Cannabidivarin is an orally-active intestinal anti-inflammatory non-psycotropic phytocannabinoid

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Background/Aim *Cannabis*use is common in inflammatory bowel disease (IBD) patients and it has been shown to subjectively ameliorate symptoms [1]. In addition to THC, its main active ingredient, *Cannabis sativa* produces over 100 non-psychotropic cannabinoids of therapeutic interest. Among these, cannabidivarin (CBDV) is a safe compound under phase II clinical evaluation as a treatment for epilepsy (GW Pharma, Cambridge UK; https://clinicaltrials.gov/). However, there is no information about its possible intestinal antinflammatory effects. Here, we investigated the effect of CBDV on colonic inflammation.

Methods: Colitis was induced in mice by intracolonic dinitrobenzene sulfonic acid (DNBS) injection and animals were euthanized three days after its administration. Inflammation was assessed by evaluating inflammatory parameters (colon weight/colon length *ratio* and myeloperoxidase activity) and by immunohistochemistry (Ki67 and p53); interleukin (IL)-1b levels were measured by ELISA; intestinal permeability was assessed using a fluorescent method. CBDV (GW Pharma, Cambridge UK) was given, intraperitoneally or by oral gavage, once a day for three consecutive days starting from one day after the inflammatory insult. The exposure of the colon to CBDV was assessed by measuring CBDV colonic levels at the end of treatment by means of isotope dilution HPLC-IT-ToF mass spectrometry.

Results Oral or intraperitoneal CBDV (0.3-10 mg/kg) reduced colon weight/colon length *ratio*, myeloperoxidase activity and IL-1 b levels in the inflamed colon. CBDV was more active when given orally than intraperitoneally. Furthermore, CBDV (orally) reduced intestinal permeability and stimulated tissue regeneration, as revealed by Ki67 and p53 immunoreactivity in DNBS-treated mice. Interestingly, CBDV exerted significant antinflammatory effects at doses that were approximately 10-15 fold less than those producing anticonvulsant effect in mice [2]. Analytical data showed that CBDV accumulated in the colon following both intraperitoneal and oral administration.

Conclusions: Our study reveals, for the first time, the ability of CBDV to attenuate the severity of intestinal inflammation. Its ability to decrease the degree of inflammation following the administration of oral low-doses, is of interest for a possible experimentation in IBD patients.

References

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