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Marine Environment: A Potential Pool of Isolating Antibiotic Producing Bacteria with Novel Characteristics

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Authors' contributions

This work was carried out in collaboration between both authors. Author SS designed the study and wrote the first draft of the manuscript and managed literature searches. Author AI checked the first draft of manuscript and analyzed the data. Both authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Aims: This review article analyze the data based on antibiotic producing bacteria isolated from different poles of marine environment globally and further more their antibiotic potential against different pathogenic microbes.
Microorganisms are potential source of metabolites with useful antimicrobial, antiviral and anticancer properties. Especially microbes of different environment show versatility in antibiotic producing ability. Thus there is always a need for exploring new microbes for promising antibiotic producing ability with an alternative mode of action and new chemical structures. Bacterial pathogens are gradually becoming more resistant to conventional antibiotics. So these resistance bacterial pathogens generating an emergence of infectious diseases and they are becoming a great problem in the field of public health.
Conclusion: Marine bacteria can be proved a source of novel antibiotics against many resistant pathogens.

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1. INTRODUCTION

An agent that inhibits bacterial growth or kills bacteria and other microorganism is called antibiotic. Antibiotic is a substance that is produced by a microorganism that is antagonize the growth of other microorganisms in high intensity [1]. It is essential to control the growth of unwanted microorganisms in every aspect of life that causes infectious diseases in plants, animals and humans [2,3]. The basic difference between antibiotics and chemotherapeutic drugs is that antibiotics are synthesized by numerous bacteria and fungi so these are natural drugs, while chemotherapeutic are synthesized by man, so these are categorized under synthetic drugs [4]. Although chemotherapeutic drugs are good but in medical implication the multiplicity of microorganisms and their secondary metabolites is supreme and matchless [5]. In modern pharmaceutical industry some of the most important products have been yielded from microorganisms because they are a productive source of structurally diverse bioactive metabolites [6]. This article focuses on the potential role of antibiotics producing bacteria isolated from marine environment of different countries against different human pathogens.

2. HISTORY OF ANTIBIOTICS

History of antibiotics began in 1928 when a British scientist Alexander Fleming observed that bacterial growth can be inhibited by another organism. He observed that a mold, which contaminated the Petri plate he was working on, inhibited the growth of bacterium *Staphylococcus aureus*. The mold was *Penicillin notatum* and the antibiotic which was isolated after some time were named as penicillin [7]. S.A Waksman introduced the term antibiotic in 1942 [4]. The antibiotic research from the innovation of Fleming to our days has been a charming, stirring, continuously changing and mounting venture [8]. Many other drugs chlortetracycline, streptomycin, chloramphenicol, rifamycin, erythromycin, cephalosporin C, lincomycin, vancomycin, amphotericin, nystatin, nalidixic acid, erythromycin and daunorubicin has been discovered from microorganisms after Penicillin got isolated [9].

3. MECHANISM OF ANTIBIOTICS ACTION

The mechanism of antibiotics action is well understood on its molecular basis and the major targets are well identified. Antibiotics are classified on the basis of their major target of action, where they restrain bacterial growth by interrupting crucial cellular functions [10]. It is a multistep procedure that involves a number of steps starting from the physical interaction of antibiotics to its target of action and hence a series of changes involving biochemical, molecular, and structural change. The main targets of action of antibiotics are: 1) DNA replication, 2) RNA synthesis, 3) Cell wall synthesis, and 4) Protein synthesis. Major antibiotics with their target of action are summarized in Table 1.

3.1 DNA Replication

Topology of the DNA is controlled by DNA gyrase (topoisomerase). This reaction has a significant value in DNA and mRNA synthesis. Quinolone (Ciprofloxacin, Levofloxacin, Norfloxacin) makes a complex with topoisomerase that is called the complex-quinolone topoisomerase-DNA, it prevents the DNA replication by interrupting the DNA cleavage that leads towards the bacterial death [11].

