

Marine bacteria and their uses as a source of antimicrobial metabolites to control multidrug-resistant bacteria

Maha Atig Alsubhi¹, Lina Ahmed Bahamdain¹ & Magda Mohammed Aly^{1,2,3}

¹Department of Biological Sciences, Faculty of Science, King Abdul-Aziz University, Jeddah, Saudi Arabia

²Department of Botany and Microbiology, Kafrelsheikh University, Kafr El Sheikh, Egypt

³Princess Doctor Najla Bint Saud Al Saud Center for Excellence Research in Biotechnology, Jeddah, Saudi Arabia

*Corresponding author, e-mail: mmmohammad@kau.edu.sa

ABSTRACT

Marine bacteria are considered to be an excellent source of new therapeutics. About 70% of the earth's surface is covered with water and it comprises 500,000 live species divided into 30 different phyla. Many researchers carried out the isolation and exploitation of bacteria from the marine environment to study the ability of strains to produce antimicrobial agents against pathogens to manage the problem of the emergence of antibiotic-resistant bacterial species. Examples of marine bacterial genera that have been isolated are *Bacillus*, *Enterobacter*, *Nocardiopsis*, *Pseudomonas*, and phylum Actinobacteria which are the richest sources of natural products. Moreover, these bacteria are commonly used in bioremediation processes and had an excellent role in the removal of different environmental pollutions due to their vital environmental conditions and reduction capability and adaptability. In conclusion, marine bacteria have an advantage over terrestrial bacteria and are used in extreme environmental conditions to provide a useful source for new antimicrobial agents or can be used in the bioremediation process.

KEY WORDS

Marine environment; antimicrobial agents and bioactive compounds.

Received 18.10.2023; accepted 15.11.2023; published online 30.12.2023

INTRODUCTION

In the biosphere, the marine environment covers 70% of the Earth's surface, and their phylogenetic diversity is considerably greater than that of the terrestrial environment because of the differences in location, temperature, and salinity. Marine habitats are home to 50–80% of all life on Earth where there are about 500,000 marine organisms divided into 30 different phyla. The oceans are a unique and abundant supply of bioactive compounds for the pharmaceutical industries owing to marine entities' enormous genetic and ecological diversity. Marine environments are characterized by high salinity and

differ in their physical and chemical conditions from the optimal conditions in which most microbes thrive. Marine environments have many unique features that vary from other environments (Srinivasan et al., 2021). They contain various dissolved salts and minerals that make up about 85% of the solids in seawater. The remaining 15% includes various elements such as sulfates, calcium, potassium, magnesium, bicarbonate, borates, strontium, bromide, fluoride, and others. The salinity characteristic of the marine environment allows some microorganisms to produce biologically active compounds distinct from other microbes on land (Sarkar & Suthindhiran, 2022).

The marine environment is very diverse with complex microbial populations. The microbial communities are various and new species abound, whether found in the water, sediments or associated with marine animals (El-Kurdi et al., 2021). Marine organisms have evolved biochemical and physiological mechanisms that include the production of bioactive compounds with unique structural characteristics for different purposes such as reproduction, communication, and protection against predation, infection, and competition. However, the sea provides impressive biological variety beyond chemical diversity (Doshi et al., 2011). Additionally, the emergence of antibiotic-resistant bacterial strains has become a global threat and a matter of concern. It is estimated that antimicrobial resistance contributes annually to 700,000 deaths worldwide and is likely to increase to 10 million in the year 2050 (El Samak et al., 2018), this is why it is important to search for new biologically active compounds from distinct sources to obtain novel types of antimicrobial agents. Mancini et al. (2007) considered marine metabolites to have become an important role in the discovery of medicines due to their structurally unique molecules, as these molecules are produced naturally by marine organisms to protect themselves from other organisms.

According to a study done by Qureshi et al. (2020), it was isolated eight bioactive marine bacterial strains from four mangrove sediment samples sourced from the coastal areas of four major cities of Saudi Arabia (Jeddah, Yanbu, Dammam and Jubail). The isolates were identified as *Bacillus pumilus* NCTC10337, *B. cereus* JEM-2, *B. cereus* FRI35, *B. safensis* KCTC12796BP, *B. pumilus* W3, *B. pumilus* NJ-V2, *Escherichia coli* 0157, and *Klebsiella oxytoca* AR-0147. The results suggested that the eight marine strains could be used to produce novel antimicrobial agents. This study may also lead to the discovery of new molecular templates and compounds for producing effective drugs. Until now, the biological diversity of the marine environment is considered partially unknown and invaluable (Hassanali & Mahon, 2022).

The sea has some unique marine habitats, including sea-grass beds, salt pans, mangroves, coral reefs, and salt marshes, in addition to existent numerous fish species and microbial communities (Abdelfattah et al., 2016). The Red Sea is one of the

most saline and warmest water bodies (Ameen et al., 2022) and has a rich biodiversity. In this short review, information about the importance of marine environments and the essential sources for isolating marine bacteria and extracting bioactive compounds are discussed.

