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Review Article

Marine sponge's biological activities: Their Biotechnological Uses

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Abstract: The most of the time, marine sponges are an invertebrate species found in the tropics, subtropics, and temperate zones of the oceans and seas. They are acknowledged as being among the most important sources of bioactive chemicals, which are found in marine habitats and can then be recovered from those settings. These bioactive chemicals are found in marine environments and can then be extracted from those environments. It is common knowledge that the chemicals that are extracted from these sponges demonstrate a wide range of bioactivities, such as antibacterial activity, anticancer activity, and general cytotoxicity. These bioactivities can be found in the isolated chemicals. In this article, we discuss the bioactive chemicals that have been found in marine sponges and their potential applications. These compounds have the potential to serve as antibacterial, antiviral, and antimalarial agents against human infections as well as fish pathogens in the aquaculture industry. In addition, these compounds may also operate as antifungal agents. Sponge organisms found in the ocean have also been shown to have these chemical compounds. This article discusses the importance of marine sponges to the fields of chemistry, microbiology, cell biology, and molecular biology from a biotechnological standpoint. Researchers of marine natural products have discovered new potential medications as a result of their efforts to exploit the remarkable chemical variety that can be found in sponges.

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INTRODUCTION

Most marine invertebrates are aquatic, such as sponges, bryozoans, cnidarians, echinoderms, and tunicates (Grosberg et al., 2012). They lack morphological defenses like thorns or shells, have soft bodies, move slowly or are sessile (Proksch, 2018). As a result, these species developed chemical defense mechanisms to shield them against predators and the emergence of dangerous microbes (Hay, 1996; Hentschel et al., 2002).
Sea sponges have been the subject of the majority of studies using bioactive secondary metabolites (Porifera). Because sponges are such good filter feeders, the microorganisms in the waters around them are actively stirred up by the fluxes of currents that are driven by sponges. Some of the bacteria are digested right away, while others are stored within the body of the sponge for later use. It has been demonstrated that related microorganisms, which are more diverse than can be assessed using the methods that are currently available, can contribute up to sixty percent of the fresh weight of marine sponges (Wang, 2006; Hardoim et al., 2009). It is believed that unicellular algae, cyanobacteria, bacteria, and fungi may contribute to the creation of natural compounds acquired from sponges. This is despite the fact that the link between the sponge and related microorganisms is exceedingly complex (Proksch et al., 2002).
On the other hand, among marine invertebrates, sponges are the species that have received the most attention from researchers, and a wide variety of bioactive compounds have been extracted from them (Hu et al., 2015). In the marine environment, these molecules are sometimes referred to as a chemical factory due to the massive manufacturing of a wide variety of chemical compounds that they are responsible for. These compounds, in addition to displaying an astonishing range of chemical properties, are also notable for the bioactivities they exhibit (Kim and Dewapriya, 2012). In addition to this, it was believed that they were a rich source of chemical compounds and antibiotic metabolites that have long-lasting inhibitory effect against bacteria, fungus, and other pathogens. According to studies, several bioactive chemicals discovered in diverse species of sponges have the potential to assist in the development of new antibiotics and antimicrobial treatments. These compounds can be found in the sponges' tissues (Shen et al., 2012).
According to a number of studies, the microorganisms that are associated with sponges could perhaps play a part in the production of physiologically active metabolites as well as defense against chemical hosts (Thakur and Anil, 2000, Piel et al. 2004). Sponge research has resulted in the discovery of approximately thirty percent of the world's marine environment's total flora and fauna, with nearly 5000 different substances having been extracted from sponges so far. During two hundred newly identified bioactive sponge products have been reported each year over the past 10 years (Hu et al., 2011). It is believed that sponges utilized a wide array of metabolic pathways in order to produce such a wide variety of and unique bioactive combinations. This was done in order for them to sustain their longevity in the water. This involves defense against microbial contamination as well as utilization as an agent in competitiveness within the congested habitat of marine reefs (Mehbub et al., 2014).
Because many of them operate effectively as chemical protectiv e factors against rivals, predators, and other ecological pressures , marine invertebrates are now a substantial source of biologicall y active natural compounds. This is due to the fact that many of t hem function as chemical defense mechanisms against competit ors. It has been determined that the microorganisms that live alo ngside invertebrates appear to be the true source of the majority of marine natural commodities. The majority of invertebrates ar e susceptible to parasite predation and destructive microbial infe ction because they are sessile, have delicate bodies, and move ve ry slowly. This makes them ideal targets for parasites. Because o f this, in order for them to mount some form of chemical defense , they require a large array of secondary metabolites, which are c reated by the bacteria that are symbiotic with them (Jimnez 2018 ; Wang et al. 2008). It is possible that this is the reason why mar ine natural products, which are manufactured by marine inverteb rates and the symbiotic microbes that live with them, are rich so urces of a wide variety of bioactive secondary metabolites (Mart ins et al. 2014; Mayer et al. 2010; Newman and Cragg 2016b).
Because of this, invertebrates and the many different microbes t hat live in close proximity to them have garnered a lot of attentio

n for their ability to produce novel structural metabolites that have the potential to have bioactive applications (Blunt et al. 2018).

