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# Beneficial Effects of EVOO on Gastrointestinal Health

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## Abstract

Among many oil products, Extra Virgin Olive Oil (EVOO) has unique properties due to its compositional profile. EVOO provides several nutritional and medical benefits. In this review, the studies demonstrating the beneficial effects of EVOO on gut microbiota and gastrointestinal disorders, including oral diseases, inflammatory bowel disease, ulcerative colitis, infant colic, constipation, functional dyspepsia, gastrointestinal barrier dysfunction, acute GVHD and food allergies, have been summarized.

**Keywords:** EVOO; Gastrointestinal disorders; Gut microbiota; Inflammatory bowel disease

**Abbreviations:** NF-κB: Nuclear Factor kappa-light-chain-enhancer of activated B cells; COX-2: Cyclooxygenase-2; IL-8: Interleukin 8; iNOS: inducible Nitric Oxide synthase; GSH: Glutathione; HOCl: Hypochlorous Acid; MOG35-55: Myelin Oligodendrocyte Glycoprotein; EAE: Encephalomyelitis; I-FABP: Intestinal Fatty-Acid Binding Protein; CD14: Cluster of Differentiation 14; hs-CRP: high-sensitivity C-Reactive Protein; GSRS: Global Substance Registration System; GvHD: Graft-versus-Host Disease; ESR: Erythrocyte Sedimentation Rate

## Introduction

The digestive system's path from the oral cavity to the anus is known as the Gastrointestinal tract (GI tract). The gut microbiota, which consists of more than 1,000 various strains of bacteria and numerous other species, is found in the GI tract. It plays a variety of roles related to maintaining a state of immunological function and metabolism. Hormones are released by GI tract cells to assist in controlling the digestive process. Olives are used to make olive oil, a liquid lipid that is created by pressing the olives intact. It is frequently employed in cooking, whether it is to fry meals or make salad dressing. EVOO has a strong resistance to oxidative damage because of its triacylglycerol composition, which has minimum concentrations of polyunsaturated fatty acids, as well as a group of phenolic antioxidants made mainly of polyphenols and tocopherols. Studies have suggested that EVOO's particular lipid composition (rich in MUFAs and OA) and high concentrations of squalene, vitamin E, and phenolic compounds are responsible for these health benefits [1]. Numerous studies suggest that the polyphenols in EVOO are responsible for the gut microbiota's anti-inflammatory, anticancer, antioxidant, and modulatory activities. The Mediterranean diet, which usually involves a consumption of 25 to 50 mL of extra Virgin Olive Oil (EVOO) per day, has been linked to a reduced risk of heart ailments and cognitive decline caused by age, according to numerous other epidemiological studies and some cancers particularly colon. In observational studies, there are links between following the Mediterranean diet and consuming olive oil and the main outcomes of both general cancer and cancer forms linked to obesity. The EVOO diet appears to have a potential link to IBD. The Mediterranean diet prevents bowel changes and encourages a healthy intestinal microbiota [2].

## Literature Review

The studies included in this review were obtained by searching for various keywords such as 'EVOO,' OR 'extra virgin olive oil,' AND 'gut microbiota,' AND 'gastrointestinal disorders,' 'inflammatory bowel disease ' in databases and websites such as Elsevier, Springer, Wiley online library, Google Scholar, PubMed, Refseek, and MDPI [3].

## Gut microbiota

EVOO has been shown to modulate the microbiota of the gut, contrary to other fats. EVOO includes. 90% to 95% of ingested phenolic compounds fail to be digested in the small intestine and pass into the colon, where they can be broken down into bioactive second-generation structures, which are metabolic products of the phenolic compounds' original parent molecules and can change the makeup of the gut microbiota. In a study of 612 elderly Europeans over a period of 12 months, Ghosh et al. examined the impact of a Mediterranean diet on gut microbiota and discovered that implementation of the diet raised the number of many bacteria linked to better cognition and was inverted related to pro-inflammatory markers like C-RP and IL-17. A Mediterranean diet enriched with 40 g/day EVOO given to eighteen overweight or obese recipients for twelve weeks produced significant improvements. Another randomized controlled double blind crossover human trial examined fecal quantitative alterations in the community of bacteria after 3 weeks of intake of 25 mL/day of phenolic-enriched olive oil, revealing both a rise in bifidobacteria and an elevation in hydroxytyrosol and dihydroxyphenylacetic acids, which are bacterial byproducts of phenolic ingredients that regulate their antioxidant effects. It was proven that ingesting EVOO regularly for over twelve weeks improved survival and raised the concentration of bacteria. In

