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Wound Healing agents from Marine Flora: A Review

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ABSTRACT

Wound is defined as the disruption of the cellular and anatomic continuity of a tissue. Wound may be produced by physical, chemical, thermal, microbial or immunological insults to the tissue. The process of wound healing consists of integrated cellular and biochemical events leading to re-establishment of structural and functional integrity with regain of strength in injured tissues. This review discuss about wound healing potential of marine species, its zoological name, common name, family and references, which are helpful for researcher to develop new wound healing formulations for human use.

Key Words: *Wound healing, marine species, tissues.*

INTRODUCTION

Marine environment is an exceptional reservoir of bioactive natural products, many of which exhibit structural/chemical features not found in terrestrial natural products. Marine organisms have evolved biological and physiological mechanisms that include the production of bioactive compounds for such purposes as reproduction, communication, and protection against predation, infection and competition. Because of the physical and chemical conditions of the marine environment, almost every class of marine organism exhibits a variety of molecules with unique structural features [1].

Marine floras, such as bacteria, actinobacteria, cyanobacteria, fungi, microalgae, seaweeds, mangroves, and other halophytes are extremely important oceanic resources, constituting over 90% of the oceanic biomass. They are taxonomically diverse, largely productive, biologically active, and chemically unique offering a great scope for discovery of new drugs for various activities [2].

The past 2 decades have produced more advances in wound care than have the previous 2000 years as a result of rapid expansion in the knowledge of the healing process at the molecular level [3].

There are several examples of recent advances in the application of above technologies to the discovery and development of novel drugs from marine origin [1]. In this review we have focussed on the pharmacologically active marine natural products that have been shown to have wound healing activity which has been investigated both in invitro and invivo models.

Marine Species having wound healing activity:

1. Chlamys farreri (Pectinidae):

It is a popular seafood native to china has a wide distribution along the coasts of north china, Korea, Japan and eastern Russia. It had been a dominant scallop species for culture, and its production has reached approximately 80% of the total scallop production in china [4].

Fig. 1: Chlamys farreri

Pharmacologically it is having phenoloxidase activity, anti-bacterial activity [5], cytoprotective activity [6], anti-oxidant activity [7], anti-tumor activity [8] and wound healing activity [9]. The recombinant protein of scallop *Chlamys farreri* promoted sheep fibroblast migration into scraped spaces in vitro. It promotes wound healing by fibroblast migration.

2. Clupea harengus Linn (Clupeidae):

Also called as atlantic herring which is found in the palagic zone of marine waters, as well as coastal zones of throughout their geographic reach. It is popular sea food and also used for research and education [10]. It contains highest amount of EPA and DHA and also contains the enzyme cathepsin D which was isolated and characterized [11]

Pharmacologically it is having anti-atherogenic property [12], acetyl-cholinesterase activity [13] and wound healing activity [14]. And the larvae shows wound healing activity by means of mass migration of epidermal cells from the periphery to the skin lesion invivo.

Fig. 1: Clupea harengus Linn

It plays an important role in the supply of essential fatty acids, which has great pharmaceutical and medical benefits [15].

***3. Sepia officinalis* (Sepiidae):**

The common cuttlefish or European common cuttlefish (*Sepia officinalis*) is one of the largest and best-known cuttlefish species. The common cuttlefish is native to at least the

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Mediterranean Sea, North Sea, and Baltic Sea, although subspecies have been proposed as far south as South Africa [16].

Pharmacologically it is having myosuppressor activity [17], anti-oxidant, analgesic, cytotoxic activity [18] and shows wound healing activity [19]. It produces wound healing by means of migration of blood cells toward the wound and by massive synthesis of collagen, followed by the spreading of epithelial cells over the wound.

Fig. 3: Sepia officinalis

It is commercially fished and eaten by humans. Its ink has many uses including homeopathic medicinal uses and use as dyes and paint. Many people keep cuttlefish as pets. People often give cuttlebones from cuttlefish to their pet birds as dietary supplements and to keep their birds' beaks in good health [20].

