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*RESEARCH ARTICLE*

# POTENTIAL TARGETS FOR ANTI-INFLAMMATORY AND ANTICANCER ACTIVITIES OF MARINE ALGAE *GELIDIUM SESQUIPEDALE* AND *LAMINARIA OCHROLEUCA*

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## *Abstract*

Marine algae are a source of compound endowed with ingenious structure and potential biological activities. In this study, extracts of red marine algae *Gelidium sesquipedale*and brown marine algae*Laminaria ochroleuca*, harvested from the coast of El Jadida-Morocco were investigated for their anti-inflammatory activity against phospholipase $A_2$ and Elastase and for their cytotoxic activity using the test of brine shrimp lethality for larvae and then both algae were tested on KB cell lines (human buccal epidermal carcinoma), K562 cell lines (Human chronic myelocytic leukemia) and HeLa cell lines (human epitheloid cervix carcinoma). For anti-inflammatory activity, both algae showed anti-elastase activity higher than 80%, however, only *Gelidium sesquipedale* showed a total inhibition of phospholipase $A_2$ activity.*Gelidium sesquipedale* showed an anticancer activity against all cells lines used, however, *Laminaria ochroleuca*showed significant cytotoxic activity of 100% inhibition against *Artemia salina*and an antitumor activity against KB cells lines.



## Introduction:-

The inflammatory and cancer diseases are among the most common diseases all over the world. The prevalence, severity, and complexity of these diseases are rapidly rising and considerably adding to the burden of healthcare costs. Although, the synthetic and combinatorial chemistry have given rise to notable successes in the development of novel anti-inflammatory and anti-cancer drugs (Vo et al., 2012). Meanwhile, the perceived value of natural products in the treatment of these diseases has yet to be fully explored. Thus, the extensive studies of alternative anti-inflammatory and anti-allergic drugs from natural products are essential. Notably, marine algae have been utilized in food products as well as in pharmaceutical products due to their biological activities and health benefit effects. Algae are an important source of various bioactive compounds such as antioxidants,antimicrobials and antivirals (Pulzet al., 2004). These compounds are also important for protecting the algal cells against stressful conditions. To enable rapid adaptation to new environmental conditions, algae produce a great variety of secondary metabolites that cannot be found in other organisms (Rodriguez-Meizoso et al., 2010).The biomass of macroalgae, represented mainly by a few species of Rhodophyta and Phaeophyta, is traditionally used to produce phycocolloids such as agar-agar, alginates and carrageenan.

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Recently, marine algae have attracted a special interest as great sources of anti-inflammatory and anti-cancerproperties (Lee et al., 2013). Inflammation has molecular links to carcinogenesis(Vendramini-Costa et al., 2012; Poehlmann et al., 2012). Therefore, pro-oxidant natural products are commonly chosen when developing anti-cancer drugs (Martin-Cordero et al., 2012; Farooqi et al., 2012; Yen et al., 2012).

In this study, we evaluated the anti-inflammatory and anti-canceractivities of two marine algae *Gelidium sesquipedale* and *Laminaria ochroleuca*collected from the coast of El Jadida-Morocco.

## Materiel and Methods:-

**Algal materials:-**

Seaweeds *Gelidium sesquipedale* and *Laminaria ochroleuca* were collected at low tide and during the spring tide by hand-picking in the period of March toApril from SidiBouzid-El Jadida coast (33°- 33°16'09''N, 8°30'-8°45'W). The algae were cleaned, washed in distilled water, then dried at room temperature and crushed until a fine powder was obtained.

**Preparation of extracts:-**

The powder of dried algae was extracted in methanol, hexane, dichloromethane,dichloromethane /methanol and wateras described by Caccamese and Azolina (1979). The resulting extracts were concentrated to dryness in a rotary evaporator under reduced pressure (at 45°C) until a crude extract was obtained and was conserved at 4°C.

**Anti-inflammatory activity:-**

**$PLA_2$ inhibition assay:-**

Bioassay was based on a colorimetric bioassay (De Araujo et al., 1987). Each extract (10µg dissolved in DMSO (10 µL)) was incubated in 96 well plates for 1h at 25°C, with *Apismellifera*venom $PLA_2$ (Sigma, 2 µL of a 1 mg/mL DMSO stock solution). Substrate solution (198 µL) containing L-α-phosphatidylcholine(L-α-lecithin, 3.5 mM), red phenol (0.055 mM), NaCl (100 mM), $CaCl_2$ (10 mM) and Triton (7 mM) at pH 7.6 were added. Manoalidewas used as a positive control. Colorimetric measurements were made as duplicates at time 0 and after 5 min thereafter read at 550 nm.

