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Review Article

# Efficacy of Olive Oil in the reduction of the risk for Colorectal Cancer – A Systematic Review

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***Abstract*—Aims and objectives:** The purpose of the systematic review is to determine whether extra virgin olive oil can effectively lower the risk of colorectal cancer.
**Materials and method:** In accordance with PRISMA guidelines, we searched electronic databases from conception until 2023. In this systematic review, the original studies that were conducted among experimental rodents who were given olive oil as a diet were included. Quality assessment was done using the Office of Health Assessment and Translation (OHAT) Scale.
**Results:** From a total of five studies consisting of randomized control trials it has been analysed that EVOO significantly lowers CRC through anti-inflammatory and antioxidant properties. Studies have shown that EVOO can alter gut microbiota, inhibit tumour growth, and impact key biomarkers of cancer and their gene expression. The notable findings on EVOO were the prevention of dysbiosis associated with CRC, the reduction in tumour size observed in animal models, and the modification of epigenetic markers associated with cancer progression.
**Conclusion:** Although all these results are very encouraging, further large-scale studies in human subjects are called for to fully establish the benefits mentioned above and to refine dietary recommendations. Consumption of EVOO might present a cost-effective and preventive strategy against CRC, improving public health and reducing cancer treatment costs.

***Keywords*—** Olive Oil, Colorectal Cancer, Chemoprevention, Tumor suppression, Phenolic compounds

## 1. Introduction

Colorectal cancer (CRC) is the third largest cancer in the entire globe [1]. About 1.2 million new cancer cases are identified to be CRC each year, and about 601,000 deaths happen due to CRC every year. This occurrence statistic is said to grow twice as in 2030 (According to which data). The incidence trend is alarming as the incidence rate has spiked more than 1.5% in adults below 50 during the last decade. Mortality has increased by 2% since then [2].

Genetic, environmental, and other modulating factors, including inflammatory bowel disease (IBD) and changes in gut microbiota, originating with the stomach mucosal epithelium, are linked to colorectal cancer (CRC). However, about three-fourths of the cases are sporadic and have no familial history. Earlier, IBD was one of the main underlying causes behind CRC after Familial Adenomatous Polyposis and Hereditary Non-Polyposis CRC [3]. The most crucial determinant of the outcome of any cancer is at what stage it is diagnosed. Therefore, the demand for early cancer diagnosis in the clinical set-up is essential to cancer treatment success.

Given olive oil's anti-inflammatory and antioxidant effects, it is better for preventing colon cancer than relying on cures. Adding olive oil into the diet can reduce the chances of developing cancers at a lower cost and less suffering than establishing a cure. Poor economic performance,

unemployment, or rising inflation rates in developing countries like India will exacerbate horrible conditions. Low socioeconomic groups can benefit from this approach by improving their health and reducing healthcare costs [4].

Adverse consequences of radiation therapy and chemotherapy leave a lifetime impression on the patient's overall well-being and lower the quality of life. The most popular treatment for colorectal cancer is 5-fluorouracil, which has adverse effects such leukopenia, bone marrow suppression, mucosal and submucosal damage, nausea, vomiting, and diarrhoea.. So, there has been a long search for alternative treatments for CRC [5].

Olive oil is a preventive measure against colon cancer owing of its anti-inflammatory and antioxidant properties. Monolaurin is a chemical produced by lauric acid. It is well known that lauric acid and monolaurin both impede the growth of oral microflora. Lauric acid appears to be abundant in both olive and coconut oils [6]. It reduces cancer risk by reducing inflammation and oxidative stress. Attention may, hence, focus on the easier prevention route through dietary choices like olive oil to avoid the harsh consequences and costs associated with cancer treatment, improving the quality of life and public health.

Since olive oil has been a part of many ethnic populations' diets for many years, it and its active components can be employed as alternative treatment options in this scenario. Much literature is available regarding olive oil's activity against multiple cancers. Evidence says that daily intake of olive oil may reduce the risk of CRC. The study aims to determine olive oil's effectiveness in reducing colorectal cancer risk.

