

Haruan Fish Extract as Potential Agent for Cancer Therapy

I Buhari^{1,2*}, AH Roslida², M T³ and AM Mat Jais^{2*}

¹Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, University Putra Malaysia (UPM), 43400 Serdang, Selangor Darul Ehsan, Malaysia

²Department of Human Physiology, Faculty of Medical Sciences, Bauchi State University, PMB 065 Gadau, Nigeria

³Department of Human Anatomy Faculty of Medicine and Health Sciences, University Putra Malaysia (UPM), 43400 Serdang, Selangor Darul Ehsan, Malaysia

Abstract

Cancer occurs as a result of contributions from environmental and genetic factors. These factors lead to disturbance in genomic composition of a cell. The change in the cellular genome distorts the normal physiological activities of the cells like, cell division, cell differentiation, angiogenesis and cell migration to cause cancer. Current anti-cancer drugs cause side effects to patients. Natural products from animals, plants and microorganism offer a lot of anticancer drugs due to the effectiveness of their bioactive compounds. Haruan fish extract contains eicosapentaenoic acid (EPA) and decosahexaenoic acid (DHA) collectively called omega-3 polyunsaturated fatty acids. Several researchers reported that the fatty acids prevent the development of breast, colon, pancreatic and prostate cancers. However, the anti-cancer effects of Haruan fish extract has not been established. Considering the side effects cause by anti-cancer drugs as well as the drug resistance nature of cancer cells, it is necessary to search for effective drugs from natural products that can cure cancer alone or in combination with other chemotherapeutic agents. Therefore, in this review, we analysed and suggest how anti-cancer effects of the Haruan fish extract could be explored using cell culture, animal models and human epidemiological studies.

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

Introduction

Cancer occurs as a result of interconnected factors leading to disturbance in genomic composition of a cell [1]. The disturbance may be triggered by organismic, 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 examples 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 inform 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 derived from marine animals such coral, sponges, microorganisms and fishes was shown to possess anti-inflammatory, anti-viral and anti-cancer activities [7].

Haruan fish is a carnivorous air breathing fish species widely known for its wound healing [8-10] and anti-inflammatory effects [11,12]. The fish is rich in omega-3 fatty acids [13-17], namely, eicosapentaenoic acid (EPA) and decosahexaenoic acid (DHA) . These fatty acids were reported to have anti-oxidant [18] as well as anti-cancer effects [19]. However, the anti-cancer effects of Haruan extract have not been

established. Therefore, in this review, we suggest the use of Haruan fish extract as an anti-cancer agent.

Natural products as an alternative in cancer treatment

Natural products used for medicinal purposes refer to the compounds with biological activities derived from plants, animals or 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

***Corresponding author:** Buhari Ibrahim, Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, University Putra Malaysia (UPM), 43400 Serdang, Selangor Darul Ehsan, Malaysia, Tel: +60162662704; E-mail: doctbuhari54@yahoo.com

AM Mat Jais, Department of Human Physiology, Faculty of Medical Sciences, Bauchi State University, PMB 065 Gadau, Nigeria, Tel: +60389472334; E-mail: abmanan@upm.edu.my

Received March 01, 2015; Accepted June 16, 2015; Published June 22, 2015

Citation: Buhari I, Roslida AH, Hidayat MT, Mat Jais AM (2015) Haruan Fish Extract as Potential Agent for Cancer Therapy. J Cancer Sci Ther 7: 186-189. doi:10.4172/1948-5956.1000347

Copyright: © 2015 Buhari I, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

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 bioactive 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 including, 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 these 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]
Theorine	[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]
Thyrosine	[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. These 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]. Berquine 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, DHA 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.