**Elastase Inhibition assay:-**

This activity is measured by the calorimetric method (La Barreet al., 1996). Bioassay was monitored by measuring the inhibition of the amidolysis of N-succinyl-alanylalanyl- prolyl-leucyl p-nitroanilide (Sigma) by the elastase (EC 3.4.21.36 Type II-A) from porcine pancreas (Sigma) at 410 nm. The reaction was carried out in 0,2M Tris-HCl buffer (pH 8.0) containing 200µl elastase (0.2mg/ml), 100µg of each extract prepared in 10µl of DMSO was added to the reaction mixture, and the elastase inhibition was assessed at 25 °C. The reaction mixture was preincubated for 10 min before addition of 2µl the substrate (7.2µg/100µl of DMSO). The change in absorbance was measured at 410 nm in a 96-well reader.

**Cytotoxic activity test:-**

**Brine shrimp lethality bioassay:-**

Brine shrimp lethality test for larvae nauplii was used to determine the toxicity of methanol/dichloromethane extract of seaweeds (McLanghlinet al., 1993). The eggs of brine shrimp (*Artemia salina*Leach) were collected and hatched in an Erlenmeyer at 30 °C with constant oxygen supply. Two days were allowed to hatch and mature the nauplii. Stock solution of the extract sample was prepared by dissolving 25, 50, 75, 100, 250 and 500 µg of extract in 4 µl of pure dimethyl sulfoxide (DMSO). 10 living nauplii were taken to each of the vial containing different concentrations of test sample with pipette Pasteur. Then, specific volumes of sample were transferred from the stock solution to the vials to get final sample concentration. In the control vials, same volumes of DMSO (as in the sample vials) were taken. After 24 hours, the vials were observed and the number of nauplii survived in each vial was counted. As controls, *A. salina*nauplii were submitted to seawater and that containing 1% DMSO (100% survival).

The number of survivors was counted and the percentage of death was calculated. Larvae were considered dead when they did not exhibit any internal or external movement during several seconds of observation. The 50% lethal concentrations ($LC_{50}$) of the extracts were determined, values of $LC_{50}$ that were greater than 100 µg/ml were considered to represent an inactive extract (Moshi et al.,2009), the test was repeated five times.

**In vitro antitumor activity assay:-**
KB cells (human buccal epidermal carcinoma), Cell strains K562 (Human chronic myelocyticleukemia) and HeLa cell lines (human epitheloid cervix carcinoma) were used using the method of Arisawa et al. (1997) with minor modifications. The cell suspension $3.10^3 ml^{-1}$was placed in 96-well tissue culture microplates. Sample were dissolved in 0.2% DMSO and added to the cell suspension at 10 µg.$ml^{-1}$. The cells lines were counted by using neutral red as dye and absorbance were measured at 540 nm in a microplate reader.

**Statistical Analysis:-**
The results were analyzed by one-way ANOVA using the SPSS 17 statistical software to compare the mean values of each treatment. The results are expressed as means ± SD. Probability levels of less than 0.01 were considered highly significant. All tests were performed in triplicate.

## Results and Discussion:-

***Gelidium sesquipedale*:-**

**Anti-inflammatory activity:-**
The search for anti-inflammatory activity of *Gelidium sesquipedale* was evaluated through the inhibition of phospholipase $A_2$ and the inhibition of elastase.Extracts of the algae were tested for their anti-inflammatory capacity in quantity of extracts of 100, 250 and 500 µg.Only the dichloromethane / methanol extract is represented, the other extracts prepared in methanol, hexane, dichloromethane and water showed no positive activity (Fig 1).

The results of the inhibition of phospholipase $A_2$ and elastase by different quantity of *Gelidium sesquipedale* extractshow that the inhibition is proportional to the amount of extract tested.They show that 100%of inhibition of phospholipase $A_2$ and 98% of the elastase was obtained with 500 µg of extract.