Table 1. Some common antibiotics with their target of action

Antibiotics				
Inhibiting DNA replication	**Inhibiting synthesis of RNA**	**Inhibiting cell wall synthesis**	**Inhibiting protein synthesis**	**Disrupting cytoplasmic membrane**
Ciprofloxacin	Rifampicin	Penicillin	Tetracyclin	Daptomycin
Novobiocin	Actinomycin	Carbapenems	Streptomycin	Polymyxin
Levofloxacin		Vancomycin	Kanamycin	Platensimycin
Norfloxacin		Fastomycin	Gentamycin	
Fludarabine		Bacitracin	Erithomycin	
		Daptomycin	Cindamycin	
			Chloramphenicol	

3.2 Synthesis of RNA

The transcription process is mediated by RNA polymerase, in other words gene expression in prokaryotes is controlled by RNA polymerase as a main regulator in the process of transcription. So, this process is a striking target for antibiotics. Rifamycin is the common example of antibiotics which inhibits RNA synthesis [12].

3.3 Cell Wall Synthesis

Peptidoglycan is the main component of the bacterial cell wall which helps the cell to maintain its integrity in diverse environments for survival. The peptidoglycan synthesis occurs in three steps, the first step is synthesis of low molecular weight precursors in cytosol, in second step membrane-bound enzymes catalyze cell wall synthesis, the third step is the attractive target for antibiotics by acting on transpetidades and preventing the β-lactams and polymerization of the glycan synthesis of cell wall enzymes [13].

3.4 Protein Synthesis

Initiation, elongation, and termination are three steps in which mRNA translation occurs. Ribosomes are the main component of cell where translation occurs. The main target of the antibiotics are ribosomal subunits which are 30S and 50S. Macrolides block the 50S subunit, tetracycline has the affinity for 30S, tetracyclines are very active molecule that have well defined target especially against bacteria, spectinomycin acts on peptidyl-tRNA and disturb its stability by binding to the ribosomes, 16S rRNA of 30S ribosome is the target of action for kanamycin, gentamicin and streptomycin [14].

3.5 Cytoplasmic Membrane

The cytoplasmic membrane is a semi permeable membrane which allows the selective diffusion of molecules through it. Daptomycin disturbs the potassium balance by being inserted in the cytoplasmic membrane and forming ion channels which results in the intracellular potassium release. Disruption of the membrane can be caused by several antibiotics. Polymyxins are the best example of such types of antibiotics which cause the disruption of cytoplasmic membrane but they are not widely used because they produce renal and nervous toxicity [11,12,13]. Another antibiotic with different mechanism of action, that disrupts the cytoplasmic membrane synthesis by interfering the fatty acids production through inhibition of beta-ketoacyl synthases I/II (FabF / B), was launched by Merck in 2006 [15].

3.5.1 Antibiotic production by soil bacteria

A number of soil bacteria have the ability to produce antibiotcs [16]. Many kinds of antibiotic are produced by *Bacillus* species which contribute to broad range antimicrobial activity. For example *Bacillus licheniformis* produce bacitracin which is active against many Gram positive organisms, anaerobic cocci, *Cornyebacter* and *Clostridia* but not against other Gram negative bacteria [17]. *Bacillus brevis* produce gramicidin which inhibits phosphate group ATPase [16]. *Streptomyces* is the largest genus and it is very important medically because of its ability to produce a vast variety of antibiotics. Stanley Waksman's discovery of streptomycin was of significant importance because it efficiently combats tuberculosis and he got the Nobel Prize in 1952. Streptomycetes produce about two thirds of the antimicrobial agent which are used in human and as well as veterinary medicine. Amphoteracin B, neomycin, nystatin, erythromycin, chloramphenicol and tetracycline are some common antibiotics which are produced by Streptomycetes [18]. Many kind of antibiotic is also produced by *Lactobacillus* species. Nicin is one of the antibiotics produced by *Lactobacillus lactis* and it shows a full range of antimicrobial activity against many gram positive bacteria [19].

3.5.2 Antibiotics resistance and need of novel antibiotic

Even though a number of antibiotics have been discovered with the help of advance technology but still infectious diseases are the second leading causes of death worldwide affecting mainly the elderly and children. Bacterial infections are the causes of death of approximately 17 million annually [20]. The main cause of failure of available antibiotics to treat infectious disease is the rapid development of resistance to the antibiotics [21]. Antimicrobial resistance (AMR) is one of the biggest threats to human health according to the World Health Organization (WHO). The important factor which contributes to the antibiotics resistance is overuse of antibiotics and self-medication, thus emphasizing the continuous need for screening and development for new antibiotics [22]. Until recently, terrestrial microorganisms were the major source of antimicrobial compounds, however from the last two decades importance of

this source has decreased because of discovery of clinically unexpected metabolites as in the case of actinomycetes [9]. Recently new metabolites discovery rate from terrestrial actinomycetes has decreased while the re-isolation of known compounds has increased [23]. Thus, it is crucial to pursue discovery of new antibiotics from unexplored or underexploited habitats. For more than two decades, marine environment has become the point of focus as enduring pursuit for discovery of new drugs [24].

