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Annotated Bibliography on

Anticancer Properties in Sea

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Introduction:

Cancer remains one of the most lethal diseases worldwide. There is an urgent need for new drugs with novel modes of action and thus considerable research has been conducted for new anticancer drugs from natural sources, especially plants, microbes and marine organisms. Marine populations represent reservoirs of novel bioactive metabolites with diverse groups of chemical structures. This highlights the impact of marine organisms, with particular emphasis on marine plants, algae, bacteria, actinomycetes, fungi, sponges and soft corals. Anti-cancer properties in Sea. This annotated bibliography contains articles abstracts from 2020-2022.

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Articles Abstracts:

1- Algotiml, R., Gab-Alla, A., Seoudi, R., Abulreesh, H. H., El-Readi, M. Z., & Elbanna, K. (2022). Anticancer and antimicrobial activity of biosynthesized red sea marine algal silver nanoparticles. Scientific Reports, 12(1).

Abstract: Biosynthesis of silver nanoparticles (AgNPs) is emerging as a simple and eco-friendly alternative to conventional chemical synthesis methods. The role of AgNPs is expanding as antimicrobial and anticancer agents, sensors, nanoelectronic devices, and imaging contrast agents. In this study, biogenic AgNPs were synthesized using extracts of different marine algae species, including Ulva rigida (green alga), Cystoseira myrica (brown alga), and Gracilaria foliifera (red alga), as reducing and capping agents. The Physiochemical properties, cytotoxicity, anticancer and antimicrobial activities of the biosynthesized AgNPs were assessed. Surface plasmonic bands of the biosynthesized AgNPs capped with U. rigida, C. myrica, and G. foliifera extracts were visually observed to determine a colour change, and their peaks were observed at 424 nm, 409 nm, and 415 nm, respectively, by UV–Vis spectroscopy; transmission electron microscopy (TEM) indicated an almost spherical shape of AgNPs with nanoscale sizes of 12 nm, 17 nm, and 24 nm, respectively. Fourier transform-infrared (FTIR) spectroscopy analysis suggested that different molecules attached to AgNPs through OH, C=O, and amide groups. The major constituents of the aqueous algal extracts included, terpenoids, polyphenols, sulfonates, polysaccharides, fatty acids, chlorophylls, amide proteins, flavonoids, carotenoids, aliphatic fluoro compounds, volatile compounds, alkalines, pyruvic acid and agar groups. The cytotoxicity and anticancer activities of the biosynthesized AgNPs were assessed using Artemia salina nauplii, normal skin cell lines (HFb-4), and breast cancer cell lines (MCF-7 cell line). The lethality was found to be directly proportional to the AgNP concentration. The IC_{50} values of C. myrica and G. foliifera AgNPs against A. saline nauplii were 5 and 10 μg ml^{-1} after 4 h and 16 h, respectively, whereas U. rigida AgNPs did not exhibit cytotoxic effects. Anticancer activity of the biosynthesized AgNPs was dose dependent. The IC_{50} values of the biosynthesized AgNPs were 13, 13, and 43 μg ml^{-1} for U. rigida, C. myrica, and G. foliifera, respectively. U. rigida AgNPs particularly exhibited potent anticancer activity (92.62%) against a human breast adenocarcinoma cell line (MCF-7) with high selectivity compared the normal cells (IC_{50} = 13 μg/ml, SI = 3.2), followed by C. myrica AgNPs (IC_{50} = 13 μg/ml, SI = 3.07). Furthermore, the biosynthesized AgNPs exhibited strong antifungal

activity against dermatophyte pathogenic moulds and mild antibacterial activity against the food borne pathogen bacteria. The highest antimicrobial activity was recorded for the U. rigida AgNPs, followed by those capped with C. myrica and G. foliifera extracts, respectively. AgNPs capped with the U. rigida extract exhibited the highest antimicrobial activity against Trichophyton mantigrophytes (40 mm), followed by Trichosporon cataneum (30 mm) and E. coli (19 mm), with minimal lethal concentration of 32 and 64 μg ml^{-1} respectively. The study finally revealed that extracts of marine algal species, particularly U. rigida extracts, could be effectively used as reducing agents for the green synthesis of AgNPs. These AgNPs are considered efficient alternative antidermatophytes for skin infections and anticancer agents against the MCF-7 cell line.

2- Amelia, T. S. M., Suaberon, F. A. C., Vad, J., Fahmi, A. D. M., Saludes, J. P., & Bhubalan, K. (2022). Recent advances of marine sponge-associated microorganisms as a source of commercially viable natural products. Marine Biotechnology, 24(3), 492-512.