In literature, studies on phospholipase $A_2$ activity and elastase in seaweed are infrequent. The most significant works are those of Mayer et al. (1993) which showed an anti-phospholipase $A_2$ activity in 10 species of algae.

Many researches reports that marine algae possess anti-inflammatory activity.Chen et al. (2013) showed that an aqueous extract of *Gracilariatenuistipitata* suppressed virus-induced inflammation; also, Lim et al. (2006)indicated that the anti-inflammatory effects of a methanol extract of*Neorhodomelaaculeata* in neurological diseases included inhibiting cellular reactive oxygen species (ROS) generation, $H_2O_2$-induced lipid peroxidation, and inducible nitric oxide synthase.

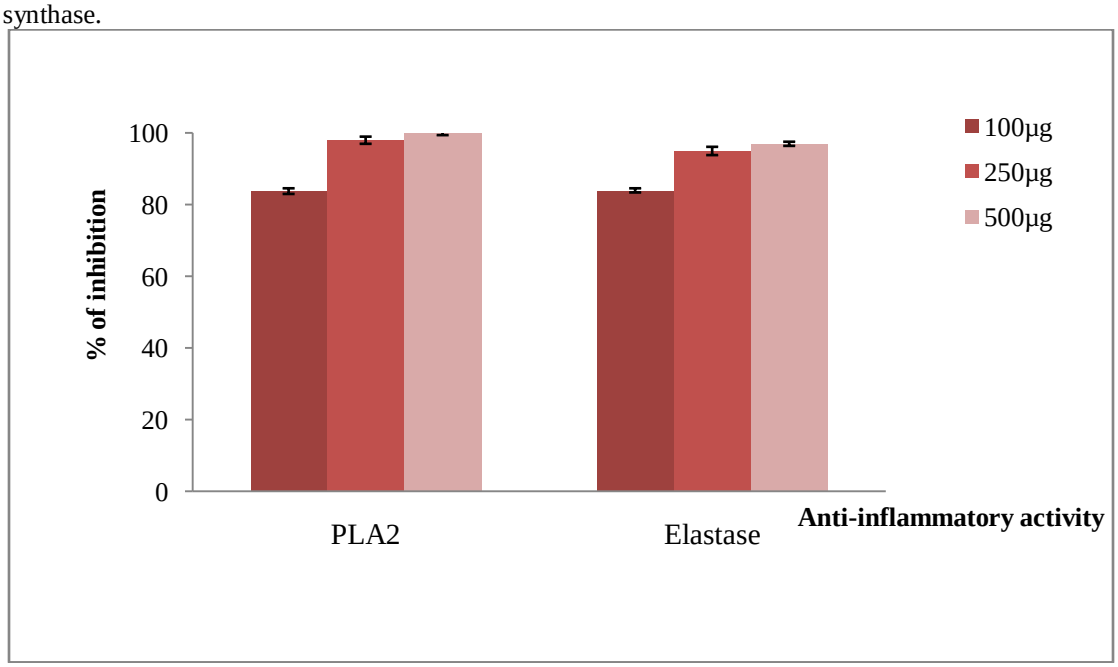


**Figure 1:-** Percent inhibition of $PLA_2$ and elastase according to the quantity of DC / MeOH extract of the algae*Gelidium sesquipedale*.

**Cytotoxic activity:-**

Since the isolation of the Halomon by Fuller et al. (1992), special attention was paid to the cytotoxic activity of the algae. Several species were tested for cytotoxicity on cancer cells, hepatocytes or tumors. In our study, the cytotoxic activity was investigated in the dichloromethane / methanol extract of *Gelidium sesquipedale* (Table 1).

The extract of *Gelidium sesquipedale* showed significant cytotoxic activity of 100% inhibition for a quantity of 100 µg against *Artemia salina*. *Gelidium sesquipedale*extract was also tested against KB cells, against cervical carcinoma Human cell lines (HeLa) and against chronic myelogenous leukemia cell lines of (K562).

The extract showed a high antitumor activity against KB with 100% ofcytotoxicity, also, anticancer activity against HeLa and K562 cell lines. $IC_{50}$ values of the MTT test is 36.01µg / ml for HeLa and 17.41 µg / ml for K562.

