WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 14, 429-449. Review Article ISSN 2277–7105

A COMPREHENSIVE REVIEW: ANTIBIOTICS FROM MARINE ORIGIN AS PROMISING SOURCE

Rutuja S. Dhaigude, Pragati D. Kale, Tejasvi S. Jadhav and Sukanya P. Paricharak*

Shardabai Pawar Institute of Pharmaceutical Sciences and Research Shardanagar.

Article Received on
25 Sept. 2021,

Revised on 15 Oct. 2021,
Accepted on 05 Nov. 2021

DOI: 10.20959/wjpr202114-22281

***Corresponding Author**
Sukanya P. Paricharak
Shardabai Pawar Institute of Pharmaceutical Sciences and Research Shardanagar.

ABSTRACT

In recent years two producers of marine derived antibiotics isolated from deep sea habitat from the surface of marine invertebrates and algae. Antibiotics are extremely important in fight against infections. There is also increasing problem of antimicrobial resistance. That is why appropriate use of antibiotics is great importance. Antibiotic is an essential part of modern medicine. This review covers marine drugs used for antibiotics. The increasing emergence of new forms of multi-drug resistance among human pathogenic bacteria, coupled with the consequent increase of infectious diseases, urgently required the discovery and developmentof novel antimicrobial drug with new mode of action. Members of each class of metabolite- ribosomal and non- ribosomal peptides, alkaloid, polyketides and terpenes they show antibacterial activity. It is marine world that will provide the Pharmaceutical industry with the next generation of antibiotics. Marine antibiotics are antibiotic obtained from the marine organism. The discovery of various antibiotic from marine bacteria. In review, various antibiotic obtained from marine microorganism, also its classification, discovery and development, Problem arises with the use of AMS, failure of use of AMA (chemotherapy). Need for this topic is very important. The concerted effort to discover new antibacterials from marine sources has the potential to contribute significantly to the treatment of ever increasing drug- resistant infectious disease. The present article provide an overview of various antibiotics obtained from marine sources.

KEYWORDS: Marine bacteria, antibiotics, antibacterial activity, antibiotic resistance, antibioticfrom deep sea microorganisms, AMA(chemotherapy).

INTRODUCTION

The molecule that either kill or stop the growth of microorganisms is called as antibiotic.

Selman Waksman was first coined the term "antibiotic". The antibiotic streptomycin was discovered by Albert Schatz and Elizabeth Bugie and Selman Waksman together at Rutgers University. The antibiotic is a chemical substance which is produced by microorganisms which has ability to stop the growth or to destroy the other microorganisms in dilute solution. After some years scientists have found synthetic compounds with antibiotic characteristics. And also found that synthetic antibiotics are much more better than natural antibiotics in different ways. So that simply antibiotic is defined as to cure the infection of human being.

Antibiotic have ability to stop the growth of microorganisms and cause small damage to host cell. The antibiotic term is vast because there are some classes are antibacterial, antiviral, antifungal, anticancer, antimicrobial antibiotics. But cancer is not considered as infection. But there are some similarities in cancer and infection. Related to this study, an interesting fact that cancer is caused by tapeworm in human being not by human cells, this case was reported recently. Sometime antibiotic is also called as an anti-infective. Antimicrobial is defined as a chemical substance which can stop the growth of microorganisms or kill it. The "antibacterial" term is defined as, to kill or stop the growth of bacteria by using a chemical substance.[1] Antimicrobial is further classified as.

