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UNVEILING NEGOMBATA MAGNIFICA: A PROMISING FRONTIER IN ANTICANCER RESEARCH

Shifali Choudhary
Department of Biotechnology, School of Biosciences and Technology, Vellore Institute of Technology (VIT), Vellore, Tamil Nadu, India

ABSTRACT

Over the last several years, marine organisms have shown to be a rich resource of novel bioactive compounds for use in the creation of new medicines. Therefore, many researchers have been trying to isolate new active compounds from marine organisms since the middle of the twentieth century. The rich variety of secondary metabolites found in marine sponges has made them a potential treasure trove. Many chemicals identified from sponges have anticancer potential. "The current research looked at whether or not Negombata magnifica has any antiproliferative properties." Multiple cellular and molecular mechanisms, including DNA protection, cell-cycle modulation, apoptosis, and anti-inflammatory activities, as well as the ability to chemosensitize cancer cells to conventional antiblastic chemotherapy, may account for the chemopreventive and potential anticancer activity of compounds from Negombata magnifica. The purpose of this article is to illustrate the interplay between the several systems responsible for Negombata magnifica's chemopreventive and therapeutic actions. Researchers have shown that NPs may serve as either a new therapeutic molecule or a useful framework for the production of novel bioactive compounds, both of which are crucial steps in the drug development process. The need of demonstrating practical mariculture technology of possible candidate marine sponges in India is also highlighted in the study, as this would allow for the pharmaceutical demands to be met without impacting the wild population.

Keywords: - Marine, Cancer, Sponges, Cells, Biological.

I. INTRODUCTION

Even now, cancer is the second leading cause of mortality in the globe. On average, there are about 10 million new cases of cancer each year, with over 6 million associated deaths (Rady et al., 2017). Since radiation-based therapy and chemotherapy are the mainstays of current treatment strategies, figuring out the best technique to treat this disease is an immediate priority. However, this approach is linked to toxic consequences including hair loss and other severe negative outcomes. Complementary and alternative medicine (CAM) is gaining popularity as a viable cancer treatment option. Natural products have shown remarkable promise in a number of cancer models (Tsuda et al., 2004).

Bioactive chemicals found in water are thought to improve adaptability, provide a chemical barrier against, and even provide protection from, other organisms. Antioxidant, antibacterial, and anticancer characteristics are just a few of the biological benefits provided by these bioactive

chemicals. Due to their diversity in taxonomy and pharmacological actions, marine organisms including sponges, mollusks, echinoderms, ascidians, and corals are of great interest in the hunt for new cancer treatments. It has been 50 years since scientists first began searching for marine derivative products, but in the previous several decades, scientists have isolated over 3,000 novel chemicals from marine sources and evaluated them for their potential to fight cancer (Hong Cui et al., 2020). Many bioactive chemicals found in marine environments that exhibit anticancer properties have been extracted, described, recognized, and evaluated at the preclinical level; some of these compounds are now being tested in human clinical trials. Bioactive chemicals and therapeutic agents have been difficult to come by, but marine natural resources have recently been recognized as the most promising source. In recent decades, marine organisms have been identified as a source of natural compounds known as secondary metabolites (Chin et al., 2006). When compared to primary metabolites like carbohydrates, amino acids, and fatty acids, which are chemically nearly identical across all organisms, secondary metabolites have a greater degree of chemical diversity and have traditionally been viewed as metabolic waste products or the remains of primary metabolic overflow with no obvious biological function. Recent advances in underwater technology and the establishment of ecologically relevant bioassays have contributed to marine chemical ecology's reputation as a relatively new field. "This is because researchers have only recently begun looking into the natural compounds that mediate interactions between marine invertebrates."

The bioactive compounds found in sea extracts have been linked to a variety of therapeutic medicinal benefits, including antiangiogenic, anticoagulant, antihypertensive, anti-inflammatory, antimicrobial, antioxidant, antithrombotic, antitumor, and wound healing (Chen et al., 2011). Many creatures, such as tunicates, sponges, soft corals, bryozoans, cephalopods, and echinoderms, have had bioactive chemicals isolated, described, and purified from them. Marine holothurians, which are echinoderm invertebrates with spiky skin, are one such economically significant category. Therefore, several bioactive chemicals that may improve health and serve as innovative medications may be isolated from marine fauna (O. Cuvillier, 2002).

II. BIOACTIVE METABOLITES OF MARINE ORGANISMS

More than 12,000 unique compounds were identified from marine species in 2001 alone (Mendola, 2003), demonstrating the marine environment's importance as a source of bioactive metabolites. Members of the phylum Porifera are the most prolific producers of such natural products among marine species, with 247 (or 36%) of the 677 newly reported compounds in 2002 coming from sponges.

Few compounds have made it to the latter phases of clinical trials despite the large number of novel bioactive metabolites derived from marine sponges (Newman et al., 2000). "This is because many of the bioactive metabolites found in sponges are very poisonous, which in turn results in a poor therapeutic index."

Some characteristics of sponges make them promising for the creation of immortal cell lines; nevertheless, all previous efforts to do so have failed, and only primary cell lines have been generated. Sponge tissue culture (primmorphs) is another approach that has been investigated, although there is still a lot of room for improvement. Cloning the genes responsible for bioactive metabolite synthesis into fermentable microorganisms is a promising new area of marine biotechnology. Several scientists have attempted to cultivate marine sponges in their natural environments. In these studies, sponges were maintained in recirculated systems where environmental factors were carefully managed. Sponge studies have shown great rates of survival, but low rates of growth.