**Table1:-** Cytotoxic activityof dichloromethane/methanol extract of *Gelidium sesquipedale*.

| ***A. salina*** | **KB** | **HeLa** | **K562** |
|---|---|---|---|
| 100 % of death | 100 % of death | $IC_{50}$ : 36,01µg/ml | $IC_{50}$ : 17,41 µg/ml |

Metidji et al. (2015) showed that methanolic extracts of *Gelidium sesquipedale* showed prominent result in brine shrimp cytotoxicity assay. The $LD_{50}$ value was 2.22 µg/ml. In addition, they found that the degree of lethality was found to be directly proportional to the concentration of the extract.

Many of the secondary metabolites produced by the marine red algae are well known for their cytotoxic property. As noted by Harada et al. (1997), the extract from a red alga, *Amphiroazonata*exhibited strong cytotoxicity to human leukemic cell line. El-Baroty et al. (2007)demonstrated the cytotoxic activities of powdered *Asparaguses taxiformis*and its water extract on *Daphna magna*.

Many studies of cytotoxic activity of other red algae are already reported. Zubia et al. (2009) reported that *Asparagopsisarmata*hada strong cytotoxic activity against cancer cell lines. Similarly, Manilal et al. (2009) reported the cytotoxicity of active fraction of *Laurenciabrandenii*showed value of 93µg/ml for the $LC_{50}$ from brine shrimp lethality.

Zandi et al. (2010a,b) showed thataqueous extracts of *Gracilariacorticata*and *Sargassumoligocystum*inhibited the proliferation of human leukemic cell lines. Yeh et al. (2012a,b) reported thatboth ethanol and methanol extracts of *Gracilariatenuistipitata* had anti-proliferative effects on Ca9-22 oral cancer cells and were involved in cellular apoptosis, DNA damage, and oxidative stress. Similarly, caspase-dependent apoptosis induced by a methanol extract of *Plocamiumtelfairiae* has been demonstrated using HT-29 colon cancer cells (Kim et al. 2007).

***Laminaria ochroleuca*:-**

**Anti-inflammatory activity:-**

The dichloromethane / methanol extractof *Laminaria ochroleuca* was tested for its ability to inhibit phospholipase $A_2$ and elastase in 100, 250 and 500 µg.Extracts prepared in methanol, hexane, dichloromethane and water showed no activity.

The results represented in figure 2 showed that the extract of *Laminaria ochroleuca* showedalow anti-$PLA_2$ activity with a percent inhibition less than 60%, by cons, this extract has a high ability to inhibit elastase with percentage inhibition greater than 80% at 100 µg of extract.

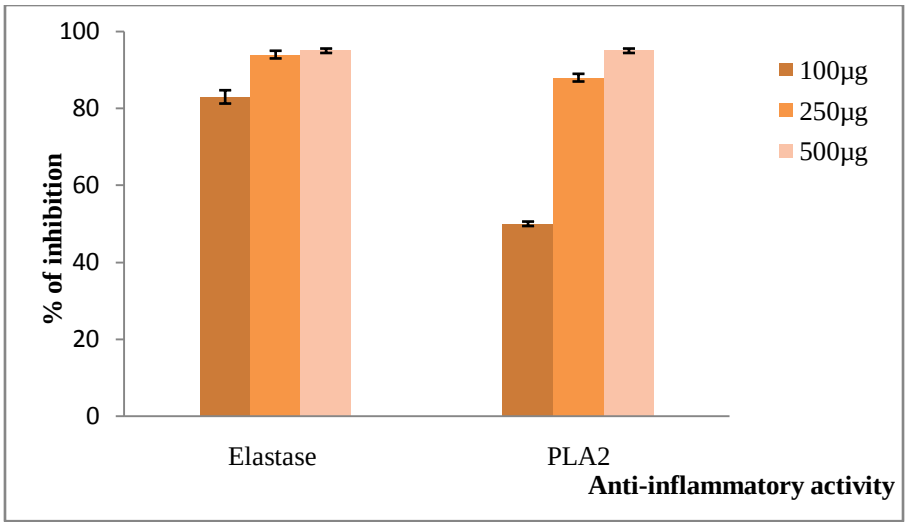


**Figure 2:-** Percent Inhibition of elastase and $PLA_2$ depending on thequantity of DC / MeOH extract of *Laminaria ochroleuca*.

