Global J. Environ. Sci. Manage.,4(1): 81-90, Winter 2018
DOI: 10.22034/gjesm.2018.04.01.008

ORIGINAL RESEARCH PAPER

In vitro investigating of anticancer activity of focuxanthin from marine brown seaweed species

M. Karkhane Yousefi[1], M. Seyed Hashtroudi[2,*], A. Mashinchian Moradi[1], A.R. Ghasempour[3]

[1]Department of Marine Biology, School of Marine Science, Science and Research Branch, Islamic Azad University, Tehran, Iran

[2]Department of Marine Living Science, Iranian National Institute for Oceanography and Atmospheric Science, Tehran, Iran

[3]Department of Medicinal Plant and Drug Research, Shahid Beheshti University, Tehran, Iran

Received 8 June 2017; revised 28 October 2017; accepted 30 November 2017; available online 1 January 2018

ABSTRACT: Breast cancer is the most common cancer type among women all over the world. Chemotherapy is the use of anticancer medicines for treating cancer but it has many side effects and cells may become resistant to these chemical medicines. Therefore, finding new compounds of natural origin could be a promising solution to this problem. The aim of the current study was to evaluate anticancer activity of fucoxanthin which is the most important carotenoid found in the marine brown seaweeds and diatoms. fucoxanthin has many properties (antioxidant, antibacterial, anticancer, antiobesity, anti-inflammatory and etc.) due to its unique structure. Samples with different concentrations (10, 25 and 50 µg/ml) and at various incubation times were collected (6, 24 and 48 hours) from four different species (*Padina tenuis, Colpomenia sinuosa, Iyengaria stellate* and *Dictyota indica*) of brown seaweeds from Qeshm Island, Persian Gulf. Moreover, the anticancer activity of fucoxanthin-containing extracts on breast cancer cells line and normal human skin fibroblast cells line was assessed by MTT [3-(4,5-dimethylthiazolyl)-2,5-diphenyl-tetrazolium bromide] assay to specify the cytotoxic effects. The results showed that fucoxanthin extract from *Dictyota. indica* at 24-hour treatment and 50 µg/ml concentration has the most effective anticancer activity on the breast cancer cells line, without toxic effects to the normal cells. According to the obtained results, it seems that *Dictyota. Indica* is a good candidate for further analysis and can be introduced to the food and pharmaceutical industries.

KEYWORDS: *Anticancer; Colpomenia sinuosa; Dictyota indica; Fucoxanthin; Iyengaria stellate; MTT [3-(4,5-dimethylthiazolyl)-2,5-diphenyl-tetrazolium bromide] assay; Padina tenuis.*

INTRODUCTION

Cancer is a disease that stems from physical, environmental, metabolic, chemical and genetic factors and there is no main reason for it as it pervades by uncontrolled cell growth. Breast cancer is the most usual cancer type among women and is considered the major reason of women mortality in many regions (Giacinti *et al.,* 2006; Lordan *et al.,* 2011). According to the statistics and records, cancer is increasing in developed and developing countries (Pereira *et al.,* 2011). Normally, treatment of cancer is divided into four steps: surgery, chemotherapy, radiotherapy and using medicine. Unfortunately, chemotherapy has many side effects and induces cells resistance due to the use of cytotoxic and chemical drugs (Koch *et*

*Corresponding Author Email: *hashtroudi@inio.ac.ir*
Tel.: +98 21 6694 4873 Fax: +98 21 6694 4869

Note: Discussion period for this manuscript open until April 1, 2018 on GJESM website at the "Show Article".

al., 2003). Therefore, finding an effective anticancer taken from natural compounds would be a promising solution for patients. For this reason, scientists from all over the world are interested in this field. Marine macro algae are abundant in marine environments and can be divided into three groups in terms of their color: green, red and brown (Rodriguez-Jasso *et al.,* 2011). Brown algae or Phaeophyceae are the major source of foucoxanthin. In other words, the dominant pigment of brown seaweeds is fucoxanthin (Hong *et al.,* 2007). It is a marine xanthophyll that has especial structure. It contains an allenic moiety and some other functional groups containing oxygen like epoxy, alcohol and ester (Konishi *et al.,* 2005). Previous studies estimate that 10% of the whole carotenoid is made in environment (Miyashita and Hosokawa, 2008; Terasaki *et al.,* 2009). Fucoxanthin is a bioactive compound (Carotenoid) which has several proven biological properties, including antioxidant, anti-inflammatory, antimicrobial (Heo *et al.,* 2010; Shiratori *et al.,* 2005), antiobesity (Maeda *et al.,* 2005; Maeda *et al.,* 2007), anti-angiogenic and anticancer properties (Nakazawa *et al.,* 2009). Indeed, all of these make fucoxanthin very applicable in pharmaceutical and food industries (Plaza *et al.,* 2008). According to previous researches, fucoxanthin has anticancer effects. Takahashi *et al.* (2015) studied the anticancer effects of fucoxanthin and fucoxanthinol on colorectal cancer cell lines. They reported that these two carotenoids from brown seaweeds have many anticancer properties and can be used in chemotherapeutic agents (Takahashi *et al.,* 2015). Martin (2015) reviewed cancer prevention and treatment of fucoxanthin and its metabolite fucoxanthinol in many different kinds of cancer cell lines (liver cancer, bladder cancer, prostate cancer, breast cancer, leukemia, cervical cancer, osteosarcoma cancer and skin cancer). He concluded that these compounds (fucoxanthin and its metabolite) are effective on treatment of cancer cells development with no sex differences effect. Persian Gulf and Oman Sea are rich of seaweeds. Erfani *et al.* (2015) investigated cytotoxic activity of ten different species of seaweeds from the Persian Gulf and Oman Sea on human breast cancer cell lines and found two species of the studied seaweeds (*Gracilaria foliifera* and *Cladophoropsis* sp.) good candidates for further analysis to produce new anticancer medicine. In this study, four species of brown seaweeds (widespread along the Persian Gulf) were chosen for extracting fucoxanthin and comparing their anticancer activity against breast cancer cells line (MDA-MB-231) and normal human skin fibroblast cells line (NHDF) in three different concentrations of solution containing fucoxanthin (10, 25 and 50 µg/ml) at three various time (6, 24 and 48 h) treatments. The aim of this study is to test some of the brown seaweeds' anticancer properties to suggest these natural resources as a potential anticancer medicine to the pharmaceutical industry. In addition, in this study, four different species of brown seaweeds were compared to find the best one with high anticancer activity. This study has been carried out in Marine Biology Laboratory, Science and Research Branch, Islamic Azad University of Tehran in 2016.