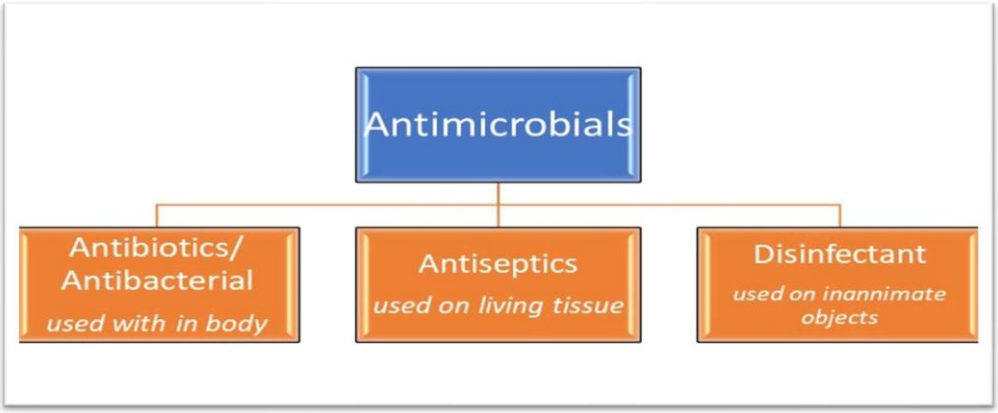


Figure No 1: Classification of antimicrobial agent.

- **Problems Arise due to use of Antimicrobial agents (AMAs)**

In 20th century, antibacterial drugs give their biggest contribution for therapeutic effects. Antimicrobial drugs has different drug categories as sulphonamides, diaminopyrimidines, quinolone, β-lactam, macrolides etc. Earlier, antibiotics are synthesized fungi, bacteria, actinomycetes, etc. But there are some problems arised due to us of antimicrobial agents (AMAs).

1) **Toxicity:-** Toxicity is of two types namely Local Irritancy and Systemic Irritancy. In the

local irritancy, drug is administered with i.m. Injection it causes gastric irritation, pain, etc. E.g. Erythromycin, tetracyclines, cephalosporins, and chloramphenicol.

Systemic Irritancy is caused by all antimicrobial drugs to the body organ. E.g. Penicillin, some cephalosporins, aminoglycosides, erthromycin, tetracyclines, etc.

2) **Hypersensitivity Reactions :-** Hypersensitivity Reactions are caused by all antimicrobial agents, because they have ability to produce unwanted reactions like rashes to anaphylactic shock. E.g. Penicillin, cephalosporins, sulfonamides, etc.

3) **Drug resistance:-** Drug resistance is of two types, Natural resistance and Acquired resistance. Sometimes resistance is caused due to gene transfer or mutation.[2]

In 1940, Penicillin was used for human being as an antibiotic, but from this 60 years, it was used and also misused. Antibiotics are developed for treating human infection but someafter they are used in veterinary, animal and plant agriculture,aquaculture.

Relationship between Antibiotic use &Antibiotic Resistance

Antibiotic resistance were foregoing to antibiotic. Antibiotic resistance is widely seen in natural antibiotic producing microorganisms. With the increased number, volume and diversity of antimicrobial use, bacterial resistance has developed. When the new drug is get developed and it used clinically, someafter their bacterial resistance are seen. In case of low immunity patient, the use of antibiotic organism can cause hazardous effect to the patient. It is not easyto decide the proportion of quantity of antibiotic applied and development of resistance.