The work of Etahiri (2002) is in agreement with our results, it showed that the extract of *Laminaria ochroleuca* has a weak anti-$PLA_2$ activity.

In literature, Kim et al. (2007) indicated that a murine asthma model showed that an ethanol extract of *Ecklonia cava* reduced allergic airway reactions and inflammation and inhibited LPS-induced inflammation in human endothelial cells (Kim et al. 2010). An ethanol extract of *Ishigeokamurae* also showed anti-inflammatory effects (Kim et al. 2009).

Additionally, anti-inflammatory effects have been demonstrated for the *Myagropsismyagroides*-dervied carotenoid fucoxanthin(Heo et al. 2010), for *Eiseniabicyclis*, *Ecklonia cava*- and*Eckloniakurome-derived* polyphenol phlorotannins(Kim et al. 2011), and for *Sargassumsiliquastrum*-derived sargachromanol G (Yoon et al. 2012). Phloroglucinol, a monomer of phlorotannins that is abundant in brown algae, reportedly had an anti-oxidative stress effect and inhibited the production of inflammatory mediators in LPS-stimulated cells (Kim et al. 2010).

**Cytotoxic activity:-**

Marine macroalgae belonging to the group of Pheophyceae possess anti-tumor activity against several culture cell lines (Tang et al., 2002).

Several cytotoxic compounds such as fucoidans, laminarians and terpenoids, reported to be abundant in brown algae, have anti-cancer, anti-tumor and antiproliferativeactivities (Gerwick et Bernat, 1993 ; Carte, 1996 ; Smit, 2004 ; Manilal et al., 2009 ; Synytsya et al., 2010 ; Vinayak et al., 2010 ; Ayyad et al., 2011).

The dichloromethane / methanol extract of *Laminaria ochroleuca* showed significant cytotoxic activity of 100% inhibition for 100 µg against *Artemia salina*. The extract of *Laminaria ochroleuca* was also tested against KB, HeLa and against K562. The extract showed an antitumor activity against KB cells lines with 100% of activity.

Studies of brown algae have shown that glycoproteins from *Laminaria japonica* (Go et al., 2010)and fucoidans from *Sargassumhornery*, *Eclonia cava*, and *Costariacostata*(Ermakovaet al., 2011) had anti-cancer effects on human colon cancer cells. Heterofucans from *Sargassumfilipendula*exhibited anti-proliferative effects on cervical, prostate, and liver cancer cells (Costa et al., 2011). A carotenoid fucoxanthin cold inhibit the growth of LNCap prostate cancer cells by arresting these cells in the G1 phase via the GDD45A and SAPK/JNK pathways (satomi et al., 2012).

## Conclusion:-

The results of the present work showed that dichloromethane/methanol extract of both algae *Gelidium sesquipedale* and *Laminaria ochroleuca* offer potential for use as anti-inflammatory and anticancer candidate. These findings of this work are useful for further research to identify, isolate and characterize the specific compound which is responsible for these activities.

