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Omega-3 Fatty Acids from Fish: A Novel Approach in Cancer Therapy

Kashif Abbas[1], Fatima Kamil[1], Yusra Tanveer[1], Mudassir Alam[2]*, Zerafshan Zehra[1], Mohd Mustafa[3], Nazura Usmani[1] and Safia Habib[3]

[1]Department of Zoology, Faculty of Life Sciences, Aligarh Muslim University, Aligarh, India.
[2]Indian Biological Sciences and Research Institute (IBRI), Noida, India.
[3]Department of Biochemistry, J.N. Medical College, Aligarh Muslim University, Aligarh, India.

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Omega-3 fatty acids (OFAs) are essential macromolecules which are frequently used to provide nutritional support in cancer patients. They have been recognised as immunonutrients, as they play important role in strengthening the immune responses against various disease including cancer. OFAs such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have shown great promise in cancer prevention and its management. Epidemiological studies have demonstrated a correlation between fish consumption and reduced cancer risk, evidence suggests that increased fish consumption is linked to a lower risk of cancer, potentially due to the high levels of bioactive fatty acids in fish. Experimental studies revealed that OFAs are capable of modulating cell signalling pathways, gene expression and influencing cell membrane composition, which can promote apoptosis and inhibition of cell proliferation. Moreover, antioxidant property of fatty acids has been reported in prevention of oxidative stress-induced DNA damage. Apart from anticancer properties OFAs have also shown good results in managing the cancer related complications such as inflammation, gastrointestinal reactions, and anorexia-cachexia syndrome. Several studies showed their efficacy in relieving cancer associated cachexia anorexia syndrome with significant improvements in weight loss. Moreover, OFA supplementation has shown antidepressant results and enhanced well-being in cancer individuals. Despite the promising effects of OFAs many challenges remain like optimal dose determination, variable impact across cancer types and the risks associated with high fatty acids intake. Further large scale randomized control trials (RCTs) are needed to strengthening the OFAs assisted cancer treatment.

Keywords: Cancer; DHA; EPA; Fish oil; inflammation; Omega-3 fatty acids.

In 2020, it was estimated that there were approximately 19.3 million new cancer diagnoses and 10 million fatalities reported worldwide, making it a major cause of death[1,2]. This strong evidence has led to in-depth studies on methods to prevent cancer with an emphasis on nutritional mediation. Omega-3 fatty acids (OFAs) have become a hopeful area of study for preventing cancer. Cold-water fish such as salmon, mackerel, tuna, and sardines are well known for being excellent reservoir of OFAs like eicosapentaenoic acid (EPA) and docosahexanoic acid (DHA)[3]. These vital polyunsaturated fatty acids (PUFA) are pivotal in multiple bodily functions. The nutritional gains of OFAs go beyond cancer prevention and also have an impact on cardiovascular health,

*Corresponding author E-mail: syedalamalig@gmail.com

brain function, and inflammatory responses [4]. Their anti-inflammatory properties are related to a diminished risk of chronic conditions, such as cancers. The possible anti-cancer properties of OFAs are due to several mechanisms such as the modulation of cellular cascades, alterations in genetic expression, and influence on the makeup and role of cell membranes[5]. It is reported that fish consumption can prevent cancer risk. For instance, a meta-analysis found that increased intake of fish was linked with a 4% decrease in the risk of colorectal cancer[6]. The antioxidant properties of OFAs are significant in decreasing oxidative stress, a critical element in the onset and advancement of cancer. Research has shown that EPA and DHA may reduce lipid peroxidation and DNA damage, which could potentially decrease cancer risk[7]. Additionally, OFAs have demonstrated the capacity to hinder the proliferation of cancer cells through different pathways. Several *in vitro* and *in vivo* researches have demonstrated that OFAs can trigger cell death in cancer cells, hinder cell growth, and regulate crucial signalling pathways for tumorogenesis[8,9]. For instance, a study focusing on breast cancer cells discovered that DHA triggered cell death by activating caspase-8 and caspase-3 [10]. In addition to their direct impact on cancer cells, OFAs also exhibit potential in addressing complications associated with cancer. Cancer-related anorexia cachexia syndrome which is a significant contributor to illness and death affects as many as 80% of advanced cancer patients [11]. EPA, a type of OFA, has displayed promise in preventing or easing this syndrome by preserving muscle mass and enhancing nutritional status [12]. A study revealed that EPA supplementation prevents weight loss and enhanced standard of living in cancer patients [13]. Receiving a cancer diagnosis and going through treatment frequently leads to considerable emotional turmoil. Approximately 60% of individuals diagnosed with cancer have shown to suffer from Major Depressive Disorder (MDD)[14,15]. The relationship between diet, mental health, and cancer outcomes is shown by the potential for treating depression in cancer patients with omega-3 fatty acids. The protective roles OFAs from fish have been observed in cancer progression. OFAs offer potential solution for preventing and targeting cancer due to their antioxidant, anti-inflammatory properties, while addressing cancer-related issues such as cachexia and nutritional deficiency.