Abstract: Many industrially significant compounds have been derived from natural products in the environment. Research efforts so far have contributed to the discovery of beneficial natural products that have improved the quality of life on Earth. As one of the sources of natural products, marine sponges have been progressively recognised as microbial hotspots with reports of the sponges harbouring diverse microbial assemblages, genetic material, and metabolites with multiple industrial applications. Therefore, this paper aims at reviewing the recent literature (primarily published between 2016 and 2022) on the types and functions of natural products synthesised by sponge-associated microorganisms, thereby helping to bridge the gap between research and industrial applications. The metabolites that have been derived from sponge-associated microorganisms, mostly bacteria, fungi, and algae, have shown application prospects especially in medicine, cosmeceutical, environmental protection, and manufacturing industries. Sponge bacteria-derived natural products with medical properties harboured anticancer, antibacterial, antifungal, and antiviral functions. Efforts in re-identifying the origin of known and future sponge-sourced natural products would further clarify the roles and significance of microbes within marine sponges.

3- Haq, S. A., Mir, M. A., Lone, S. M., Banoo, A., Shafi, F., Mir, S. A., . . . Masoodi, K. Z.

(2022). Explicating genetic diversity based on ITS characterization and determination of antioxidant potential in sea buckthorn (hippophae spp.). *Molecular Biology Reports, 49*(6), 5229-5240.

Abstract: Background: Sea buckthorn (Hippophae) is in the focus of interest mainly for its positive effects on health of both human and animal organisms. Due to the similarities in vegetative morphology, Hippophae species are often misidentified. Therefore, current study was focused on ITS based sequence characterization of sea buckthorn species and comparative biochemical evaluation for its antioxidant properties. Methods and results: DNA was extracted from leaf samples. Primer pairs K-Lab-SeaBukRhm-ITS1F1- K-Lab-SeaBukRhm-ITS1R1 and K-LabSeaBukTib- ITSF1- K-LabSeaBukTib-ITSR1 were used for PCR amplification. The purified PCR products were outsourced for sequencing. Phylogenetic tree was constructed based on neighbor-joining (NJ) method. Moreover, comparison of antioxidant potential of leaves of two sea buckthorn species (Hippophae rhamnoides and Hippophae tibetana) collected from different regions of Ladakh viz., Stakna, Nubra, DRDO Leh and Zanskar was determined by 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2-azino-bis (3- ethylbenzothiazoline-6-sulphonic acid) diammonium salt (ABTS), and Total antioxidant capacity (TAC) by phosphomolybdenum assays. The present investigation led to the differentiation of two sea buckthorn species viz., H. rhamnoides and H. tibetana based on Internal Transcribed Spacer (ITS) region. Moreover, significant variation was observed in antioxidant potential of leaf extracts collected from different regions. Conclusions: Primary ITS sequence analysis was found to be powerful tool for identification and genetic diversity studies in sea buckthorn. Leaves of sea buckthorn have pronounced antioxidant properties and can be used in food, neutraceuticals and pharmaceutical industries etc. The current study will pave the way to discover small bioactive molecules responsible for antioxidant and anticancer properties in sea buckthorn. © 2021, The Author(s), under exclusive licence to Springer Nature B.V.

4- Wargasetia, T. L., Ratnawati, H., & Widodo, N. (2022). Sea cucumber compounds targeting NF-κB in cancer treatment. Bioinformatics and Biology Insights, 16

Abstract: Cancer is a major health problem worldwide and the leading cause of death in many countries. It remains challenging to find anticancer treatments that work efficiently for varying types of cancer cells. Several studies revealed that nuclear factor kappa B (NF-κB) is a family of

dimeric transcription factors that induce tumor promotion, progression, and therapeutic resistance, providing evidence that NF-kB may be a promising target for cancer drugs. Some research has found that sea cucumber biocompounds have anticancer properties, but further research is essential to confirm anticancer targets. This manuscript discusses the mechanisms of anticancer targeting the NF-κB signaling pathway induced by sea cucumber-derived compounds. Additional database analysis showed the protein targeted by the compounds involved in several pathways related to the NF-κB network. Moreover, SwissADME predicted druglikeliness properties of the active compounds of sea cucumber. The discussion is expected to provide new insight into the promising potential of these marine natural products for the treatment of many different types of cancers. © The Author(s) 2022**.**

5- Selim, S., Almuhayawi, M. S., Alharbi, M. T., Nagshabandi, M. K., Alanazi, A., Warrad, M., . . . Ali, A. S. (2022). In vitro assessment of antistaphylococci, antitumor, immunological and structural characterization of acidic bioactive exopolysaccharides from marine bacillus cereus isolated from saudi arabia. Metabolites, 12(2).