## References:-


1. Arisawa, M., Hayashi, K., Nikaido, T., Koike, K., Fujita, D., Nunomura, N., Tanaka, M. and Sasaki, T. (1997): Screening of some Marine Organism extracts for cAMP Phosphodiesterase Inhibition, Cytotoxicity and antiviral activity against HSV-1. Inter. J. Pharm., 35 (1): 6-11.
2. Ayyad, N.S., Ezmirly, S.T., Basaif, S.A., Alarif, W.M., Badria, A.F. and Badria, F.A. (2011): Antioxidant, cytotoxic, antitumor, and protective DNA damage metabolites from the red sea brown alga *Sargassum*sp. Pharmaco. Res., 3: 160-165.
3. Caccamese, S. andAzzolina, R. (1979): Screening for antimicrobial activities in marine algae from eastern Sicily. Planta Med.,37 : 333-339.
4. Carte, B.K. (1996): Biomedical potential of marine natural products. Biosci., 46: 271-286.
5. Chen, K.J., Tseng, C.K., Chang, F.R., Yang, J.I., Yeh, C,C., Chen, W.C., Wu, S.F., Chang, H.W. and Lee, J.C. (2013): Aqueous extract of the edible *Gracilariatenuistipitata* inhibits hepatitis C viral replication via cyclooxygenase-2 suppression and reduces virus-induced inflammation. PLoS One., 8(2):e57704.
6. Costa, L.S., Fidelis, G.P., Telles, C.B., Dantas-Santos, N., Camara, R.B., Cordeiro, S.L., Costa, M.S., Almeida-Lima, J., Melo-Silveira, R.F. and Oliveira, R.M. (2011): Antioxidant and antiproliferative activities of heterofucans from the seaweed *Sargassumfilipendula*.Mar. Drugs., 9(6):952-966.
7. De Araujo, A. L. and Radvani, F. (1987): Determination of phospholoipase $A_2$ activity by a colorimetric assay using a pH indicator.Toxin.,25: 1181-1188.
8. El-Baroty, G.S., Moussa, M.Y., Shallan, M.A., Ali, M.A., Sabh, A.Z. andShalaby, E. A. (2007): contribution to the aroma, biological activities, minerals, protein, pigments and lipid contents of the red alga: *Asparagopsistaxiformis* (Delile) Trevisan.J. App Sci. Res.,3: 1825-1834.
9. Ermakova, S., Sokolova, R., Kim, S.M., Um, B.H., Isakov, V. andZvyagintseva, T. (2011): Fucoidans from brown seaweeds *Sargassumhornery*, *Eclonia cava*, *Costariacostata*: structural characteristics and anticancer activity. Appl. Biochem. Biotechnol., 164(6):841-850.
10. Etahiri, S.(2002) : Isolement et caractérisation de composés pharmacologiquement actifs à partir des algues marines de la côte d'El Jadida (Maroc). Thèse de doctorat en Science. Fac. Sci. El Jadida, Maroc. p68-92.
11. Farooqi, A.A., Butt, G. andRazzaq, Z. (2012): Algae extracts and methyl jasmonate anti-cancer activities in prostate cancer: choreographers of 'the dance macabre'. Cancer Cell Int., 12(1):50.
12. Fuller, R. W., Cardellina, J. H., Kato, Y., Brinen, L. S., Calrdy, J., Snader, K. M. and Boyd, M. R.(1992): A pentahalogenated monoterpene from the red algae *Portierahorrmemennii*produces a novel cytotoxicity profile against a diverse panel of human tumor cell lines. J. Med. Chem.35: 3007-3011.
13. Gerwick, W.H., Bernart, M.W. (1993): In: Marine Biotechnology. (Eds.): Attaway, D. and Zaborsky, O., Plenum Press, New York 101-152.
14. Go, H., Hwang, H.J. and Nam, T.J. (2010): A glycoprotein from *Laminaria japonica* induces apoptosis in HT-29 colon cancer cells. Toxicol., 24(6):1546-1553.
15. Harada, H. and Kamei, Y. (1997): selective cytotoxicityof marine algae extracts to several human leukemic cell lines. Cytotech., 25: 213-19.
16. Heo, S.J., Yoon, W.J., Kim, K.N., Ahn, G.N., Kang, S.M., Kang, D.H., Affan, A., Oh, C., Jung, W.K. and Jeon, Y.J. (2010): Evaluation of anti-inflammatory effect of fucoxanthin isolated from brown algae in lipopolysaccharide-stimulated RAW 264.7 macrophages. Food Chem.Toxicol., 48(8-9):2045-2051.
17. Kim, J.Y., Yoon, M.Y., Cha, M.R., Hwang, J.H., Park, E., Choi, S.U., Park, H.R. and Hwang, Y.I. (2007): Methanolic extracts of *Plocamiumtelfairiae* induce cytotoxicity and caspase-dependent apoptosis in HT-29 human colon carcinoma cells. J. Med. Food., 10(4):587-593.
18. Kim, S.K., Lee, D.Y., Jung, W.K., Kim, J.H., Choi, I., Park, S.G., Seo, S.K., Lee, S.W., Lee, C.M. and Yea, S.S. (2008) : Effects of *Ecklonia cava* ethanolic extracts on airway hyperresponsiveness and inflammation in a murine asthma model: role of suppressor of cytokine signaling. Biomed.Pharmacother., 62(5):289-296.
19. Kim, M.M., Rajapakse, N. and Kim, S.K. (2009):Anti-inflammatory effect of *Ishigeokamurae*ethanolic extract via inhibition of NF-kappaB transcription factor in RAW 264.7 cells. Phytother. Res., 23(5):628-634.