Fishes as rich source of Omega-3 fatty acids

In recent decades, significant upsurge in community consciousness regarding nutritious diets is observed, resulting in a rise in the use of nutraceuticals. OFAs are one of the most sought-after nutraceuticals. Nowadays, marine OFAs from oily fish like anchovy, sardine, and mackerel are widely consumed[16]. The manufacturing of fish and fish products has risen to four times its previous level over the past fifty years. The increase in fish intake has led to a rise in fish waste. Concerns about the excess fishing of these varieties have grown in recent years, prompting the investigation of marine by-products as a substitute of OFAs source[17]. Over 70% of the fish collected globally undergo processing for processing, preparing, or cleaning resulting in by-products such as heads, skeletons, internal organs, and dermis, which make up exceeding 50% of the fish's body[18]. Consuming fish that contain OFAs like EPA and DHA can help prevent and control various forms of cancers such as colorectal, pancreatic, and breast cancer[19]. Certain fish including salmon, trout, and tuna possess significant quantities of EPA and DHA in their residuals. These by-products are ideal for making fish oil and OFA products [20]. Hence, there is substantial opportunity for reusing these leftovers as they have abundant biologically active substances which can be transformed into beneficial products for the food, livestock feed, and drug industries. Fish and fish oil are rich sources of OFAs and they have been thoroughly researched for their positive effects on health. Oil extracted from fish has been extensively utilized to enhance animal feeds and various food products which is a novel strategy that is popular among consumers[21]. Recent time has experienced increasing emphasis on acquiring OFAs from fish by-products due to their significant source of not just OFAs but also collagen and minerals[22]. Consequently, the increasing need for fish oil has prompted the industry to utilize fish processing residues for oil extraction. These leftovers possess diverse nutritive potential and could be repurposed also as flours or for oil extraction. Pressing is the conventional technique used on a global scale to obtain fish oil on an industrial level. But alternative methods such as ultrasonic-assisted, microwave-assisted, or

Soxhlet methods of extraction are also available[23]. Fish oil is mainly made up of triglycerides, free FA, phospholipids, sphingolipids, and oxidized lipids. It provides multiple health advantages because of its antiinflammatory, anticancer, anti-oxidant, and anti-microbial properties[24]. OFAs are easily oxidized, leading to decreased nutritional content and shorter lifespan of food items. In order to prevent oxidation of these oils, antioxidants are often used owing to their efficacy and cost efficiency [25]. Nevertheless, artificial anti-oxidants have proven to be very poisonous and cancer-causing. Consequently, there exists an increasing focus on investigating organic-based antioxidants for healthy-friendly alternatives, like antioxidants from plants and animal sources[26].

Omega-3 fatty acids and its implication in human health

OFAs are vital, elongated, PUFAs with important roles in preserving membrane flexibility, cell communication, controlling inflammation, and protecting against oxidative load[27]. They oppose the inflammation-promoting impacts of eicosanoids and supplementary constituents produced from omega-6 fatty acid and arachidonic acid (AA)[28]. The most bio-actively potent OFAs are EPA and DHA, which can integrate in plasma bilayer and are abundant in cold water fish[29]. EPA and DHA are further transformed into resolvins (RS) and protectins (PC), that help to control or diminish inflammation. EPA can also be converted into eicosanoids[30]. Apart from that, those derived from EPA typically have diminished inflammatory effects compared to those from omega-6 AA[31]. Alpha-linolenic acid (ALA) is not efficiently embedded into plasma bilayer, as only about 6% is transformed into EPA and DHA[32]. Because omega-3 and omega-6 FA share the same elongase, desaturase, and cyclooxygenase (COX) enzymes, along with numerous lipoxygenase enzymes, a diet high in one specific FA lowers the conversion to the final products of the other[33]. Increasing the consumption of EPA and DHA may lead to a decrease in the production of pro-inflammatory eicosanoids, leukotrienes (LK), and thromboxanes (TMX) due to lowering of the conversion of AA from omega-6 FA in the diet[34]. Research has looked into ingesting OFAs from fish or nutraceutical to reduce chances of cancer (specifically breast, colon, and prostate cancers), heart disorder, and dementia; enhanced insulin resistance and hepatic steatosis linked to obesity[35]. They have also shown to ease symptoms of rheumatoid arthritis and inflammatory bowel disease—both involving inflammation[36].