MATERIALS AND METHODS

Seaweeds collection

Specimens of live brown seaweeds (P. *tenuis*, C. *sinuosa*, I. *stellate and* D. *Indica*) were collected from seashore of Qeshm Island, Persian Gulf, Iran (26° 56.059′ N and 56° 16.485′ E), in winter 2016. The seaweeds were washed with sea water carefully to remove external substances (epiphytes, other particles and invertebrates) before being transferred to the laboratory. They were washed again with tap water and distilled water and kept at shadow to be dried. Afterwards, the dried seaweeds were ground by mixer into small particles and kept in glass vials in dark and cold condition to avoid any degradation until further analysis.

Characterization of selected seaweeds

The collected seaweeds were identified according to Atlas of Sea Algae of the Persian Gulf and Oman Sea coasts (Gharanjik and Rohani Ghadikolaei, 2009). Table 1 briefly explains the characterization of each seaweed sample.

Fucoxanthin extraction

Fucoxanthin extraction was carried out according to Haugen method (Haugen *et al.,* 1992) with slight modifications. All extraction solvents and fucoxanthin standards were of analytical grade and purchased from Sigma Aldrich (Steinheim, Germany). 2 g of the algal sample was mixed with 20 ml of methanol and stirred by a magnetic bar for 24 hours at laboratory temperature. After settlement of the insoluble part, the upper layer was centrifuged (5 min, 6000 rpm)

Table 1: Characterization of the studied samples

Seaweeds Species	Color	Shape	Tallus	Photo
Colpomenia. Sinuosa	yellowish brown	Globular, irregularly convoluted to hollow smooth, irregular shape and even polygonal	About 5 - 10 cm or more	
Iyngaria. Stellate	greenish brown	Hemispherical and globular in surface, irregular shape and it looks like the compressed grapey	about 5-10 cm or more	
Padina. Tenuis	greenish brown	Large, thick and dark brown sporocyte, with several flabellate lobes	10 cm in length	
Dictyota. Indica	dark brown	Erect and forming upright tufts, angles of their straps are about 30-50 degrees, smooth margins with many proliferations except the base	about 10-20 cm in height	

and supernatant was collected. This procedure was repeated for three times. 60 ml of distilled water and 60 ml of hexane were added to the previous supernatants. The obtained solution was decanted by a separatory funnel and its aqueous phase was collected and organic phase was discarded. Then, 40 ml chloroform was added to the aqueous phase and again the two phases were decanted by decanter. The organic phase was collected and evaporated using a rotary evaporator (temperature of rotary adjusted at 30 ˚C). The residue was kept for next analysis. Fucoxanthin was detected using a high performance liquid chromatography system (Terasaki *et al.,* 2009). The detection wavelength was set at 450 nm. Fig. 1 shows the HPLC chromatogram of the fucoxanthin standard.

Cell line culture

Breast cancer cells line (MDA-MB-231) and normal human skin fibroblast cells line (NHDF) were obtained from Pastour Institute Center. Cancer cells line was cultured at complete culture medium (RPMI) and normal cells line was cultured at DMEM culture medium (Gibco company USA) as supplemented with 10% fetal bovine serum (FBS), 1% antibiotic solution (100 U/ml penicillin and 100 µg/ml streptomycin) and then incubated for 6, 24 and 48 h at 37 ˚C in 5% CO_2 and humidity of 80% for cells attachment (Jin *et al.,* 2010).

MMT assay

MTT method was used to assess the capacity of fucoxanthin extract on cell viability in cancer cells (Mosmann, 1983). Cancer cells were plated in 96 well culture plates (Cell quantity: density of $1.0x10^6$ cells/well) and incubated for 24 hours. Cells were then exposed to three different concentrations of fucoxanthin (10, 25 and 50 µg/ml) extracted from four species of algae (P. *tenuis*, C. *sinuosa*, I.*stellate* and D.*Indica*) and incubated at various incubation times (6, 24 and 48 h) at 37 ˚C and 5%CO_2 atmosphere. After finishing incubation time, MTT

([3-(4,5-dimethylthiazolyl)-2,5-diphenyl-tetrazolium bromide]) stock solution (5 mg/ml in phosphate buffer saline (PBS)) was added and again incubated for 3 h at 37 ˚C and 5%CO_2 atmosphere. Afterwards, solution of ethanol-DMSO (1V/1V) was added to purple formazan crystals to dissolve it and absorbance was measured at 570 nm by ELISA reader (TECAN, Switzerland) (Mosmann, 1983). All experiments were performed in triplicate. MTT assay is a chlorometric method based on changing tetrazolium salt MTT to formazan by dehydrogenases of viable cells at cell's mitochondria.