3.5.3 Importance of microbes from marine environment

The 70% of Earth's surface is covered by the ocean that is an enormous pool of natural wealth. Still, the degree of oceanic biodiversity, particularly of microbes, is scarcely known [25]. Marine bacteria can be defined as bacteria which need sea water and specially sodium for their growth [26]. The secondary metabolites produced by marine organisms have more novel and unique structures in comparison with terrestrial organisms. It is due to their adaptation to the complex living circumstance and diversity of species, and the bioactivities are much stronger [27]. In addition, along with the deep studies of marine natural products biosynthesis, some substantiation indicates that many bioactive compounds formerly originate in marine animals and plants were in fact produced or metabolized by related microorganisms [28,29,30]. Antibiotic producing bacteria are distributed throughout the marine environment like deep sea [31], aquaculture system [32], sea ice [33,34].

An attempt was made to collect the data of most of the bacterial strains isolated from marine environment by researchers from different countries from 2000 to 2013 in Table 2. In 1966, the first antibiotic was identified and characterized from a marine bacterium which was a pyrrole antibiotic [54]. After that, work for research of new antibiotics from marine source have little focused until 2002 when the first convincing verification for the extensive and unrelenting incidence of native actinomycetes populations in marine sediments was reported by Mincer and coworkers. They isolated large number of strains from geographically different tropical and subtropical locations, nominated MAR 1. The study of morphological characteristics, small-subunit rRNA gene signature nucleotides and presence of sea water for their growth proved that they are different from terrestrial actinomycetes. On the basis of phylogenetic analysis done by 16S rRNA gene sequencing they have monophyletic link with the family Micromonosporaceae which suggested the novelty of strain at genus level [55]. In 2002 Shehane and Sizemore isolated *Vibrio vulnificus* from USA. In 2003 *Pseudoalteromonas phenolica* was isolated by Isnansetyo and Kamei from Japan which showed antibacterial activity against methicillin-resistant *Staphylococcus aureus*. In 2007 Desjardine and coworkers isolated *Brevibacillus laterosporus* from New Guinea and Ahmed and coworkers isolated *Bacillus subtilis, Bacillus lecheniformis, Pseudomonas aeruginosa, Pseudomonas putida* and *Brevibacterium frigoritolerans* from Arabian sea of Pakistan. Raveh and Carmeli also isolated *Cyanobacterium fischerella* and Macherla isolated a strain of genus *Marinispora* which showed the potential harboring power of marine environment.

In 2008 McArthur and coworker isolated a strain of Actinomycete. A strain of *Nocardiopsis*. Sp was isolated by Vimal and coworkers in 2009. Charyulu and coworker isolated a strain of *pseudomonas* from India in 2009, which showed antimicrobial activity against many pathogenic microbes shown in Table 3. In 2010 Cetina and coworker isolated a strain of *Pseudoalteromonas.* Sp with antimicrobial activity. In 2012 research was carried out in Iran and Ghana by Darabpour and coworkers, Tawiah and coworkers, *Pseudoalteromonas piscicida, Pseudomonas auerginosa were* isolated respectively with antimicrobial activity. In 2013 research was carried out in Korea, Iran, Malaysia & India and marine microbes belong to different species were isolated with high antimicrobial activity. Some of marine isolated with their antimicrobial activity in term of inhibition zone (mm) against common pathogenic bacteria are shown in the Table 3. For convenience their antifungal activity is not shown.

Most of the strains which were isolated from marine environment with antimicrobial activity were tested against the most common pathogenic bacteria *MRSA* (methicillin resistant *Staphylococcus aureus*). These bacterial strains showed different zone of inhibition as mentioned in table. MMG-28 showed the maximum zone of inhibition 22mm isolated from India while FStm2 and SCtm12 isolated from Malaysia showed minimum zone of inhibition 10 mm. MN38 showed maximum zone of inhibition 27mm, PRps9 with minimum zone of inhibition 8mm when these bacterial strains were tested against *Bacillus subtillis*.