There is no evidence to suggest that either the sponge or the bacteria associated with it are responsible for the production of the beneficial chemicals (Unson and Faulkner, 1993; Faulkner et al., 1994; Unson et al., 1994; Brantley et al., 1995; Bewley et al., 1996; Lin et al., 2001). Therefore, the sponge can either generate its own metabolites (Garson et al., 1992; Pomponi and Willoughby, 1994), or it can obtain them from other sources. It is believed that the only sources are the free-living bacteria that exist in the marine environment as well as the symbiotic microorganisms (Lindquist et al., 2005). This is demonstrated by the fact that the structures of many naturally occurring compounds formed from sponges, such as non-ribosomal peptides and complicated polyketides, are very similar to those of molecules that are only known to be produced by bacteria. On the other side, the sponges are responsible for the production of some metabolites. For example, the chemical avarol is found in the sponge Dysidea avara, while the sponge Axinella corrugate contains stevensine (George and Wilson, 2012). Additionally, the sponge naturally produces a variety of of cytotoxic brominated isoxazoline alkaloids (Khleifat et al., 2007; Allimoun et al., 2015; Aljundi et al., 2010a; Aljundi et al., 2010b; Khlaifat et al., 2019; Khleifat et al., 2019; Andrade et al., 1999; Turon et al., 2000; Uriz et al., 1996). In addition, enzymes derived from sponges have been isolated and studied for their potential applications in medicine. For example, it was discovered that the bacterium Axinella polypoides contains the enzyme ATP N-glycosidase. This enzyme is responsible for the breakdown of adenosine-5-triphosphate (ATP) into adenine and ribose-5-triphosphate (Reintamm et al., 2003).

Extraction process

During the extraction process, the natural chemicals of interest are isolated and separated from the starting materials, which are the sea sponges (Zhang et al., 2018). The crude extract can be obtained by a variety of different means (Getachew et al., 2020). It is common knowledge that the crude extract is a complicated concoction of a number of different metabolites, including peptides, quinones, terpenoids, and alkaloids (Bayona et al., 2018; Nn, 2015). When it comes to the extraction process, there are two distinct types of approaches that fall into one of two categories: traditional extraction techniques and recently created technologies that are based on the energy or mechanism (Getachew et al., 2020).

Traditional extraction method

Extraction using a solvent or extraction using a solidliquid mixture are the two primary techniques that make up the classic extraction method (Getachew et al., 2020). Maceration requires soaking the sample in the solvent and intermittent stirring, whereas the Soxhlet method calls for boiling the sample and solvent together for a predefined amount of time with or without stirring. Maceration can also be performed without stirring (Abubakar and Haque, 2020). These are just a few of the many methods that can be used to separate solids from liquids. These methods have seen widespread application for a significant amount of time. However, utilizing these methods does come with a few drawbacks, including the commitment of time, the high volume of solvent that is required, the possibility of the compound being lost during the concentration step as a result of volatilization, the possibility of the compound being hydrolyzed as a result of harsh conditions, such as high temperatures, and the contribution of solvent waste to environmental pollution (Grosso et al., 2015).

As their respective solvents, these processes can either make use of a single solvent or a combination of solvents whose polarities span a wide spectrum (Pantidos et al., 2014; Lopes et al., 2012). Methanol, ethanol, trichloromethane, acetone, and water are some examples of discrete solvents. Other examples include trichloromethane. Additionally, they are capable of being mixed with other organic solvents such as ethanol and acetone (Catarino et al., 2019; Parys et al., 2010).It is estimated that over 80% of the world's plant and animal species can be discovered in the open oceans and deep seas, which account for approximately 70% of the surface area of the globe (Sutton et al., 2017 , Barzkar et al., 2019). It is recognized that a variety of living species, including prokaryotic bacteria, marine invertebrates, multicellular complex organisms like sharks and whales, and other living things, may be found in water (Ebada and Proksch, 2012). Despite the harsh conditions of the marine environment, it is now possible to access novel compounds from marine organisms located at various depths of the ocean thanks to advancements in technologies such as manned submersibles, remotecontrolled cars, closedcircuit computerized mixed gas rebreathers, and scuba diving equipment (Petersen et al., 2020; Carte, 1993).