THE IMPORTANCE OF MARINE ENVIRONMENTS

The ocean abounds with different organisms possessing distinct compounds with pharmacological effectiveness. The marine compounds are structurally novel and possess a unique mechanism of action and potent biological activities different from those of terrestrial organisms. Over the last 50 years, more than 20,000 natural compounds have been identified in the marine ecosystem. This complex environment includes plants, animals, microbes associated with marine organisms, and microorganisms derived from marine water and sediments (Doshi et al., 2011, Srinivasan et al., 2021). Over 35,000 research papers on organic chemical compounds with marine origins have been published in the last 25 years, which has led to an expansion of the field of marine drug discovery (Gavriilidou et al., 2021). This is also shown by the rapid discovery of new secondary metabolites and a large number of marine-derived therapeutic candidates in clinical trials or awaiting approval. Thus, the marine environment is expected to provide the pharmaceutical sector with the next generation of antimicrobial agents (Srinivasan et al., 2021).

MARINE BACTERIA DISTRIBUTED IN VARIOUS PLACES

Marine bacteria are distributed in various places such as sediment, moving inanimate surfaces, plants, animals, and the internal spaces of invertebrates. Because of the complex nature of the marine environment, marine bacteria have developed complicated biochemical and physiological systems with which they can be adapted to extreme habitats and unfavorable conditions of this environment. Marine bacteria live in biologically competitive habitats with unique conditions of salinity, pressure,

temperature, light, oxygen, pH, and nutrient. For survival and defense mechanisms, bacteria produce individual secondary metabolites. Even though these biologically active compounds are produced in response to stress, many have shown value in pharmaceutical and biotechnological applications (Biswas et al., 2016).

The phylum actinobacteria is a diverse group of Gram-positive bacteria that contains high G+C content (Qin et al., 2016). These bacteria with extensive metabolic versatility have the ability to form filamentous or hyphal structures and spores, which allow them to be present and survive in a wide range of soil environments (Farda et al., 2022). Actinobacteria have been isolated from diverse ecosystems, including alkaline saline soil, marine sponges, deep-sea sediments, hot springs, gut, and medicinal plants. Actinobacteria in extreme habitats represent extensive taxonomic diversity and high genetic differences in their biosynthetic pathways for synthesizing novel biological compounds (Qin et al., 2016).

Cyanobacteria compose of prokaryotic organisms regrouped into the bacterial taxonomic group. Because of their capability of developing photosynthesis, cyanobacteria constitute one of the components of the primary producers in aquatic food chains. Marine cyanobacteria have been considered a rich source of secondary metabolites with potential biotechnological applications, namely in the pharmacological field. Chemically diverse compounds were found to induce cytotoxicity, anti-inflammatory and antibacterial activities. However, the potential of marine cyanobacteria as anticancer agents has been the most explored (Costa et al., 2012).

HABITATS OF MARINE BACTERIA

Marine bacteria are the greatest primary colonizers on the surface of organisms in the marine environment and have been isolated from various biological and ecological niches (Karthick & Mohanraju, 2020). The coastal ecosystems could provide diverse environments for exploring the interspecies connectivity within bacterial assemblages. The shallow coastal area is occasionally affected by discharging waste into the seawater (Cui et al., 2019). Thus, microbial contaminants can po-

tentially spread and this in turn leads to enhancing the emergence of new antimicrobial resistance strains (Fonti et al., 2021). Hamed et al. (2019) conducted research on the Gulf of Suez and Hurghada, and they isolated actinomycetes from sediment samples of National Institute and Oceanography Beach. The activity of these isolates was studied and found that of *Streptomyces* sp. MK388207 has a strong antimicrobial agent against some pathogens such as *Candida albicans*. The study's results suggested using the compounds of this strain as antibiotics for future applications in the pharmaceutical industry.

The deep sea receives global attention as one of the most essential microbial-driven ecosystems, and microbes in the deep sea play a vital role in ecological and biogeochemical cycles (Chang et al., 2021). The number of bacterial species in the deep sea is much more significant than previously thought. In a study by Chbel et al. (2022), 31 marine bacteria isolated by marine agar were collected from deep ocean water on the central coast of Safi City, Morocco. The six marine bacteria *Vibrio* sp., *Pseudoalteromonas* sp., *Staphylococcus haemolyticus*, *Planococcus maritimus*, *Hispanic B 35*, and *Cobetia marina* strain A7 were able to produce molecules that inhibited three pathogenic bacterial strains which were *Escherichia coli*, *Staphylococcus aureus* and *Listeria monocytogenes* with high inhibition zones reaching 27 mm.

Microbes present in mangrove forests play a fundamental role as a source of valuable biotechnological products, and play significant roles in various environmental activities and applications (Auta et al., 2017). Microorganisms make an essential contribution to the productivity of the mangrove ecosystem. They are able to recycle nutrients, produce and consume gases that affect the global climate, destroy pollutants, and treat anthropogenic wastes, and can also be used for biological control of plant and animal pests. Bacteria from mangrove environments are a major source of antimicrobial agents and also produce a wide range of critical medicinal compounds, including enzymes, antitumor agents, insecticides, vitamins, immunosuppressants, and immune modulators (Thatoi et al., 2013).

Bibi et al. (2017) isolated 46 bacteria from the soil, roots, and leaves of different mangroves collected from the coastal area of Thuwal in Jeddah Governorate (Saudi Arabia). By using different en-

zymatic media, these bacterial strains were capable of producing industrially important enzymes (cellulase, protease, lipase, and amylase). These strains were identified as belonging to 10 different genera, *Erwinia*, *Vibrio*, *Psychrobacter*, *Aidingimonas*, *Marinobacter*, *Chromohalobacter*, *Halomonas*, *Microbulbifer*, *Alteromonas*, *Bacillus* and *Isoptricola*.