The effect of the fucoxanthin extracts on the cancer cell death was expressed as the percent of cell viability to negative control (cells treated only with 5% of DMSO(according to Eq. 1.

$$\frac{A\,570\ of\ \ treated\ \ cells}{A\,570\ of\ \ control\ \ cells}\times 100 = \%\ Cell\ \ viability \qquad (1)$$

Statistical analysis

The experiments were done in triplicate. Data are reported as mean ± standard deviation (SD). The values were analyzed by one-way ANOVA using SPSS version 17.0 software, and individual comparisons were performed by post-hoc Tukey's test (significant differences: P value ≤ 0.05).

RESULT AND DISCUSSION

Potential cytotoxic effects of four different seaweeds extracts containing fucoxanthin on breast cancer cells line (MDA-MB-231) and normal human skin fibroblast cells line (NHDF) were measured. For this purpose, cancer cells line was cultured at various concentrations of fucoxanthin extract (10, 25 and 50 µg/ml) at different incubation times (6, 24, 48 h) and examined by MMT method. Fig. 2 shows the percentage of cells viability of cancer cells at different concentration treatments of fucoxanthin from P. *tenuis*, C. *sinuosa*, I. *stellate* and D. *Indica* algae at 6 h incubation time. As shown in Fig. 2, lower percentage of cell viability belonged to D. *Indica* at 50 µg/ml concentration. According to Fig. 2, lower percentage of cell viability in all treatments belonged to D. *Indica*. Although the death of cancer cells at 6-h incubation time was not very high for all species, fucoxanthin extract from D. *Indica* had a higher cytotoxicity effect on cells line (percentage of cell death: 49%). The anticancer capacity of fucoxanthin extract from D. *Indica* and P. *tenuis* were significantly different from each other, on the other hand, there were no significant differences between anticancer activity of the extracts from C. *sinuosa* and I.*stellate*.

As shown in Fig. 3, fucoxanthin significantly increased percentage of death cancer cells at 50 µg/ml. The increase was around 90%, 80%, 51% and 55.5% in cancer cells at this concentration of fucoxanthin extract from D. *Indica,* P. *tenuis*, I. *stellate* and C. *sinuosa* respectively. Hence foucoxanthin extract from D. *Indica* showed a higher anticancer property as compared to other species at 24 h treatment time. According to the result from Fig. 3, anticancer activities of all species were higher in 24 h than in other incubation times.

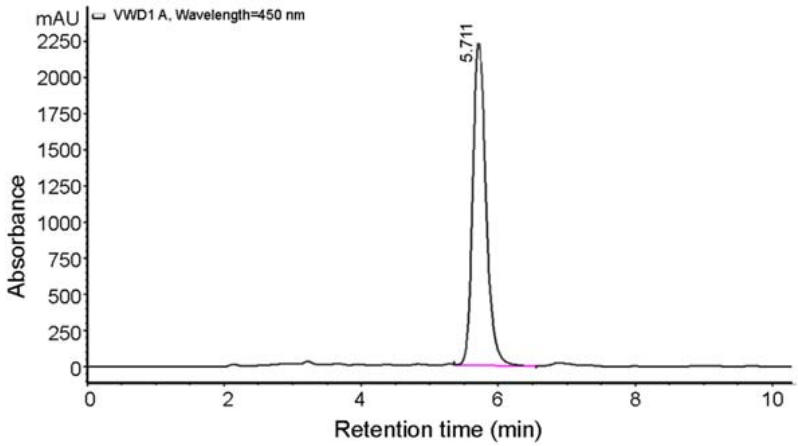

Fig. 1: HPLC chromatogram of a 500 µg/L fucoxanthin standard

As summarized in Fig. 4, in different concentrations of focuxanthin treatment at 48-h incubation time, similar to other incubation times, D. *Indica* shows higher percentage of death cancer cells. Comparison of the three different incubation times shows that 24 h is the best incubation time, 6 h has a lower cytotoxic effect and 48 h has a moderate effect. Thus, it can be concluded that incubation time of 24 h for all the four studied species of brown seaweeds, is the best incubation time. Furthermore, extract of *D. Indica* showed a significant number of cell death of breast cancer cells at 24 h incubation time and 50 µg/ml concentration of fucoxanthin. Although the fucoxanthin from P. *tenuis* extract had a good anticancer effect as well, C. *sinuosa*, and I. *stellate* approximately showed a similar effect of lower than that of the two previous species.

The concentration of extract in all treatments and for all species significantly affect the percentage of cell death ($p<0.05$). Indeed, it can be concluded that higher amount of fucoxanthin concentration plays an undeniable role in determining the anticancer properties of brown seaweed. This suggests that cancer cells growth inhibition effect of fucoxanthin depends on the dose and time, similar to the findings in a study conducted by Wang *et al.* (2014) who investigated the potential functional biomaterials against cancer

A normal human skin fibroblast cells line (NHDF) was also assessed to specify the cytotoxic effects of extract containing fucoxanthin. Normal cells were