General overview of mechanism of action of Omega-3 fatty acid in cancer

The biological effects of OFAs involve the reduction in the synthesis of prostaglandin E2 (PGE2) metabolites, TMX A2 (which causes platelet accumulation), and LK B4 (which affects leukocyte chemotaxis and adherence)[37]. They also lead to reduced efflux of inflammatory cytokines such as IL-1â and platelet-derived growth factor[38]. EPA and DHA, by lowering prostaglandin synthesis, may decrease aromatase action, estrogen production, and estrogen related cascade[39]. EPA and DHA exhibit peroxisome proliferator-activated receptor gamma agonist action and encourage differentiation and cell death by enhancing lipid peroxidation, maintaining mitochondrial calcium balance, and increasing p53 expression[40]. They enhance adiponectin release and PTEN expression and decrease proliferation and signalling via ERK and PI3 kinase cascade[41]. In obese animal models, they decrease insulin resistance by reducing NFêâ signalling and increasing the expression of insulin sensitivity related genes GLUT 4 and IRS-1[42]. With wide range of biological cascade modifications detected mainly in preliminary experiments, it is reasonable to anticipate the prevention of tumors in cases where inflammation contributes to promotion or progression. Although EPA and DHA nutraceuticals are commonly utilized several persistent illnesses aforementioned, typically consumed with the aim of alleviating heart related disorders[43]. Elevated administration of EPA and DHA effectively lower triglyceride levels in patients of dyslipidemia, nonetheless their function in averting recurring conditions in patients with persistent cardiopathy who are commonly on several other medications for the disease alleviation remains indeterminate at current[44]. Figure 1 summarise the general metabolic pathway of omega 3 and omega 6 fatty acids and their role in inflammation and cancer.

Omega-3 fatty acid in cancer

Omega-3 PUFAs are essential FA with a carbon chain of 18 to 22 and the first bivalent bond located at the third carbon from the omega terminus. They are composed of three active

substances namely ALA, EPA, and DHA. ALA is produced in plants and are found in seeds, kernels, and plant oils[45]. The body does not produce EPA and DHA, which are mainly found in the flesh of cold water fish[46]. It is important to note that ALA can be transformed into EPA and DHA through a series of extension and desaturation reactions, nonetheless these transformations yield limited quantities of EPA and DHA in body[47]. Both AA and linoleic acid (LA) share metabolic pathways and compete with each other as they are transformed to EPA and DHA by the same enzymes that metabolize ALA[48]. In inflammatory processes, phospholipase A2 (PLA2) cleaves membrane phospholipids to release AA which leads to the synthesis of extremely inflammatory eicosanoids like PGE2 and LK B4 via COX and lipoxygenases activity[49]. Modifying the plasma bilayer lipid configuration from an omega-6 PUFA to an omega-3 PUFA profile is crucial as it enhances the formation of omega-3-derived substances, like TMX A3 and prostacyclin I3, which are weak inflammatory triggers[50]. Studies have shown that omega-3 PUFAs can decrease TMX B2 serum concentration in vulnerable cardiac disease subjects and decrease LK B4 levels in unhealthy patients' neutrophils[51-53]. Another study investigated the FA configuration of CD4+T plasma bilayer after EPA and DHA nutraceutical intake[54]. Furthermore, a study revealed that EPA or DHA gestation augmented the plasma bilayer composition of omega-3 PUFAs[55]. Similarly, another study observed identical omega-3 PUFA rich bilayer composition in elderly persons' lymphocytes when they administered with omega-3 PUFA fortification for six weeks[56]. Additionally, EPA and DHA nutraceuticals are frequently used in the nutri-therapeutic intervention of carcinoma patients and have been shown to have valuable impact on carcinoma prognosis as they modulate plasma bilayer composition[57].