20. Kim, M.M. and Kim, S.K. (2010): Effect of phloroglucinol on oxidative stress and inflammation.FoodChem. Toxicol., 48(10):2925-2933.
21. Kim, T.H. and Bae, J.S. (2010): *Ecklonia cav*a extracts inhibit lipopolysaccharide induced inflammatory responses in human endothelial cells. Food Chem.Toxicol., 48(6):1682-1687.
22. Kim, S.K. andHimaya, S.W. (2011): Medicinal effects of phlorotannins from marine brown algae.Adv. Food Nutr. Res., 64:97-109.
23. La Barre, S., Longeon, A., Barthlemy, M.and Guyot, M. (1996): Characterization of a novel elastase inhibition from a fan coral, Life Sci., 319(5):365-370.
24. Lee, J.C., Hou, M.F., Huang, H.W., Chang, F.R., Yeh, C.C., Tang, J.Y. and Chang, H.W. (2013): Marine algal natural products with anti-oxidative, anti-inflammatory, and anti-cancer properties.Cancer Cell Int., 13(55): 1475-2867.
25. Lim, C.S., Jin, D.Q., Sung, J.Y., Lee, J.H., Choi, H.G., Ha, I. and Han, J.S. (2006): Antioxidant and anti-inflammatory activities of the methanolic extract of *Neorhodomela aculeate* in hippocampal and microglial cells. Biol. Pharm. Bull., 29(6):1212-1216.
26. Manilal, A., Sujith, S., Kiran, G.S., Selvin, J. and Shikar, C. (2009): Cytotoxic potentials of red alga, *Laurenciabrandenii*collected from the Indian Coast. Global J. Pharma., 3: 90-94.
27. Manilal, A., Sujith, S., Selvin, J., Kiran, G.S., Shakir,C., Gandhimathi, R. andPanikkar, M.V.N. (2009): Biopotentials of seaweeds collected from southwest coast of india. J. Mar. Sci.Tech.,17 (1): 67-73.
28. Martin-Cordero, C., Leon-Gonzalez, A.J., Calderon-Montano, J.M., Burgos-Moron, E. and Lopez-Lazaro, M. (2012): Pro-oxidant natural products as anticancer agents. Curr.Drug.Targets., 13(8):1006-1028.
29. Mayer, A. M. S., Paul, V. J., Fenical, W., Norris, J. N., DeCarvalho, M. S. and Jacobs, R. S.(1993): Phospholipase $A_2$ inhibitors from marine algae.Hydrobiol.,260: 158-168.
30. McLaughlin, J.L., Chang, C. and Smith, D.L. (1993): Simple bench-top bioassays (brine-shrimp and potato discs) for the discovery of plant antitumour compounds, in: Human Medicinal Agents from Plants. (Eds.): Kinghorn, A.D., Balandrin, M.F., Washington, D.C.: Amer. Chem. Soc., 112-137.
31. Metidji, H., Dob, T., Toumi, M., Krimat, S., Ksouri, A. andNouasri, A. (2015): antimicrobial and cytotoxic properties of *Gelidium sesquipedale*Thuret et Bornet red seaweed from Algeria. J. Mater. Environ. Sci. 6 (11) :3184-3196.
32. Moshi, M.J., Innocent, E., Masimba, P.J., Otieno, D.F., Weisheit, A., Mbabazi, P., Lynes, M., Meachem, K., Hamilton, A. and Urassa, I. (2009): Antimicrobial and brine shrimp toxicity of some plants used in traditional medicine in Bukoba District, north-western Tanzania. Tanz. J.Health Res., 11: 23-28.
33. Poehlmann, A., Kuester, D., Malfertheiner, P., Guenther, T. and Roessner, A. (2012): Inflammation and Barrett's carcinogenesis. Pathol. Res.Pract., 208(5): 269-280.
34. Pulz,O. and Gross,W. (2004): Valuable products from biotechnology of microalgae.Appl. Microbiol.Biotechnol.,65: 635-648.
35. Rodriguez-Meizoso, I., Jaime, L., Santoyo, S., Señoráns, F. J.,Cifuentes,A.and Ibáñez,E.(2010): Subcritical water extraction and characterization of bioactive compounds from *Haematococcuspluvialis*microalga.J. Pharm. Biomed. Anal., 51: 456-463.
36. Satomi, Y. (2012): Fucoxanthin induces GADD45A expression and G1 arrest with SAPK/JNK activation in LNCap human prostate cancer cells. Anticancer Res., 32(3):807-813.
37. Smit, A.J. (2004): Medicinal and pharmaceutical uses of seaweed natural products. A review J. Applied Phycol., 16: 245-262.
38. Synytsya, A., Kim, W.J., Kim, S.M., Pohl, R., Synytsya, A., Kvasnicka, F., Copikova, J. and Park ,Y. (2010): Structure and antitumor activity of fucoidan isolated from sporophyll of Korean brown seaweed *Undariapinnatifida*. Carbohydrate Polymers., 81: 41-48.
39. Tang, H. F., Yang-hua, Y., Yao, X. S., Xu, Q. Z., Zhang, S. Y. and Lin, H. W.(2002):Bioactive steroids from the brown alga *Sargassumcarpophyllum*.J. Asian. Nat. Prod. Res.,4(2): 95-105.
40. Vendramini-Costa, D.B. andCarvalho, J.E. (2012): Molecular link mechanisms between inflammation and cancer. Curr Pharm Des., 18(26): 3831-3852.
41. Vinayak, R.C., Sabu, A.S. and Chatterji, A. (2010): Bioprospecting of a few brown seaweed for their cytotoxic and antioxidant activities. eCAM., 1-9.
42. Vo, T.S., Ngo, D.H. and Kim, S.K. (2012): Potential targets for anti-inflammatory and anti-allergic activities of marine algae: an overview.Inflamm. Allergy Drug Targ.,11(2):90-101.
43. Yeh, C.C., Tseng, C.N., Yang, J.I., Huang, H.W., Fang, Y., Tang, J.Y., Chang, F.R. and Chang, H.W. (2012a): Antiproliferation and induction of apoptosis in Ca9-22 oral cancer cells by ethanolic extract of *Gracilariatenuistipitata*. Molecules., 17(9):10916-10927.