4. Arius bilineatus (Ariidae):

It is found in various places such as Indo-West Pacific/South and south East Asia, New Guinea and Australia: Andaman Islands, Australia, China, Gulf of Oman, India, Indonesia, Japan, Malaysia, Papua New Guinea, Pakistan, Philippines, Thailand and Vietnam [21].

Fig. 4: Arius bilineatus

Pharmacologically it is having anti-inflammatory activity [22], vasoconstrictor activity [23], tyrosine specific esterase activity [24], platelet activating factor (PAF) activity [25], and wound healing activity [26]. It promotes the wound healing process through its action on capillaries and the associated release of neutrophils.

5. Phallusia nigra Savigny (Ascidiidae):

It is a simple ascidian found in East North Atlantic, European waters, Gulf of Mexico, Indian Ocean, Mediterranean Sea, Panamanian part of the Caribbean Sea and Red Sea [27]. Its methanolic extract contains Methyl 3-bromo-1- adamantine acetate, n-Hexadecanoic acid, 11-Hexadecen-1-ol, (Z)-, 2,6-Dimethyl-6-trifluoroacetoxyoctane [28].

Fig. 5: Phallusia nigra Sav

Pharmacologically it is having anaesthetic activity [29], analgesic activity [30], anti-pyretic activity [30], anti-tumor activity [31], immunomodulatory activity [31], anti-bacterial activity [32], histamine like effect [33], anti-malarial activity [34] and wound healing activity [35]. It shows wound healing activity due to the presence of flavonoids and anti-oxidant compound n-Hexadecanoic acid which appears to be responsible for wound contraction and elevated rate of epithelialisation.

It is occurring as the major component of fouling community on the hull of ships, piers, pilings, harbour installations and materials used for aquaculture operations in the Tuticorin port area.

6. Salmo salar (Salmonidae):

Also called as Atlantic salmon which is found in the northern Atlantic Ocean and in rivers that flow into the north Atlantic and, due to human introduction, the north Pacific. Other names used to reference Atlantic salmon are bay salmon, black salmon, caplin-scull salmon, Sebago salmon, silver salmon, fiddler, or outside salmon [36].

Fig. 6: Salmo salar

The larvae shows wound healing activity by means of mass migration of epidermal cells from the periphery to the skin lesion invivo [14]. It is used as an edible meat in United States because it is rich in omega-3 fatty acids. Unlike commercial fishing, which is the harvesting of wild fish, aquaculture is raising fish for harvest under controlled conditions.

7. Channa striatus (Channidae):

Other names are snakehead murrel, common snakehead, chevron snakehead and striped snakehead. It is native to South and Southeast Asia, and has been introduced to some Pacific Islands and Madagascar.

Pharmacologically it is having anti-microbial activity [37], haemolytic activity [38], anti-bacterial activity [39], anti-oxidant activity [40], anti-depressant activity [41], anti-nociceptive, anti-inflammatory, anti-pyretic activity [42] and wound healing activity [43]. It promotes wound healing process due to the presence of docosahexaenoic acid (DHA).

Fig. 7: Channa striatus

It is used for osteroarthritis [44], tuberculosis [45] and at high doses it is neurotoxic in nature [46]. It has been considered as a very good source of health food among Asians because it contains high levels of amino acids and fatty acids [46]. Traditionally, this fish is believed to alleviate post-operative pain and discomfort [47].

8. Cypraea moneta (Cypraeidae):

It is a mollusc found in entire tropical Indian and Pacific Oceans, from east Africa to Central America, including northern Australia.

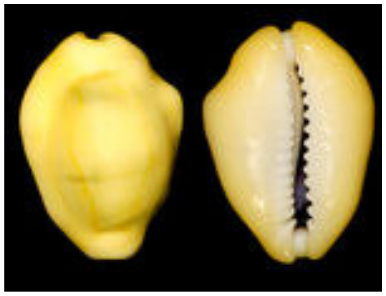

Fig. 2 Cypraea moneta

Pharmacologically it is having anti-pyretic, anti-microbial activity and wound healing activity [48]. It is also having anti-inflammatory activity to considerable extent [49]. The wound healing activity is due to the presence of phosphate, fluoride, carbonate of calcium, magnesium, phosphate and manganese.