The identification of pro-resolution mediators of inflammation obtained from omega-3 PUFAs has provided support for the idea that a membrane enriched with omega-3 PUFAs could be beneficial for managing diseases. Identifying RS, PC, and maresins (MR) over the last ten years has been a significant development[58]. It is now widely acknowledged that addressing inflammation rather than simply inhibiting it presents an intriguing approach for treating various chronic conditions like cancer. In acute inflammation, the essential regulation of blood flow and increase of endothelial permeability rely on the generation of prostaglandins through the function of COX-1 and -2[59]. Furthermore, LK is necessary for leukocyte trafficking. It was earlier assumed that every inflammatory process factors, including eicosanoids, prostanoids, cytokines, and chemokines, become reduced progressively, leading to inflammatory resolution[60]. Nonetheless, research has shown that lipoxins which is a subset of lipid pro-resolving agent originating from AA play key role in halting pro-inflammatory signals, suggesting that resolution of inflammation is a dynamic mechanism[61]. Lipoxins prevent new neutrophils from entering and activate macrophages to remove dying neutrophils[62]. Omega-3 PUFAs are important in creating strong pro-resolution mediators that are similar in effects to lipoxins, like RS, PC, and MR. RS are categorized as series E (RvE) and series D (RvD), which come from EPA and DHA, respectively[63]. DHA gives rise to PC, and MR, with MR specifically produced by macrophages. These resolution agents are able to reduce the entrance of white blood cells and particles of cells, eventually resulting in the stop of the inflammatory process[64]. RvD1, RvD2, and RvE1 were found to impede the advancement of cancer resulting from debris by boosting macrophage phagocytosis and reducing inflammation promoting cytokines in cancer[65-67]. Moreover, neuroprotectin D1, MR 1, RvD1, and RvD5, all derived from DHA and known as pro-resolution mediators, exhibited significant pain-relieving properties in a murine model of postoperative pain after osteo-surgery[68]. In context of how resolution agents impact depression, injecting RvE1 and RvE2 directly into the brain significantly decreased depressive behavior associated with lipopolysaccharide (LPS) by activating the ChemR23 receptor, as seen in murine model of LPS-induced depression[69,70].

Omega-3 PUFAs have the ability to activate GPCR which leads to internal effects. Initially, free fatty acid receptor 1 (FFA1) which was previously known as GPR40, was identified as a receptor for free fatty acids. They observed that human embryonic kidney cells that express FFA1 exhibited a concentration dependent rise in calcium level within the cell when exposed to long-chain FA[71]. The existence of the FFA1 receptor

indicates its importance in regulating metabolism, especially in the gut, pancreatic â-cells, and brain[72]. The metabolic effect of FFA1 receptor activation is associated with the release of glucagon-like peptide-1 (GLP-1) and cholecystokinin[73]. Recent studies reveal that the FFA1 receptor is present in the melanocortin system, especially within the neuropeptide Y/Agouti-related peptide (NPY/AgRP) and proopiomelanocortin/cocaine- and amphetamine-regulated transcript (POMC/CART) neurons[74,75]. It is important to note that the levels of FFA1 expression are elevated in various tissues during pathological circumstances, like periodontitis, that is linked to metabolic disorder[76]. FFA1 has been thoroughly researched for its potential in treating diabetes because of its involvement in glucose-triggered insulin secretion through PKC/IP3 activation, resulting in higher levels of intracellular calcium and subsequent insulin secretion[77]. Considering this effect, a synthetic selective FFA1 activator, known as TAK-875, underwent testing up to phase II of clinical trials for treatment of diabetic patients. Regrettably, the clinical study was halted due to patients experiencing liver toxicity and hepatic malfunction[78,79]. The function of the FFA1 receptor in the central nervous system has attracted attention. Stimulation of this receptor by DHA has shown pain-relieving impacts in various models for pain related study[80]. When it comes to FFA1 ligands, long-chain FA, specifically DHA, are seen as natural activators, however, research has indicated that oleic acid is also a strong FFA1 activator[81]. Following the discovery of FFA1 as a receptor for free FA, FFA4, previously recognized as GPCR 120, was also documented as part of this new group of this protein family[82]. EPA, ALA, and DHA are regarded as endogenous ligands for FFA4, with DHA exhibiting lower potency[83]. Similar to FFA1, FFA4 is activated by long-chain FA and has metabolic activities[84]. The manifestation of the receptor can be triggered by a diet rich in fish oil. Osteoclasts and osteoblasts express FFA4, and in the presence of elevated concentrations of OFAs, it can enhance bone formation and suppress bone resorption[85]. FFA4 receptors are present in liver, adipose tissue, intestines, macrophages, and pancreas[86,87]. Strikingly, the human FFA4 receptor has two isoforms namely long and short. The long isoform has a sixteen-residue segment in the third intracellular loop that decouples the receptor from the G protein[88]. However, both isoforms can activate â-arrestin-2, recruiting the TGF-â activated kinase 1(TAK1)-binding protein 2 (TAB2), which suppresses TAK1 and thus leading to anti-inflammatory effects[89]. Activation of FFA4 triggers Gq/11 protein activation, promoting IP3 production and elevating intracellular calcium levels, leading to hormone secretion[90]. FFA4 initiation by omega-3 PUFAs decreases appetite, food reward, and anxiety-like behavior in NPY-positive neurons, suggesting an effect on obesity[91,92]. FFA4 activation stimulates adipose tissue browning which indicates another mechanism against obesity development[93]. It has been demonstrated that FFA4 stimulation by omega-3 PUFAs might protect tumour bone metastasis and cachexia[94].