Research into natural products obtained from marine organisms was initiated when Bergmann and his colleagues discovered the compounds spongothymidine and spongouridine, which were derived from the Caribbean sponge Tectitethya crypta (de Laubenfels, 1952). (Petersen et al., 2020). In recent years, the primary source of newly discovered naturally occurring bioactive compounds has been various marine taxa. Some examples of these marine species are sea slugs, sponges, and flexible corals (Carson and Clarke, 2018; Kiuru et al., 2014; Pandey, 2019). More than 40,000 marine natural products have been discovered so far thanks to contributions from sponges, cnidarians, mollusks, tunicates, bryozoans, echinoderms, red algae, green algae, brown algae, and microbes (Carroll et al. 2019; Deshmukh et al. 2018; Jiménez 2018; Leal et al. 2016; Newman and Cragg 2016). The vast majority of naturally occurring compounds discovered throughout the entire history of marine natural product research and in the field of drug discovery at the present time originate from marine invertebrates, particularly marine sponges. This particular exporter discovers hundreds of compounds each year (Ebada and Proksch, 2012; Laport et al., 2009).In the jellylike layer that is found between the two thin layers of cells that make up marine sponges, one may find the skeleton of spicules made of silica, calcium carbonate, and a protein known as spongin. Spongin is a component of marine sponges (FAO, 2017). The many types of sponges can be distinguished from one another based on the dimensions and contours of their spicules (FAO, 2017). Marine sponges are filter feeders that remove potentially harmful particles from their environment by producing helpful compounds that have been neutralized. About 11 different genera of sponges have been responsible for making the discovery of bioactive chemicals possible. Three of these genera, Haliclona, Petrosia, and Discodemia, are known to produce compounds with potent antiinflammatory and anti-cancer capabilities (Jha and Zi-rong, 2004; Blunt et al., 2004).

Sponge metabolism results in the production of a wide variety of chemically distinct bioactive compounds, including nucleosides, terpenes, sterols, cyclic peptides, and alkaloids (Laport et al., 2009). Instead, the majority of the wide variety of bioactive compounds are produced by the microbial symbionts that live inside the sponges (Ebada and Proksch, 2012; FAO, 2017). Sponges produce powerful cytotoxic substances in the form of mucuscontaining toxins in order to protect themselves from other marine species. Because of this, sponges are able to outcompete animals that develop swiftly and can even take over corals or rocks that have a dense population. They could, however, use these toxins sparingly without putting themselves in danger of being harmed by them (Perdicaris et al., 2013).

Sponge samples have been subjected to a staggering number of statistical tests, which have been conducted on natural products that have been derived from marine organisms, and the results have shown that sponges contain a remarkable quantity of physiologically active chemicals that have been isolated.Hu et al. were able to identify the temporal trend, chemical structure distribution, bioactivity groups, and species distribution of biologically active compounds derived from marine organisms during the course of the 28 years that spanned from 1985 until 2012. (Hu et al., 2015).

According to the findings of the researchers, the researchers collected the greatest proportion of bioactive compounds from sponges. The researchers also observed that approximately 75% of the chemicals were sourced from marine invertebrates. According to the findings of another study, out of the 9812 marine natural p roducts that were recovered from invertebrates between the year s 1990 and 2009, sponges had the highest concentration of meta bolites, accounting for 40.8% of the total. (Leal et al., 2012). Th e use of sponge extracts as an antibacterial agent has been the subject of a great number of studies. These studies did not make use of any of the different types of sponges that are native to the Gulf of Aqaba. The purpose of this study was to evaluate the antibacterial efficacy of polar, semi-polar, and non polar extract fractions that were generated from a variety of sponge species that were collected from the Aqaba Gulf.

Emerging technology

Because the conventional extraction method has a number of drawbacks, new strategies that take less time and have demonstrated to be more effective in the extraction process are being adopted. New approaches that are widely used as alternative extraction procedures include pressure solvent extraction (PSE), ultrasound-assisted extraction (UAE), and microwave-assisted extraction (MAE) (Getachew et al., 2020; Grosso et al., 2015). MAE is a technique that speeds up the removal of various chemicals from natural matrices using microwave irradiation (Getachew et al., 2020). By using this technique, heat and mass gradients act in the same direction, causing the matrix to get hotter as a result of friction between the polar molecules (Rostagno et al., 2009; Kaufmann & Christen, 2002). Electric fields cause molecules to vibrate or oscillate, which causes friction between molecules as well as friction within individual molecules (Grosso et al., 2015). This results in the matrix heating up quickly (within seconds), which creates a pressure effect and tears the cell membrane and wall. As a result, the chemicals are transferred from the cells to the solvent at a faster pace (Getachew et al., 2020). Another method that alters the material's physical and chemical characteristics after reacting with it employs ultrasonic waves (Herrero et al., 2003; Chemat et al., , 2011). The procedure' advantages include a significant reduction in extraction time and an increase in extraction yield (Zou et al., 2013). By generating cavitation bubbles in the solution, this is accomplished (Zou et al., 2013). The cavitation bubble formed in the liquid during the expansion phase is widely recognized. According to Picó (2013) and Santos et al. (2014), cavitation bubble formation depends on the characteristics of the solvents, the ultrasonic wave, and the surrounding environment. When a cavitation bubble forms, it bursts during the compression cycle, compressing the liquid molecules and generating a high-velocity micro-jet that flows in the direction of the matrix particle, forcing the solvent to mix with the matrix (Rostagno et al., 2009; Picó, 2013). This procedure allows for the achievement of 1000 bar of pressure and 4726.85 °C of temperature, respectively (Picó, 2013; Santos et al., 2014). By breaking down the cell wall and membranes, this causes the solid particle to quickly dissolve, releasing the intracellular chemicals for the solvent to easily permeate (Varijakzhan et al., 2021). PSE is a novel technology that works with pressures and temperatures between 35 and 200 bar and 50 to 200 °C. In order to keep the solvents in a liquid condition, the temperature and pressure utilized in this approach are lower than the critical temperature (Tc) and critical pressure (Pc) of the solvents (Wang, 2006; Wang, 2011; Herrero et al., 2013). The solvent is heated over its boiling point by the high pressure utilized in this process, which lowers its viscosity and surface tension while also improving the solvent's solubility and rate of mass transfer (Herrero et al., 2013; Kadam et al., 2013). Water, propane, and dimethyl ether make up the trio of solvents that are most frequently utilized in this procedure (Parys et al., 2010; Rostagno et al., 2009; Kaufmann & Christen, 2002).