Abstract: A strain of Bacillus cereus was isolated from the Saudi Red Sea coast and identified based on culture features, biochemical characteristics, and phylogenetic analysis of 16S rRNA sequences. EPSR3 was a major fraction of exopolysaccharides (EPS) containing no sulfate and had uronic acid (28.7%). The monosaccharide composition of these fractions is composed of glucose, galacturonic acid, and arabinose with a molar ratio of 2.0: 0.8: 1.0, respectively. EPSR3 was subjected to antioxidant, antitumor, and anti-inflammatory activities. The results revealed that the whole antioxidant activity was 90.4 ± 1.6% at 1500 µg/mL after 120 min. So, the IC50 value against DPPH radical found about 500 µg/mL after 60 min. While using H2O2, the scavenging activity was 75.1 ± 1.9% at 1500 µg/mL after 60 min. The IC50 value against H2O2 radical found about 1500 µg/mL after 15 min. EPSR3 anticytotoxic effect on the proliferation of (Bladder carcinoma cell line) (T-24), (human breast carcinoma cell line) (MCF-7), and (human prostate carcinoma cell line) (PC-3) cells. The calculated IC50 for cell line T-24 was 121 ± 4.1 µg/mL, while the IC50 for cell line MCF-7 was 55.7 ± 2.3 µg/mL, and PC-3 was 61.4 ± 2.6 µg/mL. Anti-inflammatory activity was determined for EPSR3 using different methods as Lipoxygenase (LOX) inhibitory assay gave IC50 12.9 ± 1.3 µg/mL. While cyclooxygenase (COX-2) inhibitory test showed 29.6 ± 0.89 µg /mL. EPSR3 showed potent inhibitory activity against methicillin-resistant

Staphylococcus aureus (MRSA) and coagulase-negative staphylococci. The exposure times of EPSR3 for the complete inhibition of cell viability of methicillin resistant S. aureus was found to be 5% at 60 min. Membrane stabilization inhibitory gave 35.4 ± 0.67 µg/mL. EPSR3 has antitumor activity with a reasonable margin of safety. The antitumor activity of EPSR3 may be attributed to its content from uronic acids with potential for cellular antioxidant and anticancer functional properties. © 2022 by the authors.

6- Sadarun, B., Rahmatika, N. S., Mahatva Yodha, A. W., Fristiohady, A., Sundowo, A., Baharum, S. N., & Sahidin, I. (2022). Antioxidant and cytotoxic properties of soft coral nepthea sp. Ilmu Kelautan: Indonesian Journal of Marine Sciences, 27(1), 29-36.

Abstract: Soft coral Nepthea sp. grows in the seas of South-East Sulawesi, Indonesia. However, information on the chemical and pharmaceutical aspects of this genus is still limited. Therefore, this research aims to explore the chemical contents and biological activities of Nepthea sp. The sample was collected from the waters of Saponda Island by SCUBA diving. It was extracted by ethyl acetate and fractionated using vacuum liquid chromatography. The chemical content was analyzed by phytochemical screening, LC-MS/MS analysis, Total Phenolics Content and Total Flavonoids Contents. Antioxidant potency was evaluated by DPPH (2,2-diphenyl-1-picrylhydrazyl) radicals and ABTS (2,2'-azino-bis-3-ethylbenzthiazoline-6-sulphonic acid). Cytotoxicity property was analyzed by MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assays. The result showed that the fractionation of Nepthea ethylacetate extracts produced six fractions (A-F). Fractions A and B contain non-polar compounds. Based on LC-MS/MS data, the non-polar compounds in Fraction A and B include achillin, atractylenolide II, buthyl isobuthyl phthalate, rengyolester, 2a-acetoxycostic acid, ocotillol acetate, petasitolone and some unidentified compounds that are C33H58O4, C15H21NO, C21H33NO, and C16H20O4. In general, the antioxidant and cytotoxic properties of all samples are in the weak category, however, when examined for each sample, the antioxidant properties of fraction B is slightly better than fraction A based on the IC50 value of DPPH and ABTS. Cytotoxicity of Fraction A is better than Fraction B against Breast Cancer cell lines MCF-7. The non-polar fraction of Nepthea sp. can be developed as raw material for the discovery of new compounds, antioxidant and anticancer agents, especially breast cancer. © Ilmu Kelautan, UNDIP

7- Tekle, S., Bozkurt, F., Akman, P. K., & Sagdic, O. (2022). Bioactive and functional properties of gelatin peptide fractions obtained from sea bass (dicentrarchus labrax) skin. Food Science and Technology (Brazil), 42.

Abstract: Fish skin is one of the most common resources of gelatin, which can be hydrolyzed bioactive peptides. In this study, gelatin from sea bass skin (SBS) was hydrolyzed with flavourzyme® to obtain peptide fractions with different molecular weights and determined their bioactive and functional properties. All peptide fractions obtained showed antioxidant activity (DPPH and FRAP). The bass gelatin peptide fraction 1 (BF1) (≤5 kDa) showed the highest DPPH (44.9%) and FRAP (42.04 mmol Fe+2 /g and 22.98 mmol trolox/g) activities. Besides, the BF1 (≤5 kDa) peptide fraction showed the highest in vitro cytotoxic effect (16.58%) at 20 mg/mL concentration compared to the other peptide fractions. The highest emulsifying capacity (389.5 m2/g), emulsifying stability (53.2 min), foaming capacity (30.47%), and foaming stability (10.40%) were obtained from the control gelatin sample. Moreover, the BF3 (≥10 kDa) peptide fraction showed an excellent fat binding capacity (9.39 mL/g). Enzymatic hydrolysis decreased emulsifying and foaming capacity of gelatin while increasing its fat binding capacity. In particular, antioxidant and anticancer activities of peptide fractions with low molecular weight were found to be high. The results demonstrated that gelatin and hydrolysates from the SBS offer an important alternative as a functional food ingredient for food technology.

