ALINEA

NUTRITION

FEBRUARY 2023

www.alineanutrition.com

TABLE OF

CONTENTS

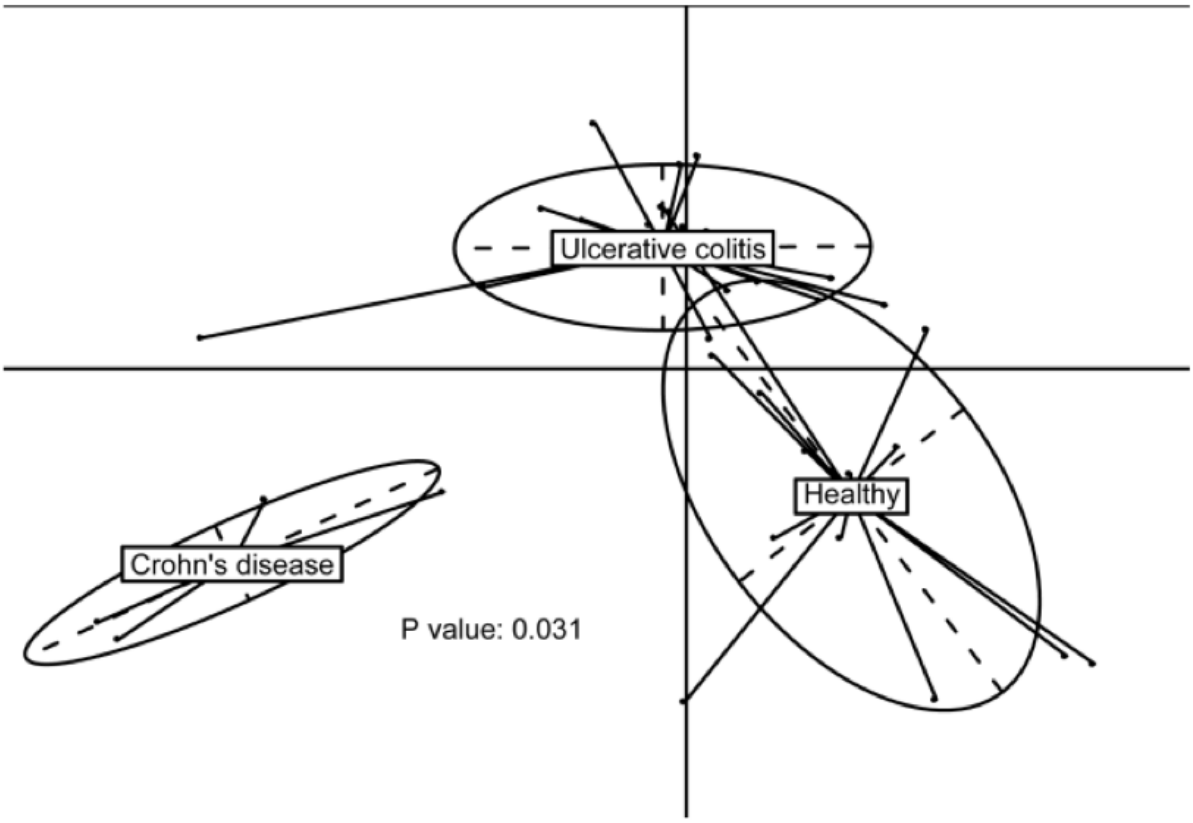
Morvaridi M, Jafarirad S, Seyedian SS, Alavinejad P, Cheraghian B. The effects of extra virgin olive oil and canola oil on inflammatory markers and gastrointestinal symptoms in patients with ulcerative colitis. Eur J Clin Nutr. 2020 Jun;74(6):891-899.

What We Know, Think We Know, or Are Starting to Know

Inflammatory Bowel Disease [IBD] is an umbrella term for gastrointestinal conditions characterised by chronic inflammation, including Crohn's Disease [CD] and Ulcerative Colitis [UC]. There is evidence of a complex interplay between environmental factors, dysbiosis i.e., disturbed balance in the gut microbiota, diet, and genetics, in risk for developing IBD [1–4].