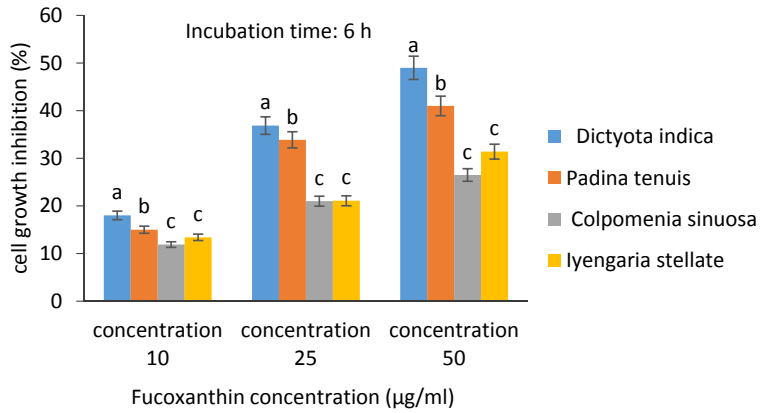

Fig. 2: Percentages of cell growth inhibition at different concentrations of fucoxanthin extract from fourspecies of brown seaweeds (P. *tenuis*, C. *sinuosa*, I.*stellate and D.Indica)* at 6 h incubation time.
Data are expressed as mean±standard deviation (n=3). Different letters (a, b, c) indicate significant mean differences between seaweeds species at a level of $p < 0.05$

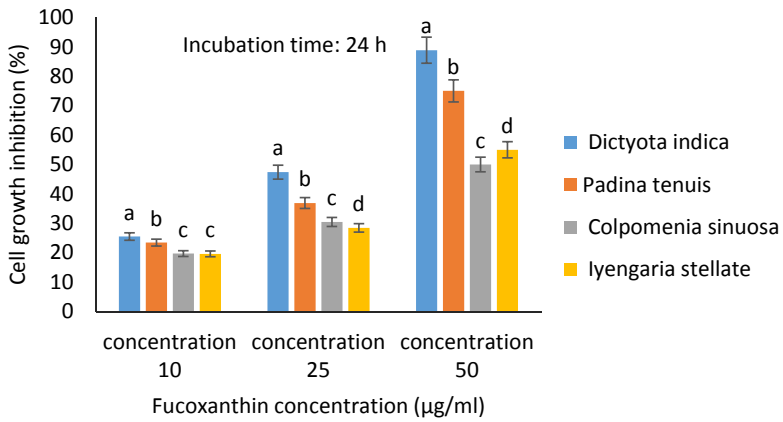

Fig. 3: Percentages of cell growth inhibition at different concentrations of fucoxanthin extract from four species of brown seaweeds (P. *tenuis*, C. *sinuosa*, I. *stellate and D. Indica)* at 24 h incubation time
Data are expressed as mean±standard deviation (n=3). Different letters (a, b, c, d) indicate significant mean differences between seaweeds species at a level of $p < 0.05$

exposed to different concentrations of fucoxanthin extract from four species at 24-h incubation time as the best incubation time obtained in this study. The result shows no significant effect on the cell growth inhibition before and after treatment by fucoxanthin extract (Fig. 5). Some researches indicated that fucoxanthin has no effect on normal cells (Ishikawa *et al.,* 2008; Yamamoto *et al.,* 2011). In some cases, at very high concentration of fucoxanthin (about 2000 mg/kg) it has an adverse effect on normal cells in mice (Beppu *et al.,* 2009). Anticancer property is one of the main features of marine seaweeds. Many algae have showed cytotoxicity effect on cancer cell lines; for instances, anticancer activity of red algae (*Gelidiela acerosa* and *Acanthiphora spicifera*) was investigated and it was revealed that these seaweeds had an acceptable anticancer effect (Duraikannu *et al.,* 2017). Moreover, Alghazeer *et al.,* (2016) studied the anticancer activities of chlorophyta (*Ulva lactuca*, *Codium tomentosum*), phaeophyta (*Cystoseira crinita, Cystoseira stricta*, and *Sargassum vulgare*), and Rhodophyta (*Gelidium latifolium* and *Hypnea musciformis*) and reported considerable cytotoxicity activities of phaeophyta as compared to chlorophyta and rhodophyta. Findings of these studies are in accordance with the findings

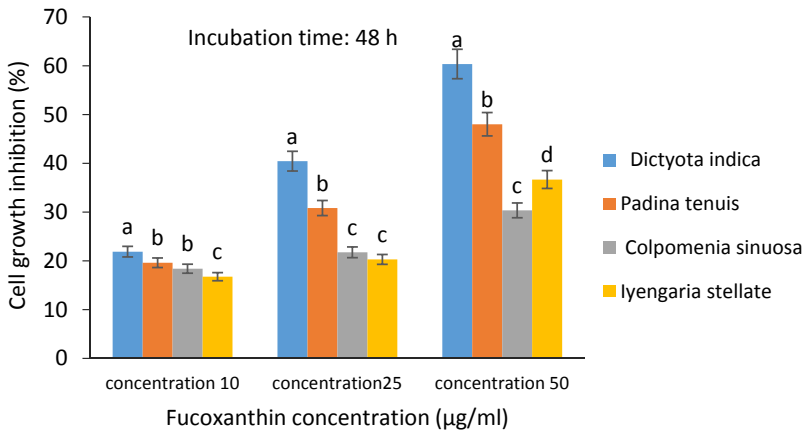

Fig. 4: Percentages of cell growth inhibition at different concentrations of fucoxanthin extract from four species of brown seaweeds (P. *tenuis*, C. *sinuosa*, I.*stellate and D.Indica)* at 48 h incubation time

Data are expressed as mean±standared deviation (n=3). Different letters (a, b, c, d) indicate significant mean differences between seaweeds species at a level of $p < 0.05$.