References

- Hanahan D, Weinberg RA, Francisco S (2000) The Hallmarks of Cancer Review University of California at San Francisco. *Cell* 100: 57–70.
- Kawabe T (2004) G checkpoint abrogators as anticancer drugs. *Mol Cancer Ther* 3: 513-519.
- Maione P, Rossi A, Airoma G, Ferrara C, Castaldo V, et al. (2004) The role of targeted therapy in non-small cell lung cancer. *Crit Rev OncolHematol* 51: 29-44.
- Mandal CC, Ghosh-Choudhury T, Yoneda T, Choudhury GG, Ghosh-Choudhury N (2010) Fish oil prevents breast cancer cell metastasis to bone. *BiochemBiophys Res Commun* 402: 602-607.
- Newman DJ, Cragg GM (2012) Natural products as sources of new drugs over the 30 years from 1981 to 2010. *J Nat Prod* 75: 311-335.
- Gupta P, Wright SE, Kim SH, Srivastava SK (2014) Phenethylisothiocyanate: a comprehensive review of anti-cancer mechanisms. *Biochim Biophys Acta* 1846: 405-424.
- Newman DJ, Cragg GM (2007) Natural products as sources of new drugs over the last 25 years. *J Nat Prod* 70: 461-477.
- Baie SH, Sheikh KA (2000) The wound healing properties of Channa striatus-cetrimide cream-- tensile strength measurement. *J Ethnopharmacol* 71: 93-100.
- Febriyenti, AzminMohd N, Baie SB (2011) Physical evaluations of Haruan spray for wound dressing and wound healing. *Int J Drug Deliv* 3: 115-124.
- Febriyenti, AzminMohd N, Baie SB (2008) Formulation of aerosol concentrates containing Haruan (channa striatus) for wound dressing. *Malaysian Journal of Pharmaceutical Sciences* 6: 43–58.
- Manan A and Jais M (2007) Pharmacognosy and pharmacology of Haruan (Channa striatus), a medicinal fish with wound healing properties 6: 52-60.
- Sadegh A, Fatemeh EF, Mohd. Khairi H, Zuraini A, Abdul MM J (2012) Effects of Haruan (Channa striatus) Based Cream on Acute Inflammation in Croton Oil Induced Mice Ear Edema Model. *Research Journal of Biological Sciences* 7: 181-187.
- Jais AM, Matori MF, Kittakoop P, Sowanborirux K (1998) Fatty acid compositions in mucus and roe of Haruan, Channa striatus, for wound healing. *Gen Pharmacol* 30: 561-563.
- Zuraini A, Somchit MN, Solihah MH, Goh YM, Arifah AK, et al. (2006) Fatty acid and amino acid composition of three local Malaysian Channa spp. *Fish Food Chem* 97: 674-678.
- Zakaria ZA, Mat Jais AM, Goh YM, Sulaiman MR, Somchit MN (2007) Amino acid and fatty acid composition of an aqueous extract of Channa striatus (Haruan) that exhibits antinociceptive activity. *Clin. Exp. Pharmacol. Physiol* vol 34: 198-204.
- Manan A, Jais MAT, McCulloch R, Croft K (1994) Pergamon Fatty Acid and Amino Acid Composition in Haruan as a Potential Role in Wound Healing 25: 1980-1983.
- NAM, Mohamad JM (2012) Fatty Acids Composition of Selected Malaysian Fishes. *Sains Malaysiana* 41: 81-94.
- Siddiqui RA, Zerouga M, Wu M, Castillo A, Harvey K, et al. (2005) Anticancer properties of propofol-docosahexaenoate and propofol-eicosapentaenoate on breast cancer cells. *Breast Cancer Res* 7: 645–654.
- Berquin IM, Edwards IJ, Chen YQ (2008) Multi-targeted therapy of cancer by omega-3 fatty acids. *Cancer Lett* 269: 363-377.
- Saha SK, Khuda-Bukhsh AR (2013) Molecular approaches towards development of purified natural products and their structurally known derivatives as efficient anti-cancer drugs: current trends. *Eur J Pharmacol* 714: 239-248.
- França HS, Rocha L, Fernande CP, Ruiz ALTG, de Carvalho JE (2013) Antiproliferative activity of the hexanic extract and phloroglucinols from *Hypericum brasiliense*. *Rev Bras Farmacogn* 23: 844–847.
- Nema R, Khare S, Jain P, Pradhan A, Gupta A, et al. (2013) Natural Products Potential and Scope for Modern Cancer Research. *Am J Plant Sci* 4: 1270-1277.
- Beesoo R, Neergheen-Bhujun V, Bhagooli R, Bahorun T (2014) Apoptosis inducing lead compounds isolated from marine organisms of potential relevance in cancer treatment. *Mutat. Res. Fundam. Mol. Mech. Mutagen* 768: 84-97.
- Suarez-Jimenez GM, Burgos-Hernandez A, Ezquerro-Brauer JM (2012) Bioactive peptides and decapeptides with anticancer potential: sources from marine animals. *Mar Drugs* 10: 963-986.
- Yang MH, Kim J, Khan IA, Walker LA, Khan SI (2014) Nonsteroidal anti-inflammatory drug activated gene-1 (NAG-1) modulators from natural products as anti-cancer agents. *Life Sci* 100: 75-84.
- Picot L, Bordenave S, Didelot S, Fruitier-Arnaudin I, Sannier F, et al. (2006) Antiproliferative activity of fish protein hydrolysates on human breast cancer cell lines. *Process Biochem* 41: 1217-1222.
- Chalamaiah M, Dinesh Kumar B, Hemalatha R, Jyothirmayi T (2012) Fish protein hydrolysates: proximate composition, amino acid composition, antioxidant activities and applications: a review. *Food Chem* 135: 3020-3038.
- Naqshbandi A, Khan MW, Rizwan S, Rehman SU, Khan F (2012) Studies on the protective effect of dietary fish oil on cisplatin induced nephrotoxicity in rats. *Food Chem Toxicol* 50: 265-273.
- Bougatef A, Nedjar-Arroume N, Manni L, Ravallec R, Barkia A, et al. (2010) Purification and identification of novel antioxidant peptides from enzymatic hydrolysates of sardinelle (*Sardinella aurita*) by-products proteins. *Food Chem* 118: 559-565.
- Kim SK and Wijesekera I (2010) Development and biological activities of marine-derived bioactive peptides: A review *J Funct Foods* 2: 1-9.
- Mat Jais AM, Dambisya YM, Lee TL (1997) Antinociceptive activity of Channa striatus (haruan) extracts in mice. *J Ethnopharmacol* 57: 125-130.
- Abdul Manan MJ (2007) Pharmacognosy and pharmacology of Haruan (Channa striatus). a medicinal fish with wound healing properties 6: 52-60.
- Park PJ, Jung WK, Kim SK, Jun SY (2004) Purification and characterization of an antioxidative peptide from enzymatic hydrolysate of yellowfin sole (*Limanda aspera*) frame protein. *Eur Food Res Technol* 219: 20-26.
- Shirota T, Haji S, Yamasaki M, Iwasaki T, Hidaka T, et al. (2005) Apoptosis in human pancreatic cancer cells induced by eicosapentaenoic acid. *Nutrition* 21: 1010-1017.
- Spencer L, Mann C, Metcalfe M, Webb M, Pollard C, et al. (2009) The effect of omega-3 FAs on tumour angiogenesis and their therapeutic potential. *Eur J Cancer* 45: 2077-2086.
- Strouch MJ, Ding Y, Salabat MR, Melstrom LG, Adrian K, et al. (2011) A high omega-3 fatty acid diet mitigates murine pancreatic precancer development. *J Surg Res* 165: 75-81.
- Glaser A, Chandel NS (2014) Targeting antioxidants for cancer therapy. *Biochem Pharmacol* 92: 90-101.
- Mohd SM, Abdul Manan MJ (2012) Therapeutic potential of the haruan (Channa striatus): from food to medicinal uses. *Malays J Nutr* 18: 125-136.
- Lands WE, Hamazaki T, Yamazaki K, Okuyama H, Sakai K, et al. (1990) Changing dietary patterns. *Am J Clin Nutr* 51: 991-993.
- Rose DP, Connolly JM (1999) Omega-3 fatty acids as cancer chemopreventive agents. *Pharmacol Ther* 83: 217-244.
- Liu XH, Rose DP (1995) Suppression of type IV collagenase in MDA-MB-435 human breast cancer cells by eicosapentaenoic acid in vitro and in vivo. *Cancer Lett* 92: 21-26.