44. Yeh, C.C., Yang, J.I., Lee, J.C., Tseng, C.N., Chan, Y.C., Hseu, Y.C., Tang, J.Y., Chuang, L.Y., Huang, H.W. and Chang, F.R. (2012b): Anti-proliferative effect of methanolic extract of*Gracilariatenuistipitata* on oral cancer cells involves apoptosis, DNA damage, and oxidative stress. BMC Complement Altern. Med., 12(1):142.
45. Yen, C.Y., Chiu, C.C., Haung, R.W., Yeh, C.C., Huang, K.J., Chang, K.F., Hseu, Y.C., Chang, F.R., Chang, H.W. and Wu, Y.C. (2012): Antiproliferative effects of goniothalamin on Ca9-22 oral cancer cells through apoptosis; DNA damage and ROS induction. Mutat. Res., 747(2): 253-258.
46. Yoon, W.J., Heo, S.J., Han, S.C., Lee, H.J., Kang, G.J., Kang, H.K., Hyun, J.W., Koh, Y.S. andYoo, E.S. (2012): Anti-inflammatory effect of sargachromanol G isolated from *Sargassumsiliquastrum* in RAW 264.7 cells. Arch. Pharm. Res.,35(8):1421-1430.
47. Zandi, K., Tajbakhsh, S., Nabipour, I., Rastian, Z., Yousefi, F., Sharafian, S. andSartavi, K. (2010a): In vitro antitumor activity of *Gracilariacorticata* (a red alga) against Jurkat and molt-4 human cancer cell lines. Afr. J. Biotechnol.,9(40):6787-6790.
48. Zandi, K., Ahmadzadeh, S., Tajbakhsh, S., Rastian, Z., Yousefi, F., Farshadpour, F. and Sartavi, K. (2010b): Anticancer activity of *Sargassumoligocystum* water extract against human cancer cell lines. Eur. Rev. Med.Pharmacol. Sci., 14(8):669-673.
49. Zubia, M., Fabre, M.S., Kerjean, V., Le Lann, K., Stiger-Pouvreau, V., Fauchon, M. andDeslandes, E. (2009): antioxidant and antitumorale activities of some Pheophyta from Brittany coasts. Food. Chem.,116(3): 693-701.