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addition, the growth of pathogenic bacteria, such as *Escherichia coli*, can be suppressed by polyphenols. Many bacterial taxa, such as *Desulfovibri*, play a role in regression approaches for physiologic factors associated to metabolic syndrome. In a comparison of the impact of Refined Olive Oil (ROO) and EVOO on the gut microbiota of mice. The antibacterial action of virgin olive oil polyphenols is thought to be responsible for the maintenance of minimal amounts of this genus. After administration of polyphenol-rich EVOO, the proportion of IgA-coated bacteria rose, suggesting an enhancement in gut immunity. Olalla et al. investigated the effect of daily extra virgin olive oil intake on the microbiota and lipid profile of patients with HIV over the age of 50. The results revealed a discernible rise in alpha diversity in men and a decline in pro-inflammatory taxa like Dethiosulfovibrionaceae, indicating an enhancement in alpha diversity in the intestinal microbiota [4].

## Oral diseases

Applying OO as a 2% emulsion or 2% mouth rinse led to preventing enamel and dentin erosion; however, applying 100% pure OO has no preventive impacts. On the other hand, the 2% OO emulsion is less potent than fluoride solution [5].

Abd El-Shafy assessed the antibacterial activity of EVOO extract as mouthwash against *S. mutans* in children's oral cavities. The mean number of *S. mutans* was significantly lower in children who washed 2 ml of OO extract twice a day for 21 days. Suggesting that *S. mutans* might be rendered inactive by ozonized olive oil formulations, so averting the oral cavity's salivary dilution impact [6].

In a comparison of ozonized olive oil and olive oil, the findings showed that ozonized olive oil can effectively help regulate the gingivitis-causing agents while minimizing its clinical symptoms.

Zumbo et al. compared the efficacy of fruity oil and EVOO in treating gingivitis. When the three groups were compared, it was evident that EVOO improved PI and BI and was an additive in the management of inflammation of the gingival tissue. After one month of EVOO treatment, group A experienced a 48% decrease in the mean plaque index and a 64% drop in the bleeding index. After thirty days, group B's mean plaque index indicated a 35% drop and a decline of 43% in the bleeding scale.

Another clinical trial was conducted on patients with gingivitis demonstrated that toothpaste containing EVOO, xylitol, and betaine used by patients with gingivitis exhibited the best results, which include declines in gingival bleeding and supragingival biofilm as well as a rise in pH after four months when compared to a commercial toothpaste.

Sinesi et al. investigated the effects of EVOO on patients with angular cheilitis, Administration of EVOO for one week showed a better looking and healing lesion. Extending the remedy for another ten days resulting in healing of bilateral cheilitis [7].

## Oral mucositis

A clinical trial was conducted to assess the effectiveness of honey or olive oil with placebo in reducing the degree of OM pain among kids with leukemia. The children who took the olive oil had fewer feelings of pain than the control group, but honey-fed children had lower pain than children given OO. EVOO exhibited antitumor activity, but at a lower level than DOX [8].

In an *in vitro* study, it may lower the proportion of live cells and EGFR, promote apoptosis, and raise caspase expression.

Based on observed results, Alkhouli assessed the efficacy of olive oil in preventing chemotherapy-induced oral mucositis. The results showed that the olive oil group experienced less severe Oral Mucositis (OM) grades compared to the sodium bicarbonate group, with a statistically significant variance reported by the second week of the study phase. Furthermore, a statistically significant difference was found between the patients in the olive oil group (OM) and the Sodium Bicarbonate group (SB) according to the Mann-Whitney U test. So, in contrast to sodium bicarbonate, olive oil delayed the onset of Oral Mucositis (OM) [9].

A retrospective analysis of 20 cases was conducted by Nardi et al. to assess the efficacy of a gel based on EVOO in the medication of Peri-Implant Mucositis (PM). Clinical results (bleeding on probing, plaque index, and probing depth) showed statistically substantial enhancements when the baseline values were compared to the 3 surveillance periods. The finding shows that ozonated EVOO gel could be used to treat PM efficiently. Because of its organoleptic properties and lack of side effects, it can also be a useful treatment for the chemical control of PM and can be used on a daily basis in conjunction with supportive therapy [10].