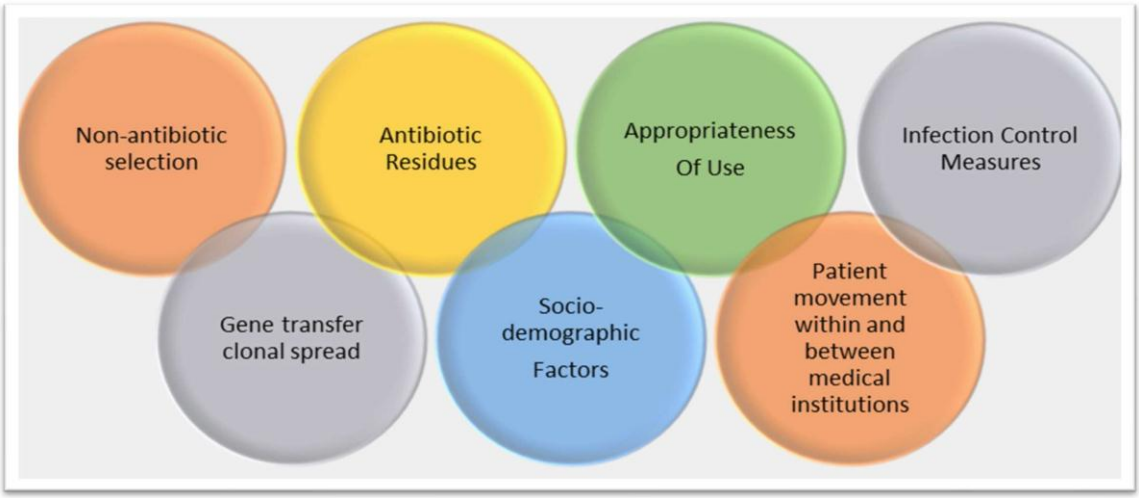


Figure No.2 - Antibiotic Use & Antibiotic Resistance.[3]

- **Failure Of Use Of Antimicrobial Agents (Chemotherapy).**

The growth of antibiotic resistant pathogens risk to increase the death of cancer patients. Chemotherapy gives their contribution to the coming antibiotic resistant bacteria within the gut. In the bloodstream, pathogens are overgrowth and translocated with the combination of antibiotics. When chemotherapy drugs are combined with antibiotic it increases the infection of bloodstream by multiresistant organisms. Primarily it disorder the commensal intestinal microbiota and then generate change by destroying the host of the intestinal nature chemotherapy will result in precipitation of dysbacteriosis, which promote the spread of pathogens. Secondly, it activate bacterial SOS response, chemotherapy activate the *de novo* antibiotic resistance mutations in population of pathogen. Thirdly on introducing antibiotics, that affect on resistant bacteria. Fourth thing is that, it destroy the intestinal barrier and by protecting the host, rate of translocation of bacteria from the gut will growth by chemotherapy.[4]

Need for Study of Marine Drugs

The sources of marine drugs are marine plants and animals and microorganisms. The earth' surface is covered by water is about 70 %, i.e marine ecosystem is the largest ecosystem of the earth. Of this marine ecosystem there are about 5,00,000 lives species are available which were distributed in 30 different phyla. Marine ecosystem is the best ecosystem for Research and Development of various natural products and also marine drugs. The ocean is filled with unique organisms, and their natural products are structurally novel, they have potent biological activities and pharmacological activities.

Many medicines are originated from plants and animals on land, which having curative properties of chemical. Biological and chemical diversity is the large source of marine ecosystem. This sources which found from marine ecosystem which are used for industrial development as cosmetics, Pharmaceutical, nutritional supplement, molecular probes, fine chemicals and agrochemicals.

Marine organisms have been used in production of bioactive compounds for purposes such as reproduction, communication, protection against predation, infection and chemical condition in the marine ecosystem. Every class of marine organisms having unique characteristics. There are 34 fundamental phyla of life, in which 17 are occur on land and 32 occur in the ocean. By the fundamental point of view of biodiversity, the marine ecosystem is most useful as compared to plants and animals found on land ecosystem.[5]

Review of literature

The number of patient with drug resistance disease is increasing. In 2017,10 million people were diagnosed with tuberculosis and 1.6 million people were died from the disease. The group of pathogens associated with severe drug resistance infections was identified which was named "ESKAPEBUGS"(antibiotic insensitive pathogens this is a Latin name: Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumanii, Pseudomonas aeruginosa and Enterobacter SPP.) to their ability ESCAPE the effects of the commonly used antibiotics.[6] Antimicrobials drugs are the greatest contribution of the 20th century to therapeutics. There advent changed the outlook of the physician about the power drugs can have on disease. They are one of the few curative drugs.

Their importance is magnified in the developing countries, where infective disease predominate. a class, they are one of the most frequently used as well as misused drugs. Drugs in this class differ from all others in that they are designed to inhibit/ kill the infecting organism and to have no / minimal effect on the recipient. This type of therapy is generally called chemotherapy which has come to mean treatment of systemic Infections with specific drugs that selectively suppress the infecting microorganism without significantly affecting the host. The basis of selective microbial toxicity is the action of the drug on a component of the microbe(e.g. bacterial cell wall) or metabolic process (e.g. folate synthesis) that is not found in the host or high affinity for certain microbial biomolecule (e.g. trimethoprim for bacterial dihydrofolate reductase) Due to analogy between the malignant cell and the pathogenic microbes, treatment of neoplastic disease with drugs is also called 'chemotherapy'.