## 2. Related works

In the past decade, phytochemicals and probiotics have been studied extensively by the authors to prevent cancer, such as gingerol, citrus peel extract and fermented rice. Gingerol's anticancer activity is especially noteworthy in the case of colorectal cancer, where it can potentially inhibit tumor growth. Through its modulation of critical signaling pathways, gingerol can trigger apoptosis, inhibit cell proliferation, and suppress metastasis in colorectal cancer cells [7]. Researchers have shown that citrus peel extract suppresses tumor growth, as well as reduces oxidative stress, suppresses inflammatory enzymes, and promotes anticancer activity in animal models [8]. It has been found that eating fermented brown rice and fermented brown rice drinks changed the gut microbial environment and protected the digestive system and accessory organs. [9]

## 3. Materials and Method

### 3.1 Information sources

According to PRISMA guidelines, the following electronic databases were searched from conception until 2023: PubMed, Elsevier Science Direct, Google Scholar, Wiley Online Library, and SpringerLink.

### 3.2 Search category

Boolean operators were used in the search strategies for the following keyword combinations: "olive oil", "extra virgin olive oil", "colorectal cancer", "cancer prevention", "cancer reduction", "oral administration", "cancer risk", "animal models", "phenolic compunds", and "tumour prevention".

### 3.3 Eligibility criteria

We have included clinical trials conducted on experimental rats and mice orally, subcutaneously and via the intra-peritoneal route, a significant cancer prevention strategy available through various sources. Only the original research studies with full texts available and published in English were included. The study contained research that had been conducted using proper statistical analysis. This study includes studies that were made by using validation tools and standardized measurement techniques. Exclusion criteria: Researches that were deemed to be irrelevant and duplicates were not included. Articles in languages other than English were excluded.

### 3.4 Methodology

Studies which fulfilled the eligibility parameters were listed. The data included the citation (author/year), the place of the study, the number and type of samples collected, the intervention provided, the techniques and methods of measurement, and the results and inferences drawn from the study. Quality assessment was done using the Office of Health Assessment and Translation (OHAT) Scale [10].

## 3. Results

In this study, original articles from conception until the present were collected. Five full-text articles out of the 165 total articles were evaluated separately. Five articles were included in the study which met the inclusion criteria after the eligibility that assessed using the inclusion and exclusion criteria, elimination of duplicate articles and those with simple abstracts, and other additional procedures were carried out. An overview of the steps according to PRISMA guidelines involved in the included studies is shown in the flowchart below.

 

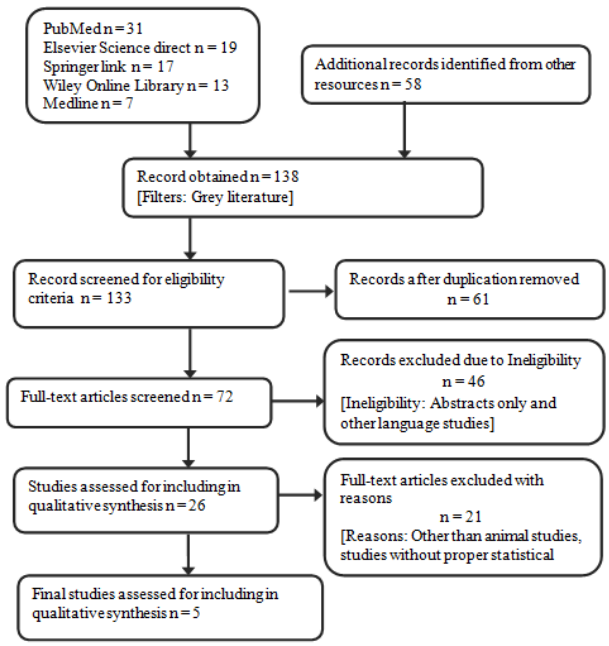


**Figure 1:** A flowchart depicting the steps in the studies included

## 4. Discussion

In numerous countries, olive oil is an essential fat source. The metabolites of olive oil have a significant anti-inflammatory and anti-tumorigenesis action, especially in risk reduction of CRC. However, systematic review studies are available in this domain on how effective olive oil is in reducing the risk of CRC. This study aims at how Olive Oil and its key metabolites play an important role in reducing oxidative damage, and inflammation, promoting cellular apoptosis and reducing the risk of developing colorectal cancer.