It is used in bone formation, regulation of plasma volume, acid-base balance, nerve and muscle contraction [50], and also used in stroke and heart diseases [49]. It is traditionally used in indigestion, colic, peptic ulcer, eye diseases, dysentery, diuretic, anti-diarrhoeal, ear ache, dyspepsia, jaundice, enlarged spleen and liver, asthma and cough.

9. Crassostrea gigas (Ostreidae):

It is also called as Pacific oyster, Japanese oyster or Miyagi oyster. It has been introduced from Asia across the globe. It has been documented destroying habitat and causing eutrophication of the water bodies it invades.

Pharmacologically it is having phenoloxidase activity [51], anti-tumour and immunostimulatory activity [52], laccase like activity [53], anti-hypertensive effect [54], anti-oxidant activity [55], and wound healing activity [56]. A cDNA encoding Cg-TIMP was isolated and characterized which promotes wound healing by means of inhibition of metalloproteinases.

Fig. 9: Crassostrea gigas

It is used extensively by humans. It is cultured and harvested extensively for food. Also, it can be used to replace dying out organisms in an ecosystem. It has been introduced into Europe as a commercial species of importance for aquaculture in countries such as the UK and France.

10. Apostichopus japonicus (Stichopodidae):

It is found in shallow temperate waters along the coasts of south East Asia and is commonly known as the Japanese spiky sea cucumber or the Japanese sea cucumber. The Japanese sea cucumber is found along the coast of Russia, China, Japan and Korea. It contains 2,4-dihydroxy-5-methyl-1,3-azine; 2,4-dihydroxy-1,3-diazine; 3-O-[β-D-quinovopranosyl-(1→2)-4-O-sodium sulfate-β-D-xylopranosyl]-holosta-9(11)-ene-3β,12α,17α-triol; and 24-ethyl-5α-cholesta-7-ene-3β-O-β-D-xylopyranoside. All of these compounds are known in *A. japonicus*, and were found in the waste liquid for the first time [57] and the polysaccharides consists of glucosamine, galactosamine, glucuronic acid, mannose, glucose, galactose and fucose.

Fig. 10: Apostichopus japonicus

Pharmacologically it is having anti-oxidant and anti-hyperlipidemic activity [58], immunostimulatory activity, anti-cancer, anti-coagulant activity [59], anti-inflammatory activity, anti coagulant, wound healing activity [60]. It is used for food. It is also cultivated on a commercial scale in shallow ponds and by sea ranching in northern China.

11. Cucumaria japonica (Cucumariidae):

The other name is Japanese sea cucumber and it is distributed in the northern part of Japan, along the continental coasts of the Sea of Ochotsk and Sea of Japan, off the Kuril Islands and the Kamchatka Peninsula, and in the Bering Sea at least to Northern Kamchatka in Russia +. It contains cucumarioside, a triterpene glycoside [62].

Fig. 11: Cucumaria japonica

Pharmacologically it is having beneficial effect on cognitive performance [63], immunomodulatory activity [64]. It is popular sea food in Japan.

12. Gracilaria changii (Gracilariaceae):

It is an edible sea weed. Malaysia is endowed naturally with a very rich algae life such as the Gracilaria changii.

Fig. 12: Gracilaria changii

Pharmacologically it is having anti-inflammatory, gastroprotective, anti-ulcerogenic activity [65], anti-oxidant, antibacterial and cytotoxic activity [66], anti-fungal activity [67], anti-yeast activity [68] and wound healing activity [69]. These algae are widely applied as folk medicine for the treatment of various ailments including inflammation and gastric ailments.

13. Pleuronectes platessa Linn (Pleuronectidae):

The geographical range of the European plaice is off all coasts from the Barents Sea to the Mediterranean, also in the Northeast Atlantic and along Greenland. In some locales such as the Irish Sea this species is considered fully exploited by commercial fishing.

Fig. 13: Pleuronectes platessa Linn

Pharmacologically it is having anti-bacterial activity [17], anti-atherogenic property [12], and wound healing activity [14]. The larvae shows wound healing activity by means of mass migration of epidermal cells from the periphery to the skin lesion invivo. In North German and Danish cuisine plaice is one of the most commonly eaten fishes.