Factors affecting the extraction

The method used to extract the bioactive metabolites from marine sponges depends on the variables used in the extraction process, such as solvent polarity, temperature, and pressure (Bayona et al., 2018; Riguera, 1997). These elements affect the kinds of metabolites that are primarily present in the crude extract. According to their polarity, the types of solvents used for extraction can be divided into non-polar solvents like hexane and trichloromethane and highly polar solvents like water (Nn, 2015; Ebada et al., 2008). The yield of phenolic compounds rises when water and an organic solvent, like ethanol, are combined compared to the percentage yield when the solvents are used separately (Getachew et al., 2020).

The sponges Stylotella aurantium and Halicona molitba (de Laubenfels, 1952) were used in a study to examine the impact of solvents on the percentage yield of crude extracts. Methanol and water were used as the solvents (Hutagalung et al., 2014). Although the water solvent extract of both sponges had a greater ratio yield, the methanol extract of both sponges demonstrated superior antibacterial effectiveness against B.cereus than the water extract. Polarity is responsible for the difference in percentage yield between the two solvents. More polar chemicals can be recovered from the sponges since water has a stronger polarity than methanol, increasing the percentage of yield (Hutagalung et al., 2014). The difference in antimicrobial activity among the crude extracts suggests that the bioactive substances that inhibit bacterial cell development are primarily semi-polar; accordingly, the compounds may be extracted using methanol because it is a semi-polar solvent (Varijakzhan et al., 2021). The marine sponge Xestospongia sp. (Laubenfels, 1952) was the subject of a study by Bayona et al. (2018) to examine the link between pressure, solvent polarity, temperature, and the variety of extracted chemicals (Bayona et al., 2018). The most significant factors affecting the metabolic diversity in the extract were found to be the temperature and solvent polarity used during the extraction process. As was already mentioned, a rise in solvent polarity is positively correlated with the diversity of extracted chemicals. Because it produced a wider variety of chemicals than the solvent containing a mixture of ethanol and dichloromethane, ethanol was found to be a more appropriate solvent than dichloromethane. With a wide range of yields, it was discovered that the ethanol solvent was more efficient at extracting both polar and lipophilic fatty acid molecules. The extract included sterol and fatty acid-related substances after being cleaned with the solvent dichloromethane (Varijakzhan et al., 2021).

Additionally, compared to the lower temperature (30-500 °C), the chemical variety was decreased when the extraction was carried out at a higher temperature (60-800 °C). 100% ethanol was used for the extraction in order to investigate the effect of temperature (Bayona et al., 2018). A certain collection of chemicals were extracted by extraction at varied temperatures. Specific groups, such as aromatic compounds, were actively extracted at high temperatures, although a large chemical variety of the extracts was found at low temperatures (Varijakzhan et al., 2021).

The number of cycles used to complete the extraction, which interacted with the temperature at which the extraction process was conducted, was another factor that was demonstrated to have a significant impact on extraction (Bayona et al., 2018). When the extraction was carried out at a low temperature and with one or three cycles, the study found no change in the diversity of chemicals obtained. However, when only one cycle was used, the extract's diversity decreased as the temperature rose, whereas increasing the number of cycles increased the compound diversity (Varijakzhan et al., 2021a and b).

Bioactivities of marine sponges with regard to human diseases

The discovery of the nucleosides spongouridine and spongothymidine in the sea sponge Cryptotethya crypta in the early 1950s sparked an interest in sponges in the pharmaceutical industry (Bergmann and Feeney, 1950 and 1951). These nucleosides served as the building blocks for the creation of the first sea-derived anticancer drug, ara-C, as well as ara-A, an antiviral medication (Proksch et al., 2002). A component of the fluorinated derivative known as Ara-C is approved for the treatment of lung, pancreatic, breast, and bladder cancers in addition to lymphoma and leukemia (Momparler, 2013). (Schwartsmann, 2000). Comparatively to vertebrates, lower invertebrates have higher lipid components such sterols, fatty acids, and other unsaponifiable compounds (Bergmann and

Swift, 1951; Piel, 2004;; Piel et al., 2004). About 20,000 bioactive substances have so far been identified in marine organisms (Hu et al., 2011). But most of these biologically active chemicals—mostly terpenoids and alkaloids—have only been identified from sponges (Leal et al., 2012). Sponge production accounts for the majority of the diversity in marine chemicals. Marine sponges are used to isolate about 5300 distinct natural products and new chemicals each year (Faulkner et al., 1994; Faulkner, 2000; 2001; 2002). The likelihood of sponges producing new substances each year, including more than 200 new metabolites, is the highest (Blunt et al., 2004 and 2006; Turk et al., 2013). Around 300 novel Porifera phylum compounds were identified in 2011. (Blunt et al., 2013). Additionally, in comparison to chemicals derived from different marine phyla, some substances derived from sponges are undergoing clinical and pre-clinical studies (as anti-inflammatory or anticancer treatments) (Blunt et al., 2005: Martins et al., 2014).