Antioxidant Effects of Omega-3 Fatty Acids in Cancer

Reactive oxygen species (ROS) are continually produced in human cells as a result of metabolism and other biochemical reactions (Figure 2). ROS are normally generated through regular cellular metabolism, revelation to specific external factors like ionizing radiation, nitrogen oxide pollutants, and specific biochemical cancer-causing agents can increase ROS production[95]. Antioxidants protect the defense system of the body against ROS. However, if ROS levels exceed antioxidant levels, oxidative stress will happen[96]. ROS activity may result in cellular oxidative damage, changing metabolic pathways and causing DNA mutations, ultimately heightening the likelihood of cancer[97]. Research conducted on both in vitro and animal subjects has indicated that dietary antioxidants have the ability to prevent the growth of cancerous cells[98]. Several literatures reported regarding fish oil containing OFAs like EPA and DHA, has antioxidant and anti-cancerous feature[99-101]. Another study reported that omega-3 treatment may control the function of superoxide dismutase (SOD) and glutathione peroxidase (Gpx) in the bloodstream which improves the production of antioxidant enzymes such as SOD 1 and catalase (CAT)[102]. These antioxidant enzymes help eliminate harmful ROS from the cell. A study proposed that fish oil rich in OFAs can enhance antioxidant levels in red blood cells and plasma[103].

An elevated intake of EPA and DHA supplements has been associated with a lower chance of cancer-related deaths[104].

Protective Effects of Omega-3 Fatty Acids on Tumor Cell Suppression

Several studies have shown that DHA has functional properties that can inhibit the invasion of tumor cells[105-107]. A study showed how LA, EPA, and DHA affect the invasion capability of the MDA-MB-435 human breast cancer cell line. The study revealed that not every FA promote tumour cell metastasis, with DHA and EPA suppressing tumorigenesis while LA has no effect on tumour cells[108]. Another investigation suggested that combining DHA with nutrient genistein enhances the invasion-suppressing effect on tumour cells[109]. Genistein which is an anticancerous agent derived from soybeans, obstructs PGE2 production and COX-2 expression, thus reducing cell invasion[110] (Figure 2). Investigators have observed that the amalgamation therapy of DHA and genistein can enhance the suppression of PGE 2 and COX 2[111]. A study suggested that DHA prevents migration and invasion of human hepatocyte carcinoma cell lines[112]. Increased consumption of nutritional OFAs, particularly DHA, inhibits the onset and genesis of tumour cells[113].