BACTERIA ASSOCIATED WITH MARINE ORGANISMS

Oceans comprise 70% of the earth's area and 33–34% of animal phyla live in marine environments. The marine life constitutes almost 80% of the world's biota (Datta et al., 2015) and the symbiotic relationships are widespread in marine ecosystems. From a microbial perspective, symbiosis can be considered an ancient survival strategy that furnishes microorganisms with advantages to promote their proliferation, such as access to a nutrient-rich habitat and higher environmental stability. In this regard, even if microbial cells typically grow faster in their free-living stage, aggregates confer microbes a higher protection against external stresses e.g., desiccation, antibiotics, and predation (Lo Giudice & Rizzo, 2022).

Neave et al. (2016) explained that *Endozoicomonas* bacteria have highly diverse and flexible symbionts in numerous marine hosts inhabiting oceans worldwide. Their hosts range from simple invertebrate species, such as sponges and corals, to complex vertebrates, such as fish. The functional role of *Endozoicomonas* is to participate in host-associated protein and carbohydrate transport and cycling. It also regulates bacterial colonization of the animal host via the production of bioactive secondary metabolites or distinct mechanisms such as the competitive exclusion of pathogenic bacteria.

Bacteria associated with fish

Marine fish are important for the human diet due to their high nutritional value. In spite of this advantage, eating fish could have the risk of infectious diseases. Fish contain high moisture and protein and the pH values close to neutral; thus, bacteria can develop in this very favorable media. The microorganisms in the skin, shell, gills, intestinal contents,

and surrounding areas cause first-degree contamination and the second contamination occurs in the processing, transportation, and marketing stages (Ogur, 2022).

Based on the study by Tomaru et al. (2022), 23 genera of histamine-producing bacteria that led to food poisoning were isolated from fish purchased in Japan. The most frequently reported bacteria were *Morganella morganii* and *Photobacterium damsela*. Psychrophilic bacteria such as *Morganella psychrotolerans* and *Photobacterium phosphoreum* were also isolated.

Bacteria associated with Sponges

Sponges are sessile filter-feeding organisms that are widely distributed in marine environments. They harbor a diverse community of microorganisms, including bacteria, archaea, fungi, and viruses. Among these microorganisms, bacteria are the most abundant and diverse group associated with sponges (Versluis et al., 2017). Marine bacteria associated with sponges play important roles in the ecology of these organisms. They can provide essential nutrients to sponges, help in the removal of waste products, and protect their host against pathogens. In addition, some sponge-associated bacteria have been found to produce bioactive compounds that have potential applications in medicine and biotechnology (Taylor et al., 2007).

The diversity of bacterial communities associated with sponges is influenced by various factors such as sponge species, location, depth, and environmental conditions. Some common bacterial phyla found in sponge-associated communities include Proteobacteria, Actinobacteria, Bacteroidetes, Firmicutes, and Cyanobacteria (Webster & Taylor, 2012).

Anteneh et al. (2022) isolated a total of 1234 bacterial colonies from 12 sponge samples from two sites collected from the South Australian marine environment. This bacterial population was cultivated on seven different agar media: Soluble starch yeast extract peptone agar (SYP), asparagine peptone agar (ASP), natural seawater agar (SWA), humic acid-vitamin agar (HV), nutrient agar (NA), marine agar (MA) and tryptone soya agar (TSA) at 15 °C and 27 °C and three oxygen levels: aerobic, anaerobic and microaerophilic for three months. Depending on 16S rRNA gene analysis, the isolated

bacteria were classified into four phyla: Actinobacteria, Firmicutes, Proteobacteria and Bacteroidetes containing 21 genera. In this study, the researchers isolated a variety of bacterial species by using culture-based and culture-independent approaches. This observed variation displays the importance of utilizing both culturing methods to reflect a complete picture of the microbial population of marine sponges.

Bacteria associated with Corals

One of the biologically diverse ecosystems on the earth is a coral reef. Each square centimeter of a coral's surface harbors several thousand species of microbes and up to 107 bacterial species which are ten times more abundant, on average, than the surrounding seawater (Raina et al., 2016). Previous research has indicated that the predominant bacterial phyla, such as Proteobacteria, Bacteroidetes, Firmicutes, Cyanobacteria, and Chloroflexi, are similar among many coral species. In addition to the microbiome of the coral core which includes rare bacterial taxa, many studies support the notion that the microbiome of corals is distinct from that of the overlying seawater and that bacterial communities supported by corals fluctuate with the season (Su et al., 2021).

Raina et al. (2016) extracted an antimicrobial compound from *Pseudovibrio* sp. P12, a common coral-associated bacterium. This compound had been identified as tropodithietic acid (TDA) and it prevented the growth of two pathogens in coral, *Vibrio coralliilyticus* and *Vibrio owensii*, at very low concentrations (0.5 µg/mL) in agar diffusion assays. These results show the importance of microbial communities associated with coral reefs for their contribution to protecting corals from diseases.