Although these factors may interact, there is one common denominator: inflammation. Inflammation is the primary driver of alterations in the gut that lead to increased risk for IBD [1,4]. However, this relationship is influenced by dysbiosis in the gut microbiota, which itself is influenced by diet and environmental factors [3].

A striking illustration of this was provided by an analysis from Qin *et al*. [1] of bacterial species' abundance between healthy controls and individuals with CD or UC; as you can see from this **figure** below, the bacterial compositions differed substantially not just between those with IBD and healthy controls, but even between CD and UC.



And we know that diet has an influence on the composition of the microbiota and intestinal inflammation [3,5]. Most of the attention in this area is given to dietary fibres, as these non-digestible carbohydrates reach the colon and undergo selective fermentation by bacterial species that increase production of short-chain fatty acid [SCFA], and SCFA's, in particular butyrate, are associated with anti-inflammatory effects in the colon [6,7].

However, dietary fat intake is also a crucial characteristic of diet that may influence the microbiome, particularly by influencing production of bile acids [3,8]. However, fat subtype is important. The evidence to date suggests monounsaturated fats do not significantly influence microbial composition, while omega-3 polyunsaturated fats may increase some beneficial bacterial strains and modify bile acid composition [3,8]. The present study investigated the effects of additional extra virgin olive oil or canola [rapeseed] oil in participants with UC.

The Study

The study was designed as a randomised, crossover, single-blind, controlled trial in participants with a diagnosis of UC. The interventions in this study were 50ml of extra virgin olive oil [EVOO] or canola oil [CO] per day consumed for 20 days. The crossover design meant that participants were randomised to the order of oil intake, with a 14-day washout period between diet phases:

- **EVOO** [20-days] >Washout [14-days] >**CO** [20-days]
- **CO** [20-days] >Washout [14-days] >**EVOO** [20-days]

Clinical symptoms were assessed at baseline and after each intervention period using the Gastrointestinal Symptom Rating Scale [GSRS]. The GSRS scale ranges from 1 representing the absence of symptoms to 7 representing troublesome symptoms; each specific subscale [e.g., bloating, constipation] is summed together to give an overall symptom score.

The primary outcomes of the study were inflammatory markers [erythrocyte sedimentation rate (ESR) and high-sensitivity C-reactive protein (hs-CRP)] and changes in the GSRS. For context, normal reference ranges for ESR are 0–22mm/hr and 0–29mm/hr for men and women, respectively. For hs-CRP, normal range is <1.0mg/L, while the range of risk is evident >2mg/L.

Secondary outcomes included the Mayo score, a measure of UC disease activity categorised as remission, mild, moderate, and severe. The Mayo score ranges from 0–12, with 3–5 indicating mild disease activity, while 11–12 indicates severe UC.

Results: 32 participants completed the study; *n* = 17 in the EVOO>CO diet order [13 female], and *n* = 15 in the CO>EVOO diet order [10 female]. Participants were ~36yrs of age on average and had diagnoses of UC for ~4yrs.

***Effect of Diets on Inflammatory Markers*:** In the EVOO phase, ESR decreased by 1.18mm/h [from 14.36 to 13.18mm/h], while hs-CRP decreased by 1.31mg/L [from 2.31mg/L to 1.00mg/L]. In the CO phase, ESR increased by 1.87mm/h [from 12.01 to 13.18mm/h], while hs-CRP increased by 0.36mg/L [from 1.51mg/L to 1.87mg/L].

***Effect of Diets on Gastrointestinal Symptoms*:** In the EVOO phase, the overall GSRS score decreased by 13-points [from 38.0 to 25.0], while in the CO phase there was a decrease of 4.2 points [from 32.4 to 28.2].

For specific components of the GSRS, there were significant decreases in the EVOO phase in bloating by 1.6 points [3.9 to 2.3], in constipation by 2.15 points [3.2 to 1.06], in faecal urgency by 2.1 points [3.4 to 1.3], and in incomplete defecation by 1.7 points [3.2 to 1.5].

