Haruan Fish Extract as Potential Agent for Cancer Therapy

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Abstract

Cancer occurs as a result of contributions from environmental and genetic factors. These factors lead to disturbance in genomic composition of a cell [1]. The disturbance may be triggered by organic, environmental and or genetic factors. These factors hijack the normal physiologic conditions of the cells like, cell division, cell differentiation, angiogenesis and cell migration to cause cancer [1]. Cancers are named base on their location in the body, for example breast cancer, colon cancer, pancreatic cancer and prostate cancer all originated from breast, colon, pancreas and prostate gland respectively.

Current anti-cancer drugs cause side effects to patients. Numerous known anti-cancer drugs result in the death of normal body cells in addition to cancer cells. This manifests as adverse side effects to the patients [2]. These effects could be in form of nausea, fatigue, hair loss and anaemia [2]. Therefore, the need for anti-cancer agents with specific cytotoxic effects on cancerous cells came in. Those anti-cancer agents aim at stimulating cancer cells apoptosis, suppressing angiogenesis and arresting signal transduction [3,4].

Natural products have been identified as a source of drugs for treatment of different diseases including cancer. It was reported that 74.8% of currently used anti-cancer drugs such taxanes, vinca alkaloids, and camptothecin class of compounds are sourced from natural products [5]. These agents are given due consideration owing to their availability at low cost with reduced level of toxicity [6].

Natural products from animals, plants and microorganism. It was said that many agents implored for therapeutic applications are natural products or natural product derivatives [20]. A number of these agents or their derivatives have potent anti-cancer effects [6,20-22].

Marine natural products

Marine animals have been identified as the source of compounds with anti-cancer effects. For instance, algae, sponges and fishes were reported to contain bioactive compounds with anti-cancer effects [23-25]. In fact, agents with anti-proliferative, anti-oxidant and anti-microtubule were isolated from these animals [24]. Fish offers important source of protein universally, hydrolysis of these proteins produce important peptides with anti-cancer effects by acting via anti-proliferative [26] as well as anti-oxidant systems [27,28]. For example, peptide isolated from Sardinelle offers promising anti-oxidant effects reported was Sardinelle [29]. Haruan fish extract also contained a

Keywords: Haruan fish extract; Anti-cancer; Omega-3 fatty acids; Cancer; Cancer treatment; Cancer therapy

Introduction

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number of amino acids, peptides and proteins that may have anti-oxidant as well as anti-proliferative effects.

Haruan fish extract

Haruan fish, found in many tropical countries like Malaysia, Indonesia, and Thailand is widely known as a source of food and traditional medicinal product since pre-historic time [28]. Details of its biochemical component have been explored [15]. The components include proteins, peptides, glycoproteins, fat, and minerals [28]. Several amino acids and fatty acids were reported to be contained in Haruan fish extract (Table 1). Minerals deposit found in Haruan fish extract include magnesium, copper, calcium, manganese, iron, and zinc [29]. Nickel and lead were also reported to be found in the fish extract, but are much lower than the toxic threshold [29]. The peptides as well as the fatty acids, especially the unsaturated fatty acids, DHA and EPA content of this fish could give an effect on cytotoxicity and anti-oxidant activity. Therefore, the need to investigate the potential of this novel fish for anti-cancer activity would be attractive.

Anti-cancer activity of Haruan fish extract

Peptides and fatty acids derived from marine animals such as fish shows antioxidant activity [30], anti-proliferative activity [24] and anti-angiogenesis [30]. Furthermore, several studies show that omega-3 fatty acids have significant effects on prevention, and suppression of different types of cancers incuding, colon, breast and prostate [31]. The important polyunsaturated fatty (PUFA) acids content of Haruan fish that are beneficial to anti-cancer studies include; EPA and DHA. Several experimental models and tissue culture studies reported the protective effects of theses omega-3 fatty acids on colon [21,24], breast [23-26] and prostate cancers [27-29,32].

Anti-oxidant potential

Cancer cells produce reactive oxygen species in abundant compare to normal cells [33]. These molecules attack lipids, proteins and DNAs there by causing serious diseases like cancer [22]. Peptides derived from marine fish proteins showed higher anti-oxidant activity than α-tocopherol studied using variety of oxidative systems [34]. Haruan fish extract also possess anti-oxidant effects due to its omega-3 fatty acids content, especially EPA and DHA [35]. However, more research needs to be done to prove the mechanism of such effects.