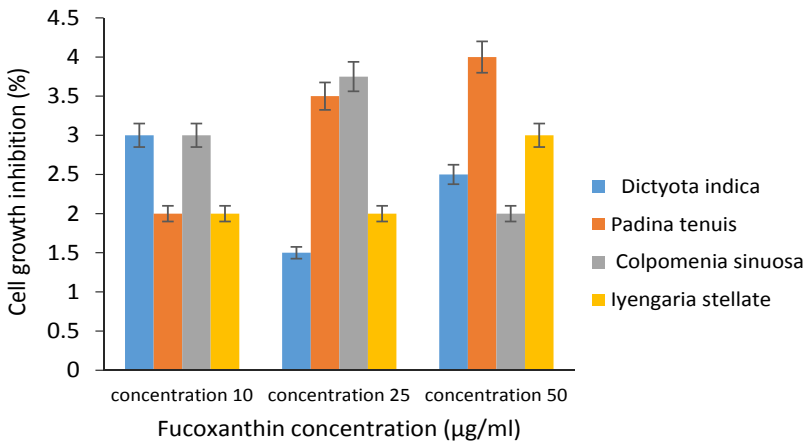

Fig. 5: Percentages of cell growth inhibition at different concentrations of fucoxanthin extract from four species of brown seaweeds (P. *tenuis*, C. *sinuosa*, I. *stellate and D. Indica)* at 24 h incubation time

Data are expressed as mean±standared deviation (n=3)

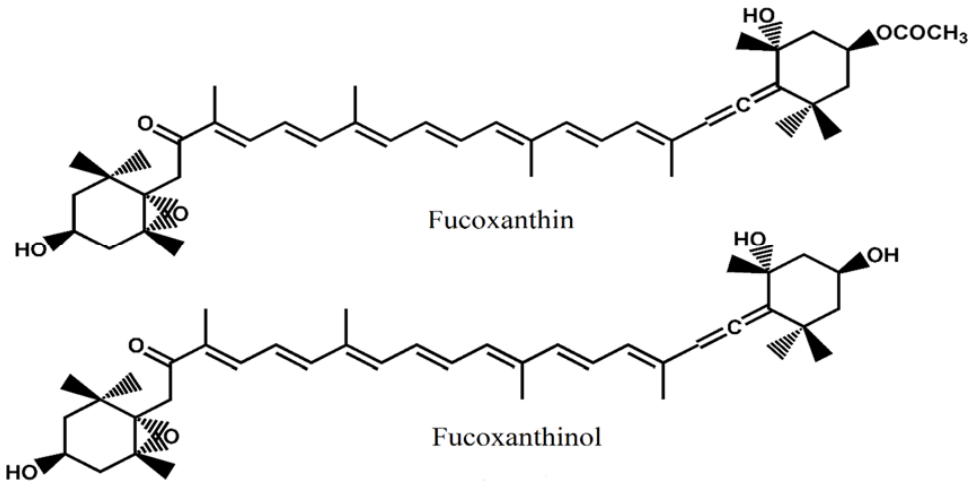

Fig. 6: The structures of Fucoxanthin and Fucoxanthinol

of the present study, proving that brown seaweeds could have a higher anticancer effect in comparison with other seaweeds. Indeed, in many studies it has been implied that brown seaweeds would be better resource for anticancer drugs due to their special bioactive. Fucoxanthin is a carotenoid pigment that is available in the chloroplasts of brown seaweeds and some popular microalgae diatoms. When humans use Fucoxanthin, it is metabolized to fucoxanthinol (deacetylated metabolite of fucoxanthin) (Peng *et al.,* 2011; D'Orazio *et al.,* 2012). Fig. 6 shows the chemical structure of fucoxanthin and fucoxanthinol.

There are some reports which verify that the main reasons of anticancer activity of brown seaweeds are fucoxanthin pigments (Rokkaku *et al.,* 2013; Kumar *et al.,* 2013) as mentioned in the current study. There is a strong correlation between anticancer activities and concentration of the fucoxanthin content extract of each species. Moreover, some researchers compered the anticancer activity of brown seaweeds and exhibited that fucoxanthin and its metabolite fucoxanthinol were the main reasons for brown seaweeds anticancer activities (Kumar *et al.,* 2013). These finding suggests that the main reason for anticancer effect of brown seaweeds can be higher rate of foucoxanthin which contributes to higher percentage of death cancer cells as compared to other red or green seaweeds extracts. Ashwini *et al.,* (2017) observed that *Gracilaria corticata* (red seaweed) extract had a cytotoxicity effect but not as much as brown seaweeds. According to previous studies, diets rich in carotenoids including fucoxanthin can decrease the possibility of breast cancer (Lordan *et al.,* 2011; Peng *et al.,* 2011; Tanaka *et al.,* 2012). In addition, Fucoxanthin was significantly cytotoxic to breast cancer cells (Ayyad *et al.,* 2011). Similar to the results obtained in the current study, which showed that fucoxanthin containing extract with a concentration of 50 µg/ml could have a marked effect on percentage of human breast cancer cell line, Rwigemera *et al.,* (2015) reported on the effects of fucoxanthin on cancer cells line as well (Rwigemera *et al.,* 2015). According to the results obtained in this study, fucoxanthin extract from the brown seaweeds collected from the Persian Gulf, has a considerable anticancer capacity (approximately 90% in some cases) and would be a good candidate for further analysis for food and pharmaceutical purposes. Namvar *et al.* (2014) have also showed the anticancer activity of some seaweeds species from the Persian Gulf. Anticancer activity of *Gracillaria corticata* (red seaweed), *Ulva fasciata* (green seaweed) and *Sargassum ilicifolium* (brown seaweed) against different cancer cell lines (MCF-7, MDA-MB-231, HeLa, HepG2, and HT-29) revealed that all extracts have significant anticancer activity (Namvar *et al.,* 2014). Some researches focused on the mechanisms of fucoxanthin's cytotoxicity in different cancer cell lines such as breast adenocarcinoma MCF-7, human lung carcinoma A549, human hepatocellular carcinoma Hep G2 and colon adenocarcinoma WiDr. They suggested three mechanisms of fucoxanthin reaction in human body: 1) Fucoxanthin can decrease cell apoptosis by