8- Mohanta, Y. K., Mishra, A. K., Nayak, D., Patra, B., Bratovcic, A., Avula, S. K., . . . Saravanan, M. (2022). Exploring dose-dependent cytotoxicity profile of gracilaria edulis-mediated green synthesized silver nanoparticles against MDA-MB-231 breast carcinoma. Oxidative Medicine and Cellular Longevity, 2022

Abstract: Green-based synthesis of metal nanoparticles using marine seaweeds is a rapidly growing technology that is finding a variety of new applications. In the present study, the aqueous extract of a marine seaweed, Gracilaria edulis, was employed for the synthesis of metallic nanoparticles without using any reducing and stabilizing chemical agents. The visual color change and validation through UV-Vis spectroscopy provided an initial confirmation regarding the Gracilaria edulis-mediated green synthesized silver nanoparticles. The dynamic light scattering studies and high-resolution transmission electron microscopy pictographs exhibited that the

synthesized Gracilaria edulis-derived silver nanoparticles were roughly spherical in shape having an average size of 62.72±0.25 nm and surface zeta potential of -15.6±6.73 mV. The structural motifs and chemically functional groups associated with the Gracilaria edulis-derived silver nanoparticles were observed through X-ray diffraction and attenuated total reflectance Fourier transform infrared spectroscopy. Further, the synthesized nanoparticles were further screened for their antioxidant properties through DPPH, hydroxyl radical, ABTS, and nitric oxide radical scavenging assays. The phycosynthesized nanoparticles exhibited dose-dependent cytotoxicity against MDA-MB-231 breast carcinoma cells having IC50 value of 344.27±2.56 μg/mL. Additionally, the nanoparticles also exhibited zone of inhibition against pathogenic strains of Bacillus licheniformis (MTCC 7425), Salmonella typhimurium (MTCC 3216), Vibrio cholerae (MTCC 3904), Escherichia coli (MTCC 1098), Staphylococcus epidermidis (MTCC 3615), and Shigella dysenteriae (MTCC9543). Hence, this investigation explores the reducing and stabilizing capabilities of marine sea weed Gracilaria edulis for synthesizing silver nanoparticles in a cost-effective approach with potential anticancer and antimicrobial activity. The nanoparticles synthesized through green method may be explored for their potential utility in food preservative film industry, biomedical, and pharmaceutical industries.

9- Singh, K. S., & Tilvi, S. (2022). Chemical diversity and bioactivity of marine sponges of the genus oceanapia: A review. Mini-Reviews in Organic Chemistry, 19(1), 66-73.

Abstract: The marine sponges of the genus Oceanapia sp. is comprised of more than 50 species and are distributed in the seas around the tropical and subtropical regions. They are mainly found in the northern Indian oceans, Japan, and the south pacific coast. They are highly colored and known to be a rich source of various secondary metabolites, particularly alkaloids. Several other secondary metabolites are also reported from this genus which include terpenes, sphingolipids, ceramides, cer-ebrosides, acetylenic acids, and thiocyanatins, etc. Many of these compounds isolated from this genus exhibited various biological properties, including anticancer, antimicrobial, anti-HIV, ichthyo-toxicity, and nematocidal activities. Although several secondary metabolites have been reported from this genus, a dedicated review of the chemicals and biological activities of this genus is so far lacking. Keeping this in mind, this review describes the various chemical entities isolated from the sponges of the genus Oceanapia, providing details of their chemical structures along with their reported biological properties.

10- Lobine, D., Rengasamy, K. R. R., & Mahomoodally, M. F. (2022). Functional foods and bioactive ingredients harnessed from the ocean: Current status and future perspectives. Critical Reviews in Food Science and Nutrition, 62(21), 5794-5823.

Abstract: With an increase in life expectancy and decrease of quality-of-life couple with the high prevalence of diseases, diet is expected to play a key function in sustaining human health. Nutritionists, food technologists and medical experts are working in synergy to cater for the increasing demand of food with associated therapeutic benefits, commonly known as functional food, that may improve well-being and reduce the risk of diseases. Interestingly, the marine ecosystem, due to its abundant and phenomenal biodiversity of marine organisms, constitutes a vital source of a panoply of healthy foods supply for the thriving functional food industry. Marine organisms such as seaweeds, sea cucumbers, sponges, and mollusks amongst others are sources of thousands of biologically active metabolites with antioxidant, anti-parasitic, antiviral, anti-inflammatory and anticancer properties. Given the growing number of research and interest to probe into the therapeutic roles of marine products, this review was designed to provide a comprehensive summary of the therapeutic properties of marine organisms (macroalgae, sea cucumbers and fish among others) which are consumed worldwide, in addition to their potentials and as sources of functional ingredients for developing novel food and fostering wellness. The gap between research development and actual commercialization, and future prospects of marine-based products also summarized to some extent.