The Protective Role of Omega-3 Fatty Acids in Anorexia Cachexia Syndrome

Cancer anorexia cachexia syndrome (CACS) is a debilitating facet present every phase of cancer, characterized by loss of appetite, weight, and muscle, and secondarily by metabolic alteration in individuals suffering with cancer[114]. Clinical data suggests that fish oil which are primary origin of OFAs, has a positive and potential impact on cancer cachexia[115]. OFAs supplementation is crucial for postoperative rehabilitation and reducing problems like infections and wounds in carcinoma patients[116]. These nutraceuticals help alleviate the body weight

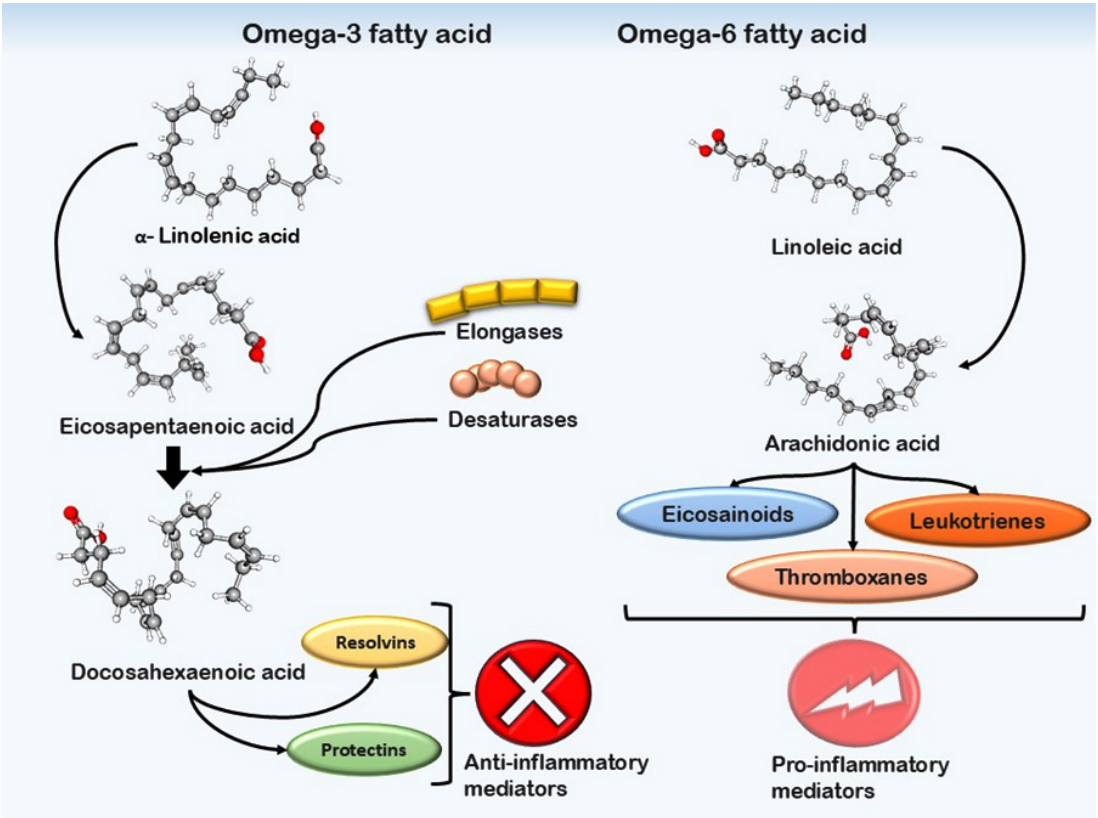

Fig. 1. General metabolic pathways involved in production of various subtypes of omega-3 and -6 fatty acids. The omega-3 fatty acids are anti-inflammatory mediators while omega-6 fatty acids belong to pro-inflammatory mediators

of gastrointestinal (GI) cancer patients. A study reported that 2g of EPA supplementation helps maintain weight and lean body mass in patients with head and neck squamous cell carcinoma and CACS[117]. A study indicates that supplementation with 53.4% EPA and DHA or 54.8% ALA recovers weight increase in rats with breast cancer[118].

Omega-3 Fatty Acids as a Key Element in Managing Major Depressive Disorder (MDD) in Cancer Patients

Approximately 6% to 62% of cancer affected individual usually experience major depressive disorder (MDD)[119]. Inflammatory cytokines like tumor necrosis factor (TNF), interleukin 1 beta (IL-1â), and interferon lambda (IFN-ã) are produced through tumor-host interaction and can access hypothalamus, triggering depressive behavior[120] (Figure 2). Cytokines also trigger the expression of serotonin and norepinephrine uptake transporters, reducing the levels of neurotransmitters in the central nervous system (CNS)[121]. Leptin hormone which is found in gastric tissue could be linked to depression in GI carcinoma[122]. A study proposed that OFAs nutraceuticals are highly essential for individuals ailing with MDD. A deficiency of OFAs in CNS can elevate the risk of MDD and mental disorders[123]. OFAs exhibit nootropic effects thus reducing the incidence of brain disorders. Studies indicated that supplementation with 1.50 gram per kg of omega-3 PUFAs (35% EPA + 25% DHA) reduces depressing behaviour in rats induced by LPS[124-126].