Environmental issues and logistical challenges related to gathering significant amounts of sponges are typically obstacles in the development and production of pharmaceuticals derived from sponges. Since a stable source of therapeutic candidates derived from sponges may be created by establishing a symbiont culture or by transferring their biosynthetic genes into culturable bacteria, the presence of potentially generating microbial symbionts is of particular relevance. For instance, manzamine alkaloids were previously extracted from the sponge Acanthostrongylophora sp. and were also derived from the associated microorganism Micromonospora sp. These compounds are promising lead substances for an extended preclinical evaluation against malaria, tuberculosis, and HIV (Hill et al., 2005). The dinoflagellate Prorocentrum lima, which was initially isolated from the host sponge Halichondria okadai, produces okadaic acid (Morton et al., 1998) (Kobayashi and Ishibashi, 1993). A Vibrio sp. synthesizes and rimid, peptide, and brominated biphenyl ethers from the sponges Hyatella sp. and Dysidea sp (Elyakov et al., 1991). So, the microbial interaction that occurs on or in sponges may be crucial in resolving the issue of lack of supply for the vast majority of medicinal chemicals produced by sponges (Anjum et al., 2016).

Antibacterial activity of various compounds isolated from marine sponges

According to the composition of their cell walls, bacteria are typically categorized as either gram-positive or gram-negative (Nazzaro et al., 2013, Moo et al., 2019). Teichoic acid, lipoteichoic acid, and proteins make up the thick peptidoglycan layer found in gram-positive bacterial cell walls, whereas gram-negative bacteria have a thinner peptidoglycan layer that is encased in an outer membrane layer made of lipopolysaccharides (Varijakzha et al., 2021a; Aljaafari et al., 2019). Despite their structural differences, a number of chemicals discovered in sea sponges have been proven to possess antibacterial activities against human pathogenic bacterial strains such Escherichia coli, Pseudomonas aeruginosa, and S. aureus. In general, bioactive substances can kill bacteria by seeping their contents into the cells and causing cell membrane rupture that results in the production of reactive oxygen species (ROS). Additionally, ROS has the ability to oxidize proteins found in bacterial cells by changing the covalent connections that maintain the structure of proteins essential for cell survival (Benzaid et al., 2019, Yang et al., 2019) Clathria compressa was gathered from Florida, USA, and its bicyclic terpenoid, clathric acid, was isolated. When tested against methicillin-resistant S. aureus ATCC 33,591 (MRSA), S. aureus ATCC 6538P, and vancomycin-resistant S. aureus (VRSA) bacterial strains with MIC values of 64 g/mL, 32 g/mL, and 64 g/mL, respectively, it demonstrated antibacterial activity (Alrawashdeh et al., 2019; Al-Sammarraie et al., 2020; Al-Limoun et al., 2020; Al-Tawarah et al., 2020; Alqaraleh et al., 2021; Gupta et al., 2012). Axinella donnani contains lectin, a glycoprotein substance. It showed antibacterial action against S. aureus bacterial cells while also demonstrating great effectiveness in anti-biofilm activity against S. aureus that produces biofilms (Alqudah et al., 2014; Allimoun et al., 2015; Al-Limoun et al., 2019; Al Qaisi et al., 2021; Alqaraleh et al., 2021; Sadanandan and Rauf, 2018). After treatment with lectin at concentrations of 15.1 g/mL to 1000 g/mL, the total biomass of the biofilm reduced depending on the concentration; treatment at 1000 g/mL showed an inhibition of more than 80%. (Khleifat et al., 2000; Khleifat et al., 2001; Khleifat et al., 2006; Khleifat et al., 2021; Aljundi et al., 2010a; Khleifat et al., 2022a; Khlaifat et al., 2019; Khleifat et al., 2019; Varijakzhan et al., 2021a).

It was discovered, however, that some of the marine sponge chemicals were less efficient against Gram-negative bacteria. For instance, when tested against Escherichia coli and Klebsiella pneumoniae at a concentration of 128 g/mL, clathric acid isolated from C. compressa showed no antibacterial action; nevertheless, as previously mentioned, the substance showed antibacterial activity against Gram-positive bacteria (Gupta et al., 2012). The compound lectins extracted from A. donnani were discovered to have antibacterial activity against Gram-negative bacteria. It also demonstrated anti-biofilm activity against Gram-negative bacterial strains of E. coli, K. pneumonia, and Pseudomonas aeruginosa as well as a potent anti-biofilm activity against P. aeruginosa, which produces biofilms (Sadanandan and Rauf, 2018). E. coli and P. aeruginosa, two Gram-negative bacterial strains, were resistant to the antibacterial effects of haliclona extract with the same efficiency as Gram-positive bacterial strains (Shushizadeh et al., 2018; Khleifat et al., 2010; Tarawneh et al., 2010; Khleifat et al., 2014; Müller et al., 2013; Khleifat et al., 2009; Khleifat et al., 2007; Qaralleh et al., 2021; Khleifat et al., 2011; Khlaifat et al., 2019; Khleifat et al., 2019).