Table 2. Some common antibiotic producing marine bacteria

Sr#	Isolated strain	Identified as	Country	References
1	*Pseudomonas* sp. UJ-6	_	Korea	[35]
2	FStm2	*Pseudomonas putida*	Malaysia	[25]
3	SWtm11	Not identified	__	__
4	SCtm12	*Vibrio protolyticus*	__	__
5	PRps9	*Vibrio protolyticus*	__	__
6	MN38	*Actinomycetes*	Iran	[36]
7	MN39	_		__
8	MN3	_		__
9	KSP-SS-06-1C/1	*Actinomycetes*	India	[37]
10	BC-1	_	India	[38]
11	MAI2	*Pseudomonas aeruginosa*	Ghana	[9]
12	PG-01	*Pseudoalteromonas piscicida*	Iran	[39]
13	C11	Not identified	India	[40]
14	C12	Not identified		
15	MS-3/48	*Pseudoalteromonas* sp.	Mexico	[41]
16	MMG-28	*Pseudomonas* sp.	India	[42]
17	VITSVK5(FJ9 73467)	*Nocardiopsis* sp.	India	[43]
18	Actinomycetes	Not identified	USA	[44]
19	NPS008920	genus *Marinispora*	USA	[45]
20	Cyanobacterium	*Cyanobacterium fischerella*	Israel	[46]
21	*Bacillus*	*Bacillus subtilis*	Pakistan	[47]
22	*Bacillus*	*Bacillus lecheniformis*	_	_
23	*Pseudomonas*	*Pseudomonas aeruginosa*	__	_
24	*Pseudomonas*	*Pseudomonas putida*	_	_
25	*Brevibacterium*	*Brevibacterium frigoritolerans*	_	_
26	PNG276	*Brevibacillus laterosporus*	PAP New Guinea	[48]
27	Nov.O-BC30t	*Pseudoalteromonas phenolica*	Japan	[49]
28		*Vibrio vulnificus*	USA	[50]
29		*Vibrio(Beneckea) Harveyi*	Texas	[51]
30	strain 18 (=NCMB 1890)	*Alteromonas rubra*	France	[52]
31		*Vibrio marinus*		[53]
32		*Pseudomonas bromoutilis*	New York	[54]

Table 3. Showing antimicrobial activity of isolated marine strain against common pathogenic microbes

	Marine isolated strain with antimicrobial activity	Test strain	Inhibition zone(mm)
1	FStm2	*MRSA*	10
	_	*Bacillus subtilis*	10
	_	*Vibrio parahaemolyticus*	8
	_	*Escherichia coli*	9
	_	*Serratia marcescens*	9
	_	*Aeromonas hydrophila*	10
2	SCtm12	*MRSA*	10
		Sthapylococcus aureus	15
		Vibrio parahaemolyticus	14
		Escherichia coli	12
		Serratia marcescens	8
		Aeromonas hydrophila	12
3	SWtm11	*MRSA*	13
		Sthapylococcus aureus	13
		Bacillus subtilis	8

	Marine isolated strain with antimicrobial activity	Test strain	Inhibition zone(mm)
		Vibrio parahaemolyticus	18
		Escherichia coli	15
		Serratia marcescens	8
		Aeromonas hydrophila	13
4	PRps9	*MRSA*	12
		Sthapylococcus aureus	12
		Bacillus subtilis	8
		Vibrio parahaemolyticus	13
		Escherichia coli	9
		Serratia marcescenss	8
		Aeromonas hydrophila	13
5	MS-3/48	*MRSA*	19
		P. aeruginosa	10
6	KSP-SS-06-1C/1	*Bacillus subtilis*	22.4
		Staphylococcus aureus	21.9
		Escherichia coli	20.4
		Saccharomyces cerevisiae	19.5
		Candida albicans	13.9
		Aspergillus niger	11.7
		Pseudomonas aeruginosa	12.8
7	MMG-28	*Klebsiella pneumonia*	16
		Staphylococcus aureus	20
		Shigella flexneri	18
		Pseudomonas aeruginosa	17
		Bacillus subtilis	18
		MRSA/ORSA	22
8	MAI2	*Bacillus thuringiensis*	24
		Bacillus subtilis	26
		Enterococcus faecalis	22
		Proteus vulgaris	25
9	VITSVK 5	*Escherichia coli*	20
		Pseudomonas aeruginosa	18
		Klebsiella pneumonia	15
		Enterococcus faecalis	20
		Bacillus cereus	13
		Staphylococcus aureus	6
10	MN38	*Staphylococcus aureus*	20
		Bacillus subtilis	27
		Escherichia coli	20
11	MN39	*Bacillus subtilis*	23
		Escherichia coli	23
		Klebsiella pneumonia	24
12	MN3	*Pseudomonas aeruginosa*	20
13	*Bacillus lecheniformis*		
		Kokoris marina	17
		Rothia. Sp.	14
14	*Bacillus subtilis*	*Aeromonas punctata*	15
		Rothia. Sp.	18
		Vibrio. Sp.	21
		S.aureus	16
		S.epidermis	15
15	*Pseudomonas aeruginosa*	*Aeromonas punctata*	17
		Kokoris marina	15
		Rothia. Sp.	18
		Vibrio. Sp.	17