Bacteria associated with Algae

Marine bacteria are a diverse group of microorganisms that can live in close association with various types of algae. These bacteria play important roles in the ecology and physiology of their algae hosts and are involved in a range of processes, including nutrient cycling, symbiosis, and disease resistance. In addition, the secondary metabolites produced and secreted by different macroalgae can

selectively attract or repel specific bacteria (Wang et al., 2022).

Schwenk et al. (2014) isolated 17 bacterial species from four algae cultures *Chlorella pyrenoidosa*, *Scenedesmus obliquus*, *Isochrysis* sp., and *Nitzschia microcephala* from the Baltic, Finland. The algae was cultivated on special media for three days. Then, 1 ml of each culture was suspended in 9 ml of marine broth and then additional dilutions were made for these suspensions. About 0.1 ml of each dilution was spread onto marine agar plates and incubated at 25 °C for 7 days. All obtained bacterial strains belong to one of three families, Rhodobacteraceae, Rhizobiaceae, and Erythrobacteraceae and the majority of the isolated bacteria belong to Rhodobacteraceae. Based on 16S rDNA sequences, the online tool UniFrac indicated that the bacterial community of *Isochrysis* sp. differs significantly from the other communities associated with other algae. In contrast, communities found in other algae are not remarkably different from each other. The different marine habitats in Saudi Arabia that have been used to isolate novel bacterial strains are illustrated in Fig. 1.

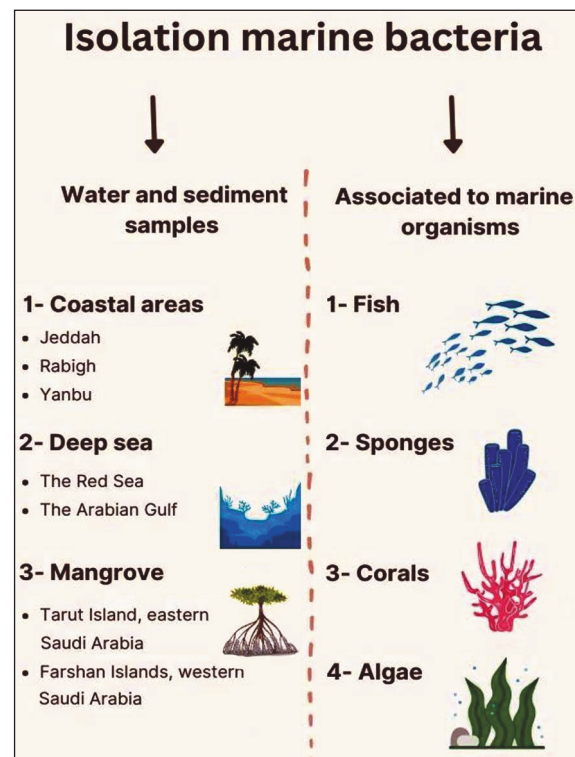


Figure 1. Some marine sources in Saudi Arabia for the isolation of new bacterial species.

SALINITY-TOLERANT MECHANISMS OF MARINE BACTERIA

Halophilic bacteria are a group of microorganisms that thrive in high salt concentrations. They have evolved unique mechanisms to survive in these extreme environments. One of these mechanisms is the accumulation of compatible solutes. Amino acids, betaines, and sugars are examples of these solutes which are small organic molecules that help maintain cell turgor and prevent dehydration (Gregory & Boyd, 2021). Another mechanism for salinity resistance is an accumulation of big quantities of potassium needed for the stability and activity of the enzymes, ribosomes, and transport proteins (Rao et al., 2022). Also, the cell membrane of bacteria adapts to withstand high concentrations of salt as the membrane contains more negatively charged phospholipids, which repel sodium ions and prevent them from entering the cell (Gandhi & Shah, 2016). Some halophilic bacteria use a salt-in strategy, where they actively transport sodium ions into the cell to balance the high concentration of salt outside the cell (Rao et al., 2022).

THE IMPORTANCE OF BIOACTIVE COMPOUNDS FROM MARINE BACTERIA

Bacteria isolated from marine waters, sediments, and marine organisms can produce a wide range of novel therapeutic compounds with broad applications. Many biotechnologically useful compounds were identified from marine bacteria, such as antibacterial, antiviral, antifungal, anti-quorum-sensing, and anticancer substances (Srinivasan et al., 2021). Table 1 summarizes some marine bacterial isolates that have been shown to be effective as producers of natural bioactive compounds. Marine bacteria provide new avenues for developing novel compounds and therapeutic agents, potentially providing antimicrobials necessary to fight drug-resistant pathogens for the next 100 years (Srinivasan et al., 2021).

In the study conducted by El Samak et al. (2018), 50 bacterial strains were isolated by marine agar, starch casein agar, and International Streptomyces Project-2 (ISP-2) agar from eight different Red Sea marine invertebrates and screened for their

antimicrobial activity against common pathogenic bacteria (*Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis*) and yeast (*Candida albicans*) using the well diffusion assay. The results showed that *Bacillus* sp., *Paracoccus* sp. and *Nocardiopsis* sp. had antifungal activity against *C. albicans* with no activity recorded against pathogenic bacterial strains. Many marine bacteria belonging to a wide range of bacterial taxa were found to produce β -glucosidase inhibitors. These compounds are abundantly present in bacteria of the phylum Firmicutes followed by the phylum Actinobacteria. The results nurture the hope of finding new compounds that can inhibit glucosidases from marine bacteria. Thus, microbial cells can be utilized as producers of pharmacologically essential enzyme inhibitors (Pandey et al., 2013).