## Gastrointestinal disorders

The beneficial effects of EVOO on gastrointestinal disorders are attributed to its antioxidant, anti-inflammatory, immunomodulatory, and cytotoxic properties. In enterocyte-like cells, the phenolic fraction produced from olives is shown to be responsible for improving the integrity of the epithelium and healing membrane damage caused by oxidation following peroxidative stress. In rat model, diets containing EVOO reduces indomethacin-induced gastric damage in rats. This effect may be partly due not only to reducing oxidative stress and neutrophil-induced toxicity but also to enhancing the glutathione antioxidant defense system [11].

An *in vitro* model of alternariol (a mycotoxin known AOH) induced cytotoxicity in Caco-2 cells showed the protective benefits of EVOO due to its cytotoxic properties and enhanced ROS generation AOH and polyphenols or AOH and EVOO together lessen cytotoxicity and ROS production. Polyphenols and EVOO extract also protected Caco-2 cells against AOH cytotoxicity. EVOO decreased IL-8 promoter action in cells that received IL-1 (representing the middle stage of inflammation), but also increased IL-8 stability of mRNA and expression of proteins, with the latter mechanism predominating over the former. INOS-mediated NO generation is one sign of an immunological response that can be unregulated, and this can result in chronic inflammatory illnesses like IBD. Transcriptional regulators like NF-B control the expression of iNOS and other activated genes, including COX-2, IL-6, and IL-8, during inflammatory and immune responses [12].

EVOO polyphenols may have a preventive impact on the development and progress of IBD. In research by Serra and colleagues, an olive oil polyphenolic extract was able to prevent $H_2O_2$ and NO generation that was brought on by oxysterols and maintains cellular GSH concentrations. Additionally, the phenolics in olive oil inhibited important oxysterol-driven inflammatory processes such as NF-B activation, iNOS expression, and the generation of IL-8 and IL-6. Research has been done on the effects of Oleocanthal (OC), Tyrosol (Tyr), and Oleocanthalic Acid (OA) on cell viability. The

results showed that the ability of OC and Tyr to scavenge ROS, especially HOCl and $O_2$·, was amply proven. The fact that all chemicals successfully penetrated the intestinal co-culture model is further evidence of their potential to do so, suggesting their potential against oxidative illnesses [13].

## Discussion

The contributions of TH to the prevention of ulcerative colitis, crohn's disease, gastric ulcer, colorectal cancer, gastroesophageal reflux disease, and eosinophilic esophagitis by hydroxytyrosol through a number of mechanisms have been summarized. These actions include a rise in antioxidant enzyme activity and the restoration of oxidative equilibrium. The suppression of the NF-B pathway and the release of inflammatory cytokines, immunomodulatory, antibacterial, pro-apoptotic, and anti-proliferative activity. The phenolic compounds found in EVOO have been shown in *in vivo* tests on animals to be efficient in both reducing and curing inflammation of the intestinal tract and associated damage. Adding EVOO to a Mediterranean diet or chocolate was shown to decrease permeability in the gut and low-grade endotoxemia [14].

Dameski et al. conducted a clinical trial to evaluate the impact of the topical application of OO on infantile colic symptoms. According to a clinical trial's findings, applying olive oil to the abdomen has the same symptom-reducing benefits as applying paraffin oil. The effect of abdominal massage with extra-virgin olive oil on constipation in elderly people was assessed by Faghihi et al. The findings showed that the olive oil group's mean score for constipation fell more than that of the water-only massage group and the control group. A clinical trial was done by Asl et al. To assess the effectiveness of olive oil ointment in the treatment of constipation in children ages 1-4, children given olive oil ointment experienced considerably higher enhancements in frequency of stools beginning on day 1 and lasting until day 4, when compared to the placebo group without adverse effects. Yoki assessed the effectiveness of olive oil enemas for extremely constipated children. Olive oil was successful in healing the impaction of feces in 77.6% of patients who received an enema and in 76.9% of patients who received it as a lubricant. Patients with various underlying diseases had equal levels of success with fecal disimpaction treatment. Overall, over 75% of kids with severe chronic constipation find benefit from olive oil enemas. It has been shown that ingesting extra virgin olive oil enhances omega-3 unsaturated fatty acids, which has beneficial synergistic effects on antioxidant defense and the metabolism of fat in people with metabolic syndrome. In the wistar rat model, the hypocholesterolemic impact of OO was caused by the rise in bile flow, biliary cholesterol and bile acid amounts, and subsequently increased excretion of feces [15].