14. Stichopus badionotus (Stichopodidae):

This species is widespread throughout the Caribbean. It occurs from the southern U.S. (North Carolina) to northern Brazil, and east to the mid-Atlantic including Ascension Island, and Gulf of Guinea in western Africa.

Fig. 14: Stichopus badionotus

Pharmacologically it is having anti-bacterial activity [70], anti-oxidant activity [71], used for pleurisy [72] and wound healing activity [73].

CONCLUSION

Natural derivatives play an important role to heal the wound as synthetic drug formulations cause various harmful side effects to human beings. Marine floras are potential source of wound healing compounds, but they are least explored. This review outlines the marine organisms which are proved to have wound healing activity by means of various methods with their mechanism of action to some extent. Further studies have to be carried out in order to find out the chemical compound which is responsible for the pharmacological action as well as the effectiveness.

REFERENCES:

1. Sarfaraj Hussain Md, Sheeba Fareed, Saba Ansari and Mohd Sajid Khan. Marine natural products: A lead for anti-cancer, Indian journal of Geo-marine Sciences, **2012**; 41(1): 27-39.
2. N. Sithranga Boopathy and K. Kathiresan. "Anticancer Drugs from Marine Flora: An Overview", Journal of Oncology, **2010**; 1-18.
3. JoAn L. Monaco, W. Thomas Lawrence. "Acute wound healing -An overview", Clinics in Plastic Surgery, **2003**; 30: 1-12.
4. Yang Zhang, Xiaojun Zhang, Chantel F. Scheuring, Hong-Bin Zhang, Pin Huan, Fuhua Li, Jianhai Xiang. Construction and Characterization of Two Bacterial Artificial Chromosome Libraries of Zhikong Scallop, *Chlamys farreri* Jones et Preston, and Identification of BAC Clones Containing the Genes Involved in Its Innate Immune System, Marine Biotechnology, **2008**; 10(4): 358-365.
5. Zhou Z, Ni D, Wang M, Wang L, Wang L, Shi X, Yue F, Liu R, Song L. The phenoloxidase activity and antibacterial function of a tyrosinase from scallop *Chlamys farreri*, Fish Shellfish Immunology, **2012**; 33(2): 375-81.
6. Yao RY, Wang CB. Protective effects of polypeptide from *Chlamys farreri* on Hela cells damaged by ultraviolet A, Acta Pharmacology Sin., **2002**; 23(11): 1018-22.
7. Yan-Tao Han, Zhi-Wu Han, Guo-Ying Yu, Yue-Jun Wang, Rui-Yao Cui, Chun-Bo Wang. Inhibitory effect of polypeptide from *Chlamys farreri* on ultraviolet A-induced oxidative damage on human skin fibroblasts in vitro, Pharmacological Research, **2004**; 49(3): 265-274.
8. Gu Qianqun,Fang Yuchun,Wang Changyun et al, Studies on the chemical composition and an-titumor activity of the glycoprotein from *Chlamys* (azumapecten) *farreri*, Chinese Journal of Marine Drugs, **1998-03**.
9. Li F, Huang S, Wang L, Yang J, Zhang H, Qiu L, Li L, Song L. A macrophage migration inhibitory factor like gene from scallop *Chlamys farreri*: Involvement in immune response and wound healing, Dev. Comp, Immunology, **2011**; 35(1): 62-71.
10. http://animaldiversity.ummz.umich.edu/accounts/Clupea_harengus/
11. Nielsen LB, Nielsen HH. Purification and characterization of cathepsin D from herring muscle (*Clupea harengus*), Comp. Biochem. Physiol. B. Biochem. Mol. Biol., **2001**; 128(2): 351-63.
12. Tzortzis Nomikos, Haralabos C. Karantonis. Constantinos Skarvelis, Constantinos A. Demopoulos, Ioannis Zabetakis, Antiatherogenic properties of lipid fractions of raw and fried fish, Food Chemistry, **2006**; 96(1): 29-35.
13. Magdalena Podolska and Dorota Napierska. Acetylcholinesterase activity in hosts (herring *Clupea harengus*) and parasites (*Anisakis simplex* larvae) from the southern Baltic, ICES Journal of Marine Sciences, **2006**; 161-168.
14. G.M. Hickey. Wound healing in fish larvae, Journal of Experimental Marine Biology and Ecology, **1982**; 57(2-3): 146-168.