Some of the secondary metabolites found in the genus Negombata (formerly Latrunculia) of sponges include macrolides (latrunculins), pyrroloiminoquinone alkaloids (discorhabdins) (Li F et al., 2020), terpene peroxides cyclic 2-oxecanone glycosides, diterpenes, ceramides, and peptides. Microfilament disruption, anticancer properties, antiviral properties, antiangiogenic properties, antimigratory properties, and anti-cancer properties were all seen in latrunculins. Antimicrobial, immunomodulatory, caspase-inhibiting, antiviral, feeding-deterrent, and antimalarial characteristics have been shown in pyrroloiminoquinone alkaloids, and these compounds also have significant in vivo inhibitory potential against mammalian topoisomerase II. Other chemical entities from the genus Negombata have been shown to have pharmacological properties such as cytotoxicity, antifeeding, antiepileptic, and anti-inflammatory, as well as powerful inotropic effects and blockage of the cardiac Na/Ca exchanger.

The organic extract of the sponge Negombata magnifica was analysed as part of our expanding efforts to identify biologically active leads among marine resources.

III. VARIOUS BIOLOGICAL APPLICATIONS OF MARINE SPONGES

Sponge research holds great promise for finding a solution to the rising (or prospective) prevalence of new infectious illnesses in humans (Dikid et al., 2013).

Anti-inflammatory, anti-tumor, immuno-suppressive, cardiovascular, neuro-suppressive, muscle-relaxing, anti-viral, anti-malarial, anti-fouling, antibiotic, and fungicide properties have all been shown in sponges (Anjum et al., 2016). Thakur and Muller (2004) note that Ara-C (Arabinosysl Cytosine), an anti-tumor chemical sold by Pharmacia & Upjohn Company under the trade name Cytosar-UR, was isolated from sponges. In addition, they may be able to kill off malaria parasites, bacteria, and cells (Pedpradab et al., 2010).

Some sponges' secondary metabolites have been shown to be cancer- and disease-fighting (Longakit et al., 2005). They suppress the growth of hepatocellular carcinoma, colorectal carcinoma, and breast adenocarcinoma cells (Elhady et al., 2016) and are anti-tumor (Gordaliza, 2010). It has been suggested that their pumping activity is crucial in the treatment of psoriasis

(Pietschmann et al., 2004), as an antifoulant (Riberio et al., 2012), in cosmetics (Swatschek et al., 2002), in marine environmental bioremediation in integrated aquaculture practices (Milanese et al., 2003), in bioremediation in polluted sea water (St To that end, they are included into the production of silver nanoparticles (Inbakandan et al., 2012), which are being studied as potential innovative cancer therapies (Ong et al., 2013). (KirubaSankar, et al., 2016) say that sponges may be used as bioindicators of pollution levels. They may be used as a source of antibiotics for controlling shrimp illness (Selvin and Lipton, 2004a).

It is also well-documented that sponges play a significant role in keeping coral reefs thriving. Antimicrobial activity (Vijayalakshmi, 2015), mosquito larvicidal activity (Sonia and Lipton, 2012), anti-inflammatory activity (Kumar et al., 2014), immunomodulatory activity (Krishnan and Keerthi, 2016), anti-tumor activity (Chairman and Singh, 2013), and anti-cancer activity have all been studied in Indian sponges and their associated microbes. Implications for bioprospecting and ecology resulting from the interactions between sponges and microbes were also highlighted (Selvin et al., 2010). Painters, lithographers, janitors, artists, leather workers, window cleaners, car mechanics, tile setters, and hospitals are just some of the various industries that rely on sponges (Stevely et al., 1978). Bell (2008) reviews the research on the several functions played by sponges, including bioerosion, reef formation, substrate stability, carbon cycling, silicon cycling, nitrogen cycling, primary production, secondary production, camouflage, etc. The potential uses of sponges are vast; the problem is getting enough biomass (Thakur & Muller, 2004) since these invertebrates only create little amounts of metabolites.

Some sponges, including Tethya citrina (Bari et al., 2014), Spongia tubulifera and S. pertusa (Oronti et al., 2012), Stylissa massa, Neopetrosia spp. (Schiefenhovel and Kunzmann, 2012), Dysidea avara, Chondrosia reniformis (Osinga et al., 2010 Sponge larval culture (Decaralt et al., 2003), deep water boreal sponge Geodia barretti (Hoffmann et al., 2003), mariculture of fishes (Sea bass) with spong, Ephydatia fluviatilis (Francis et al., 1990), Aaptos suberitoides, Amphimedon paraviridis, Callyspongia biru, Hyrt Since sponges are slow growing creatures, at least a year or two of culture time would be needed to produce a commercially viable size.

Cultivation of Marine Sponges in India

Narinder Chadha (2017) assesses the value of marine sponge cultivation in the context of pharmaceutics and drug discovery. Despite widespread recognition of sponges' potential for medicinal use, the practice of sponge mariculture remains largely untapped in India. Since sponges yield very low number of bioactive compounds, mariculture technologies need to be standardized to ensure steady supply of sponges in required quantities without disturbing the wild sponge populations, which produces bioactive metabolites that have potential applications in drug development. Several prospective sponges in India are highlighted in the study, including Stylissa massa, Hyrtios erectus, Mycale sp., Dysidea sp., and Plakortis sp., all of which have been shown to have significant bioactive potential and might be pursued in mariculture. Aquaculture potential,

including those involving the use of sponges, are also highlighted. Marine species, especially sponges, show great potential in addressing crucial difficulties in medication development in light of the rise of rare and uncommon illnesses. Without harming their natural population, the reviewers stress the need of showing that mariculture technology may be used to prospective candidate marine sponges in India in order to meet the pharmaceutical demands.

Natural goods derived from marine sponges are plentiful and vital. One way to alleviate the 'supply problem' that impedes research into the creation of new chemicals from sponges is via mariculture. Three species of sponges, Negombata magnifica, Amphimedon chloros, and Theonella swinhoei, were cultured for a lengthy period of time (767 days) in the ocean at depths of 10 and 20 m, and the resulting latrunculin-B, halitoxin, and swinholide-A were reported by Bergman, Oded et al., 2011. "In order to determine whether or not the stability of the bacterial communities in cultivated vs wild sponges is related to sponge health, we investigated whether or not sponge-associated microbes are the genuine manufacturers of many of the natural compounds present in sponges." The sponges' growth rates varied greatly across species (from 308 to 61 and -19 (%) (year (-1) in N. magnifica, A. chloros, and T. swinhoei, respectively), but not between the two depths at which the species were cultured. Inconsistent survival rates ranged from 96% to 57%. All species cultured throughout this study still contained the target natural substance. Sponge-associated bacterial consortiums were analyzed by denaturing gradient gel electrophoresis, which demonstrated that T. swinhoei and A. chloros had different communities in cultivated and wild sponges. N. magnifica was the best candidate for the culture approach for natural product production, whereas T. swinhoei and A. chloros were less successful due to lower growth and survival rates and changes in their bacterial consortiums.