	Marine isolated strain with antimicrobial activity	Test strain	Inhibition zone(mm)
16	*Pseudomonas putida*	*S.aureus*	17
		S.epidermis	18
		E.coli	16
		MRSA	16
		Poteus vulgaris	18
		Aeromonas punctata	15
		Rothia. Sp.	15
		Vibrio. Sp.	14
17	*Brevibacterium frigoritolerans*	*S.aureus*	18
		S.epidermis	16
		E.coli	14
		MRSA	16
		Poteus vulgaris	17
		Rothia. Sp.	20
		Vibrio. Sp.	19
		S.aureus	17

4. CONCULSION

Most of the natural antibiotics available are derived from terrestrial microbes. Microbial resistance against them intensifies the need of new bacterial strain with novel antibiotic production. In this study bacterial strain isolated from marine sources were found to be promising antibiotic producing agents that can be further use to control the spreading of antibiotic resistant pathogens, which cause life threatening infections. This study also highlighted the role of other sources apart from soil community in screening of potential candidates that might be helpful for the discovery of new antibiotics.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Hashemi S, Nasrollah A, Rajabi M. Irrational antibiotic prescribing. A local issue or global concern? EXCLI Journal. 2013;12:384-395.
2. Vicente M, Hodgson J, Massidda O, Tonjum T, Henriques-Normark B, Ron EZ. The fallacies of hope: Will we discover new antibiotics to combat pathogenic bacteria in time? FEMS Microbiol Rev. 2006;30:841-852.
3. Wagner-Döbler I, Biebl H. Environmental biology of the marine *Roseobacter* lineage. Ann Rev Microbiol. 2006;60:255–280.
4. Nair A. Studies on production of antibiotics by induction of marine bacteria with human pathogens. (thesis); 2012.
5. Fenical W. Chemical studies of marine bacteria: Developing a new resource. Chem. Rev. 1993;93:1673-83.
6. Cragg G M, DJ Newman. Medicinals for the millennia. The historical record. Ann. NY. Acad. Scie. 2001;953:3-25.
7. Nester R, J Nester, Sherwood N. Microbiology of human perspective. 5th ed. London Mc Graw Hill Publisher; 2009.
8. Bérdy. Bioactive microbial metabolites. J.Antibiot. 2005;58(1):1–26.
9. Tawiah A, Gbedema S, Adu F, Boamah V, Anna K. Antibiotic producing microorganisms from River Wiwi, Lake Bosomtwe and the Gulf of Guinea at Doakor Sea Beach, Ghana. BMC Microbiology. 2012;12: 234.
10. Kohanski MA, Dwyer DJ, Collins JJ. How antibiotics kill bacteria: From targets to networks. Nat Rev Microbiol. 2010;8:423-35.
11. Chopra I, Hesse L, O'Neill AJ. Exploiting current understanding of antibiotic action for discovery of new drug. J Appl Microbiol. 2002;92:4S-15S.
12. Brotz-Oesterhelt H, Brunner NA. How many modes of action should an antibiotic have? Curr Opin Pharmacol. 2008;8:564-73.
13. Nikaido H. Multidrug Resistance in bacteria. Annu Rev Biochem. 2009;78:119-46.
14. Fuoco D. Classification Framework and Chemical Biology of Tetracycline-