Antibiotics

These are the substance produced by microorganism, which selectively suppress the growth of or kill other microorganisms at very low concentration. This definition excludes order natural substances which also inhibit microorganism but are produced by higher form(e.g. antibiotics)or even those produced by microbes but are needed in high concentration (ethanol, lactic acid, H202).[7]

Antibiotics are used as enzyme inhibitors, antitumor, immunosuppressive agents, hypocholesterolemic and antiparasitic agent in addition to their applications as antibiotics. some microorganisms are naturally resistance to antibiotics and antibiotic resistance can be an inherent property of microorganisms or can be acquired. They have inherent resistance to

an antibiotic because for example microorganisms may lack the target an antibiotic inhibits be impermeable to antibiotic be able to alter antibiotics to an inactive form or may modify the target of the antibiotics or be able to pump out an antibiotic entering the cell.

Marine microorganism as resource of antibiotic

The oceans are a resource of biodiversity that greatly exceeds that of terrestrial environments. The oceans cover 71% of the earth surface and 80% of life on the planet is found under the ocean surface.

Antibiotics from marine bacteria

Bacteria in the marine environment are diverse and more than 40% of sponge weight may contain bacteria. It bacteria are considered as an emerging source of novel bioactive metabolite with respect to their existence diversity and function in the marine environment the promising antibiotic derived from marine bacteria.

1. Lomaiviticins
2. Pelagiomicins
3. Tetrocarcins
4. *Bacillus laterosporus* antibiotics
5. Macrolactins
6. Haliangicin
7. Massetolides

Lomaiviticins

The antitumor antibiotics lomaiviticins A and B were isolated from halophilic strain LL-371366 and identified as the new species Micromonospora lomaivitiensis. The strain was isolated from the inner core of the ascidian Polysyncraton lithostrotum. In a plate assay, the antibiotics demonstrated potent activity against S aureus and E faecium with MIC values of 6to 25 ng/sp.[8]

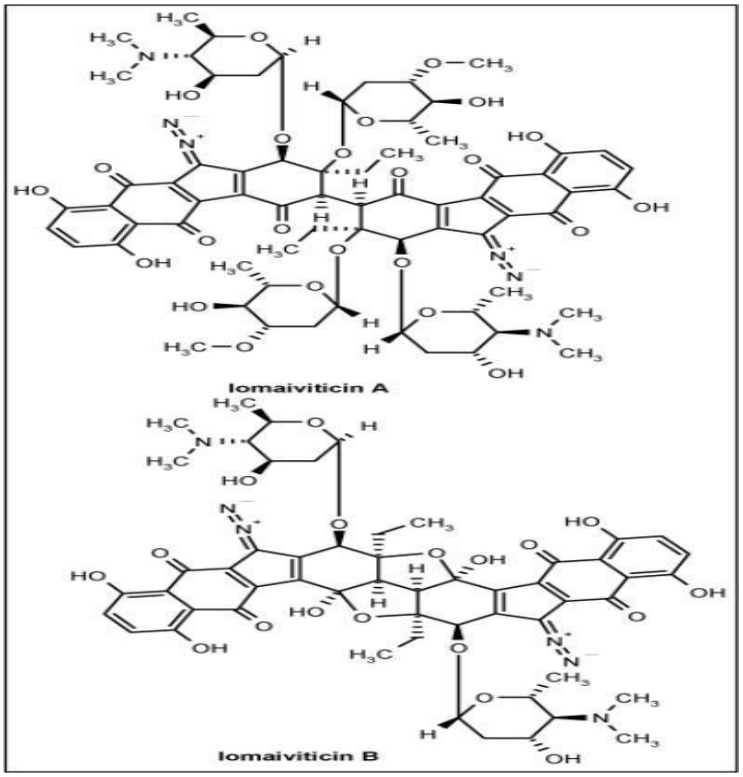


Figure No. 3: Structure of Lomaiviticin.