15. Adriana Mika, Marek Gołębiowski, Edward F. Skorkowski, Piotr Stepnowski. Composition of fatty acids and sterols composition in brown shrimp Crangon crangon and herring *Clupea harengus* membras from the Baltic Sea, Oceanological and Hydrobiological Studies, **2012**; 41(2): 57-64.
16. www.wikipedia.com
17. L.F. Marvin, C. Zatylny, J. Leprince, H. Vaudry, J. Henry. Characterization of a novel *Sepia officinalis* neuropeptide using MALDI-TOF MS and post-source decay analysis, Peptides, **2001**; 1391-1396.
18. Sohair R. Fahmy and Amel M. Soliman. Invitro antioxidant, analgesic and cytotoxic activities of *Sepia officinalis* ink and *Coelatura aegyptiaca* extracts, African journal of pharmacy and pharmacology, **2013**; 7(22): 1512-1522.
19. Jean-Pierre Féral. Wound healing after arm amputation in *Sepia officinalis* (Cephalopoda: Sepioidea), Journal of Invertebrate Pathology, **1988**; 52(3): 380-388.
20. http://animaldiversity.ummz.umich.edu/accounts/Sepia_officinalis.
21. http://www.fishwise.co.za/Default.aspx?TabID=110&SpecieConfigId=201973&GenusSpecies=Arius_bilineatus
22. http://www.patentbuddy.com/Patent/20130108705)
23. Hayat A. Al-Bow, Jassim M. Al-Hassan, Martha Thomson, Olav Thulesius, Abdullah Elkhawad. Multiple vasoactive factors in epidermal secretions of the arabian gulf catfish, *Arius bilineatus* (valenciennes) General Pharmacology: The Vascular System, **1997**; 28(5): 737-744.
24. Martha Thomson, J.M. Al-Hassan, Sanaa Fayad, R.S. Criddle. Tyrosine specific esterase activity in the epidermal secretions from the Arabian Gulf catfish, *Arius bilineatus* (valenciennes), Comparative Biochemistry and Physiology Part B: Comparative Biochemistry, **1989**; 93(3): p. 621-627.
25. Brent Summers, Jassim M. Al-Hassan, Martha Thomson, Alan Chun, R.S. Criddle. Platelet activating factors (AGEPC) from epidermal secretions of the Arabian Gulf catfish, *Arius bilineatus*, Biochim Biophys Acta, **1991**; 1091(3): 329-36.
26. Mei-Mei Wang, Martha Thomson, Muslim Ali, Cecil R. Pace-Asciak, Jassim M. Al-Hassan. Catfish gel extract causes increase in vascular permeability in the rat skin, Inflammopharmacology, **2001**; 8(4): 397-403.
27. http://eol.org/pages/512620/overview
28. S. Gopalakrishnan, V. K. Meenakshi and D. Shanmuga priya. Chemical investigation of the simple ascidian *Phallusia nigra* savigny, 1816 of Tuticorin coast by GC-MS, International Journal of Pharma and Bio Sciences, **2011**; 2(4): 382-387.
29. S. Gopalakrishnana, V. K. Meenakshib and D. Shanmuga priya. Anaesthetic activity of *Phallusia nigra* Savigny, Annals of Biological Research, **2012**; 3(4): 1863-1865.
30. S. Gopalakrishnan, V. K. Meenakshi and D. Shanmuga Priya. Antipyretic and Analgesic activity of *Phallusia nigra* Savigny, 1816, Annals of Biological Research, **2011**; 2(4): 192-196.
31. Meenakshi V.K., Paripooranaselvi M., Senthamarai S., Gomathy S., and Chamundeswari K.P. Antitumor and Immunomodulatory Activity of *Phallusia nigra* Savigny, 1816 Against Ehrlich Ascites Carcinoma, Research Journal of Pharmaceutical Science, **2012**; 1(2): 7-12.
32. S. Bragadeeswaran, K. Ganesan, N. Sri Kumaran, S. Thangaraj and K. Suganthi. Antibacterial and Cytotoxic Activities of Ascidians *Polyclinum madrasensis* Sebestian, 1952 and Phallusia nigra Savigny, 1816 from Tuticorin Coast of India, World Applied Sciences Journal, **2010**; 9(12): 1387-1391.
33. Costa LV, Malpezzi EL, Berlinck RG, Rowan EG, de Freitas JC. This histamine-like effects of *Phallusia nigra* extract: evidences for direct activity at H1 receptors, Comp. Biochem. Physiol. C Pharmacol. Toxicol. Endocrinol., **1997**; 117(1): 111-5.
34. Judith Mendiola, Hilda Hernández, Idalia Sariego, Lázara Rojas, Anabel Otero, Angel Ramírez, María de los Angeles Chávez, Juan Abreu Payrol, Aida Hernández. Antimalarial activity from three ascidians: an exploration of different