Structure-Based Drugs. Antibiotics. 2012;1(1):1-13.
15. Wang J, Soisson SM, Young K, et al. Platensimycin is a selective FabF inhibitor with potent antibiotic properties. Nat. 2006;441:358-61.
16. Waites MJ, Morgan NL, Rockey JS, Higton, M. Industrial Microbiology an Introduction. 4th ed. London, Blackwell Publisher; 2008.
17. Mc Evoy G, Ahes drug information Amr. Soc. Hospital Pharm. USA; 1993.
18. Willey HJ, Linda PS, Shewood M. Microbiology. 5th ed. London McGraw Hill Publisher. 2008;1035
19. Abdulkadir M, Waliyu S. Screening and Isolation of the Soil Bacteria for Ability to Produce Antibiotics. European Journal of Applied Sciences. 2012;4:211-215.
20. Procópio-R, Silva I, Martins M, Azevedo J, Araújo J. Antibiotics produced by *Streptomyces.,* Braz J Infect Dis. 2012;16(5):466-471.
21. Singer RS, Finch R, Wegner HC, Bywater R, Walters J, Lipstich M. Antibiotic resistance- The interplay between antibiotic use in animals and Human beings. Lancet Infect Dis. 2012;3:47-51.
22. Gould IM. Antibiotic resistance: The perfect storm. Int J Antimicrob Agents. 2009;34(53):S2-5.
23. Fenical W, Jensen PR. Developing a new resource for drug discovery: Marine actinomycete bacteria. Nat Chem Biol. 2006.;2:666–673.
24. Anand, TP, AW Bhat, YS Shouche, U Roy, J Siddharth, SP Sarma. Antimicrobial activity of marine bacteria associated with sponges from the waters off the coast of South East. India. Microbiol. Res. 2006;161(3):252-262.
25. Hamid R, Usup G, Ahmad A. Antimicrobial activity of bacteria associated with various marine sources. Advances in Environmental Biology. 2013;7(2):356-365.
26. Bush K. Antibacterial drug discovery in the 21st century. Clin Microbiol. Infect. 2004;10(4):10-17.
27. Schwartsmann G, Rocha AB, Berlinck RGS, Jimeno J. Marine organisms as a source of new anticancer agents. Lancet Oncol. 2001;2:221-225.
28. Davidson SK, Allen SW, Lim GE, Anderson CM, Haygood MG. Evidence for the biosynthesis of bryostations by the bacterial symbiont Candidatus Endobugula sentula of the bryozoans Bugula neritina. Appl. Environ. Microb. 2001;67:4531-4537.
29. Luesch H, Moore RE, Paul VJ, Mooberry SL, Corbett TH. Isolation of dolastatin 10 from the marine cynobacterium Symploca species VP642 and total stereochemistry and biological evaluation of its analogue symplostatin. 1. J. Nat. Prod. 2001;64:907-910.
30. Proksch P, Edrada RA, Ebel R. Drugs from the sea-current status and microbiological implications. Appl. Microbiol. Biotechnol. 2002;59:125-134.
31. Fusetani N, Ejima D, Matsunaga, Hatsumoto K et al. 3-Amino-3-deoxy-D-glucose: an antibiotic produced by deep-sea bacterium. Experientia. 1987;43:464-465.
32. Jorquera MA, Riquelme CE, Loyola LA, Muñoz LF. Production of bactericidal substances by a marine *Vibrio* isolated from cultures of the scallop *Argopecten purpuratus*. Aquaculture International. 2000;7(6):433-448.
33. Al-Zereini W, Schuhmann I, Laatsch H, Helmke E, Anke H. New Aromatic Nitro Compounds from *Salegentibacter* sp. T436, an Arctic Sea Ice Bacterium: Taxonomy, Fermentation, Isolation and Biological Activities. The Journal of Antibiotics. 2007;6:301–308.
34. Wietz M ,Månsson M, Bowman J, Blom N, Ng Y, Gram Y. Wide distribution of closely related, antibiotic-producing *Arthrobacter* strains throughout the Arctic Ocean. Applied and environmental microbiology. 2012;78(6):2039-42
35. Lee D, Eom S, Je Y, Kim Y, Le M, Kim YM. Antibacterial Activity of an Ethyl Acetate Extract of *Pseudomonas* sp. UJ-6 against Methicillin-Resistant *Staphylococcus aureus*. Fisheries and Aquaict Sciences. 2013;16(2):79-84.
36. Mohseni M, Norouzi H, Hamedi J, Roohi A. Screening of antibacterial producing actinomycetes from sediments of Caspian Sea. Int J Mol Cell Med. 2013;2(2):64-71.
37. Kumari P, Mantada, Sankar G, Prabhakar GT. Isolation and Characterization of Potent Antibiotic Producing Marine Actinomycetes from Tiruchendur and Kulasekarapattinam, Tamilnadu. Global Journal of Science Frontier Research Bio-Tech & Genetics. 2013;13(2):1-5.
38. Poosarla A, Ramana V, Krishna M. Isolation of potent antibiotic producing Actinomycetes from marine sediments of