Production of antibacterial agents

Antibiotics are medicines used to treat infections caused by bacteria and also known as antibacterial. They are chemicals derived from the metabolism of living cells and most of which are obtained through synthesis or semi-synthesis. These substances, in very diluted solutions, have the property of stopping the multiplication or even destroying certain microorganisms. Most antibiotics target growth processes or bacterial functions, they can target the bacterial cell wall or cell membrane or interfere with DNA replication, metabolism, or protein synthesis (Gabriela et al., 2010). The first antibiotic substance obtained from the marine environment was identified by Burkholder. This substance was extracted from the marine bacterium *Pseudomonas bromoutilis* which was isolated from *Thalassia* (turtle grass) in Puerto Rico. The discovered antibiotic was shown to be highly active against Gram-positive bacterial strains of *Staphylococcus aureus*, *Diplococcus pneumoniae*, and *Staphylococcus pyogenes* (Burkholder et al., 1966).

Bacteria associated with brown algae represent a rich source of bioactive metabolites. Twenty-three marine bacterial strains associated with brown algae *Sargassum* were isolated using marine agar from Panjang island, Jepara, North Java. The disk-diffusion method was used to screen for antibacterial activity against pathogenic bacteria methicillin-resistant *Staphylococcus aureus* (MRSA) and *Staphylococcus epidermidis*. The results

| | Marine sources | Marine bacteria | Bioactive compounds | References |
|---|---|---|--|---|
| 1 | Deep Atlantic Ocean, Morocco (water) | <i>Pseudoalteromonas</i> , <i>Vibrio</i> , <i>Staphylococcus haemolyticus</i> , <i>Planococcus maritimus</i> | Antibacterial compounds against <i>Staphylococcus aureus</i> | Chbel et al., 2022 |
| 2 | Limski Channel in Croatia and Punta de Santa Ana, Blanes (sponge) | <i>Rhodococcus erythropolis</i> | Bioactive secondary metabolites | Versluis et al., 2018; Gavriilidou et al., 2021 |
| | | <i>Pseudovibrio</i> , <i>Psychrobacter</i> , <i>Brevibacterium</i> | Active against cancer cell lines | |
| 3 | Harminder Bay, Little Andaman (algae) | <i>Lysinibacillus odysseyi</i> | A broad spectrum of antibacterial activity against <i>Klebsiella pneumoniae</i> , <i>Shigella flexneri</i> , <i>E. coli</i> , and <i>Vibrio cholerae</i> | Karthick and Mohanraju, 2020 |
| 4 | Red Sea, Jazan Region, Saudi Arabia (coastal region) | <i>Streptomyces</i> strain Al-Dhabi-100 | Antimicrobials and promising antitubercular and antioxidant activities | Abdullah Al-Dhabi et al., 2020 |
| 5 | The Gulf of Suez and Hurgada, Egypt (sediment) | <i>Streptomyces</i> sp. | Antimicrobial agent against some pathogens such as <i>Candida albicans</i> | Hamed et al., 2019 |
| 6 | Red Sea invertebrates (corals and sponge) | <i>Bacillus</i> sp. <i>Paracoccus</i> sp. <i>Nocardiopsis</i> sp. | Antifungal activity against <i>C. albicans</i> | El Samak et al., 2018 |
| 7 | Red Sea, Sharm el Sheikh, Egypt (sediments) | <i>Streptomyces</i> | Antimicrobial and anticancer drugs with cytotoxic activity against breast cancer cell line | Abdelfattah et al., 2016 |
| 8 | Panjang Island, Indonesia (algae) | <i>Bacillus subtilis</i> | Potential sources of antibacterial compounds against MRSA and <i>Staphylococcus epidermidis</i> | Susilowati et al., 2015 |
| 9 | Bay of Bengal, India (sponge) | Firmicutes Actinobacteria | β -glucosidase essential enzyme inhibitors | Pandey et al., 2013 |

Table 1. Some effective natural products isolated from marine bacteria.

showed that the active bacterial strain associated with algae belongs to *Bacillus subtilis* and this strain may contribute to the search for new resources of antibacterial substances (Susilowati et al., 2015).

Karthick & Mohanraju (2020) obtained four bacterial isolates from red algae by using marine agar media. One isolate, namely *Lysinibacillus odysseyi*, has an inhibitory effect on the tested pathogens. The crude extract obtained from the

minimal media at pH 7 produced a broad spectrum of antibacterial activity against enteropathogenic *Escherichia coli*, *Klebsiella pneumoniae*, *Shigella flexneri*, *Shigella boydii*, *Salmonella typhi* and *Vibrio cholerae*.

Abdelfattah et al. (2016) isolated 27 strains of actinomycetes from Red Sea sediments. Among them, five strains of *Streptomyces* produced biologically active secondary metabolites such as antimicrobial and anticancer and can be used in testing to obtain pharmaceutical products. The results also showed that one strain was found to have cytotoxic activity against breast cancer cell line MDA-MB-231 due to the presence of many anthraquinone compounds.