11- Stephen, N. M., Maradagi, T., Kavalappa, Y. P., Sharma, H., & Ponesakki, G. (2021). Seafood nutraceuticals: Health benefits and functional properties. Research and technological advances in food science (pp. 109-139).

Abstract: Sea is acknowledged for its unexplored complex small molecules with potential health benefits in the field of nutraceutical research. The unique properties of marine compounds set an important part in our diet that play a major therapeutic role against various human diseases. Seafood including finfish, shellfish, and marine algae are rich in proteins, essential amino acids, omega-3 polyunsaturated fatty acids, carotenoids, vitamins, and minerals. Moreover, the by-products of fish processing industries include shell, bones, intestines, fin, and skin contains valuable bioactive molecules such as fish oils, carotenoids, collagen, gelatin, peptides, chitin,

chitosan, glycosaminoglycans, and trace elements. These components possess varying health benefits including cardioprotective, neuroprotective, antioxidant, antiinflammatory, anticancer, antiobesity, anticoagulant, antimicrobial, and immunomodulatory activities. Thus, this chapter presents the currently available information/data of seafood bioactive components and their potential health benefits in human nutrition and health care.

12- Tortorella, E., Giugliano, R., De Troch, M., Vlaeminck, B., de Viçose, G. C., & de Pascale, D. (2021). The ethyl acetate extract of the marine edible gastropod haliotis tuberculata coccinea: A potential source of bioactive compounds. Marine Biotechnology, 23(6), 892-903.

Abstract: The phylum Mollusca represents one of the largest groups of marine invertebrates. Nowadays, molluscan shellfish belonging to the classes Bivalvia and Gastropoda are of commercial interest for fisheries and aquaculture. Although bioactive properties of bivalve molluscs have been widely investigated and several dietary supplements have been brought to the market, the bioactive potentialities of marine gastropods are poorly documented. The present study investigated the bioactive properties of tissue extracts derived from Haliotis tuberculata coccinea, or "European abalone," an edible abalone species distributed in the Mediterranean Sea and the northeast Atlantic Ocean. A bioactive organic compound-rich extract was obtained using ethyl acetate as extracting solvent. It showed antimicrobial activity towards the methicillin-resistant Staphylococcus epidermidis strain RP62A, the emerging multi-drug-resistant Stenotrophomonas maltophilia D71 and Staphylococcus aureus ATCC 6538P, being the most sensitive strain. It also showed anthelmintic activity, evaluated through the toxicity against the target model helminth Caenorhabditis elegans. In addition, the ethyl acetate extract demonstrated a selective cytotoxic activity on the cancer cell lines A375, MBA-MD 231, HeLa, and MCF7, at the concentration of 250 µg/mL. The fatty acid composition of the bioactive extract was also investigated through FAME analysis. The fatty acid profile showed 45% of saturated fatty acids (SAFA), 22% of monounsaturated fatty acids (MUFA), and 33% of polyunsaturated fatty acids (PUFA). The presence of some biologically important secondary metabolites in the extract was also analysed, revealing the presence of alkaloids, terpenes, and flavonoids.

13- Alhadrami, H. A., Alkhatabi, H., Abduljabbar, F. H., Abdelmohsen, U. R., & Sayed, A. M.

(2021). Anticancer potential of green synthesized silver nanoparticles of the soft coral cladiella pachyclados supported by network pharmacology and in silico analyses. Pharmaceutics, 13(11).

Abstract: Cladiella-derived natural products have shown promising anticancer properties against many human cancer cell lines. In the present investigation, we found that an ethyl acetate extract of Cladiella pachyclados (CE) collected from the Red Sea could inhibit the human breast cancer (BC) cells (MCF and MDA-MB-231) in vitro (IC50 24.32 ± 1.1 and 9.55 ± 0.19 µg/mL, respectively). The subsequent incorporation of the Cladiella extract into the green synthesis of silver nanoparticles (AgNPs) resulted in significantly more activity against both cancer cell lines (IC50 5.62 ± 0.89 and 1.72 ± 0.36, respectively); the efficacy was comparable to that of doxorubicin with much-enhanced selectivity. To explore the mode of action of this extract, various in silico and network-pharmacology-based analyses were performed in the light of the LC-HRESIMS-identified compounds in the CE extract. Firstly, using two independent machine-learning-based prediction software platforms, most of the identified compounds in CE were predicted to inhibit both MCF7 and MDA-MB-231. Moreover, they were predicted to have low toxicity towards normal cell lines. Secondly, approximately 242 BC-related molecular targets were collected from various databases and used to construct a protein–protein interaction (PPI) network, which revealed the most important molecular targets and signaling pathways in the pathogenesis of BC. All the identified compounds in the extract were then subjected to inverse docking against all proteins hosted in the Protein Data bank (PDB) to discover the BC-related proteins that these compounds can target. Approximately, 10.74% of the collected BC-related proteins were potential targets for 70% of the compounds identified in CE. Further validation of the docking results using molecular dynamic simulations (MDS) and binding free energy calculations revealed that only 2.47% of the collected BC-related proteins could be targeted by 30% of the CE-derived compounds. According to docking and MDS experiments, protein-pathway and compound-protein interaction networks were constructed to determine the signaling pathways that the CE compounds could influence. This paper highlights the potential of marine natural products as effective anticancer agents and reports the discovery of novel anti-breast cancer AgNPs.