The major phenolic compounds of olive oil were identified and quantified into three classes: simple phenols (hydroxytyrosol, tyrosol), secoirioids (oleuropein) [16], and the lignans (acetoxy pinoresinol and pinoresinol). All three classes are effective anti-inflammatory agents but will not get metabolized in the colon. Only less than 50% of total phenols get absorbed in the colon. The amount of hydroxytyrosol and tyrosol reaching the colon was quantified to be less than 4mol/100mol, whereas the other two classes' absorption rate and quantity remain unknown. Based on an In-Vitro study by Gill et al., the incidence of CRC in Mediterranean regions is lower than in European countries. The study examined the effect of active olive oil phenols on DNA damage, barrier function, invasion, and cell viability in CRC cell lines. The phenols in olive oil were observed to reduce the DNA damage induced by hydrogen peroxide in HT-29 cell lines with a significant linear trend ($p<0.001$), thus suggesting a protective effect against DNA damage. Olive oil phenols (50 and 100 µg/ml) significantly improved the epithelial resistance, increasing the barrier function in CACO2 cell lines ($p = 0.004$ and $p = 0.002$, respectively). The phenols inhibited the invasion of HT-115 cells through Matrigel in a dose-dependent manner ($p < 0.01$ for 25, 50, 75, and 100 µg/ml). Further increased concentrations (75 and 100 µg/ml) prominently reduced the cell attachment ($p<0.001$ and $p<0.006$). However, the phenols do not lessen the metastatic gene expression in HT-115 cells even when tested across various concentrations [17].

In a similar study, the impact of a high-fat diet on the gut microbiota of female CD1 mice was observed based on how this influenced CRC risk. The mice were split into four different groups of 11 each based on the type of diet that they were fed, i.e., chow diet, coconut oil, sunflower oil, and Olive oil, respectively. The intake of different kinds of fat in a diet highly influences the gut microbiota, causing alterations in the bacteria ratio. Consuming coconut oil and sunflower HFDs created a proinflammatory environment by reducing Akkermansia and increasing the other harmful bacteria. In contrast, olive oil HFD resulted in maintaining the population of Akkermansia and increasing the ratio of Firmiculates/Bacteroidetes. EVOO was seen to reduce the risk of CRC, while other HFDs implied increased risk for CRC [11,18,19].

A study by Neha Nanda et al. examined the effects of EVOO on colon cancer in a rat model. The study involved three groups of Sprague Dawley rats: normal controls, rats treated with 1,2 –dimethylhydrazine (DMH) alone, and rats treated with DMH along with olive oil. Olive oil was administered for three weeks orally, and the tumour development and progression were observed. The rats were found to have increased body weight in DMH and olive oil-treated rats more significantly than the only DMH-fed rats. Olive oil feeding reduced the rat's incidence, multiplication, and tumour progression compared to DMH. Over ten weeks of Olive oil administration, the polyp incidence was reduced, and after 20 weeks, the tumour was completely absent. The anti-inflammatory action of olive oil was proved by analyzing the expression of inflammatory and pro-cancerous markers such as NF-κB, VEGF, and MMP-9, which were reduced after olive oil administration [20]. Olive oil was also found to promote the pro-apoptotic proteins caspase-3 and caspase-6. Olive oil also proved to have optimistic DNA methylation results favorable in reducing the oncogenic markers. Also, the expression of Mi-RNAs (miR-143 and miR-145) was increased that were reduced in DMH treatment. This explains that olive oil counteracts the epigenetic silencing of these miRNAs. This study affirms olive oil's protective effect against colon cancer by modulating tumour growth, enhancing apoptosis, and influencing gene expression and DNA methylation [12].

Fezai et al study concerned with rats and mice investigated anti-inflammatory, analgesic, and anticancer properties. The carrageenan-induced paw oedema model was used to evaluate EVOO's anti-inflammatory effects [21], a well-established test for assessing anti-inflammatory effects. EVOO showed a significant reduction in swelling of the paws as it surpassed ASA (32%) but fell slightly behind dexamethasone (69%), registering a 79% inhibition at 5 hours. Accordingly, this highlights that EVOO has bioactive compounds possessing potent anti-inflammatory activities, such as hydroxytyrosol and oleuropein, previously reported to lower inflammatory markers and cytokine production. This discovery supports the traditional use of EVOO in inflammatory conditions and suggests its potential as a natural alternative or adjunct to conventional anti-inflammatory drugs.