There are 584 species of marine sponges in India, divided among 288 genera and 81 families, all of which belong to 21 different orders. As a result, this accounts for 30% of all animal species on Earth. Andaman and Nicobar Islands, Lakshadweep, and the East and West Coasts are all highlighted for their unique characteristics. Sponge diversity is higher in the East Coast, particularly in the Gulf of Mannar, than it is along the West Coast. This research examines the sponge resources and ecological connections across different environments. Possible solutions to the decline in sponge growth and future cultivation methods are presented. Sponges have economic and biomedical importance, and threats to sponge biodiversity are highlighted (Sivaleela, Gunasekaran, & Venkataraman, Krishnamoorthy, 2007).

In his 2017 study, Philip Nemoy delves into the connections between marine sponge biology and the long-term viability of sponge mariculture. The current thesis investigates one approach to achieving these goals, which is essential for the long-term sustainability of maricultural practices. The Integrated Multi-Trophic Aquaculture (IMTA) strategy recommends co-cultivating organisms from various trophic levels in close proximity to each other in order to improve the environmental performance of mariculture. The "fed species" (such as predator finfish) are grown alongside 'extractive species' (organisms from lower trophic levels) such as primary producers, filter-

feeders, and detritivores in IMTA. Feeding wastes into extractive organisms as a source of energy and/or nutrients lowers organic and inorganic effluents and improves the environment for the development of extractive species. Production from IMTA may be increased by making advantage of the goods and services provided by extractive organisms. In addition to marine and land-based mariculture of finfish, the current research explores the possibility of cultivating sponges as extractive organisms.

IV. BIO ACTIVE PROPERTIES OF NEGOMBATA MAGNIFICA

Negombata magnifica, commonly known as **toxic finger-sponge**, is a species of sponge found from the Red Sea and the Indian Ocean. Its reddish-brown narrow crooked branches can grow up to 70 centimetres (28 in). *Negombata magnifica* is extremely toxic because of the toxin latrunculin.

Table 1: Scientific classification of the sponge

Kingdom	Animalia
Phylum	Porifera
Class	Demospongiae
Order	Poecilosclerida
Family	Podospongiidae
Genus	Negombata
Species	Negombata Magnifica
Common Name	Toxic Finger sponge

The Negombata magnifica may be found in the northern Red Sea, on shallow coral reefs. In contrast to the majority of the sponges found in these waters, Negombata magnifica prefers to grow out in the open, rather than hiding between corals and rocks or even beneath the surface. Fish in the area avoid it, protecting it from harm. Touching it causes it to secrete a pungent, scarlet liquid that drives the fish away immediately. Artificial cultivation of Negombata magnifica for the extraction of latrunculin has been documented (Lieske, Ewald; Myers, Robert 2004).

Red Sea and Indian Ocean negrombatica magnifica. It may to a height of 70 centimeters (28 inches), with a trunk that is reddish brown and thin and twisted. The latrunculin in Negombata magnifica makes it very poisonous.

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Fish in the area avoid it, protecting it from harm. Touching it causes it to secrete a pungent, crimson liquid that drives fish away immediately.

Source: https://encrypted-tbn2.gstatic.com/licensed-image?q=tbn:ANd9GcT3bp2iuTyCDMd5kpqlFb5TmYWRNERtsHoF4m53x-Z4q-hodPEgnmWFJN0qJStAeE0R-Ru4f60ZtjpqfG4

There is a growing need for innovative medication treatments, thus researchers are exploring marine creatures for bioactive compounds with therapeutic potential. One such creature is the sea sponge, which belongs to the improbable phylum Porifera. Sea sponges, which lack a brain and central nervous system, get along with the help of specialized cells. These primitive organisms have developed defense mechanisms that use poisonous compounds to ward off predators, and these same chemicals may be deadly to human cancer cells and microorganisms due to their structural simplicity and sedentary lifestyle (El-Naggar et al., 2022). Negombata magnifica (finger sponge) and Callyspongia siphonella (tube sponge) were the subjects of a research published in Applied Sciences. This built on prior research showing that all eight finger-sponge and tube-sponge extracts tested induced cell death and suppressed proliferation in liver, breast, and colorectal cancer cell lines (El-Naggar et al., 2022).

This new study focused solely on the methanolic extracts of Negombata magnifica (NmE), a type of sponge, whereas the previous one had used four different solvents to produce sponge extracts.

NmE dose-dependently impeded their growth by inducing cell cycle arrest in the liver cancer lines by inhibiting the cell division protein CDK6. D1 and E1 cyclins, which govern cell cycle progression, were likewise inhibited, halting mitotic development in all three cell types (Alao, 2007). Furthermore, NmE induced apoptosis in all cell lines by increasing Bax (a pro-apoptotic regulatory protein) and caspase-3 (a death protease that cleaves cellular proteins) and decreasing BCL2 (an anti-apoptotic regulatory protein) (Blanco and Garca-Sáez, 2018). Evidence for this may be found in (Ponder & Boise, 2019; Youle & Strasser, 2002). When tested for its antibacterial efficacy, NmE showed a positive response to just two strains (El Naggar et al., 2022).

NmE's cancer-fighting qualities suggest it might one day be used to treat the disease in humans.