14- Pagliara, P., De Benedetto, G. E., Francavilla, M., Barca, A., & Caroppo, C. (2021). Bioactive potential of two marine picocyanobacteria belonging to cyanobium and

synechococcus genera. Microorganisms, 9(10).

Abstract: Coccoid cyanobacteria produce a great variety of secondary metabolites, which may have useful properties, such as antibacterial, antiviral, anticoagulant or anticancer activities. These cyanobacterial metabolites have high ecological significance, and they could be considered responsible for the widespread occurrence of these microorganisms. Considering the great benefit derived from the identification of competent cyanobacteria for the extraction of bioactive compounds, two strains of picocyanobacteria (coccoid cyanobacteria < 3 μm) (Cyanobium sp. ITAC108 and Synechococ-cus sp. ITAC107) isolated from the Mediterranean sponge Petrosia ficiformis were analyzed. The biological effects of organic and aqueous extracts from these picocyanobacteria toward the nauplii of Artemia salina, sea urchin embryos and human cancer lines (HeLa cells) were evaluated. Methanolic and aqueous extracts from the two strains strongly inhibited larval development; on the contrary, in ethyl acetate and hexane extracts, the percentage of anomalous embryos was low. Moreover, all the extracts of the two strains inhibited HeLa cell proliferation, but methanol extracts exerted the highest activity. Gas chromatography–mass spectrometry analysis evidenced for the first time the presence of β-N-methylamino-L-alanine and microcystin in these picocyanobacteria. The strong cytotoxic activity observed for aqueous and methanolic extracts of these two cyanobacteria laid the foundation for the production of bioactive compounds of pharmacological interest.

15- Abdelhafez, O. H., Fahim, J. R., El Masri, R. R., Salem, M. A., Desoukey, S. Y., Ahmed, S., . . . Abdelmohsen, U. R. (2021). Chemical and biological studies on the soft coralNephtheasp. RSC Advances, 11(38), 23654-23663.

Abstract: Soft corals belonging to the family Nephtheidae have been appreciated as marine sources of diverse metabolites with promising anticancer potential. In view of that, the current work investigates the anti-proliferative potential of the crude extract, different fractions, and green synthesized silver nanoparticles (AgNPs) of the Red Sea soft coral,Nephtheasp. against a panel of tumor cell lines. The metabolic pool of the soft coral under study was also exploredviaan LC-HR-ESI-MS metabolomics approach, followed by molecular docking analysis of the characterized metabolites against the target proteins, EGFR, VEGFR, and HER2 (erbB2) that are known to be involved in cancer cell proliferation, growth, and survival. Overall, then-butanol fraction ofNephtheasp. exhibited the highest inhibitory activities against MCF7 (breast cancer) and A549

(lung cancer) cell lines, with interesting IC50values of 2.30 ± 0.07 and 3.12 ± 0.10 μg ml−1, respectively, whereas the maximum growth inhibition of HL60 (leukemia) cells was recorded by the total extract (IC50= 2.78 ± 0.09 μg ml−1). More interestingly, the anti-proliferative potential of the total soft coral extract was evidently improved when packaged in the form of biogenic AgNPs, particularly against A549 and MCF7 tumor cells, showing IC50values of 0.72 ± 0.06 and 9.32 ± 0.57 μg ml−1, respectively. On the other hand, metabolic profiling ofNephtheasp. resulted in the annotation of structurally diverse terpenoids, some of which displayed considerable binding affinities and molecular interactions with the studied target proteins, suggesting their possible contribution to the anti-proliferative properties ofNephtheasp.viainhibition of tyrosine kinases, especially the EGFR type. Taken together, the present findings highlighted the relevance ofNephtheasp. to future anticancer drug discovery and provided a base for further work on the green synthesis of a range of bioactive NPs from marine soft corals.

16- Veríssimo, A. C. S., Pacheco, M., Silva, A. M. S., & Pinto, D. C. G. A. (2021). Secondary metabolites from marine sources with potential use as leads for anticancer applications. Molecules, 26(14).