Lemos et al. (1985) demonstrated that bacteria from the surfaces of seaweed produce antibacterial compounds. They also conducted further studies in the laboratory and showed that high proportions of marine epibiotic bacteria secrete secondary metabolites with antibacterial properties. Armstrong *et al.* (2001) screened the bacterial isolates associated with seaweed and invertebrate and reported that over 25% of these isolates can produce compounds capable of killing MRSA and vancomycin-resistant *Enterococcus* (VRE). This is a much higher proportion than found with free-living or soil-associated bacteria. In another study, the researchers obtained crude extracts from 21 bacterial strains isolated from marine sponges and determined their antibacterial and cytotoxic activity. 16S rRNA gene analysis revealed that these strains belong mainly to four phyla, Proteobacteria, Actinobacteria, Bacteroidetes, and Firmicutes. Actinobacteria and Proteobacteria were considered the most prolific sources of bioactive secondary metabolites. In fact, marine bacteria of these taxa had been highlighted before for their antimicrobial activity. Also, the results from this study showed that only one strain was identified as *Rhodococcus erythropolis*, which possesses anti-MRSA potential. In addition, four extracts obtained from isolated strains belonging to the genera *Pseudovibrio*, *Psychrobacter*, and *Brevibacterium* showed the highest activity mainly against A2058, A549, and MiaPaca2 cancer cells (Gavriilidou et al., 2021).

A novel strain Al-Dhabi-100 belonging to the genus *Streptomyces* was isolated from the marine areas in the Jazan region, Saudi Arabia, and it was screened for antibacterial activity. The results indi-

cated that the minimum inhibitory concentration (MIC) values of the fraction noted as 62.5 µg/ml for *Enterococcus faecalis*, 31.25 µg/ml for *Bacillus subtilis*, 125 µg/ml for *Staphylococcus aureus*, 250 µg/ml for *Staphylococcus epidermidis* and 125 µg/ml for *Klebsiella pneumoniae*. Also, this new strain had the additional advantage of anti-tubercular and antioxidant potentials (Al-Dhabi et al., 2020).

CONCLUSIONS

After new strains of bacteria resistant to antibiotics emerged, it became important to search for new biological compounds. Marine environments, with their wide biological, physiological and chemical diversity, have proven to be a good source for isolating marine bacteria and extracting biologically active compounds. This contributes to discovering new molecular templates and compounds for producing effective antimicrobial drugs.

REFERENCES

- Abdelfattah M.S., Elmallah M.I.Y., Hawas U.W., El-Kassem L.A., & El-Desoky A.H., 2016. Isolation and characterization of marine-derived actinomycetes with cytotoxic activity from the Red Sea coast. *Asian Pacific Journal of Tropical Biomedicine*, 6: 651–657.
- Al-Dhabi N.A., Esmail G.A., Ghilan A.K.M., Arasu M.V. & Duraipandiyar V., 2020. Metabolite profiling of *Streptomyces* sp. Al-Dhabi-100 isolated from the marine environment in Saudi Arabia with anti-bacterial, anti-tubercular and anti-oxidant potentials. *Journal of King Saud University-Science*, 32: 1628–1633. <https://doi.org/10.1016/j.jksus.2019.12.021>
- Ameen F., Alnadhari S. & Al-Homaidan A.A., 2022. Marine fungi showing multifunctional activity against human pathogenic microbes and cancer. *Plos one*, 17(11), e0276926.
- Anteneh Y.S., Yang Q., Brown M.H. & Franco C.M., 2022. Factors affecting the isolation and diversity of marine sponge-associated bacteria. *Applied Microbiology and Biotechnology*, 106: 1729–1744. <https://doi.org/10.1007/s00253-022-11791-8>
- Armstrong E., Yan L., Boyd K.G., Wright P.C. & Burgess J.G., 2001. The symbiotic role of marine microbes on living surfaces. *Hydrobiologia*, 461: 37-40.
- Auta S.H., Emenike C.U. & Fauziah S.H., 2017. Screening for polypropylene degradation potential of bac-