marine invertebrate phyla, Transactions of the Royal Society of Tropical Medicine and Hygiene, **2006**; 100(10): 909–916.
35. Gopalakrishnan S, Shanmuga Priya and Meenakshi VK. Wound healing activity of the methanolic extract of *Phallusia nigra* Sav., International Journal of Chemical and Pharmaceutical Sciences, **2012**; 3(3): 45-51.
36. http://www.marinespecies.org/aphia.php?p=taxdetails&id=127143.
37. Pravin Kumar N, Marimuthu K, Vengkades Rao R, Xavier R, Kathiresan S, Suresh CV, Sreeramanan S. Antimicrobial activity of different tissues of snakehead fish *Channa striatus* (Bloch), Asian Pacific Journal of Tropical Disease, **2012**; S302-S305.
38. Loganathan K, Arulprakash A, Prakash M, Senthilraja P and Gunasekaran G. Studies on the antimicrobial and hemolytic activity of the mucus of fresh water snakehead fish *Channa striatus*, International journal of biology, pharmacy and allied sciences, **2013**; 2(4): 866-878.
39. Ong yeong wei, R. Xavier, K. Marimuthu. Screening of antibacterial activity of mucus extract of Snakehead fish, *Channa striatus* (Bloch), European Review for Medical and Pharmacological Sciences, **2010**; 675-681.
40. Narsing Rao Galla, Balaswamy Karakala, Satyanarayana Akula, Prabhakara Rao Pamidighantam. Physico-chemical, amino acid composition, functional and antioxidant properties of roe protein concentrates obtained from *Channa striatus* and *Lates calcarifer*, Food Chemistry, **2012**; 132(3): 1171-1176.
41. Saleem AM, Taufik Hidayat M, Mat Jais AM, Fakurazi S, Moklas M, Sulaiman MR, Amom Z. Antidepressant-like effect of aqueous extract of *Channa striatus* fillet in mice models of depression, Eur. Rev. Med. Pharmacol. Sci., **2011**; 15(7): 795-802.
42. Zakaria ZA, Kumar GH, Mat Jais AM, Sulaiman MR, Somchit MN. Antinociceptive, antiinflammatory and antipyretic properties of *Channa striatus* fillet aqueous and lipid-based extracts in rats, Methods and Findings in Experimental and Clinical Pharmacology, **2008**; 30(5): 355-362.
43. Abdul Manan MAT JAIS. Pharmacognosy and pharmacology of Haruan (*Channa striatus*), a medicinal fish with wound healing properties, Bol. Latinoam. Caribe Plant. Med. Aromaticas, **2007**; 6(3): 52-60.
44. Ng Yeen Tan Michelle, Ganabadi Shanthi, Mohamad Yusof Loqman. Effect of Orally Administered *Channa striatus* Extract Against Experimentally-Induced Osteoarthritis in Rabbits, Intern. J. Appl. Res. Vet. Med., 2(3): 200.
45. Novita Paliliewu, Eulis A. Datau, Julia C. Matheos, Eko E. Surachmanto. Channa striatus capsules induces cytokine conversion in pulmonary tuberculosis patients, J. Exp. Integr. Med., **2013**; 3(3): 237-242.
46. Surajit Karmakar, SC Dasgupta and A Gomes. Pharmacological and haematological study of shol fish (*Channa striatus*) skin extract on experimental animal, Indian journal of experimental biology, **2002**; 115-118.
47. Mat Jais AM, Matori MF, Kittakoop P, Sowanborirux K. Fatty acid compositions in mucus and roe of Haruan, *Channa striatus*, for wound healing. Gen. Pharmacol., **1998**; 30(4): 561–563