 

**Table 1:** Characteristics of the studies included in the study

| Studies | Year of Study | Place of study | Type of Study | Sample | Sample size | Intervention | Technique |
|---|---|---|---|---|---|---|---|
| Carmen Rodriguez et al [11] | 2020 | Spain | Randomized clinical trial | Female CD1 mice | 44 | CD1 MICES were divided into four groups (11 in each) and fed with different diets: Chow Diet, Coconut Oil, Sunflower Oil, and Extra Virgin Olive Oil. All the groups were fed with a chow diet for two weeks, and then the three groups were switched to High Fat Diet (HFD) but the chow diet group was continued with the same diet. This diet routine was followed for 16 weeks. | Colonic mucosa-associated microbiota was analyzed using Polymerization Chain Reaction (PCR) amplification and sequencing of the 16S rRNA gene. |
| Neha Nanda et al [12] | 2018 | Maryland, USA | Randomized clinical trial | Healthy male Sprague Dawley rats | 12 | Rats were divided into three groups, each group having 12 rats. Group 1 rats served as controls. Group 2 rats were subcutaneously injected once weekly with 1,2-dimethylhydrazine (DMH) in normal saline at 30mg/kg of body weight for two-time durations of 10 and 20 weeks. Group 3 was given Extra Virgin Olive Oil (EVOO) twice a week at a dose of 1g/kg body weight through oral garaging in addition to DMH treatment as was given to Group 2 rats for 10 and 20 weeks. | Immunohistochemistry (IHC) study of tumour markers |
| Myrium Fezai et al [13] | 2013 | Tunisia | Randomized clinical trial | HCT 116 CELLS and Albino Wistar female rats and albino swiss male mice | 8 | Athymic 6-week-old female mice inoculated with 200$\mu$Lof PBS 1X or EVOO (8ml/kg) thrice a week for four weeks. | Tumour size was evaluated twice a week using a calliper. Histopathology, IHC |
| S. Sánchez-Fidalgo et al [14] | 2010 | Seville, Spain | Randomized clinical trial | Six-week-old femaleC57BL/6 mice | 84 | Mice were divided into two groups- (Sunflower Oil) SFO fed & EVOO fed as lipid components that were a part of the AIN76A diet (900mg/kg iron diet). The mice were fed this diet for two weeks before the induction of colitis and during the experiment. Colitis was induced by administration of DSS(0.7%w/v) | IHC, Cytokines, Cytoplasmic proteins |
| R Bartolí et al [15] | 2000 | Badalona, Spain | Randomized clinical trial | Sprague-Dawley rats | 108 | The rats were divided into three groups, and each group were fed a diet rich in the following fats-n6 (linoleic acid-sunflower oil), n3 (eicosapentaenoic acid-fish oil) and n9 (oleic acid-olive oil). Then, the rats were subjected to carcinogen treatment -Azoxymethane (AOM) subcutaneously once weekly for 11 weeks to induce colon cancer. The control rats received injections of saline instead of AOM. | The colon tissue samples' histopathology was done to analyze the tumorigenesis and other precancerous changes. Prostaglandin E2 measurement was done using enzyme immunoassay technique. Gas chromatography examined the type of fatty acids involved in cancer outcomes. |

Table 1 shows the characteristics of the intervention across all the included trials. The administration of olive oil on mice in the prevention of colorectal cancer was taken in all of the aforementioned research, which were written by Carmen Rodriguez et al., Neha Nanda et al., Myrium Fezai et al., Sánchez-Fidalgo et al., and Bartolí R et al.