Abstract: The development of novel anticancer agents is essential to finding new ways to treat this disease, one of the deadliest diseases. Some marine organisms have proved to be important producers of chemically active compounds with valuable bioactive properties, including anticancer. Thus, the ocean has proved to be a huge source of bioactive compounds, making the discovery and study of these compounds a growing area. In the last few years, several compounds of marine origin, which include algae, corals, and sea urchins, have been isolated, studied, and demonstrated to possess anticancer properties. These compounds, mainly from securamines and sterols families, have been tested for cytotoxic/antiproliferative activity in different cell lines. Bioactive compounds isolated from marine organisms in the past 5 years that have shown anticancer activity, emphasizing the ones that showed the highest cytotoxic activity, such as securamines H and I, cholest-3β,5α,6β-triol, (E)-24-methylcholest-22-ene-3β,5α,6β-triol, 24-methylenecholesta-3β,5α,6β-triol, and 24-methylcholesta-3β,5α,6β-triol, will be discussed in this review. These studies reveal the possibility of new compounds of marine origin being used as new therapeutic agents or as a source of inspiration to develop new therapeutic agents.

17- Gravili, C. (2021). Mediterranean blooms of jellyfish and comb jellies: Problems vs opportunities. The cnidaria: Only a problem or also a resource? (pp. 255-279).

Abstract: In the Mediterranean Sea, we are witnessing the effects of the rise of water temperature that is accompanied by migrations and the associated expansion of tropical jellyfish and comb jellies. Multiple factors are probably responsible for their blooms, such as coastal development, nutrient loading, transport of non-indigenous species (NIS), aquaculture, climate change, and overfishing. Benthic stages of several jellyfish are common components of harbours and fouling communities, and are often transported on ship hulls, while their planktonic stages are frequently found in ballast water. Therefore, the biodiversity of Mediterranean gelatinous Cnidaria and Ctenophora (CC) has changed considerably in the past two decades. The decline and disappearance of the species with cold-water affinity resulted in the prevalence of tropical, non-indigenous species that invade new regions and habitats, influencing in many ways the already fragile Mediterranean ecosystem. Jellyfish and comb jellies negatively affect tourism, fish farms, power plants, and fisheries. The present analysis shows that, among the 59 CC NIS existing in the Mediterranean Sea, 58% are of Indo-Pacific origin, while 35% of them have an Atlantic origin, and only 7% originate from the Southern Ocean. There are several problems to be addressed, but the link between the gelatinous bloom events and a decrease in the fishery sectors is, at present, difficult to quantify. Unfortunately, the lack of historical databases, the difficulties inherent to regular conduction of biodiversity surveys, and the increasing paucity of taxonomists hinder our knowledge of NIS throughout the Mediterranean Sea. Besides these, several studies are noteworthy on the account of the uses of jellyfish as foods, biofuels, and as an immense reservoir of bioactive peptides used in nutraceutical, cosmeceutical, and pharmaceutical fields, notably for their antioxidant activity. Recent studies have focused on bioactive molecules with potential anticancer and anti-inflammatory properties. The high reproductive potential of jellyfish may represent a possible socioeconomic opportunity with far-reaching beneficial implications, even though further studies are needed to improve some encouraging, preliminary results.

18- Terasaki, M., Kubota, A., Kojima, H., Maeda, H., Miyashita, K., Kawagoe, C., . . . Tanaka, T. (2021). Fucoxanthin and colorectal cancer prevention. Cancers, 13(10).

Abstract: Colorectal cancer (CRC), which ranks among the top 10 most prevalent cancers, can obtain a good outcome with appropriate surgery and/or chemotherapy. However, the global

numbers of both new cancer cases and death from CRC are expected to increase up to 2030. Diet-induced lifestyle modification is suggested to be effective in reducing the risk of human CRC; therefore, inter-ventional studies using diets or diet-derived compounds have been conducted to explore the prevention of CRC. Fucoxanthin (Fx), a dietary carotenoid, is predominantly contained in edible brown algae, such as Undaria pinnatifida (wakame) and Himanthalia elongata (Sea spaghetti), which are con-sumed particularly frequently in Asian countries but also in some Western countries. Fx is respon-sible for a majority of the anticancer effects exerted by the lipophilic bioactive compounds in those algae. Interventional human trials have shown that Fx and brown algae mitigate certain risk factors for CRC; however, the direct mechanisms underlying the anti-CRC properties of Fx remain elusive. Fx and its deacetylated type "fucoxanthinol" (FxOH) have been reported to exert potential anti-cancer effects in preclinical cancer models through the suppression of many cancer-related signal pathways and the tumor microenvironment or alteration of the gut microbiota. We herein review the most recent studies on Fx as a potential candidate drug for CRC prevention.

19- Sibiya, A., Jeyavani, J., Sivakamavalli, J., Ravi, C., Divya, M., & Vaseeharan, B. (2021). Bioactive compounds from various types of sea urchin and their therapeutic effects — A review. Regional Studies in Marine Science, 44.

Abstract: Marine ecosystem is a treasure house of drugs as a plenty of marine organisms possess interesting bioactive properties that has to be explored further to find applications in the biomedical and pharmaceutical arena. Sea urchin is a seafloor dwelling invertebrate belonging to the phylum Echinodermata is having high nutritional and medicinal properties. It is rich in vitamins, minerals, proteins, fatty acids and polysaccharides and possess anticancer, anticoagulant/antithrombotic, antimicrobial and antioxidant properties. The extracts and hydrolysates of sea urchin have various bioactive compounds especially glycosides, acid polysaccharide, sphingoid, glycolipids, sulphate, polysaccharides and phospholipids. Owing to its wide range of biomedical properties, the present review aims to summarize the therapeutic applications of valuable bioactive components in sea urchins. This review could act as a key reference to identify the new potential bioactive molecules in the drug industry and unravels the applications of sea urchin.