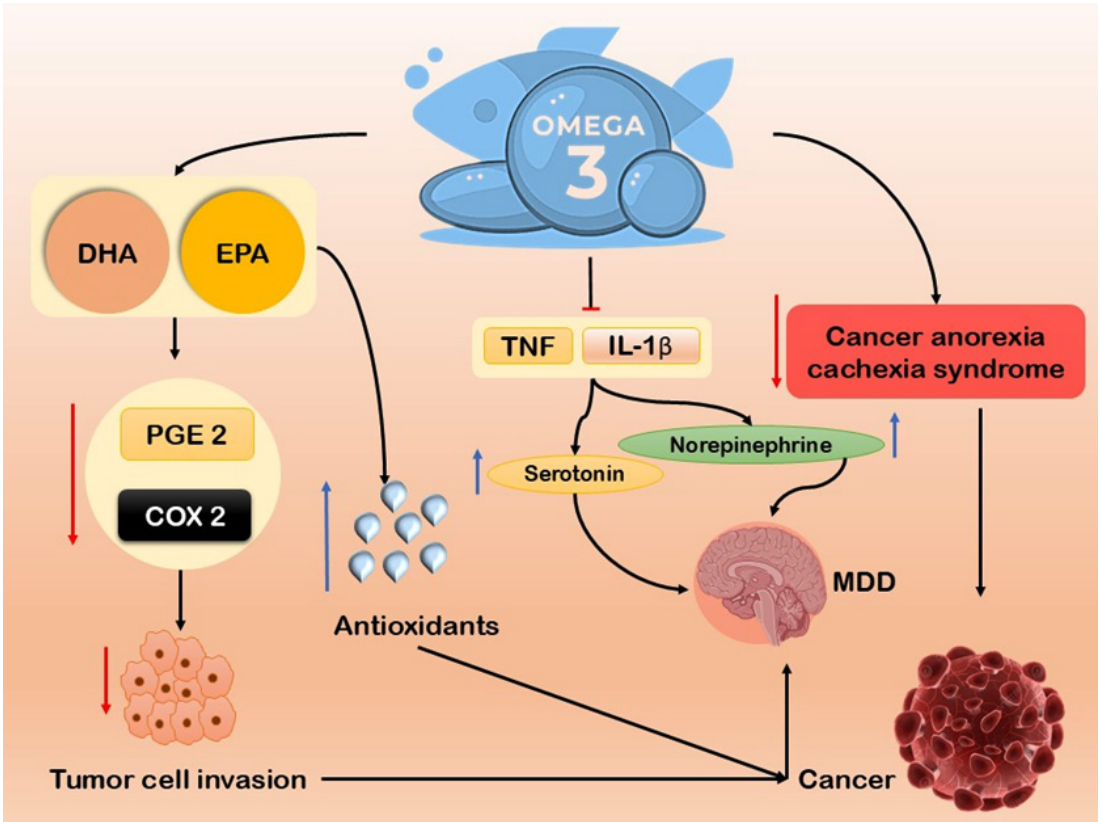

Fig. 2. Omega-3 fatty acids mainly docosahexaenoic acid (DHA), and eicosapentanoic acid (EPA) reduces the generation of prostaglandin E2 (PGE2) and cyclooxygenase 2 (COX-2) which leads to suppression of tumor cell invasion. Furthermore, EPA and DHA are natural antioxidants which control cancer formation. Omega-3 fatty acids have shown efficacy in alleviating cancer anorexia cachexia syndrome (CACS). It is also observed that omega-3 fatty acids help in managing the cancer induced Major Depressive Disorder (MDD) as it inhibits the production of tumour necrosis factor (TNF) and interleukin 1 beta (IL-1â)

