

EFFECT OF REPEATED TREATMENT WITH OLIVE-BASED PREPARATIONS ON COLITIS MODEL IN RATS

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Background: Abdominal pain is a common symptom of Inflammatory Bowel Diseases (IBDs), characterized by chronic recurrent bowels ulceration, resulting in inflamed gut and breakdown of the intestinal barrier function. Although the knowledge in this pathology is progressing, new therapeutic strategies continue to be investigated because current pharmacological therapies offer little benefit for abdominal symptoms, with frequent side effects. In this sense, the interest by dietary safe supplements that integrate the classical pharmacotherapy is growing. Scientific evidences support the potential use of nutraceuticals, such as polyphenols contained in some foods, as agents capable to prevent or accelerate healing of gastrointestinal mucosal damage. In this study the efficacy of an extra virgin olive oil, and two by-products of the milling process with different phenolic content were evaluated in preventing the development of abdominal pain on 2,4-dinitrobenzenesulfonic acid (DNBS) induced colitis model in rats.

Material and methods: Colitis was induced in the animals by the intrarectal injection of DNBS (30 mg dissolved in 0.25mL EtOH 50%). Olive extract (Ret Osm 300 mg kg⁻¹, retentate from waste waters containing 75% OH-tyrosol on total phenols), olive patè (Patè 300 mg kg⁻¹, a dry by-product without kernel residue produced during the milling, containing 87% OH-tyrosol on total phenols) and an extra virgin olive oil (EVOO 3mL, maximum administrable volume, a liquid sample containing 57% free and linked OH-tyrosol on total phenols) were orally administered once daily for 14days, starting from DNBS injection.

Results: The visceromotor response (VMR) to colon-rectal balloon distension (CRD) was used as measure of visceral sensitivity in animals 7and 14days after DNBS injection. Patè and EVOO significantly reduced visceral sensitivity of animals with 2and 3mL (balloon distension volume), both 7and 14days, while VMR to CRD in animals treated with Ret Osm resulted significantly lowered compared to animals treated with DNBS + vehicle only with 3mL, as observed on day 7and 14. Abdominal withdrawal response (AWR) and spontaneous motility were assessed in awake animals 14days after DNBS injection. Patè and Ret Osm reduced pain perception with 1, 2and 3mL balloon inflation, while EVOO reduced behavioural alterations with 2and 3mL. All three samples showed a protective effect on intestinal damage expressed as Macroscopic Damage Score (MDS), evaluated on the newly explanted tissue on 14th day. The effect of the treatments on the intestinal inflammation, fibrosis and increase in mast cells induced by DNBS was histologically evaluated on day 14, finding a protective effect of treatments on intestinal tissue.

Discussion and conclusions: The three samples were very different in terms of phenolic concentration and form of administration: Patè and Ret Osm were more concentrated and in dried forms, while the EVOO was chosen because with an high amount of total phenols and to test a liquid sample. OH-Tyr in all three matrices is present in free, and almost in EVOO in linked forms, as oleuropein derivatives. OH-Tyr is well known for its *in vivo* anti-inflammatory and antioxidant properties, neuroprotective effects and for its important role for the cardiovascular system in humans. Our data also suggest that olive-based preparations can be an interesting natural source for promoting abdominal pain relief in IBDs patients.