minimizing the proliferation of target cells, 2) It can contribute to morphological change on cells, and 3) It can directly prevent the DNA replication step and apprehend the G_0/G_1 phase of the cell cycle (Das *et al.,* 2005; Namvar *et al.,* 2013., Mikami *et al.,* 2013).

CONCOLUSION

American Cancer Society anticipated that by 2050, 27 million new cancer cases will be expected due to increasing global warming and various environmental issues. Natural products from marine environment play an important role in discovering the new alternatives for anticancer drugs instead of synthetic ones which have many sides effect on human cells and cause cell resistance. The current study investigated the activity of fucoxanthin containing extracts of four Iranian brown seaweeds (P. *tenuis*, C. *sinuosa*, I. *stellate* and D.*Indica*) collected from the Persian Gulf at concentrations of 10, 25, 50 µg/ml and various incubation times (6, 24 and 48 h) against cancer cell line. According to the results, extract of *D. Indica* showed the best anticancer activity (at 50 µg /ml and 24 h) which could be highly correlated to its fucoxanthin content. However, more research is needed to assess the anticancer activities of other natural products from seaweeds at the Persian Gullf and Oman Sea to find the most efficient resources of anticancer component for further clinical experiments.

ACKNOWLEDGMENT

The authors would like to acknowledge Ms. Zohreh Gatmiri for her kind assistance in the statistical analysis throughout the current study.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

ABBREVIATIONS

%	Percent
°C	Degree Celsius
ANOVA	Analysis of variance
cm	Centimeter
CO_2	Carbon dioxide
A	Absorbance
C. sinuosa	Colpomenia sinuosa
DMEM	Dulbecco's modified eagle's medium
DMSO	Dimethyl sulphoxide
DNA	Deoxyribonucleic acid
E	East
Eq	Equation
FBS	Fetal bovine serum
g	Gram
G_0/G_1	Gap_0/Gap_1
h	Hour
HPLC	High Performance Liquid Chromatography
I. stellate	Iyngaria. stellate
mAU	milli absorbance unit
Mg/kg	Milligram per kilogram
MTT	3-(4,5-dimethylthiazolyl)-2,5-diphenyl-tetrazolium bromide
min	Minute
µg/ml	Micro gram per milliliter
N	North
NHDF	Normal human dermal fibroblasts
nm	Nanometer
PBS	Phosphate buffer saline
P. tenuis,	Padina. tenuis
P value	probability value
rpm	Revolutions per minute
RPMI	Roswell Park Memorial Institute
SD	Standard Division
SPSS	Statistical Package for Social Sciences
U/ml	Unite of activity per milliliter
V	Volume

REFERENCES

Alghazeer, R.; Enaeli, M.; Howell, N.K., (2016). Anticancer and antioxidant activities of some algae from western Libyan coast. Pharmacol. Toxicol. Ver. 1, 2016090018.

Ashwini, S.; Manjula, S., (2017). A study on ethanolic extracts of red seaweed Gracilaria corticata (J. Agardh) J. Agardh, to assess the antiproliferative activity and morphological characterization of apoptosisi on Hela cell lines. Int. J. Phytomedicine., 9: 436-442 (**7 pages**).

Ayyad, S.E.N.; Ezmirly, S.T.; Basaif, S.A.; Alarif, W.M.; Badria, A.F.; Badria, F.A., (2011). Antioxidant, cytotoxic, antitumor, and protective DNA damage metabolites from the red sea brown alga *Sargassum* sp. Pharmacogn. Res., 3: 160-165 (**6 pages**).

Beppu, F.; Niwano, Y.; Tsukui, T.; Hosokawa, M.; Miyashita,

K., (2009). Single and repeated oral dose toxicity study of fucoxanthin (FX), a marine carotenoid, in mice. J. Toxicol. Sci., 34: 501-510 (**10 pages**).

Das, S.K.; Hashimoto, T.; Shimizu, K.; Yoshida, T.; Sakai, T.; Sowa, Y.; Komoto, A.; Kanazawa, K., (2005). Fucoxanthin induces cell cycle arrest at G0/G1 phase in human colon carcinoma cells through up-regulation of p21 WAF1/Cip1. Biochim. Biophys. Acta Gen. Subj., 1726: 328-335 (**8 pages**).

D'Orazio, N.; Gemello, E.; Gammone, M.A.; de Girolamo, M.; Ficoneri, C.; Riccioni, G., (2012). Fucoxantin: A treasure from the sea. Mar. Drugs., 10: 604-616 (**13 pages**).

Duraikannu, K.; Shameem rani, K.; Anithajothi, R.; Umagowsalya, G.; Ramakritinan, C.M., (2017). In-vivo anticancer activity of red algae (*Gelidiela Acerosa* and *Acanthophora Spicifera*). Int. J. Pharm. Sci. Res., 5(8): 3347-3352 (**6 pages**).