 

**Table 2:** Results of the included interventional studies showing the effectiveness of Olive Oil in the reduction of Colorectal Cancer Risk

| Study | Results | Inference |
|---|---|---|
| Carmen Rodriguez et al [11] | In the post bioinformatic analysis of the genomic DNA, the administration of EVOO caused dysbiosis that was associated with the reduction and prevention of the risk of CRC. In contrast, administration of other diets was known not to cause dysbiosis of the CRC promoting bacteria, enhancing the risk of CRC. | The CRC-associated risk was reduced. |
| Neha Nanda et al [12] | NF-κB, VEGF, and MMP-9 are examples of hypomethylated genes where olive oil can act as a demethylation inhibitor. Olive oil also has the capacity to demethylate the hypermethylated genes caspase-3 and caspase-9. In addition, the study revealed a connection between miRNA expression pattern and DNA methylation, which is related to the silencing of mir-143/145. It was noted that rats injected DMH could develop and spread tumors. | The DNA methylation of tumour suppressor genes reduced the risk of CRC |
| MyriumFezai et al [13] | Within three weeks of treatment, the treated group had the tumour volume reduced by 50% compared to the control group. During the treatment period, no significant weight changes, toxicity or macroscopic signs were seen, suggesting that the EVOO was well tolerated in the intraperitoneal administration. | Anti-inflammatory and anti-carcinogenic properties of EVOO were proven and have effects against CRC carcinogenesis. |
| S. Sánchez-Fidalgo et al [14] | Animals with EVOO feeding exhibited reduced disease activity, fewer tumours, less inflammation, and lower β-catenin, COX-2, and iNOS expression compared to mice fed sunflower oil. The extra virgin olive oil-enriched diet exerts protective activity against the development of colorectal cancer in the colitis-induced mouse model. It seems more efficient than sunflower oil in reducing cancer risks | Dietary enrichment with extra virgin olive oil significantly reduces the development of colorectal cancer in the mouse model of ulcerative colitis. Therefore, EVOO consumption is protective against the development of colorectal cancer through its modulation of both inflammatory and tumour-related pathways. |
| R Bartolí et al [15] | Olive oil likely influenced the metabolism of Arachidonic Acid, a precursor to proinflammatory prostaglandins. Thus, by modulating this pathway, olive oil reduced the PGE2's local synthesis, reducing inflammation and carcinogenesis. | Rats treated with the olive oil diet had reduced tumor incidence and progression compared to the other fatty acid-rich diet, especially n6 fatty acid. |

Table 2 shows the interpretation of administering olive oil to mice in the prevention of colorectal cancer in all the included studies.

**Table 3:** Quality Assessment of all the included studies

| Author name | Randomization | Allocation Concealment | Comparison group | Confounding | Experimental conditions | Blinding | Complete outcome data | Exposure Characterization | Outcome Assessment | Outcome Reporting | No other threats |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Carmen Rodriguez et al [11] | | | | | | | | | | | |
| Neha Nanda et al [12] | | | | | | | | | | | |
| MyriumFezai et al [13] | | | | | | | | | | | |
| S. Sánchez-Fidalgo et al [14] | | | | | | | | | | | |
| R Bartolí et al [15] | | | | | | | | | | | |

Table 3 shows the Risk of bias in all the included studies based on the Office of Health Assessment and Translation (OHAT) Assessment tool [10].

Definitely low risk of bias
Probably low risk of bias
Probably high risk of bias
Definitely high risk of bias

 

On the other hand, regarding its anticancer activities, the researchers employed HCT 116 human colon cancer cells with xenograft mouse models. For example, according to this study, there was a 50% decrease in tumour growth among EOVO-treated mice compared to controls; no noticeable toxicities were detected. This kind of anticancer effect could be seen as promising regarding limited systemic side effects because it demonstrates that EOVO might be useful for therapeutic purposes in the cancer management system [13].

A study was done by S. Sanchez et al. to determine the critical impact of dietary fats, such as extra virgin olive oil and sunflower oil, on developing chronic ulcerative colitis and colorectal cancer in mice. We found these dietary lipids to have differential impacts on inflammation and carcinogenesis, reflecting worthwhile information on nutritional influences on colitis and CRC. EVOO and SFO represent two extreme dietary fat profiles. In contrast to the high content of oleic acid and phenolic compounds in EVOO, SFO is rich in n-6 polyunsaturated fatty acids. All these studies conclude that diets with a high intake of n-6 fatty acids, especially those containing SFO, can cause an inflammation response and increase CRC risk. In sharp contrast, EVOO, having anti-inflammatory components, exerts some protective benefits against inflammation. Our review shows mice fed with SFO have more serious inflammation and higher disease activity indices than the EVOO group. This result was by previous observations that a high intake of n-6 fatty acids promoted inflammatory responses via COX-2 and iNOS up-regulation, leading to an increased production of eicosanoids and nitric oxide. These inflammatory mediators can create a milieu that favours the process of tumorigenesis. Our findings point to a protective role of EVOO against CRC development. Mice fed with EVOO showed decreased incidence and severity of tumours, with fewer adenocarcinomas and reduced grade dysplasia compared with SFO diet-fed animals. This protective effect is likely due to the richness of squalene and phenolic antioxidants in EVOO, which may exert an inhibitory action on several phases of carcinogenesis. On the contrary, intake of an SFO diet was related to increased tumour burden and advanced dysplasia. It reinforces the idea that a high intake of n-6 fatty acids can further enhance the risk of CRC by promoting chronic inflammation and molecular pathway alterations in tumorigenesis [14].