42. Aronson WJ, Glaspy JA, Reddy ST, Reese D, Heber D, et al. (2001) Ratio of Dietary Fish Oils in Men with Prostate Cancer. *Urology* 4295: 1-6.
43. Kobayashi, Barnard RJ, Henning SM, Elashoff D, Reddy ST, et al. (2006) Cyclooxygenase-2, and prostaglandin E2. *Clin Cancer Res* 12: 4662-4670.
44. Berquin IM, Min Y, Wu R, Wu J, Perry D, et al. (2007) Modulation of prostate cancer genetic risk by omega-3 and omega-6 fatty acids. *J Clin Invest* 117: 1866-1875.
45. Kelavkar UP, Hutzley J, McHugh K, Allen KG, Parwani A (2009) Prostate tumor growth can be modulated by dietarily targeting the 15-lipoxygenase-1 and cyclooxygenase-2 enzymes. *Neoplasia* 11: 692-699.
46. Kato T, Hancock RL, Mohammadpour H, McGregor B, Manalo P, et al. (2002) Influence of omega-3 fatty acids on the growth of human colon carcinoma in nude mice. *Cancer Lett* 187: 169-177.
47. Hawcroft G, Volpato M, Marston G, Ingram N, Perry SL, et al. (2012) The omega-3 polyunsaturated fatty acid eicosapentaenoic acid inhibits mouse MC-26 colorectal cancer cell liver metastasis via inhibition of PGE2-dependent cell motility. *Br J Pharmacol* 166: 1724-1737.