20- Tulandi, S. M., Tanzil, L., & Ulfa, D. M. (2021). Analysis of bioactive compounds from

methanol extract of diadema setosum sea urchin gonads using gas chromatography – mass spectrometry. Research Journal of Pharmacy and Technology, 14(3), 1626-1634.

Abstract: This study aimed to determine the bioactive component of gonads of the sea urchins Diadema setosum from Indonesian waters using Gas Chromatography Mass Spectrometry. Phytochemical test results qualitatively showed that the methanol extract of D. setosum gonads contained steroids-triterpenoids, saponins and alkaloids while the results of analysis using GC-MS illustrated that the largest contents were Hexadecanoic acid, methyl ester (29.53%) and Tetradecanoic acid, methyl ester (14.86%), followed by other components in small quantity including Methyl 13-methyltetradecanoate (0.55%), Pentadecanoic acid, methyl ester ss Methyl npentadecanoate (2.08%), Hexadecadienoic acid, methyl ester (0.48%), 9-Hexadecenoic acid, methyl ester (4.68%), Methyl 10-methyl-hexadecanoate (0.56%), Hexadecanoic acid (4.05%), Heptadecanoic acid, Methyl ester (4.17%), 6,9,12-Octadecatrienoic acid, Methyl ester (1.33%), 9-Octadecenoic acid (Z)-, Methyl ester (5.42%), Octadecanoic acid, Methyl ester (1.91%), 9,12-Octadecadienoic acid (Z, Z)-, Lineloic acid (8.58%), 5,8,11,14-Eicosatetraenoic acid, Methyl ester (3.21%), 9,12-Octadecadienoic acid, Methyl ester (4.71%), Cis-11Eicosenoic acid, Methyl ester (1.86%), (1S, 15S)-Byciclo [13.10] hexadecan-2-one (4.82%), Cholesta-3.5diene (0.67%), Cholest-5-en-3-ol (3β)-(4.20%). Components of the compound were reported to possess pharmacological function as antimicrobial, antifungal, antioxidant, anticancer, hipercholesterolemic agent, lubricant, antiinflammatory, nematicide, hepatoprotective, antihistaminic, pesticide, larvacidal activities, antiacne, anemiagenic, antiandrogenic, 5-alpha reduce inhibitor, antiarthritic and anticoronary properties.

21- Mateos, R., Pérez-Correa, J. R., & Domínguez, H. (2020). Bioactive properties of marine phenolics. Marine Drugs, 18(10).

Abstract: Phenolic compounds from marine organisms are far less studied than those from terrestrial sources since their structural diversity and variability require powerful analytical tools. However, both their biological relevance and potential properties make them an attractive group deserving increasing scientific interest. The use of efficient extraction and, in some cases, purification techniques can provide novel bioactives useful for food, nutraceutical, cosmeceutical and pharmaceutical applications. The bioactivity of marine phenolics is the consequence of their enzyme inhibitory effect and antimicrobial, antiviral, anticancer, antidiabetic, antioxidant, or

antiinflammatory activities. This review presents a survey of the major types of phenolic compounds found in marine sources, as well as their reputed effect in relation to the occurrence of dietary and lifestyle-related diseases, notably type 2 diabetes mellitus, obesity, metabolic syndrome, cancer and Alzheimer's disease. In addition, the influence of marine phenolics on gut microbiota and other pathologies is also addressed.

22- Hossain, A., Dave, D., & Shahidi, F. (2020). Northern sea cucumber (cucumaria frondosa): A potential candidate for functional food, nutraceutical, and pharmaceutical sector. Marine Drugs, 18(5).

Abstract: Sea cucumber (Cucumaria frondosa) is the most abundant and widely distributed species in the cold waters of North Atlantic Ocean. C. frondosa contains a wide range of bioactive compounds, mainly collagen, cerebrosides, glycosaminoglycan, chondroitin sulfate, saponins, phenols, and mucopolysaccharides, which demonstrate unique biological and pharmacological properties. In particular, the body wall of this marine invertebrate is the major edible part and contains most of the active constituents, mainly polysaccharides and collagen, which exhibit numerous biological activities, including anticancer, anti-hypertensive, anti-angiogenic, anti-inflammatory, antidiabetic, anti-coagulation, antimicrobial, antioxidation, and anti-osteoclastogenic properties. In particular, triterpene glycosides (frondoside A and other) are the most researched group of compounds due to their potential anticancer activity. This review summarizes the latest information on C. frondosa, mainly geographical distribution, landings specific to Canadian coastlines, processing, commercial products, trade market, bioactive compounds, and potential health benefits in the context of functional foods and nutraceuticals.

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