- teria isolated from mangrove ecosystems in Peninsular Malaysia. *International Journal of Bioscience, Biochemistry and Bioinformatics*, 7: 245–251. <https://doi.org/10.17706/ijbbb.2017.7.4.245-251>
- Bibi F., Ullah I., Alvi S.A., Bakhsh S.A., Yasir M., Al-Ghamdi A.A.K. & Azhar E.I., 2017. Isolation, diversity, and biotechnological potential of rhizo- and endophytic bacteria associated with mangrove plants from Saudi Arabia. *Genetics and Molecular Research*, 16: 1–12. <https://doi.org/10.4238/gmr16029657>.
- Biswas K., Paul D. & Sinha S.N., 2016. Marine bacteria: a potential tool for antibacterial activity. *Journal of Applied & Environmental Microbiology*, 4: 25–29. <https://doi.org/10.12691/jaem-4-1-3>
- Burkholder P.R., Pfister R.M. & Leitz F.H., 1966. Production of a pyrrole antibiotic by a marine bacterium. *Applied microbiology*, 14: 649–653.
- Chang R.H., Yang L.T., Luo M., Fang Y., Peng L.H., Wei Y., Fang J., Tang J.-L. & Liang X., 2021. Deep-sea bacteria trigger settlement and metamorphosis of the mussel *Mytilus coruscus* larvae. *Scientific Reports*, 11: 919.
- Chbel A., Rodriguez-Castro J., Quinteiro J., Rey-Méndez M., Delgado A.S., Soukri A. & El Khalfi B., 2022. Isolation, molecular identification and antibacterial potential of marine bacteria from deep Atlantic Ocean of Morocco. *Avicenna Journal of Medical Biotechnology*, 14: 206–215. <https://doi.org/10.18502/ajmb.v14i3.9827>.
- Costa M., Costa-Rodrigues J., Fernandes M.H., Barros P., Vasconcelos V. & Martins R., 2012. Marine cyanobacteria compounds with anticancer properties: a review on the implication of apoptosis. *Marine drugs*, 10: 2181–2207. <https://doi.org/10.3390/md10102181>
- Cui Y., Chun S.J., Baek S.H., Lee M., Kim Y., Lee H., Ko S.-R., Hwang S., Anh C. & Oh H.M., 2019. The water depth-dependent co-occurrence patterns of marine bacteria in shallow and dynamic Southern Coast, Korea. *Scientific Reports*, 9: 9176. <https://doi.org/10.1038/s41598-019-45512-5>
- Datta D., Talapatra S.N. & Swarnakar S., 2015. Bioactive compounds from marine invertebrates for potential medicines-an overview. *International Letters of Natural Sciences*, 7: 42–61.
- Doshi G.M., Aggarwal G.V., Martis E.A. & Shanbhag P.P., 2011. Novel antibiotics from marine sources. *International Journal of Pharmaceutical Sciences and Nanotechnology*, 4: 1446–1461. <https://doi.org/10.37285/ijpsn.2011.4.3.2>
- El Samak M., Solyman S.M. & Hanora A., 2018. Antimicrobial activity of bacteria isolated from Red Sea marine invertebrates. *Biotechnology Reports*, 19.
- El-Kurdi N., Abdulla H. & Hanora A., 2021. Anti-quorum sensing activity of some marine bacteria isolated from different marine resources in Egypt. *Biotechnology Letters*, 43: 455–468.
- Farda B., Djebaili R., Vaccarelli I., del Gallo M. & Pellegrini M., 2022. Actinomycetes from Caves: An Overview of Their Diversity, Biotechnological Properties, and Insights for Their Use in Soil Environments. *Microorganisms*, 10: 453. <https://doi.org/10.3390/microorganisms10020453>
- Fonti V., Di Cesare A., Šangulin J., Del Negro P., & Cellussi M., 2021. Antibiotic resistance genes and potentially pathogenic bacteria in the central Adriatic Sea: are they connected to urban wastewater inputs? *Water*, 13: 3335. <https://doi.org/10.3390/w13233335>
- Gabriela A., Goldiş V., Avram G. E. & Urtilă E., 2010. Antibiotic. *Journal Medical Aradean*, 8: 15–23.
- Gandhi A., & Shah N.P., 2016. Effect of salt stress on morphology and membrane composition of *Lactobacillus acidophilus*, *Lactobacillus casei*, and *Bifidobacterium bifidum*, and their adhesion to human intestinal epithelial-like Caco-2 cells. *Journal of Dairy Science*, 99: 2594–2605. <https://doi.org/10.3168/jds.2015-10718>
- Gavriliidou A., Mackenzie T.A., Sánchez P., Tormo J.R., Ingham C., Smidt H. & Sipkema D., 2021. Bioactivity screening and gene-trait matching across marine sponge-associated bacteria. *Marine Drugs*, 19: 75. <https://doi.org/10.3390/md19020075>
- Gregory G.J. & Boyd E.F., 2021. Stressed out: Bacterial response to high salinity using compatible solute biosynthesis and uptake systems, lessons from *Vibrionaceae*. *Computational and structural biotechnology journal*, 19: 1014–1027. <https://doi.org/10.1016/j.csbj.2021.01.030>
- Hamed M.M., Abdelfattah L.S. & Fahmy N.M., 2019. Antimicrobial activity of marine actinomycetes and the optimization of culture conditions for the production of antimicrobial agent (s). *Journal of Pure and Applied Microbiology*, 13: 2177–2188. <https://doi.org/10.22207/JPAM.13.4.30>
- Hassanali K. & Mahon R., 2022. Encouraging proactive governance of marine biological diversity of areas beyond national jurisdiction through Strategic Environmental Assessment (SEA). *Marine Policy*, 136: 104932. <https://doi.org/10.1016/j.marpol.2021.104932>
- Karthick P. & Mohanraju R., 2020. Antimicrobial compounds produced by *Lysinibacillus odyseyi* epiphytic bacteria associated with red algae. *Brazilian Journal of Microbiology*, 51: 1683–1690. <https://doi.org/10.1007/s42770-020-00341-x>
- Lemos M.L., Toranzo A.E. & Barja J.L., 1985. Antibiotic activity of epiphytic bacteria isolated from intertidal