The average Mayo score was 3 at baseline, indicating the low end of the range for mild UC, and there were no significant effects of either diet on Mayo scores.

The Critical Breakdown

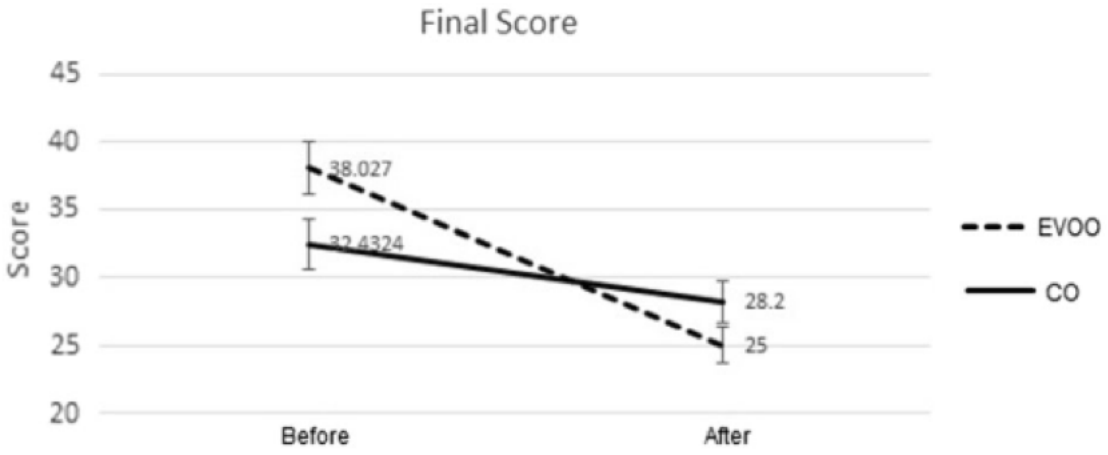
Pros: The study had clearly stated aims. The randomisation method was appropriate [computer-generated, blocks of 4 participants to ensure balance] and clearly described. The crossover design meant that each participant served as their own control. Sample size calculation was clearly stated, and the study appears to have been adequately powered with participants in each diet order group [a minimum of 15 per group was estimated]. Validated outcome measures for gastrointestinal symptoms and UC disease severity were used. The investigator conducting the statistical analysis was blinded to participant allocation to diet order.

Cons: While it appears that their sample size estimation was just met, this is a very small study and the first to test the potential effects of these oils specifically in participants with UC. Consequently, this is best considered a pilot study with hypothesis-generating, rather than confirmatory findings. The statistical analysis was rudimentary, using basic before-after tests for each group, rather than comparing one group to the other [more under ***Key Characteristic***, below]. Diet was only assessed before and after each intervention using a single 24 h recall, which may have provided inaccurate representations of diet in each group.

Key Characteristic

As stated above, the statistical analysis in the present study was fairly crude. In a crossover design like the present study, comparing the magnitude of change between diets is the purpose of such study designs, with the intention that the crossover will minimise potential inter-individual differences in response by having the same participant consume both diets.

However, the analysis only compared the before and after scores for *each* diet, rather than compare the differences *between* the effects of each diet. And this is important, for reasons that will be clear by looking at the **figure** from the paper illustrating the changes in overall Gastrointestinal Symptom Rating Scale [GSRS] scores before and after each diet phase. As you can see, the EVOO group had a 5.6 point higher overall GSRS score at baseline compared to the CO diet.



While the magnitude of the decrease is clearly greater in the EVOO diet compared to the CO diet, these baseline differences were not accounted for in the statistical analysis, which used basic statistical tests that don't allow for adjustment for additional factors, in this case differences in baseline symptom scores. Thus, the decrease from a higher baseline in the EVOO group may have overexaggerated the effects of the EVOO.

Interesting Finding

Let's get straight into the finding that anyone reading this study would likely jump at; the apparent different directions of effect of each oil on inflammatory markers. The fact that there were modest increases in the CO diet would likely bring the focus sharply onto the content of omega-6 linoleic acid [LA] in this oil. One could envisage this paper being cited as evidence that such seed oils are in fact inflammatory.