Pelagiomicins

Pelagiomicins are new anticancer compounds produced by marine bacteria, found that a new genus marine bacterium Pelagiobacter variabilis produced new phenazine antibiotics, pelagiomicins A, B and C. Those compounds were labile in water and alcohols. The absolute structure of the main component, pelagiomicin A, and the structures of the minor ones were determined from the spectroscopic data and by synthesis. Pelagiomicin A exhibits activity against Gram-positive and -negative bacteria and antitumor activity in vitro and in vivo.[9]

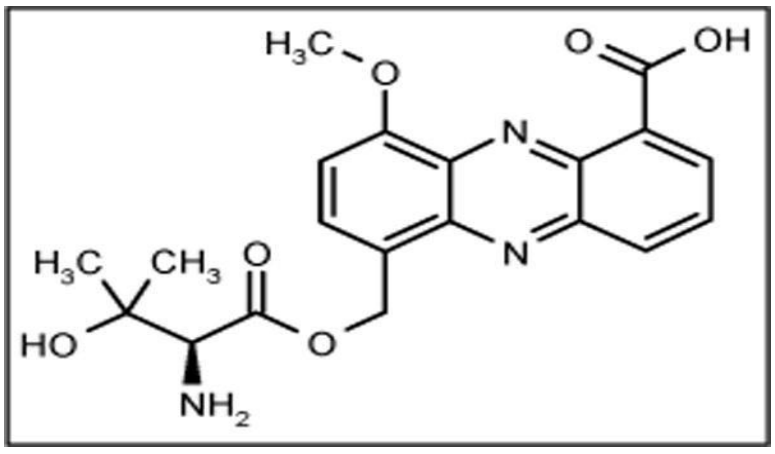


Figure No. 4: Structure of Pelagiomicins.

Tetrocarcins

Novel antitumor antibiotics designated as tetrocarcins from a broth culture of Micromonospora chalcea KY11091 isolated from A soil sample collected in Sendai-shi, Miyagi, Japan. Tetrocarcins A, B and C showed antibacterial and antitumor activity. The LD50 values of tetrocarcins in mice were 60~80 mg/kg of body weight by intraperitoneal injections. Tetrocarcins caused little reduction in the number of leucocytes in mice during treatments.[10]