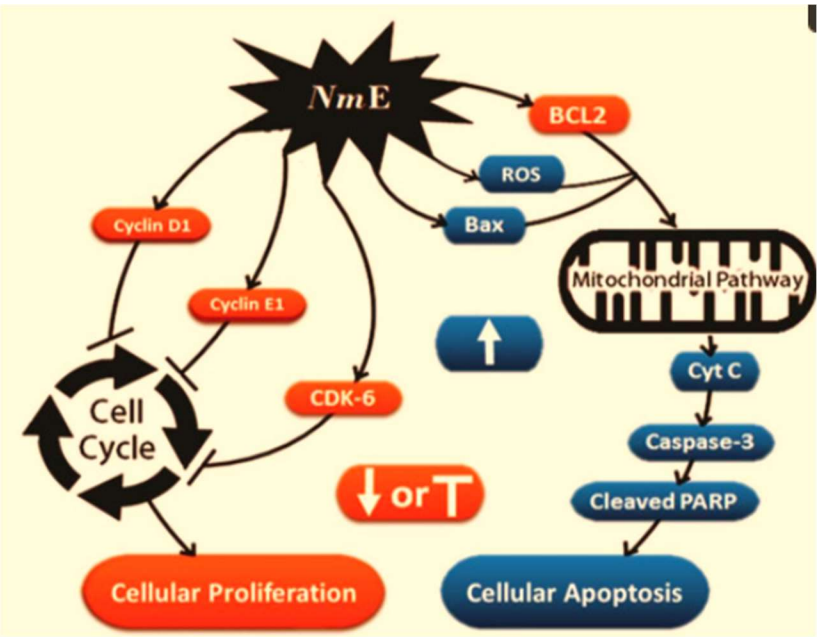
Fenretinide and ethyl iso-allocholate, for example, have been linked to anti-COVID-19 action (Orienti, et al., 2020; Poochi et al., 2020), however neither is active against cancer nor microorganisms. Given that roughly 80% of the compounds have not been linked to anti-cancer or anti-microbial mechanisms, the study highlights the importance of exploring Earth's oceans as potential sources of bioactive compounds and utilizing the biological potential of marine organisms in the creation of novel drug therapies.

V. ANTI CANCER PROPERTIES OF MARINE EXTRACTS: SPECIAL FOCUS ON NEGOMBATA SPECIES

The research conducted by El-Naggar et al. in 2022 is a continuation of our earlier studies in which we evaluated the antiproliferative and pro-apoptotic effects of crude extracts of the sponges Negombata magnifica (NmE) and Callyspongia siphonella (CsE) on cancer cells. Here, we contribute to our earlier research on these sponge species, which relied on a different methanol extraction technique, by providing more recent molecular biochemical evidence supporting N. magnifica and C. siphonella's anticancer and antibacterial properties. Sponge samples were so gathered from the Dahab area of the Gulf of Aqaba during the winter of 2020. The crude extracts, NmE and CsE, were obtained by macerating each sponge with methanol. A total of 117 chemical compounds were identified by GC-MS analysis, of which 37 were biologically active, 11 had previously been identified as components of a wild organism, and 69 did not exhibit any biological activity. Contrary to CsE, which sadly lacks any antiproliferative effect against the same cancer cell lines HepG2, MCF-7, and Caco-2 carcinoma cell lines, NmE dose-dependently suppressed the proliferation of these cancer cell lines. With its suppression of CDK6, Cyclins D1 and E1 in HepG2, MCF-7, and Caco-2 cells, NmE was reported to cause G0/G1 cell cycle arrest in HepG2 cells. By increasing pro-apoptotic proteins Bax, caspase-3, and cleavage PARP and decreasing anti-apoptotic protein BCL2, NmE also stimulated ROS generation in HepG2 cells and caused apoptosis in HepG2, MCF-7, and Caco-2 cells. Contrary to its anticancer potential, CsE clearly outperformed NmE as an antimicrobial agent with a broader range when tested against six microbial strains, whereas NmE shown good antibacterial activity only when tested against two strains.

The antiproliferative activity of Negombata magnifica was examined using petroleum ether extract (PE), total methanolic extract (ME) and two sub-fractions II and III, isolated pure compounds (palmitic acid and pregnanediol), sponge mesohyl, and primmorphs ethyl acetate extract in the study by Rady et al., (2016). The positive control utilized was palmitic acid. MTT test was used to measure the vitality of the cells, while DNA fragmentation and BCl2 gene expression were used to study apoptosis. Using flow cytometry, cell cycle analysis was carried out. PE's GLC analysis showed that it includes 84.46% hydrocarbons, 15.54% sterols, and 61.38% unsaturated fatty acids in contrast to 38.62% saturated fatty acids. Results showed that all treatments had cytotoxic effects with the exception of pregnanediol and fraction II. While fraction II stopped the cell cycle in G2/M, the primmorphs ethyl acetate extract and fraction III arrested cells in G0-G1. Cells were halted in G0-G1 and G2/M by PE extract. While ME and pregnanediol may have demonstrated pro-apoptotic effects by lowering BCL2 expression even if no DNA ladder was seen, mesohyl, PE, and fraction III may be apoptotic agents as evidenced by DNA fragmentation independent of BCL2 expression.

According to Rady, Islam and Bashar, Mansour's (2020) research, extracts from marine creatures have been found to offer a variety of anti-cancer effects. The finger sponge ‘Negombata magnifica (Nm)’ and the tube sponge ‘Callyspongia siphonella (Cs)’ were obtained from the Gulf of Aqaba (Red Sea, Egypt) during the summer of 2020. Each sponge macerated with methylene chloride (CH2Cl2), ethyl acetate (C4H8O2), acetone (C3H6O), and chloroform ($CHCl_3$) separately into four different crude extracts for each sponge species and eight extracts as a total for both marine species, where each extract was in vitro assessed for its antiproliferative and proapoptotic activity in HepG-2, MCF7, and Caco-2 cancer cell lines. HepG2 cancer cells were inhibited by Cs-CH2Cl2, Cs-C4H8O2, Cs-C3H6O, Cs-CHCl3, Nm-CH2Cl2, Nm-C4H8O2, Nm-C3H6O, and Nm-CHCl3 within IC50 values of 17.53, 11.18, 9.97, 19.21, 9.14, 10.94, 8.78, and 7.23 g/m Additionally, it was shown that all extracts increased the proapoptotic proteins Bax and caspase-3 and decreased the anti-apoptotic protein Bcl-2 in HepG2, MCF-7, and Caco-2 cancer cells, causing them to undergo apoptosis. Recent research identifies numerous extracts from two marine sponges as potential sources for future cancer therapeutic agent development.