Erfani, N.; Nazemosadat, Z., Moein, M., (2015). Cytotoxic activity of ten algae from the Persian Gulf and Oman Sea on human breast cancer cell lines; MDA-MB-231, MCF-7, and T-47D. Pharmacognosy. Res., 7(2): 133-137 (**5 pages**).

Gharanjik, B.M.; Ghadikolaei, K.R., (2009). Atlas of the sea algae of the Persian Gulf and Oman sea coasts. Iranian Fisheries Research Organization. 47-77 (**31 pages**).

Giacinti, L.; Claudio, P.P.; Lopez, M.; Giordano, A., (2006). Epigenetic information and estrogen receptor alpha expression in breast cancer. Oncologist., 11: 1-8 (**8 pages**).

Heo, S. J.; Yoon, W. J.; Kim, K. N.; Ahn, G. N.; Kang, S. M.; Kang, D. H.; Jeon, Y. J., (2010). Evaluation of anti-inflammatory effect of fucoxanthin isolated from brown algae in lipopolysaccharide-stimulated RAW 264.7 macrophages. Food. Chem. Toxic., 48(8-9): 2045-2051 (**7 pages**).

Hong, D.; Hien, H.; Son, P., (2007). Seaweeds from Vietnam used for functional food, medicine and biofertilizer. J. Appl. Phycol., 19: 817–826 (**10 pages**).

Haugen, J.A.; Akermann. T.; Liaaen-Jensen, S., (1992). Isolation of fucoxanthin and peridinin. Methods Enzymol., 213: 231–245 **(14 pages).**

Ishikawa, C.; Tafuku, S.; Kadekaru, T.; Sawada, S.; Tomita, M.; Okudaira, T.; Nakazato, T.; Toda, T.; Uchihara, J.N.; Taira, N., (2008).Antiadult T-cell leukemia effects of brown algae fucoxanthin and its deacetylated product, fucoxanthinol. Int. J. Cancer, 123: 2702-2712 (**11 pages**).

Jin, S.; Zhang, Q.Y.; Kang, X.M.; Wang, J.X.; Zhao, W.H., (2010). Daidzein induces MCF-7 breast cancer cell apoptosis via the mitochondrial pathway. Ann. Oncol., 21: 263-268 (**6 pages**).

Koch, S.; Mayer, F.; Honecker, F.; Schittenhelm, M., (2003). Efficacy of cytotoxic agents used in the treatment of testicular germ cell tumours under normoxic and hypoxic conditions in vitro. Br. J. Cancer. 89: 2133-2139 (**7 pages**).

Konishi, I.; Hosokawa, M.; Sashima, T.; Kobayashi, H.; Miyashita, K., (2005) Halocynthiaxanthin and fucoxanthinol isolated from *Halocynthia roretzi* induce apoptosis in human leukemia, breast and colon cancer cells. Comp. Biochem. Physiol. C. Toxicol. Pharmacol., 142: 53-59 (**7 pages**).

Kumar, S.R.; Hosokawa, M.; Miyashita, K., (2013). Fucoxanthin: A marine carotenoid exerting anti- cancer effects by affecting multiple mechanisms. Mar. Drugs., 11: 5130–5147 (**18 pages**).

Lordan, S.; Ross, R.P.; Stanton, C., (2011). Marine bioactives as functional food ingredients: Potential toreduce the incidence of chronic diseases. Mar. Drugs., 9: 1056-1100 (**45 pages**).

Maeda, H.; Hosokawa, M.; Sashima, T.; Funayama, K.; Miyashita, K., (2005). Fucoxanthin from edible seaweed, *Undaria pinnatifida*, shows antiobesity effect through UCP1 expression in white adipose tissues. Biochem. Bioph. Res. Com., 332(2): 392-397 (**6 pages**).

Maeda, H.; Hosokawa, M.; Sashima, T.; Funayama, K.; Miyashita, K., (2007). Effect of medium-chain triacylglycerols on anti-obesity effect of Fucoxanthin. J. Oleo. Sci., 56(12): 615-621 (**7 pages**).

Martin, L.J., (2015). Fucoxanthin and Its Metabolite Fucoxanthinol in Cancer Prevention and Treatment. Mar. Drugs., 13: 4784-4798 (**15 pages**).

Miyashita, H.M.; Hosokawa, M., (2008). Beneficial health effects of seaweed carotenoid, Fucoxanthin. In F. Shahid, C. Barrow (Eds.), Marine nutraceuticals and functional foods. Taylor and Francis Publisher, 297-308 (**12 pages**).

Mikami, K.; Hosokawa, M., (2013). Biosynthetic pathway and health benefits of fucoxanthin, an algae-specific xanthophyll in brown seaweeds. Int. J. Mol. Sci.,14: 13763-13781 (**19 pages**).

Mosmann, T., (1983). Rapid colorimetric assay for cellular growth and survival: Application to proliferation and cytotoxicity assays. J. Immunol. Methods, 65: 55-63 (**9 pages**).

Nakazawa, Y.; Sashima, T.; Hosokawa, M.; Miyashita, K., (2009). Comparative evaluation of growth inhibitory effect of stereoisomers of fucoxanthin in human cancer cell lines. J. Func. Foods, 1(1): 88-97 (**10 pages**).

Namvar, F.; Mohamad, R.; Baharara, J.; Zafar-Balanejad, S.; Fargahi, F.; Rahman, H.S., (2013). Antioxidant, antiproliferative, and antiangiogenesis effects of polyphenol-rich seaweed (sargassum muticum). BioMed. Res. Int. Article ID 604787, (**10 pages**).