Nagahamide A is a depsipeptide isolated from Theonella swinhoei (Hall et al., 2014). The weak antibacterial properties of the chemical were ineffective against E. coli and S. aureus (Okada et al., 2002). Agelas sp. provided the dimeric bromopyrrole alkaloids nagelamides Q and R, which exhibit antibacterial activity. The nagelamide Q molecule contains a pyrrolidine ring, but the bromopyrrole alkaloid nagelamide R would be the first to have an oxazoline ring (Araki et al., 2009). Both substances had MIC values of 13.0 g/mL against B. subtilis, and at doses greater than 25 g/mL, they were both effective against E. coli, M. luteus, and S. aureus (Varijakzhan et al., 2021b). For instance, the synthetic analogs of the bisindole alkaloid 2,2-bis(6-bromo-3-indolyl) ethylamine may have both antibacterial and biofilm-preventing effects. 2,2-bis(6-bromo-3-indolyl)ethylamine (Hall et al., 2014) demonstrated strong antibacterial activity against E. coli, S. aureus, and K. pneumoniae with a MIC as low as 8 mg/L when it was isolated from the New Calodenian sponge Orin asp. The biofilms formed by the pathogens E. coli, S. aureus, and K. pneumoniae could also be broken down by the molecule, which was similarly found to suppress biofilm formation by 82.2%. (Alqudah et al., 2014; Al Qaisi et al., 2021; Hajleh et al., 2022;Campana et al., 2019).

Classification of Compounds

Whereas the crude extracts of identified creatures has been discovered to consist of a wide variety of chemicals from different chemistry classes, extraction from marines sponges have primarily been found to belong to three primary classifications (C.-H. Chen et al., 2016).

Terpenes

Terpenoids make up a major portion of secondary metabolites, which are created as isoprene (C_5H_8) polymers and linked repeatedly head-to-tail (Karanam, Arumugam, & Sirpu Natesh, 2020). A variety of derivative with a broad spectrum of chemical structures and concurrently biological features is produced when the architectures of terpene-based metabolites are altered. Depending on the polarity of the solvents, terpenes could be extracted in a huge variety of structural forms (Lim, Chung, & Son, 2017). The terpenes are made up of polar terpenoids and non-polar terpenes, which seem to be linear and cyclized terpenoids. Steroids terpenes were the first terpenes found in the marine sponges. Two significant groups of terpenoids, identified as sesterterpenoid (C25) and triterpenoids

(C30), have frequently been extracted from marine sponges and are recognized to have a variety of bioactive components (C. Guo et al., 2019).

Alkaloids

A further group of metabolites from marines sponges that have been widely discovered is those dependent on alkaloids. Manzamines A, a polycyclic alkaloids produced from - carbolines, was discovered in 1986 from the marines sponges Haliclona sp. A fused and bridged tetra- or pentacyclic rings structure connected to the - carbolines characterisesmanzamines compounds (Yuzhen Zhu et al., 2018). The bioactive components of the manzamines alkaloids are diverse, including cytotoxic, antibacterial, and anti-malarial (Du et al., 2020).

In addition, bromopyrrole alkaloids produce toxins that are unique to marines sponges. The first substance from this category to be discovered was oroidin, which was discovered in 1971 from Agelasoroides (Schmidt, 1864). Oroidin seems to be the precursors for the substances categorized as bromopyrroles alkaloids because these substances contain a pyrroles-imidazoles unit that is a derivation of oroidin (Zhang et al., 2019). Instances of bromopyrroles alkaloids that have been identified from marines sponges include hymenidins, clathrodins, and sventrins, with the bioactivities being linked to the pyrroles moiety's bromination structure (De Vera & Reznik, 2019).

Peptides

Studies on bioactive substances from marines natural products is a well-established field, and it has been found that the peptides from marines sponges have distinctive patterns when comparing to bioactive substances from other origins. These peptides have amino acids that are either uncommon or nonexistent in terrestrial-based and microbiological peptides, and they can be cyclical or linear in structure (Chiou et al., 2021). It is well recognized that peptides obtained from marine sponges are secure, affordable, and have a variety of antibacterial activities (W. Yang et al., 2018).