Mechanisms may include the increased expression of proinflammatory cytokines (TNF-α, IL-6, IFN-γ) and disruption of tumour suppressor pathways, for instance, p53, as occurred in SFO-fed mice. The opposite effects exerted by EVOO and SFO on CRC might be related to their actions on cellular and molecular pathways. The translocation of β-catenin—a key event in CRC—was more relevant in SFO-fed mice, thus indicating a more aggressive tumour phenotype. In contrast, EVOO feeding was associated with less β-catenin translocation, suggesting a less aggressive disease course. Moreover, the effect of EVOO on the maintenance of the p53 level, coupled with the downregulation of COX-2 and iNOS expression, further supports its potential as a dietary intervention in CRC prevention strategies. The preserved p53 levels in EVOO-fed mice implicate its protective role in maintaining genomic stability, consequently acting to prevent tumour initiation and progression. The findings have significant therapeutic ramifications for the possible contribution of dietary fat composition to the treatment of UC and CRC. Given its anti-inflammatory and antioxidant properties, EVOO may be a dietary strategy to reduce CRC risk and manage UC.

Further studies are needed to translate these findings into human populations and validate EVOO's efficacy in CRC prevention and management. The mechanisms underlying EVOO's anti-inflammatory and anti-carcinogenic roles warrant further investigation. Interventional studies in humans, well-designed to investigate EVOO consumption at various doses and durations concerning UC and CRC, should be conducted in the context of specific dietary patterns [14].

The rising incidence of cases of colon cancer across the world calls for an effective prevention strategy. According to the present review, dietary phenolic compounds, with major emphasis on olive oil phenolics, could play a role in the potential attenuation of cancer risk. HT is already identified as one of the major phenolic components of virgin olive oil and has been related to several health benefits, including antioxidant and anti-inflammatory properties [22]. The present study further supports these observations by demonstrating that HT and its microbial metabolites may modulate the behaviour of human colon cancer cells. Results of the MTT assay revealed the dose-dependent cytotoxic properties of HT and CAT, thus indicating their anticancer potential. Cytotoxicity, as seen with HT and CAT, is following literature where these have already been reported to cause cell death in cancer cells. The study also pointed out that other metabolites, such as PA and PP, exhibited very low cytotoxicity, which may mean the effects are not that prominent or higher concentrations need to be used for them to elicit meaningful impacts. The effects of HT and its metabolites on cell cycle progression and apoptosis are particularly notable. The observation that HT causes G1 phase cell cycle arrest in both Caco-2 and HT-29 cells indicates that it is an effective cell proliferation antagonist.

The finding is in line with reports from previous studies that indicated HT can interfere with cell cycle regulatory proteins and pathways involved in cancer progression [23]. The PA, HPP, and MIX metabolites showed a more differential action on the cell cycle phases, underscoring the complexity of their actions. The influence of PA on the G2/M phase in Caco-2 but not in HT-29 cells may indicate cell line-specific responses or other mechanisms of action. The same could be a reason for different reactions to HPP and diHPP, which may relate either to differences in bioactivity or to different metabolic rates in the cells. The Annexin V−APC assay confirms the compounds' apoptotic potential. HT, CAT, and their metabolites can induce apoptosis, hence their potential in cancer cell death pathways. These compounds may exert differential apoptotic effects because of their interaction with cellular machinery or cellular uptake and metabolism differences. To complicate matters, the present study focused on microbial metabolites of HT in an attempt to better understand their anticancer potential: PA, PP, HPP, and diHPP. These metabolites would, therefore, probably have different bioactivities from their parent compound. The review calls for further studies into the mechanisms of action