Source: https://www.researchgate.net/figure/Schematic-drawing-of-the-mechanism-of-action-of-NmE-This-carton-is-based-on-the-current_fig8_358188229

Schematic drawing of the mechanism of action of *Nm*E

Hemimycale arabica (blue sponge) and Negombata magnifica (red sponge) mesohyls were tested for their anticancer efficacy in a rat model of hepatocellular carcinoma (HCC) by Ahmed et al., 2018. Forty adult female albino rats were split into five groups: (1) control; (2) HCC; (3) Doxorubcin (DOXO); (4) mesohyl of H. arabica; and (5) mesohyl of N. magnifica. The levels of a variety of serum enzymes including bilirubin, AFP, and CEA were measured. Liver tissue slices were examined histopathologically. Serum levels of AST, ALT, GGT, AFU, bilirubin, AFP, and CEA were all shown to be significantly higher in HCC-affected rats compared to control rats. DOXO therapy of HCC-inflicted rats resulted in no discernible changes to serum AST, ALT, and GGT activity, or bilirubin levels. Serum levels of AFU, CEA, and AFP were significantly reduced after therapy with DOXO compared to HCC patients. When compared to untreated HCC rats, biochemical parameters were significantly muted after treatment with mesohyl blue (Hemimycale arabica) or red (Negombata magnifica) sponges. The structural organization of the livers of the treated rats much improved, attesting to the beneficial effect of the natural remedies. Experimental evidence for the antitumor potential of Hemimycale arabica and Negombata magnifyica mesohyls in a rat model of HCC is presented here. This effect may be attributed to the active constituents' potent hepatoprotective activity, powerful free radical scavenging ability, and highly apoptotic property.

According to research by Hadas et al., (2005), marine sponges contain bioactive metabolites that have the potential to serve as lead molecules in the treatment of a wide range of human ailments.

Few of these drugs have advanced to clinical trials because of the difficulties in producing a consistent supply of such metabolites. One of the most promising approaches to solving this supply issue is sponge marine ranching. The cytotoxin latrunculin B (lat-B) may originate from the Negombata magnifica sponge found in the Red Sea. The study's overarching goal was to uncover potential growth and survival rate boosters for N. magnifica by comparing the effects of several marine ranching culture techniques. Since making bioactive metabolites is the project's end objective, we determined how much lat-B was present in the sponge tissues. Nineteen different people's bones were broken and strung together on PVC plates or fishing line. The threaded sponges were hung on horizontal ropes, while the PVC-attached sponges were secured to plastic netting. Both 10 and 20 m depths were supplied for these procedures. The average sponge grew from 11.6F0.7 to 24.5F2 gr over the course of 177 days, and the weighted mean survival rate across all treatments was 71.4%. When compared to sponges that were linked to the net, the specific growth rate (SGR) of those that were hung on nylon threads was considerably (Pb0.05) greater (0.9F0.08% day 1 vs. 0.5F0.05% day 1). There was no statistically significant difference (p>0.05) in the growth rate between the two stocking densities. The SGR of sponges produced in the presence of fouling organisms was lower than that of sponges grown in the absence of fouling organisms by a statistically significant amount (p0.05) (0.26F0.07% day 1 and 0.55F0.09% day 1, respectively). Sponge bodies cultivated for a year in the marine ranching system had 1.2–0.16 times the quantity of latrunculin B previously observed for this species (0.35 mg lat-B gr dry matter sponge 1). "This study shows that N. magnifica may be cultivated in marine ranching systems with acceptable survival and growth rates in order to produce lat-B."

In addition to the well-known latrunculin B (4) and 16-epi-latrunculin B (5), research into the Red Sea sponge Negombata magnifica yielded two novel alkaloids, magnificines A and B (1 and 2), and a new -ionone derivative, ()-negombaionone (3). The relative configurations and planar structures of the compounds were validated using NMR and HRESIMS spectral spectroscopy. By comparing the theoretical and practical ECD spectra, we were able to identify the precise configurations of magnificines A and B. Magnificines A and B include a tetrahydrooxazolo[3,2-a] that has not been described before. azepine-2,5(3H,6H)-dione backbone and are the pioneering examples of this family of natural chemicals. First of its kind, ()-Negombaionone was isolated from a sponge. In a disk diffusion experiment, compounds 1-3 showed selective action against Escherichia coli, with inhibition zones of up to 22 mm at 50 g/disc and MIC values as low as 8.0 M. The proliferation of HeLa cells was reduced by latrunculin B and 16-epi-latrunculin B with IC50 values as low as 1.4 M (Diaa et al., 2021).

Cancer cure and therapy remain a tough issue despite massive investments in research and substantial efforts and achievements in the quest for novel anticancer medications in recent decades. In the search for new molecular treatments, the oncological field has looked in many different places, including plants, animals, and minerals. A variety of secondary metabolites found in marine sponges have shown promising tumor chemopreventive and chemotherapeutic capabilities. Recently, medications produced from marine sponges have been licensed by the Food

and Drug Administration (FDA) to treat metastatic breast cancer, malignant lymphoma, and Hodgkin disease. Multiple cellular and molecular mechanisms, such as DNA protection, cell-cycle modulation, apoptosis, and anti-inflammatory activities, as well as the ability to chemosensitize cancer cells to conventional antiblastic chemotherapy, may account for the chemopreventive and potential anticancer activity of compounds derived from marine sponges. This review paper by Calcabrini et al. (2017) seeks to illustrate the many processes at play in the chemopreventive and therapeutic actions of marine sponges, as well as to critically examine the constraints and difficulties inherent in the creation of a marine sponge-based anticancer approach.