Antimicrobial peptides (AMPs) are significant sources of novel antibiotics that can be utilized in place of or in addition to already used antibiotics (Yurasakpong, Apisawetakan, Pranweerapaiboon, Sobhon, & Chaithirayanon, 2021). Discodermin A, a tetra-decapeptides that was the first bioactive peptides to be extracted from Discodermiakiiensis (Hoshino, 1977) on Shikine Island in Japan, is an illustration of AMP (Méresse, Fodil, Fleury, & Chénais, 2020). Additional research led to the identification of several analogues, particularly discodermins B, C, and D (L. Ma et al., 2020). In addition to having antibacterial properties, discodermins A-D is a strong inhibitor of the PLA2 enzymes (S. Jiang et al., 2021). Formyl-D alanines, 3-methyl-L-prolines, and 3-methyl-D-valines are a few of the aberrant residues in amino acids that are used to describe tetra-decapeptides AMPs (Yuan et al., 2017). The prolines-rich cyclopeptides are another type of peptides that has bioactivities like anti-cancers, immunosuppressant, and anti-inflammatory effects (Pham, Le, & Yang, 2021). By limiting conformational changes, the prolines residues in peptides molecules contributes to structural support. This is because the prolines ring's stiffness ensures that the rigid structures of the peptides is maintained (Liu et al., 2022).

S. carteri

*An Indonesian S. carteriethanolic extracts showed anti-cancer efficacy against the breast cancer cell line MDA MB 231 (*Zhang et al., 2019) *. According to the research, the extraction includes a variety of different chemicals, the most significant of which are 1,2-Benzenediol, dibutyl phthalates, and 9,12-Octadecadienoics acid ethyl ester (Figures 1a, 1b) (Figure 1c). Dibutyl phthalates is commonly utilized as a plasticizer in the production of plastics and is generally regarded as a contaminant.* Nevertheless, the compound's existence in the extraction may be the result of synthesis by the sea sponge's microorganism symbionts. It was discovered that the marine bacteria Pseudomonas sp. PB01, Streptomyces rubers EKH2, and Rheinheimeras japonicas KMM9513, as well as filamentous fungi Penicillium lanosumPTN121, Trichodermaasperellums PTN7, and Aspergillusnigers PTN42, produce the compounds dibutyl phthalates as secondary metabolites (M. W. Kim, Niidome, & Lee, 2019). The extracts caused the breast cancer cell lines to die in a dose-dependent way through apoptotic and also by stopping the cancer cells from migrating. Breast cancer cells have been shown to proliferate and become more aggressive when exposed to butyl phthalates (Y. Sun et al., 2020).

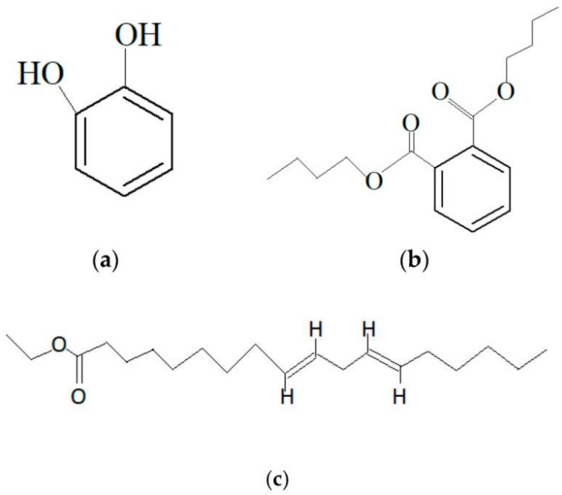

Figure 1. (a) 1,2-Benzenediols, (b) dibutyl phthalates, and (c) 9,12-Octadecadienoics acids ethyl esters chemical structures (Cheng et al., 2018).

Structure Elucidation of the Isolated Compounds

Compound 1 (Figure 2) was produced as a white powdered, and its chemical formulas, which denotes one level of unsaturations, was discovered by HRESIMS to be C32H65NNaO5 with m/z 566.4772 [M + Na]+ (calcd 566.4760). A resonating of an amide protons doublets at H 8.95 (d, J = 8.4 Hz) and the protons of a lengthy methylene chains at δH 1.25, which represents the skeletons of a sphingolipids, were both visible in the spectrum of 1H NMR (recorded in C5D5N, 400 MHz). Given to H-2, H-1, H-3, H-4, and H-2′, correspondingly, characteristics resonances of the hydrocarbons chains units 2-amino-1,3,4,2′-tetrol were seen at H 5.12 (m), (dd, J = 8.0, 4.8 Hz), 4.43 (dd, J = 8.0, 4.8 Hz), 4.29 (m), 4.62 (m), and 4.37 (m). CH3-17 and CH3-15′ are allocated reverberations at δH 0.85 (t, J = 6.8 Hz) that match to the aliphatic methyl groupings (Shen et al., 2012; Yang et al., 2021).

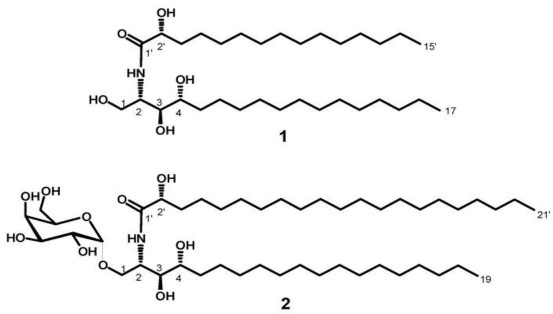

Figure 2. Chemical structures of the newly crude extracts: stylissamides A (1) and stylissosides A (2) (J. Yang et al., 2021).