DISCUSSION

The thorough investigation into how fish-derived OFAs affect cancer prevention reveals a complex and promising research area with significant implications for clinical treatment. The varied effects of OFAs, specifically EPA and DHA, on several aspects of cancer biology and patient well-being underscore their potential as a dietary approach to prevent and manage cancer. In studies on epidemiology, a constant link between reduced cancer risk and increased fish consumption has been identified. The meta-analysis showed that consuming high amounts of fish reduced the vulnerability towards colorectal cancer by 4%, indicating the protective benefits of OFAs. Studies into how OFAs fight cancer provides valuable information about how they may work. EPA and DHA can change cell signaling pathways, modify gene expression, and impact cell membrane composition, which could explain their anti-cancer properties. A study demonstrated that OFAs can trigger cell death in cancer cells by triggering caspase-8 and caspase-3 in breast cancer cells. The findings suggest that OFAs can prevent the initiation of cancer and impede the growth of existing tumor cells. OFAs also contain antioxidants that might reduce the onset and development of cancer by decreasing lipid peroxidation and DNA anomalies resulting from oxidative stress. Nevertheless, it is crucial to recognize that the connection between antioxidants and cancer is complex and requires additional studies to fully comprehend the best levels and circumstances for utilizing antioxidants in the prevention of cancer. Moreover, the study on cancer-related anorexia cachexia syndrome has shown promising results that support the significant potential of OFAs in helping with cancer related issues, highlighting their broader benefits in cancer treatment. In spite of these encouraging results, various constraints and obstacles in the area need to be tackled. The most effective dose and duration for taking OFAs to prevent cancer are still not fully understood. Further research is required to explore the absorption rate of OFAs from various sources like fish or supplements and how they may interact with other dietary elements. Moreover, the effect of OFAs could differ based on the type of cancer, its stage, and the specific characteristics of the patient, highlighting the need for more focused studies. The possible dangers of consuming excessive omega-3 fatty acids, including higher risk of bleeding from their blood-thinning properties, should be taken into account as well. Additionally, it is significant to weigh the advantages of consuming OFAs against worries about environmental pollutants like mercury and polychlorinated biphenyls (PCBs) in fish. Future research should emphasize undertaking large, long-term randomized controlled studies to assess the effectiveness of OFAs in cancer prevention. For stronger evidences, these studies should investigate other sources and amounts of omega-3 fatty acids, as well as a diverse variety of demographics. Moreover, examining how OFAs interact with other dietary components or cancer therapies may offer important information for holistic approaches to preventing and treating cancer. Conducting molecular studies is essential to comprehend how OFAs affect cancer-related pathways. By employing advanced methods such as metabolomics and proteomics, researchers may gain a deeper insight into the effect of OFAs on cellular processes in normal and cancerous cells. The evidence gathered strongly indicates that fish-derived OFAs have a substantial effect on preventing and controlling cancer. Their diverse effects, including direct anti-cancer properties, antioxidant characteristics, and positive effects on overall patient health, make them a potentially valuable dietary intervention. Nevertheless, additional research is necessary to overcome current limitations and knowledge gaps in order to translate these findings into effective public health strategies and clinical recommendations.

CONCLUSION

The OFAs which are mostly obtained from fish have received utmost attention for their wide range health benefits and therapeutic potential. This review highlights the multidimensional roles of OFAs in treatment of various ailments. We have incorporated latest studies, which emphasised on their anti-inflammatory, antioxidant, and tumor-suppressive properties. The acknowledged capacity of these FA to module key molecular cascades linked to cancer progression makes them potent additions to cancer therapy. Moreover, the benefits of integrating OFAs into the treatment regimen are underscored by their role in protecting against

CACS and reducing the symptoms of MDD in cancer patients. On-going research indicates that OFAs are important for promoting human health and providing protection against conditions such as cancer and MDD, suggesting the need for further extensive investigations in clinical settings.

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Ethics Statement

This research did not involve human participants, animal subjects, or any material that requires ethical approval.

Informed Consent Statement

This study did not involve human participants, and therefore, informed consent was not required.

Clinical Trial Registration

This research does not involve any clinical trials.

Author contributions

Kashif Abbas : Methodology, writing original draft; Mudassir Alam: Conceptualization, writing original draft and Review. Fatima Kamil : Data collection, writing, Image creation. Yusra Tanveer: Data collection, literature search and writing. Zerafshan Zehra: Writing, Data collection. Mohd. Mustafa: Visualization, Review and Editing. Nazura Usmani: Supervision, Review and Editing. Safia Habib: Review, Editing and Project administration.

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