Andaman and Nicobar Marine Islands. Journal of Microbiology and Antimicrobials. 2013;5(1):6-12.
39. Darabpour E, Ardakani R, Motamedi H, Ronagh T. Isolation of a potent antibiotic producer bacterium, especially against MRSA, from northern region of the Persian Gulf. Bosn J Basic Med Sci. 2012;12(2) 108-121.
40. Valli S, Sugasini SS, Aysha OS, Nirmala P, Vinoth Kumar P Reena A. Antimicrobial potential of *Actinomycetes* species isolated from marine environment. Asian Pacific Journal of Tropical Biomedicine. 2012;2(6):469-473.
41. Cetina A, Matos A, Garma G, Barba H, Vázquez R, Rodríguez A et al. Antimicrobial activity of marine bacteria isolated from Gulf of Mexico Rev. peru. boil. 2010;17(2):231-236.
42. Charyulu EM, Sekaran G, et al. Antimicrobial activity of secondary metabolite from marine isolate, *Pseudomonas* sp. against Gram positive and negative bacteria including MRSA. Indian J. Exp. Biol. 2009;47(12):964-8.
43. Vimal V, Rajan B, Kannabiran K. Antimicrobial Activity of Marine Actinomycete, *Nocardiopsis* sp. VITSVK 5 (FJ973467). Asian Journal of Medical Sciences. 2009;1(2):57-63.
44. McArthur KA, Mitchell SS, Tsueng G, Rheingold, et al. Lynamicins A–E, chlorinated bisindole pyrrole antibiotics from a novel marine actinomycete. J. Nat. Prod. 2008;71:1732-1737.
45. Macherla VR, Liu J, Sunga M, White et al. Lipoxazolidinones A, B, and C: Antibacterial 4-oxazolidinones from a marine actinomycete isolated from a Guam marine sediment. J. Nat. Prod. 2007;70:454–1457.
46. Raveh A, Carmeli S. Antimicrobial ambiguines from the *Cyanobacterium fischerella* sp. collected in Israel. J Nat Prod. 2007;70(2):196-201.
47. Ahmed N, Uzair B, Ayaz, S, Ahmed V. Antibacterial activity of marine bacteria from Arabian Sea of Pakistan. The Internet Journal of Microbiology. 2007;4(2):1-5.
48. Desjardine K, Pereira A, Wright H, Matainaho T, Kelly M, Andersen, RJ. Tauramamide A lipopeptide antibiotic produced in culture by *Brevibacillus laterosporus* isolated from a marine habitat: Structure elucidation and synthesis. J. Nat. Prod. 2007;70:1850-1853.
49. Isnansetyo A, Kamei. *Pseudoalteromonas phenolica sp.* nov., a novel marine bacterium that produces phenolic anti-methicillin-resistant *Staphylococcus aureus* substances. Int J Syst Evol Microbiol. 2003;53:583-8.
50. Shehane SD, Sizemore RK. Isolation and preliminary characterization of bacteriocins produced by *Vibrio vulnificus*. J Appl Microbiol. 2002;92(2):322-8.
51. McCall JO, Sizemore RK. Description of a bacteriocinogenic plasmid in *Beneckea harveyi*. Appl Environ Microbiol. 1979;38(5):974-979.
52. Gauthier MJ. *Alteromonas rubra sp*. nov, a New Marine Antibiotic-Producing Bacterium. IJSEM. 1976;26(4):459-466.
53. Magnusson S, Gundersen K, Brandberg A, Lycke E. Acta Pathol. Microbiol Sci. 1967;71(2):274-80.
54. Burkholder PR, Robert M, Pfister, Leitz FH. Production of pyrrole antibiotic by a marine bacterium. Appl. Microbiol. 1996;14(4):649-653.
55. Mincer TJ, Jensen PR, Kauffman CA, Fenical W. Widespread and persistent populations of a major new marine actinomycete taxon in ocean sediments. Appl Environ Microbiol. 2002;68:5005–5011.

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