- seaweeds. *Microbial Ecology*, 11: 149–163.
<https://doi.org/10.1007/BF02010487>
- Lo Giudice A. & Rizzo C., 2022. Bacteria Associated with Benthic Invertebrates from Extreme Marine Environments: Promising but Underexplored Sources of Biotechnologically Relevant Molecules. *Marine drugs*, 20: 617.
<https://doi.org/10.3390/md20100617>
- Mancini I., Defant A. & Guella G., 2007. Recent synthesis of marine natural products with antibacterial activities. *Anti-Infective Agents in Medicinal Chemistry*, 6: 17–48
<https://doi.org/10.2174/187152107779314151>
- Neave M.J., Apprill A., Ferrier-Pagès C. & Voolstra C.R., 2016. Diversity and function of prevalent symbiotic marine bacteria in the genus *Endozoicomonas*. *Applied microbiology and biotechnology*, 100: 8315–8324.
<https://doi.org/10.1007/s00253-016-7777-0>
- Ogur S., 2022. Pathogenic bacteria load and safety of retail marine fish. *Brazilian Journal of Biology*, 82.
<https://doi.org/10.1590/1519-6984.262735>
- Pandey S., Sree A., Dash S.S., Sethi D.P. & Chowdhury L., 2013. Diversity of marine bacteria producing beta-glucosidase inhibitors. *Microbial cell factories*, 12: 35.
- Qin S., Li W. J., Dastager S.G. & Hozzein W.N., 2016. Editorial: actinobacteria in special and extreme habitats: Diversity, function roles, and environmental adaptations. *Frontiers in Microbiology*, 7(SEP). Frontiers Research Foundation.
- Qureshi K.A., Seroor M., Al-Masabi A., Saykhan M.A., Mutairi Y.A., Elhassan G.O. & Khan R.A., 2020. Bio-characterizations of some marine bacterial strains isolated from mangrove sediment samples of four major cities of Saudi Arabia. *Journal of Environmental Biology*, 41: 1003–1012.
<https://doi.org/10.22438/jeb/41/5/MRN-1317>
- Raina J.B., Tapiolas D., Motti C.A., Foret S., Seemann T., Tebben J., Willis B.L. & Bourne D.G., 2016. Isolation of an antimicrobial compound produced by bacteria associated with reef-building corals. *PeerJ*, 4, e2275.
- Rao A.S., Nair A., Nivetha K., More V.S., Anantharaju K.S. & More S.S., 2022. Molecular adaptations in proteins and enzymes produced by extremophilic microorganisms. In: *Extremozymes and their Industrial Applications*, pp. 205–230.
<https://doi.org/10.1016/j.semcedb.2018.01.003>
- Sarkar G. & Suthindhiran K., 2022. Diversity and biotechnological potential of marine actinomycetes from India. *Indian Journal of Microbiology*, 62, 475–493.
<https://doi.org/10.1007/s12088-022-01024-x>
- Schwenk D., Nohynek L. & Rischer H., 2014. Algae-bacteria association inferred by 16S rDNA similarity in established microalgae cultures. *Microbiology Open*, 3: 356–368.
<https://doi.org/10.1002/mbo3.175>
- Srinivasan R., Kannappan A., Shi C. & Lin X., 2021. Marine bacterial secondary metabolites: a treasure house for structurally unique and effective antimicrobial compounds. *Marine Drugs*, 19: 530.
<https://doi.org/10.3390/md19100530>
- Su H., Xiao Z., Yu K., Zhang Q., Lu C., Wang G., Wang Y., Liang J., Huang W., Huang X. & Wei F., 2021. High diversity of β -Glucosidase-producing bacteria and their genes associated with Scleractinian corals. *International Journal of Molecular Sciences*, 22: 3523.
<https://doi.org/10.3390/ijms22073523>
- Susilowati R., Sabdono A. & Widowati, I., 2015. Isolation and characterization of bacteria associated with brown algae *Sargassum* spp. from Panjang Island and their antibacterial activities. *Procedia Environmental Sciences*, 23: 240–246.
<https://doi.org/10.1016/j.proenv.2015.01.036>
- Taylor M.W., Radax R., Steger D. & Wagner M., 2007. Sponge-associated microorganisms: evolution, ecology, and biotechnological potential. *Microbiology and molecular biology reviews*, 71: 295–347.
<https://doi.org/10.1128/MMBR.00040-06>
- Thatoi H., Behera B.C., Mishra R.R. & Dutta S.K., 2013. Biodiversity and biotechnological potential of microorganisms from mangrove ecosystems: a review. *Annals of Microbiology*, 63: 1–19.
- Tomaru A., Toda M. & Hara-Kudo Y., 2022. Literature Review on the Type of Fish and Histamine-producing Bacteria Associated with Histamine Poisonings in Japan. *Journal of the Food Hygienic Society of Japan*, 63: 109–116.
<https://doi.org/10.3358/shokueishi.63.109>
- Versluis D., McPherson K., van Passel M.W.J., Smidt H. & Sipkema D., 2017. Recovery of previously uncultured bacterial genera from three mediterranean sponges. *Marine biotechnology*, 19: 454–468.
<https://doi.org/10.1007/s10126-017-9766-4>
- Versluis D., Nijssse B., Naim M.A., Koehorst J.J., Wiese J., Imhoff J.F., Schaap P.J., van Passel M.W.J., Smidt H. & Sipkema D., 2018. Comparative genomics highlights symbiotic capacities and high metabolic flexibility of the marine genus *Pseudovibrio*. *Genome biology and evolution*, 10: 125–142.
<https://doi.org/10.1093/gbe/evx271>
- Wang J., Yang Z., Wang G., Shang S., Tang X. & Xiao H., 2022. Diversity of epiphytic bacterial communities on male and female *Sargassum thunbergii*. *AMB Express*, 12: 97.
<https://doi.org/10.1186/s13568-022-01439-1>