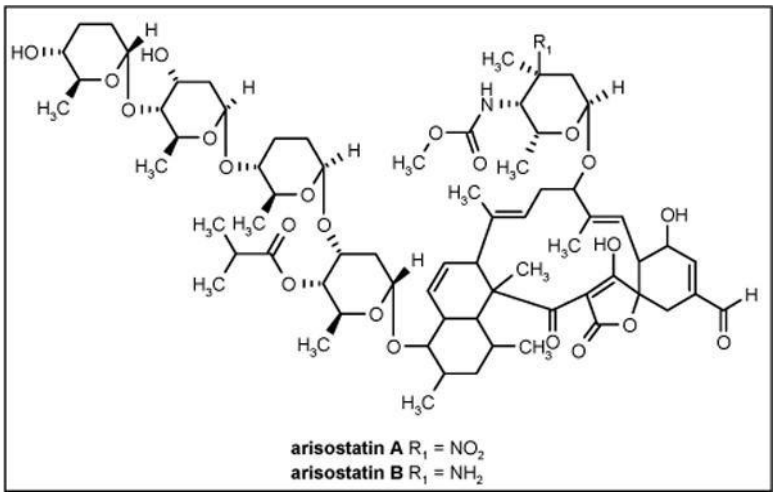
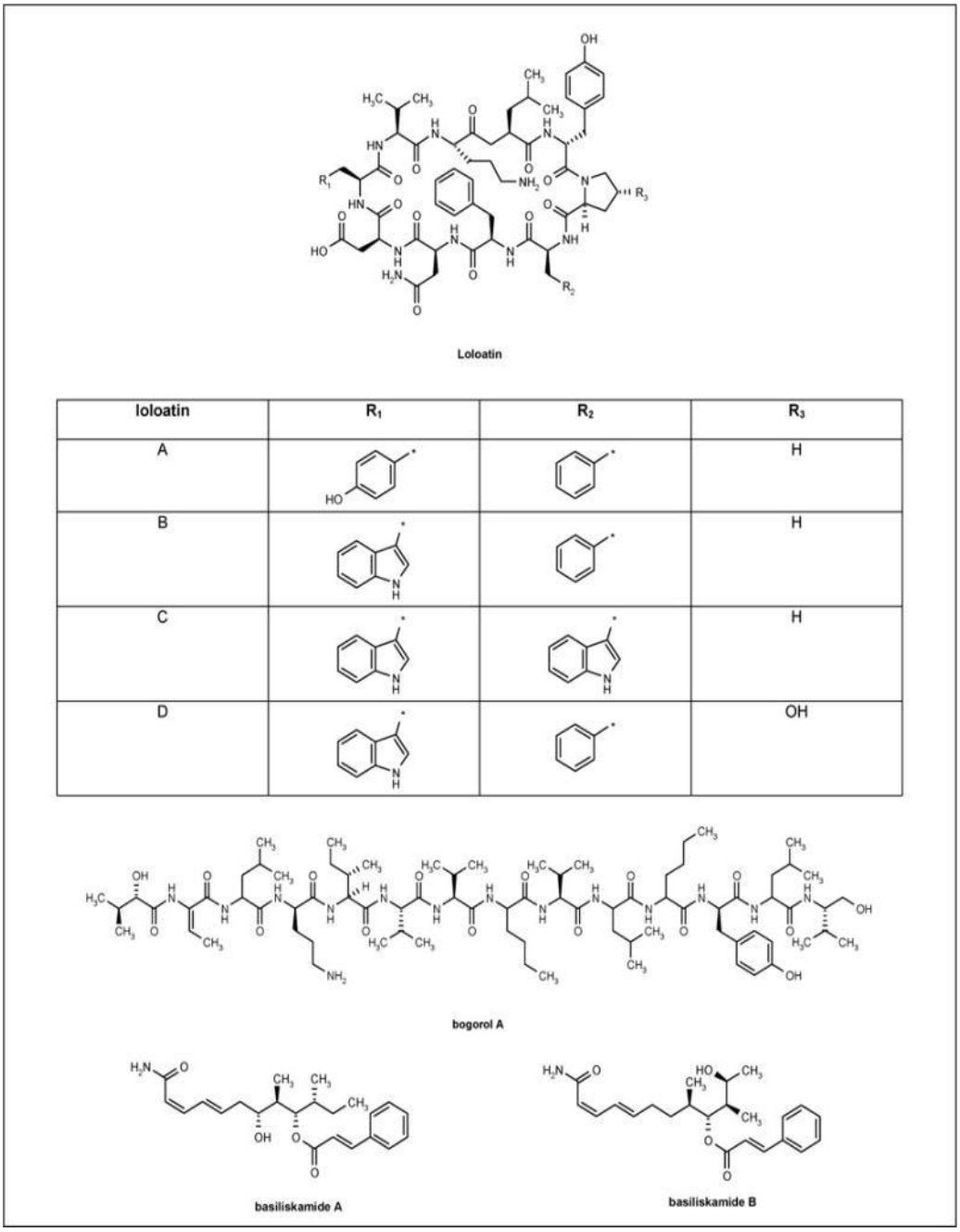


Figure No. 5: Structure of tetrocarcins.

Bacillus laterosporus antibiotics

A new antibiotic, named laterosporamine, was isolated from the culture broth of Bacillus laterosporus 340-19. The antibiotic is active against Gram-positive and Gram-negative bacteria in vitro and in vivo. It is a water-soluble basic substance, positive to ninhydrin, SAKAGUCHI's and DRACENDORFF's reagents. A non-peptidic structure with an approximate empirical formula C17H35N7O4 was suggested. In the course of our screening program for new antibiotics from the genus Bacillus, strain 340-19 was found to produce a water-soluble basic antibiotic and a basic acylpeptide antibiotic simultaneously. The water-soluble basic antibiotic active against Gram-positive and Gram-negative bacteria was isolated and named laterosporamine, since the producing organism was identified as a strain of B. laterosporus and the antibiotic contained an amine component.[11]



Ioloatin	R_1	R_2	R_3
A			H
B			H
C			H
D			OH

Figure No. 6: Structure of Bacillus laterosporus antibiotics.