The Red Sea sponge Negombata corticata (Carter) was used to identify and describe two novel metabolites, corticaglyceride (1), a diglyceride ester, and corticaceramide (5), a sphingolipid. Cholesterol (4), 24-methylenecholesterol (3), and nervonic acid (2) were also isolated for the first time from this species. "The unsaponifiable substance was found to have a high concentration of hydrocarbons (89.474%), with n-hexacosane being the most abundant component (10.979%), according to GLC analysis." Additionally, the found sterol accounts for 7.162%. Fatty acid methyl esters were analyzed using GLC, and nervonic acid was found to make up the majority (73.782%). In addition to the weak anti-oxidant effects shown by compounds 1 and 5, anti-inflammatory activity was also seen in compound 3.

Isolated and described from the Red Sea sponge Negombata magnifica, latrunculeic acid (3) is a new counterpart of latrunculin B (2a). Latrunculin B (2a), 15-methoxylatrunculin B (2b), 16-epi-latrunculin B (4), and latrunculin C (5), as well as many other recognized chemicals, were also isolated. The new chemical 3 is a polyketide unlike any other member of the latrunculin family (Vilozny et al., 2004), lacking the typical macrocyclic and thiazolidinone rings.

El Tamany et al. (2014) conducted study on Egyptian marine resource extracts in response to recent pharmaceutical advances. High potential was observed in extracts from five different sponge species, including Spheciospongia vagabunda (SAA-14), Negombata corticata (SAA-8), and Negombata magnifica (SAA-64), and two soft coral species, Sarcophyton glaucum (SAA-33) and Sarcophyton auritum (SAA-43). The Sulpho-Rhodamine-B (SRB) test was used to evaluate the cytotoxic potential of these five extracts. When compared to doxorubicin, the positive control, the anticancer activity of SAA-8, SAA-14, SAA-33, SAA-43, and SAA-64 was significantly increased at concentrations ranging from 16.3 to 19.3 g/ml in the liver cancer cell line and 24.7, 19.7, 18.7, 21.1, and 25.8 g/ml in the breast cancer cell line. In vitro studies showed that extracts derived from the plants Negom batacorticata and Sarcophyton auritum were effective against fungus belonging to the genera Candida, Cryptococcus, and Aspergillus. Negombata corticata is effective against TB, malaria, and lyme disease.

According to research by Ye, Jianjun et al. (2014), marine sponges are one of the best places to find chemicals with anticancer properties. Sponge and microbial communities produce about 5,300 unique compounds. Most sponge species have developed chemical defense mechanisms to help

them survive in the harsh sea environment. Secondary metabolites, such as those with anticancer properties, are produced as a result of this chemical adaptation. This article summarizes the last five years' worth of research on the unique secondary metabolites in sponges that have been shown to inhibit several cancer types. The chemical properties used to classify these marine sponge natural products.

The Negombata corticata sponge found in the Red Sea yielded a novel ceramide combination 1 with antiepileptic properties. Extensive spectroscopic investigation was used to identify the structures of the metabolites. Using the pentylenetetrazole-induced seizure paradigm, the anticonvulsant activity of 1 was evaluated in vivo. This result has significant ramifications for the use of this class of chemicals in biological research (Ahmed et al., 2008).

New potential therapies for a wide range of ailments may often be found in maritime environments. Several marine-based pharmaceuticals are now on the market as a consequence of earlier attempts to develop marine-derived anticancer medicines. Anticancer medications developed from MNPs have an estimated pharmaceutical value of $563 billion to $5.69 trillion. In this overview, we focus on a few marine-derived substances having the potential to control and prevent cancer by blocking key tumor cell motility and/or migratory processes in cancer metastasis. The paper also discusses the primary challenges that the MNP research scientific community often faces (Mudit, Mudit, & El Sayed, Khalid. 2016).

Recent years have seen an uptick in research on the potential anticancer effects of several bioactive components found in marine species (Rady, Islam, 2020). We obtained ethanol extracts from the black-spotted sea cucumber (Pearsonothuria graeffei), the lollyfish (Holothurus atra), and the sea hare (Aplysia dactylomela) that we caught in the winter of 2019 in the Gulf of Aqaba, Red Sea, Egypt. We tested the efficacy of these extracts against HepG2, HCT-116, and MCF-7 cancer cells in vitro. HepG2, HCT-116, and MCF-7 cells were all dose-dependently inhibited by PgE, with IC50 values of 16.22, 13.34, and 18.09 g/mL, respectively, while HaE's antiproliferative activity had IC50 values of 10.45, 10.36, and 10.48 g/mL, and AdE's IC50 values were 6.51, 5.33, and 6.87 g/mL. In addition to inhibiting CDK2 in all three cell lines, all extracts were found to induce G0/G1 cell cycle arrest in HepG2 cells and pre-G1 apoptosis in HepG2 cells, demonstrating anticancer activity through upregulation of proapoptotic proteins Bax, caspase-3, and cleaved PARP, and downregulation of antiapoptotic proteins Bcl-2. In addition, necrosis is an additional anticancer activity for each extract, as it has been largely seen in the HepG2 cell line. Based on our findings, three marine extracts preserved in ethanol may be further explored as potential natural chemotherapeutic agents for cancer prevention and treatment.

Using specialized antibodies, researchers were able to pinpoint exactly where in the sponge Negombata magnifica of the Red Sea latrunculin B is stored. Antibodies from rabbits were isolated using a latrunculin B-Sepharose affinity column after being inoculated with a latrunculin B-keyhole limpet hemocyanin (KLH) conjugate. Light and transmission electron microscopy

analysis of immune histochemical and immune gold-stained sponge sections showed latrunculin B labeling mostly underneath the sponge cortex at the ectosome-endosome boundary. The boundary was more clearly demarcated than the endosome. Sponge cells, but not their prokaryotic symbionts, were shown to have latrunculin B by immunogold localization. Labeling was denser in archeocytes and choanocytes. Archeocytes and choanocytes had many vacuoles, perhaps secretory or storage vesicles for latrunculin B, that were prominently identified by the antibodies. Defense against external epibionts, predators, and rivals may include peripheral latrunculin B (Gillor, Osnat. et al., 2000).