| Amino acids | References | Fatty acids | References |
|-------------|------------|-------------|------------|
| Aspartic Acid | 14-16 | Myristic acid (C14 : 0) | 14,15 |
| Glutamic Acid | 14-16 | Palmitic acid (C16 : 0) | 14-16 |
| Serine | 14-16 | Heptadecanoic acid (C17 : 0) | 14-16 |
| Glycine | 14-16 | Stearic acid (C18 : 0) | 14-16 |
| Histidine | 14-16 | Palmitoleic acid (C16 : 1) | 14-16 |
| Arginine | 14-16 | Oleic acid (C18 : 1) | 14-16 |
| Theorone | 14-16 | Linoleic acid (C18 : 2) | 14-16 |
| Alanine | 14-16 | Linolenic acid (C18 : 3) | 15 |
| Proline | 14-16 | Arachidonic acid (C20 : 4) | 14-16 |
| Thersidine | 14-16 | Eicosapentanoic acid (C20 : 5) | 15 |
| Valine | 14-16 | Docosahexanoic acid (C22 : 6) | 14,16 |
| Methionone | 14-16 |
| Cysteine | 15,17 |
| Isoleucine | 14-16 |
| Leucine | 14-16 |
| Phenylalanine | 14-16 |
| Lysine | 14-16 |

Table 1: The amino acids and fatty acids content of Haruan fish extract.

Anti-angiogenic potential

Act of new blood vessel formation is termed angiogenesis. Cancer tumour growth relies on new blood vessel formation. In fact, it was elaborated that, for tumour to increase in size beyond 1-2 mm³ there must be an equivalent formation of new blood vessel to cater for its nutritional needs.

EPA and DHA potentiate anti-angiogenic effects by limiting the secretion of necessary mediators of angiogenesis. Theses mediators includes, platelet-derived growth factor, endothelial cell growth factor, cyclo-oxygenase 2, prostaglandin-E2, and vascular endothelial growth factor [36].

Anti-cancer activities of omega-3 fatty acids in some selected cancer types

Breast cancer: Another important findings revealed that fish oil containing EPA and DHA successfully prevented breast cancer metastasis into the bone [4]. This support the claim that decrease in consumption of food rich in PUFA correlates with high risk of breast cancer in Japan [37]. Also, these polyunsaturated fatty acids have been reported to suppress breast cancer [38]. Furthermore, fish oil used to feed mice showed significant reduction in breast cancer tumour and in its spread to the lung [39]. All these evidences suggest that Haruan fish extract could have significant effects on prevention of breast cancer, as it contains the above named acids which play the key role on the prevention.

Prostate cancer: Omega-3 fatty acids were reported to prevent the development and progression of prostate cancer [40]. In fact, immunodeficiency mice fed with omega-3 dietary supplement show reduced level of tumour growth, final tumour volume and serum prostate-specific antigen level [41]. Berquene et al. reported the reduction in tumour growth, longer lifespan and slow histopathological progression of prostate cancer in Pten-knockout mice fed with omega-3 dietary supplement [42]. Another study shows that EPA and DHA specifically acts via 15-lipoxygenase-1 (15-LO-1) and cyclooxygenase-2 (COX-2) pathways to suppress prostate cancer progression [43].

As we mentioned earlier, both EPA and DHA are important components of Haruan fish extract. Since these fatty acids show therapeutic effects on prostate cancer, the extract can prevent prostate cancer if tested using the models highlighted in the text.

Colon cancer: Haruan fish extract can also be explored for treatment and prevention of colon cancer. The reason being that, plenty of animal research models reported the involvement of omega-3 in suppression of colon cancer [19]. For instance, DHAsaw was shown to reduce primary tumour growth in human colon carcinoma xenograft nude mice [44]. Data from histological studies conducted further prove the reduction effect of the said fatty acid [44]. Furthermore, successful inhibition of metastasis was also reported in mice fed with omega-3 fatty acids [45].

Pancreatic cancer: The therapeutic effects of omega-3 polyunsaturated fatty acids extend to pancreatic cancers. Again, (EPA) halts the development of human pancreatic cancer cell by inducing apoptosis [46]. Interestingly, the molecular mechanism of this apoptosis occurred through activation of caspase-3 and prevention of cyclo-oxygenase-2 expression [47]. Murine mice fed with dietary supplement containing omega-3 fatty acids successfully lessen the pancreatic pre-cancer by arresting the cell cycle in elastase (EL)-Kras transgenic mice [47].
Conclusions

The omega-3 fatty acid content of the Haruan fish extract, if found to be in an adequate quantity, has the potential to contribute to the treatment of various types of cancers including, breast, colon, prostate, and pancreatic cancers. This can be demonstrated using cell culture, animal models and human epidemiological studies as we exemplified in the text.

Moreover, the extract can achieve its anti-cancer activities by neutralizing the free radicals, inducing apoptosis and inhibiting angiogenesis. Considering the vast side effects caused by anti-cancer drugs as well as the drug resistance nature of cancer cells, it is necessary to search for safer and more specific drugs from natural products.

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