et al. (2015) *Br J Pharmacol.* 172, 142-58.

Izzo et al. (2012) *Br J Pharmacol.* 166, 1444-60.