Novel medications and prototypes might be made from Red Sea sponges. Sponges belonging to the genus Negombata may be found in great numbers in the Red Sea (Eid, Eman, et al., 2011). Antitumor action in the form of latrunculins produced by this sponge has been seen and reported. Negombata species are classified according to their morphology and the microscopical analysis of spicule megascleres. However, identification based on these characteristics has shown to be inaccurate. This work was designed to compare the molecular and protein profiles of the two Negombata species, N. magnifica and N. corticata, with the spicules-based taxonomy. The cytochrome c oxidase I gene, which is around 700 base pairs long, was sequenced from both Negombata species. In addition, total proteins were extracted from Negombata samples collected at various times of the year and places and separated by denaturing polyacrylamide gel electrophoresis. Protein profiles that are characteristically different between the two species were obtained. Different species of Negombata in the Red Sea may be consistently distinguished using data acquired from cytochrome c oxidase I gene sequencing and protein profiling.

VI. DIFFERENT BIOLOGICAL PROPERTIES OF MARINE SPONGES OBTAINED FROM INDIA

In this study, Kumar, Maushmi. (2022) have investigated the antifungal and antibacterial activities of methanol extracts of Cliona, Haliclona cratera, Hyrtios cavernosus, Spongia obscura, Sarcotragus foetidus, and Xestospongia carbonaria and fractions from X. carbonaria S. obscura and H. cratera. The antibacterial activity was determined by agar disc diffusion method against clinical gram-positive- Staphylococcus aureus, Bacillus subtilis and gram negative- Escherichia coli, Pseudomonas aeruginosa bacteria. The antifungal activity of the extracts and fractions was determined against Candida albicans and Aspergillus niger. S. obscura, X. carbonaria, H. cavernosus, and H. cratera exhibited good antibacterial activity against the tested gram-positive bacteria with larger zones of inhibition at 19±6 mm, 19.5±5.5mm, 20±0 mm and 23±0 mm. S. foetidus gave good inhibition of gram-negative bacteria at 19±0 mm. They showed moderate antifungal activities against C. albicans and A. niger. Cliona, H. cratera and H. cavernosus gave inhibition with 20±5 mm, 15.5±0.5 mm and 25.5±14.5 mm for A. niger. The MIC for Xc_PE_2, Sob_n but_1 and Hc_n but_3 was determined. H. cavernosus, S. foetidus, S. obscura and X. carbonaria showed presence of fatty acids and sterol type of compounds. The mass of molecular

ions in purified fractions helped in characterization of known compounds in H. cratera, X. carbonaria and S. obscura which exhibited good antimicrobial activity.

In the study of Chander, Dr. M. Punnam & Vijayachari, Paluru (2018), marine sponges found to possess were effective. To the best of our knowledge, this is the first report demonstrating the antimicrobial activity of the marine spongesfrom Andaman and Nicobar Islands, with few exceptions. These organisms need to investigate in detail, in order to isolate biologically active molecules and thus paving the way to search for novel compounds. Furthermore, the encouraging biological activity observed in this study show that the Andaman and Nicobar Islands are potential source of variety of marine organism's worthy of further investigation.

Kumar, Maushmi. (2016) presents an overview of the development and study of marine sponge's bioactive compounds for anti-inflammatory activity for last four years i.e., 2012-2016. Marine pharmacology during 2009–2011 remained a global enterprise contributing to the preclinical pharmacology of 262 marine compounds which are in pharmaceutical pipeline. There is no updated review for the studies done on marine sponge's compounds showing anti-inflammatory activity after 2011. This chapter is a sincere effort to present a systematic review of the preclinical pharmacology of marine sponge and its associated microbes/symbionts compounds for potential activity in inflammation.

The work of Dhinakaran et al., (2012) describes the biological activities using the marine sponges collected from kanyakumari. The sponges are such as the Callyspongia diffusa, Echinodictyum gorgonoides, Callyspongia reticutis, Gelliodes cellaria, and Thalysias vulpine. It is revealed that the sponges showed the antifungal activity against the various fungal strains such asthe Aspergillus niger, Pencillium notatum, and Candida albicans by using the agar well diffusion method. The sponge crudeextra cts seems to have effective cytotoxic property that was detected by Brine shrimp assay. Hence it i s assumed that the marine sponges act as the vital source for the development of anticancer drug s.

To focus on the isolation and preliminary characterization of marine sponges associated Actinobacteria particularly Streptomyces species and also their antagonistic activities against bacterial and fungal pathogens. The sponges were collected from Kovalam and Vizhinjam port of south-west coast of Kerala, India. Isolation of strains was carried out from sponge extracts using international Streptomyces project media. For preliminary identification of the strains, morphological (mycelial colouration, soluble pigments, melanoid pigmentation, spore morphology), nutritional uptake (carbon utilisation, amonoacids influence, sodium chloride tolerance), physiological (pH, temperature) and chemotaxonomical characterization were done. Antimicrobial studies were also carried out for the selected strains. With the help of the spicule structures, the collected marine sponges were identified as Callyspongia diffusa, Mycale mytilorum, Tedania anhelans and Dysidea fragilis. Nearly 94 strains were primarily isolated from these sponges and further they were sub-cultured using international Streptomyces project media.