The impact of extra-virgin olive oil supplemented with probiotics or antioxidants on functional dyspepsia was assessed in an OVA-sensitized model of animals. Subjects consuming either the antioxidant or probiotic-enriched oil meal showed a significant reduction in their symptoms of dyspepsia, with the latter having a more noticeable impact. Studies use MOG35-55-induced EAE in C57BL/6 mice to evaluate its possible a beneficial impact on gastrointestinal barrier dysfunction. Oleacein (OLE) prevented tissue damage and variations in permeability by reducing EAE-induced inflammatory conditions and oxidative Stress in the gut. OL enhanced its antioxidant ability and received protection from EAE-induced superoxide anion and the buildup of protein and lipid oxidation products in the colon. In OLE-treated EAE animals, these impacts were followed by decreased colonic IL-1 and TNF levels, while immunoregulatory cytokines IL-25 and IL-33 remained unaltered. Additionally, OLE shielded the goblet cells that contained mucin. IFABP and sCD14 levels, which are indicators of decreased intestinal epithelial barrier strength and low-grade systemic inflammation, were substantially lower in the colon and serum [16].

A mouse model of DSS-induced colitis was used by Carrielo et al. to show the beneficial impacts of EVOO from four Apulian cultivars. EVO, administered to mice, led to less body weight, decreased rectal bleeding, and decreased IL-1, TGF-, and IL-6 gene expression levels. EVO also improved the permeability of the intestinal tract and histological signs of inflammation. EVOO was compared to canola oil for its impact on the therapy of UC. After consuming EVOO, ESR and hs-CRP dramatically decreased. After consuming EVOO, symptoms like bloating, constipation, fecal urgency, incomplete defecation, and final GSRS significantly decreased. Consuming EVOO helped patients with UC by reducing indicators of inflammation and easing gastrointestinal symptoms. A PE-supplemented diet decreased the rate and degree of the acute GVHD illness and enhanced survival following transplantation in a mouse model of acute GVHD [17].

The anti-allergic effect of olive oil was assessed. The clinical signs and immune related parameters in BALB/c mice that had been given 600 mg/kg/day of olive oil for two weeks were examined before the assessment. The findings revealed that olive oil up-regulated hypothermia and a reduction in the immunological system index while down-regulating hypoallergenic sign scores in mice. Additionally, the olive oil-treated group showed a decrease in intestinal inflammation and cytokines linked to allergies. Olive oil boosted the expression of intestinal proteins involved in tight junctions and IL-22, as well as contributing to preserving the strength of the intestinal epithelial physical barrier. The intestinal mucus of the mice treated with olive oil showed higher concentrations of mucin 2 and defensin. The authors suggested that oral treatment with olive oil significantly reduced the mice's allergic immunological response to ovalbumin and enhanced intestinal epithelial mucosal immunity [18,19].

The impact of olive oil on intestinal microecology and food-allergic susceptibility was evaluated. The findings showed that supplementing sensitized mice with olive oil at a dose of 1-3 g/kg per day for seven weeks aided in reducing their allergy signs. It has been observed that the intestinal epithelium revealed restored ileum villi and increased expression of the Tight Junction (TJ) protein. In addition, the lamina propria showed lower levels of T helper 2 (Th2) cell-associated components and higher amounts of regulatory T cell-secreted cytokines, such as IL-10. Additionally, 16S rRNA sequencing revealed altered intestinal microbiota, with fewer *Burkholderiaceae* and more *Clostridiaceae*. The findings imply that, through controlling the intestinal microecological balance, a diet high in olive oil may be beneficial for preventing food allergies [20].

## Conclusion

In summary, EVOO improves the production of some beneficial bacteria and suppresses pathogenic bacteria such as *Desulfovibrio*. Due to its anti-inflammatory, immunomodulatory, and antioxidant properties, EVOO have positive effects on gastrointestinal diseases. EVOO reduces symptoms of infantile colic dyspepsia, gastrointestinal barrier dysfunction, inflammatory bowel disease, and ulcerative colitis. It is an effective remedy against constipation. It also enhances

omega-3 unsaturated fatty acids and the frequency of stools in children and elderly individuals.

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