 

of these metabolites as single entities or mixtures, emphasizing synergistic effects.
Compared with other research works reviewed in association with dietary phenolic compounds, this study complicates understanding how certain metabolites impact colon cancer cells. Effects on cell viability, cell cycle progression, and apoptosis agree with the literature describing the contribution of dietary polyphenols to cancer prevention [24]. However, it also shows where further investigation is needed; for example, the differential effect of various metabolites in different cell lines may indicate that this impact could be context-dependent. Furthermore, their metabolism and in vivo bioavailability will be extremely important in determining practical effectiveness as dietary interventions [25].

Olive oil contains the highest percentage of long-chain mono and polyunsaturated fatty acids (86.934%) amongst edible lipids, which may help prevent cancer [26]. Modification in arachidonic acid metabolism [27], an important modulator fatty acid of inflammation and carcinogenesis, associated with decreased incidence and progression of colon tumours, may support a role for an anti-inflammatory mechanism of olive oil in its protective action. This would, therefore, indicate that dietary lipids may be involved in cancer modulation through effects on inflammatory function. Findings from the study conducted by Bartoli et al.have extremely important implications for dietary recommendations to be put in place concerning cancer prevention strategies, in that olive oil could add value to the diet; however, further studies are required to validate these findings by using adequate amounts and types of olive oil relevant to cancer prevention [15].

By analysing FASN and CEA levels, S. J. Mubarak et al. suggest a unique approach to improve the prediction of colorectal cancer. Their concept incorporates mathematical techniques for accurate staging and risk assessment while ranking important risk indicators to address the flaws of traditional diagnostics. Through enabling real-time diagnosis simpler, this approach aims to improve patient outcomes and early detection [28]

The limitations of this study include a need for more generalizability. Most studies reviewed were conducted on experimental rodents; therefore, the ability to generalize the findings from these studies could be higher. Rodent models may not replicate a human response appropriately. Secondly, heterogeneity in study designs. The studies differed much in their applied animal species, formulation of olive oil, dosage, and intervention duration. All of this heterogeneity has made the results very difficult to be directly compared, drawing general conclusive results. Thirdly, there needs to be more data on long-term intervention. Most of the studies assessed short-term outcomes. There is still a lack of research on the long-term impacts of olive oil consumption on the risk of CRC in both humans and animals. Finally, from this review, data from human clinical trials are not forthcoming and available. While animal studies give some insight into it, human trials have become necessary in establishing efficacy and safety in using olive oil for CRC prevention.

## 5. Conclusion

This systematic review assesses the efficacy of olive oil in reducing the risk of colorectal cancer, as evident from the findings of different interventional studies. The results concluded olive oil showed prominent anti-inflammatory and antioxidant properties contributing to CRC risk reduction. Olive oil has been shown in the reviewed studies to modulate gut microbiota, decrease tumour growth, and alter some of the relevant tumour-related biomarkers and genetics involved in this process. Although the evidence supports olive oil's role as a preventive dietary intervention against CRC, further research, including large-scale clinical trials, is needed to confirm these benefits and to establish comprehensive nutritional recommendations. Consumption of olive oil in diet might offer a cost-effective, easily accessible way to reduce CRC risk and improve general health.

**Data Availability**

Data that supported the findings of the study will be provided upon request.

**Conflict of Interest**

Authors declare that they do not have any conflict of interest.

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None

**Authors' Contributions**

Jenardhan: Literature search
Sindhu R: Methodology
Sujitha S: Data extraction
Prabu D: Conceptualization
Rajmohan M: Tabulation of data
Dinesh Dhamodhar: Manuscript writing and editing.
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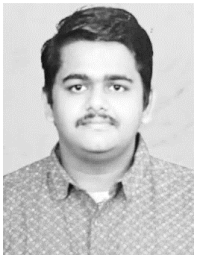
**AUTHORS PROFILE**



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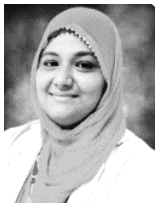

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