At δH 5.29 (1H, m), 4.63 (1H, m), 4.32 (1H, m), 4.59 (1H, m), 4.39 (1H, m), and 4.28 (1H, m), resonances characteristics of a 2-amino-1,3,4,2′-tetrol units of the hydrocarbons chains were found. These resonant frequency were allocated for H-2, H-2′, H-1b, H-1a, H-3, and H-4, correspondingly (L. Liu et al., 2022).

Additionally, resonances for CH3-19 and CH3-21′ that corresponded to aliphatic methyl groupings at H 0.85 (3H, t, J = 6.8 Hz) were identified. There were 46 carbonic signals visible in the 100 MHz C5D5N 13C NMR spectra. A 2-amino-1,3,4,2′-tetrol units of the hydrocarbon chains showed characteristics resonances at δC-50.4 (C-2), 72.4 (C-2′), 68.2 (C-1), 76.5 (C-3), and 72.3. (C-4). The two terminal methyl groupings (C-19 and C-21′) were also allocated resonances at δC 14.2 and δC 175.0, respectively, as well as the imidazole carbonyl (C-1′) at δC 175.0 (Senthilkumar and Kim, 2013; Sheng et al., 2021). Roughly 80% of the globe's plants and animals species can be found in the open oceans and deeper seas, which make up about 70 percent of the planet's surfaces (X. R. Zhang, Wang, Sun, & Wei, 2018). The ocean is recognized to be home to a variety of living creatures, including multicellular complex species like sharks and whales as well as prokaryotic bacteria and marines invertebrates (F. Wang, Wang, et al., 2015). Despite the harsh circumstances of the marine environments, the development of technologies like crewed submersibles, remotely controlled vehicles, closed-circuits computerized gas mixtures respirators, and scuba diving gear has made it possible to obtain new substances from marines organisms in different depths of the ocean (Yan et al., 2022). Over than 5000 unique natural compounds have been derived from marine creatures residing in these harsh habitats, which include photic and non-photic regions, pressures range between 1 and 1000 atm, vast heat fluctuations, and temperatures as hot as 350 °C in deeper hydrothermal vents (Tang, Lu, & Xia, 2020).

With the finding of the substances spongo thymidine and spongouridine, which were taken from the Caribbean sponge Tectitethyacrypta (de Laubenfels, 1949), studies on natural chemicals from marines creatures officially began (Wenjie Jiang et al., 2018). Numerous marines taxa, including sea slugs, sponges, and soft corals, have recently proven a significant source of novel biological active chemicals (Wu et al., 2020).

The majority of naturally occurring elements that have been found come from marines invertebrates, particularly marines sponges, with hundreds of compounds being identified from this sources each year (J. Chen et al., 2020), from the earlier phases of natural substance marines researches to the recent trends of drugs discoveries. A sponge is a sessile invertebrates that is commonly found in settings that are temperate, tropical, and polar (Hu et al., 2021). There have been found more than 8000 varieties of marines sponges, which are members of the phylum Poriferas (Chashoo, Singh, Singh, Mondhe, & Vishwakarma, 2019). Marines' sponges have two thin cells layers sandwiched between a jelly-like layers and may have spicules skeletons comprised of silicas, calcium carbonates, and a proteins called sponging (Rath, Hochmair, Plangger, & Hamilton, 2018). The size and shaping of the spicules are used to identify the species of sponges. Marine sponges are filters feeders that produce bioactive substances to neutralize potentially harmful particles (Tewari, Patni, Bishayee, Sah, & Bishayee, 2019).

Ecological and Biological Aspects Cruising the Elevated Abundant supply of Bioactive Compounds from Marine Sponges

There are two distinct life cycles for marine sponges. A larva is initially discharged into the water by the female sponges; it finally attaches to a prepared surface and develops into a non-motile (sessile) adults (J.-C. Ma et al., 2017). Marine sponges are renowned for being efficient filter feeders; water from the environment enters the sponges through tiny pores called ostia and exits through a bigger aperture called an osculum (Rath et al., 2018). The marines' sponges contains distinct cells that serve particular purposes. Water can travel in one way by the coordination of the flagella on flagellar cellular (choanocytes). The amoebocyte cells take up water-borne particulates debris (Wu et al., 2020).

Conclusion

Most sponges live in the tropics, subtropics, and temperate ocea ns. They are one of the most important sources of marine bioacti ve compounds that can be retrieved. Marine bioactive compound s can be extracted. It is well known that sponge compounds have many bioactivities, including antibacterial, anticancer, and cytot oxic properties. Isolated compounds have bioactivities. Marine s ponges contain bioactive compounds with potential uses. These chemicals may be antibacterial, antiviral, and antimalarial agains t human and aquaculture diseases. These chemicals are also antif ungal. Ocean sponges also have these chemical substances. Mari ne sponges are biotechnologically important to chemistry, micro biology, cell biology, and molecular biomedicine. Researchers u sing sponges' extraordinary chemical variability have developed new drugs.

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