The first thing to note is that the totality of available research does not support an increase in inflammatory biomarkers from either CO specifically [(9)], or LA specifically [(10)]. The second is to then consider the specific ranges and changes of the inflammatory outcome measures in the present study. For the ESR finding, it is crucial to note that the levels of ESR in participants both at baseline and after the interventions were within normal ranges, and so the very minor changes observed were within the biological range of normal for this marker. Further, the normal range for ESR is higher for women, and the majority of participants in this study were female, further emphasising that ESR exhibited minor changes well within normal range.

A similar consideration applies to hs-CRP, which shows natural variation in measured levels [(11)], and the minor change in this marker potentially reflects natural biological variation. It would also, based on wider evidence, be difficult to attribute any such effect to LA *per se*, given CO also is rich in oleic acid and omega-3 alpha-linolenic acid. A 4-week trial comparing olive oil to rapeseed oil found that both diets led to reductions in CRP, albeit the magnitude of the decrease was greater in the olive oil group [(12)].

Thus, based on both the overall wider literature and the levels of specific inflammatory markers in the present study being all within normal ranges, caution in required against interpreting the finding of very minor increases in these markers on the CO diet as evidence of a detrimental inflammatory effect in these participants with UC.

Relevance

As stated in the **Cons** section above, a study like this is best considered as a hypothesis-generating pilot study. And such research is needed; there is scant research specifically focusing on UC, and many trials of dietary fats have been in participants with CD [13,14]. At the very least, it does appear that fat composition is an important dietary factor to consider in IBD generally [3,8].

It is established that 'Western' diets high in fat, sugar, animal protein, and low in fibre negatively impacts the microbiome, effects seen as early as 1-years old [15]. High fat Western diets increase populations of bile-tolerant bacterial strains and bile acid production which, in the absence of fibre, pass to the colon and undergo metabolism to secondary bile acids that are associated with intestinal inflammation and colorectal cancer risk factors [6,7].

This increase in bile-tolerant bacteria and secondary bile acid metabolites appears to be driven primarily by animal and saturated fats [3,8]. However, the role of monounsaturated fats and polyunsaturated fats in IBD specifically is incompletely understood. For example, a randomised controlled trial in patients with UC on enteral feeding [i.e., providing nutrients direct to the gastrointestinal tract with a tube] provided two formula diets, one rich in oleic acid and the other in LA; 52% of patients on the LA-enriched formula achieved clinical remission compared to 20% in the oleic acid formula group [14].

What of olive oil itself? The data is sparse, and the present study appears to be the only study to date to specifically investigate the effects of EVOO in patients with IBD/UC. However, both animal models and other human trials on the effects of olive oil on inflammatory markers and beneficial gut bacterial species, generally suggest benefits on inflammatory markers relevant for intestinal health [16,17].

Application to Practice

Overall, like much of human gut research, we are left with broad conclusions, and as it pertains to dietary fats, it appears the general application of unsaturated fats as the preferable, predominant fats in the diet also applies to intestinal inflammatory conditions.

Nevertheless, there is a lack of evidence currently to make specific recommendations and doses for EVOO intake, or any specific oil, in individuals with IBD, UC in particular. In fact, overall there is simply an absence of evidence for UC, and there are few to none well-designed, high-powered intervention trials targeting nutritional remission of UC [18].

In the absence of more rigorous evidence for effects of specific fat subtypes and fatty acids, at the very least the evidence supports the general health benefits of unsaturated fat rich oils, including both EVOO and CO.