48. Grasian Immanuel, Berkmans Jude Thaddaeus, Muthusamy Usha, Ramasamy Ramasubburayan, Santhiyagu Prakash, Arunachalam Palavesam. Antipyretic, wound healing and antimicrobial activity of processed shell of the marine mollusc *Cypraea moneta*, Asian pacific journal of tropical biomedicine, **2012**; S1643-S1646.
49. Kulshrestha Mayank Krishna, Karbhal Kamleshwar Singh. A critical review of ayurvedic drug Kapardika (*Cypraea moneta* Linn), International research journal of pharmacy, **2012**; 3(10): 8-12.
50. Mubarak H, Masilamani G, Siddha marine drug Palagarai (*Cypraea moneta* Linn-A review, Indian journal of geo-marine species, **2012**; 41(2): 121-123.
51. Thomas-Guyon H, Gagnaire B, Bado-Nilles A, Bouilly K, Lapègue S, Renault T. Detection of phenoloxidase activity in early stages of the Pacific oyster *Crassostrea gigas* (Thunberg), Dev. Comp. Immunol., **2003**; 33(5): 653-9.
52. Wang YK, He HL, Wang GF, Wu H, Zhou BC, Chen XL, Zhang YZ. Oyster (*Crassostrea gigas*) hydrolysates produced on a plant scale have antitumor activity and immunostimulating effects in BALB/c mice, **2010**; 8(2): 255-68.
53. Luna-Acosta A, Rosenfeld E, Amari M, Fruitier-Arnaudin I, Bustamante P, Thomas-Guyon H. First evidence of laccase activity in the Pacific oyster *Crassostrea gigas*, Fish Shellfish Immunol., **2010**; 28(4): 719-26.
54. Jae-Young Je, Ji-Young Park, Won-Kyo Jung, Pyo-Jam Park, Se-Kwon Kim. Isolation of angiotensin I converting enzyme (ACE) inhibitor from fermented oyster sauce, *Crassostrea gigas*, Food Chemistry, **2005**; 90(4): 809–814.
55. Juliano Zanette, Fabrício Flores Nunes, Igor Dias Medeiros, Marília Nardelli Siebert, Jacó Joaquim, Mattos, Karim Hahn Lüchmann, Cláudio Manoel Rodrigues de Melo, Afonso Celso Dias Bainy. Comparison of the antioxidant defense system in *Crassostrea rhizophorae* and *Crassostrea gigas* exposed to domestic sewage discharges, Marine Environmental Research, **2008**; 66(1): 196-198.
56. Caroline Montagnania, Fre¨de¨rique Le Rouxb, Franck Bertheb, Jean-Michel Escoubas. Cg-TIMP, an inducible tissue inhibitor of metalloproteinase from the Pacific oyster *Crassostrea gigas* with a potential role in wound healing and defense mechanisms, FEBS Letters, **2001**; 500: 64-70.
57. Li, Chaofeng; Li, Xiancui; Li, Hong; Guo, Shuju; Zhu, Xiaobin. Chemical constituents and antioxidant activities of waste liquid extract from *Apostichopus japonicus* Selenka processing, Chinese Journal of Oceanology & Limnology, **2013**; 31(4): p850.
58. Liu X, Sun Z, Zhang M, Meng X, Xia X, Yuan W, Xue F, Liu C. Antioxidant and antihyperlipidemic activities of polysaccharides from sea cucumber *Apostichopus japonicus*, Chinese pharmacological bulletin, **2008-02**.
59. SHEN Ming. Investigation on Component and Pharmacology of Sea Cucumber, Chinese Traditional Patent Medicine, **2001-10**.
60. Popov A, Artyukov A, Krivoshapko, Kozlovskaya. Biological activities of collagen peptides obtained by enzymic Hydrolysis from Far-Eastern holothurians, American Journal of Biomedical and Life Sciences, **2013**; 1(1): 17-26.