The strains exhibited different mycelial colouration (aerial and substrate), soluble and melanoid pigmentations. The strains possessed three types of sporophore morphology namely rectus flexibilis, spiral and retinaculiaperti. Among the 94 isolates, seven exhibited antibacterial and antifungal activities with maximal zone of inhibition of 30 mm. The nutritional, physiological and chemotaxonomical characteristic study helped in the conventional identification of the seven strains and they all suggest that the strains to be grouped under the genus Streptomyces. The present study clearly helps in the preliminary identification of the isolates associated with marine sponges. Antagonistic activities prove the production of antimicrobial metabolites against the pathogens. Marine sponges associated Streptomyces are universally well known for their synthesis of many bioactive compounds such as antibiotics, enzymes, enzyme inhibitors and food grade pigments. They also have certain biotechnological applications like probiotics and single cell proteins. These marine Streptomyces bioactive metabolites can be the futuristic solution for the dreadful diseases (Dharmaraj, Selvakumar & Kandasamy, Dhevendaran 2016).

Annie et al., (2009) defines that Secondary metabolites of the marine sponges Acanthella elongata, Axinella donnani, Callyspongia diffusa, Callyspongia subarmigera, and Echinodictyum gorgonoides were collected from fishing nets and their in vitro antibacterial properties against eight virulent marine fish pathogens were studied at incubation temperatures of 20°C and 30°C. Crude methanol extracts of the tested sponges showed species-specific antibacterial activity. The most active species was A. elongata which inhibited 100% and 87.5% of the tested bacterial isolates at 20°C and 300C, respectively. Callyspongia subarmigera was the least active as it inhibited only 62.5% and 50% of the tested bacteria at those temperatures. Results suggest that fractionation and purification of the crude methanol extract of A. elongata has potential in the development of novel antibiotic substances for managing common bacterial diseases in aquaculture.

Joseph, Baby & Sujatha, s.Sujatha. (2010) describes research on novel natural pharmacological compounds isolated from marine sponges. More than 90 novel cytotoxic antitumor compounds and their synthetic analogs have shown confirmed activity in vitro tumor cell lines bioassay and are of current interest to NCI for further in vivo evaluation. A great problem, to use directly the reservoir of marine organisms for therapy is the very low availability and the isolation of only very small amounts of the biologically active substances from the natural materials. Sponges produce a wide array of secondary metabolites ranging from derivatives of amino acids and nucleosides to macrolides, porphyrins, terpenoids, aliphatic cyclic peroxides and sterols. The purpose of this article is to be present a structurally reviewed the pharmacological activities in marine sponge antitumor and cytotoxic properties of 143 marine natural products, many of them novel compounds that belongs to the family of porifera possessed the various species diverse structural classes, including polyketides, terpenes, steroids and peptides. Finally, this 2009 overview of the highlights the fact that the discovery of novel some pharmacologically important of novel naturally presented chemical compounds isolated from a wide variety of marine sponges. Naturally, the following pharmacological compounds such as Monomeric, oligomeric and polymeric 3-alkylpyridiniums,

amino acids and nucleotides to macrolides, porphyrins, terpenoids to aliphatic cyclic peroxides and sterols, the majority of which are related to sponges and 3-alkylpyridines comprise a group of biologically active compounds found in several sponges. This review will present some of the aspects of the medicinal chemistry developed recently to introduce such modifications. The structures, origins, synthesis and biological activity of a selection of N-heterocyclic marine sponge alkaloids are reviewed. The emphasis is on compounds poised as potential anticancer drugs: pyrroles, pyrazines, imidazole, and other structural families.

The sponge Sigmadocia fibulata was collected during low tides from West Coast of Mumbai. Crude extract was obtained by taking 10 gram of sponge samples in10 ml of methanol. In the investigation of Bhadekar, N & Zodape, Gautam. (2021) we found the crude protein contents in Sigmadocia fibulata as 0.096 mg/mL. The Neuromodulatory Na (+)-K+ ATPase activity and AChE on Sprague dawley rat brain and chicken brain extract may brain may contribute to the pathogenesis of metabolic complications of the central nervous system, and that the undetectable enzyme activity in chicken brain convulsing chicken brain may result from considerable damage or necrosis of brain tissue during seizures. In AChE our study is evident that both the sponge extract showed enzyme inhibitor activity at certain concentrations. In hemolytic activity showed potent toxin which is responsible for hemagglutination. Hemagglutination activity is generated by the presence of protein and the protein found in sponges which usually show hemmaglutination activity that might be because of presence of lectin which showed hemolytic activity. In CAM study showed that methanolic extract has strong antiangiogenic activity. "The protein bands showed lectins have variety of effects on cells, such as agglutination, mitogenic stimulation, redistribution of cell surface components, modifying the activity of membrane enzymes, inhibition of bacterial and fungal growth, cell aggregation, toxicity, immunomodulation."

VII. CONCLUSION

Sedentary marine sponges are colonized by a wide variety of species and invaders, forcing them to develop a suite of chemical defences. Successfully counteracting the wide range of threats posed by invaders and aggressors requires the production of a wide range of cytotoxic chemicals. Therefore, scientists might draw inspiration for the development of new anti-cancer drugs by studying the structural chemistry of such marine natural chemicals. As more is learned about the chemicals extracted from marine sponges and their capacity to target specific stages in the carcinogenetic process, these compounds show promise as potential new tools for preventative and therapeutic treatments. Based on the results presented here, derivatives of Negombata magnifica might be a useful source of anticancer chemicals. Potential antitumor activity of the compounds presented here was elicited via multiple mechanisms, including cell-cycle arrest, anti-inflammatory activity, apoptosis, ER stress induction, and interaction with numerous targets involved in the progression of cancer, such as the mitochondrial membrane, PARP, cytochrome c, Akt, and caspases.

We anticipate that providing a comprehensive account of the synthesis and cytotoxic activity will be invaluable to medicinal and synthetic chemists as they work to develop structure-activity relationship techniques for the future creation of new anticancer medicines for the treatment of various malignancies. Therefore, future studies should evaluate and utilize the clinical anticancer potential of the most promising candidates derived from marine sponges, weighing their broad-spectrum efficacy and toxicity to precisely define their risk-benefit ratio.

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