References

1. Qin J, Li R, Raes J, Arumugam M, Burgdorf KS, Manichanh C, et al. A human gut microbial gene catalogue established by metagenomic sequencing. Nature. 2010 Mar;464(7285):59–65.
2. Serrano-Moreno C, Brox-Torrecilla N, Arhip L, Romero I, Morales Á, Carrascal ML, et al. Diets for inflammatory bowel disease: What do we know so far? Eur J Clin Nutr. 2022 Sep 22;76(9):1222–33.
3. Devkota S, Chang EB. Interactions between Diet, Bile Acid Metabolism, Gut Microbiota, and Inflammatory Bowel Diseases. Digestive Diseases. 2015;33(3):351–6.
4. Peterson DA, Frank DN, Pace NR, Gordon JI. Metagenomic Approaches for Defining the Pathogenesis of Inflammatory Bowel Diseases. Cell Host Microbe. 2008 Jun;3(6):417–27.
5. Lopez-Legarrea P, Fuller NR, Zulet MA, Martinez JA, Caterson ID. The influence of Mediterranean, carbohydrate and high protein diets on gut microbiota composition in the treatment of obesity and associated inflammatory state. Asia Pac J Clin Nutr. 2014;23(3):360–8.
6. Ou J, Carbonero F, Zoetendal EG, DeLany JP, Wang M, Newton K, et al. Diet, microbiota, and microbial metabolites in colon cancer risk in rural Africans and African Americans. American Journal of Clinical Nutrition. 2013;98(1):111–20.
7. O'Keefe SJD, Li J v., Lahti L, Ou J, Carbonero F, Mohammed K, et al. Fat, fibre and cancer risk in African Americans and rural Africans. Nat Commun. 2015;6(May 2014).
8. Graf D, di Cagno R, Fåk F, Flint HJ, Nyman M, Saarela M, et al. Contribution of diet to the composition of the human gut microbiota. Microb Ecol Health Dis. 2015 Feb 4;26(0).
9. Lin L, Allemekinders H, Dansby A, Campbell L, Durance-Tod S, Berger A, et al. Evidence of health benefits of canola oil. Nutr Rev. 2013 Jun;71(6):370–85.
10. Su H, Liu R, Chang M, Huang J, Wang X. Dietary linoleic acid intake and blood inflammatory markers: a systematic review and meta-analysis of randomized controlled trials. Food Funct. 2017;8(9):3091–103.
11. Rudnicka AR, Rumley A, Lowe GDO, Strachan DP. Diurnal, Seasonal, and Blood-Processing Patterns in Levels of Circulating Fibrinogen, Fibrin D-Dimer, C-Reactive Protein, Tissue Plasminogen Activator, and von Willebrand Factor in a 45-Year-Old Population. Circulation. 2007 Feb 27;115(8):996–1003.
12. Junker R, Kratz M, Neufeld M, Erren M, Nofer JR, Schulte H, et al. Effects of diets containing olive oil, sunflower oil, or rapeseed oil on the hemostatic system. Thromb Haemost. 2001 Feb;85(2):280–6.
13. Marion-Letellier R, Savoye G, Beck PL, Panaccione R, Ghosh S. Polyunsaturated Fatty Acids in Inflammatory Bowel Diseases. Inflamm Bowel Dis. 2013 Mar;19(3):650–61.
14. Gassull MA, Fernandez-Banares F, Cabre E, Papo M, Giaffer MH, Sanchez-Lombrana JL, et al. Fat composition may be a clue to explain the primary therapeutic effect of enteral nutrition in Crohn's disease: results of a double blind randomised multicentre European trial. Gut. 2002 Aug 1;51(2):164–8.

References

15. de Filippo C, Cavalieri D, di Paola M, Ramazzotti M, Poullet JB, Massart S, et al. Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa. Proceedings of the National Academy of Sciences. 2010 Aug 17;107(33):14691–6.

16. Vrdoljak J, Kumric M, Vilovic M, Martinovic D, Tomic IJ, Krnic M, et al. Effects of Olive Oil and Its Components on Intestinal Inflammation and Inflammatory Bowel Disease. Nutrients. 2022 Feb 11;14(4):757.

17. Cárdeno A, Magnusson MK, Strid H, Alarcón de La Lastra C, Sánchez-Hidalgo M, Öhman L. The unsaponifiable fraction of extra virgin olive oil promotes apoptosis and attenuates activation and homing properties of T cells from patients with inflammatory bowel disease. Food Chem. 2014 Oct;161:353–60.