61. V. Levin. Japanese sea cucumber Cucumaria japonica in the far eastern seas of Russia, SPC Beche-de-mer Information Bulletin, **1995**; 18-19.
62. Sedov AM, Shepeleva IB, Zakharova NS, Sakandelidze OG, Sergeev VV. Effect of cucumarioside (a triterpene glycoside from the holothurian *Cucumaria japonica*) on the development of an immune response in mice to corpuscular pertussis vaccine, J. Med. Food., **2001**; 4(3): 127-135.
63. A.Yu. Gorkavaya, T.N. Slutskaya, O.I. Kirillov. Effect of *Cucumaria japonica* extract on cognitive performance in young adults, Zh. Mikrobiol. Epidemiol. Immunobiol., **1984**; (9): 100-4.
64. Aminin DL, Agafonova IG, Berdyshev EV, Isachenko EG, Avilov SA, Stonik VA. Immunomodulatory Properties of Cucumariosides from the Edible Far-Eastern Holothurian *Cucumaria japonica*, J. Med. Food, **2001**; 4(3): 127-135.
65. Meng-Hooi Shu, David Appleton, Keivan Zandi and Sazaly AbuBakar. Anti-inflammatory, gastroprotective and antiulcerogenic effects of red algae *Gracilaria changii* (Gracilariales, Rhodophyta) extract, BMC Complementary and Alternative Medicine, **2013**; 13, 61: 1-13.
66. Tee, Ching Yee. Isolation and bioactivity screening of chemical constituents extracted from *Gracilaria changii*), Master of science thesis, Universiti Malaysia Terrengannu, **2008**.
67. S Sasidharan, I Darah, K Jain. In vitro and In vivo antifungal activity of the methanol extract from *Gracilaria changii*, The Internet Journal of Pharmacology, **2007**; 6(1): p. 12.
68. Sreenivasan Sasidharan, Ibrahim Darah, Mohd Kassim Mohd Jain Noordin. Preliminary isolation and in vitro antiyeast activity of active fraction from crude extract of *Gracilaria changi*i, Indian J. Pharmacology, **2008**; 40(5): 227-229.
69. Mariana N. S, Nik K. A. N. I, Neela V. K., Norfarrah M. A. and Zamberi S. In vivo evaluation on Malaysian coastal isolates of *Gracilaria changii* and *Stichopus badionotus* through heat-burn methicillin-resistant Staphylococcus aureus (MRSA) infection animal model, African Journal of Microbiology Research, **2011**; 5(12): 1379-1382.
70. N.S. Mariana, M.A. Norfarrah, K.A.N.I. Nik, F.M. Yusoff and A. Arshad. Evaluating the Antibacterial Activity and in vivo Assay of Methanolic Extract of *Stichopus badionotus*, Chinese Pharmacological Bulletin, **2011-05**.
71. Hawa I, Zulaikah M, Jamaludin M, Zainal Abidin AA, Kaswandi MA and Ridzwan BH. The potential of the coelomic fluid in sea cucumber as an antioxidant, Mal. J. Nutr., **1999**; 5: 55-59.

72. S.Z. Idid , D.M. Jalaluddin , B.H. Ridzwan , A. Bukhori , S. Nor Hazlinah , C.C. Hoo and L.K. Marthivarman. The Effect of Two Extracts from *Stichopus badionotus* Selenka upon Induced Pleurisy in Rat, Pakistan Journal of Biological Sciences, **2001**; 4(10): 1291-1293.

73. Ronald R. Cowden. Cytological and histochemical observations on connective tissue cells and cutaneous wound healing in the sea cucumber *Stichopus badionotus*, Journal of Invertebrate Pathology, **1968**; 10(1): 151–159.

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