Namvar. F., Baharara. J., Mahdi. A.A., (2014). Antioxidant and Anticancer Activities of Selected Persian Gulf Algae. Ind. J. Clin. Biochem., 29: 13–20 (**8 pages**).

Peng, J.; Yuan, J. P.; Wu, C. F.; Wang, J. H., (2011). Fucoxanthin, a marine carotenoid present in brown seaweeds and diatoms: Metabolism and bioactivities relevant to human health. Marine. Drugs., 9(10): 1806-1828 (**23 pages**).

Pereira, D.M.; Cheel, J.; Arche, C.; San-Martin, A.; Rovirosa, J.; Silva, L.R.; Valentao, P.; Andrade, P.B., (2011) Anti-proliferative activity of meroditerpenoids isolated from the brown alga Stypopodium flabelliforme against several cancer cell lines. Mar. Drugs., 9: 852-862 (**11 pages**).

Plaza, M.; Cifuentes, A.; Ibez, E., (2008). In the search of new functional food ingredients from algae. Trends. Food. Sci. Technol., 19: 31–39 (**9 pages**).

Rodriguez-Jasso, R.M.; Mussatto, S.I.; Pastrana, L.; Aguilar, C.N.; Teixeira, J.A., (2011) Microwave-assisted extraction of sulfated polysaccharides (fucoidan) from brown seaweed. Carbohydr. Polym. 86: 1137-1144 (**8 pages**).

Rokkaku, T.; Kimura, R.; Ishikawa, C.; Yasumoto, T.; Senba, M.; Kanaya, F.; Mori, N., (2013). Anticancer effects of marine carotenoids, fucoxanthin and its deacetylated product, fucoxanthinol, on osteosarcoma. Int. J. Oncol., 43: 1176–1186 (**11 pages**).

Rwigemera, A.; Mamelona, J.; Martin, L.J., (2015). Comparative effects between fucoxanthinol and its precursor fucoxanthin on viability and apoptosis of breast cancer cell lines MCF and MDA-MB-231. Anticancer. Res., 35: 207-219 (**13 pages**).

Shiratori, K.; Ohgami, K.; Ilieva, I.; Jin, X. H.; Koyama, Y.;

Miyashita, K.; Ohno, S., (2005). Effects of fucoxanthin on lipopolysaccharide-induced inflammation in vitro and in vivo. Experimental. Eye. Res., 81(4): 422-428 (**7 pages**).

Sithrang, B. N.; Kathiresan, K., (2010). Anticancer drugs from marine flora: an overview. J. Oncol. Article ID 214186, (**19 pages**).

Tanaka, T.; Shnimizu, M.; Moriwaki, H., (2012). Cancer chemoprevention by carotenoids. Molecules., 17: 3202-3242 (**41 pages**).

Terasaki, M.; Hirose, A.; Narayan, B.; Baba, Y.; Kawagoe, C.; Yasui, H.; Miyashita, K., (2009). Evaluation of recoverable functional lipid components of several brown seaweeds (*Phaeophyta*) from Japan with special reference to fucoxanthin and fucosterol contents. J .Phycol., 45(4): 974-980 (**7 pages**).

Takahashi, K.; Hosokawa, M.; Kasajima. H.; Hatanaka. K.; Kudo. K.; Shimoyama. N.; Miyashita. K., (2015). Anticancer effects of fucoxanthin and fucoxanthinol on colorectal cancer cell lines and colorectal cancer tissues. Oncol. Lett., 10: 1463-1467 (**5 pages**).

Wang, S.K.; Li, T.; White, W.L.; Lu, J., (2014). Extracts from New Zealand *Undaria pinnatifida* containing Fucoxanthin as potential functional biomaterials against Cancer in Vitro. J. Funct. Biomater., 5: 29-42 (**14 pages**).

Yamamoto, K.; Ishikawa, C.; Katano, H.; Yasumoto, T.; Mori, N., (2011). Fucoxanthin and its deacetylated product, fucoxanthinol, induce apoptosis of primary effusion lymphomas. Cancer Lett., 300: 225-234 (**10 pages**).

AUTHOR (S) BIOSKETCHES

Karkhane Yousefi, M., Ph.D. Candidate, Department of Marine Biology, School of Marine Science, Science and Research Branch, Islamic Azad University, Tehran, Iran. Email: *mahdiekarkhane85@gmail.com*

Seyed Hashtroudi, M., Ph.D., Assistant Professor, Department of Marine Living Science, Iranian National Institute for Oceanography and Atmospheric Science, Tehran, Iran. Email: *hashtroudi@inio.ac.ir*

Mashinchian Moradi, A., Ph.D., Assistant Professor, Department of Marine Biology, School of Marine Science, Science and Research Branch, Islamic Azad University, Tehran, Iran. Email: *ali2m@yahoo.com*

Ghasempour, A.R., Ph.D., Professor, Medicinal Plants and Drug Research Institute, Shahid Beheshti University, Tehran, Iran. Email: *a-ghassempour@sbu.ac.ir*

HOW TO CITE THIS ARTICLE

Karkhane yousefi, M.; Seyed Hashtroudi, M.; Mashinchian Moradi, A.; Ghasempour, A.R., (2018). In vitro investigating of anticancer activity of focuxanthin from marine brown seaweed species. Global J. Environ. Sci. Manage., 4(1): 81-90.

DOI: 10.22034/gjesm.2018.04.01.008

url: http://gjesm.net/article_28761.html