Macrolatins

Seven new macrolactins (named G~M) and known macrolactins A and F were isolated from a culture broth of Bacillus sp. PP19-H3. The strain had been isolated from the macroalga, Schizymenia dubyi. Macrolactin A, which was 24-membered lactone, had previously been reported to show antibacterial, cytotoxic and antiviral activities. The new macrolactins include 22-membered ring or dicyclic lactone in addition to geometric isomers of known macrolactins A and F. The antibacterial activities of all themacrolactins examined in this study were relatively weak.[12]

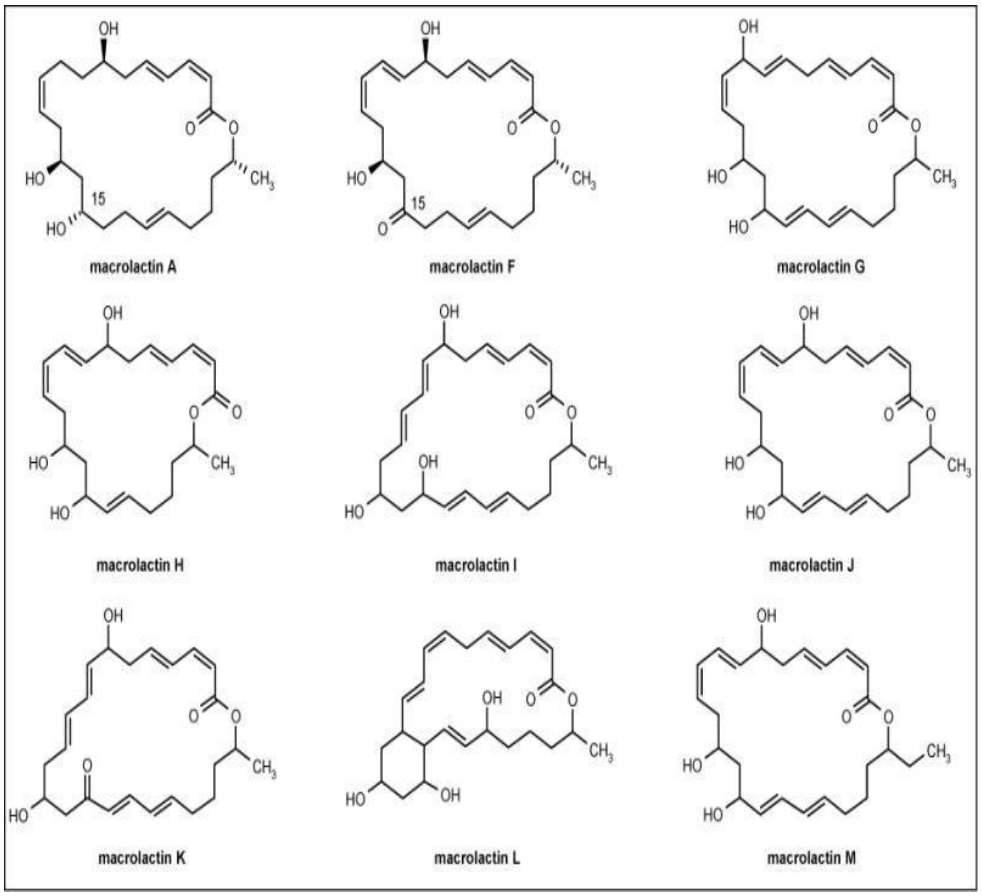


Figure no. 7: Structure of Macrolatins.

Haliangicin

Haliangicin, a novel /3-methoxyacrylate antibiotic with a conjugated tetraene moiety, was isolated from the culture broth of a marine myxobacterium. A bacterium tentatively named as Haliangium luteum required 2-3% NaCl for the growth and production of haliangicin. Haliangicin inhibits the growth of a wide spectrum of fungi but was inactive against bacteria. In mitochondrial respiratory chains, haliangicin interfered the electron flow within the b-cl segment.[13] The chemical structure of haliangicin is given in figure No.8-.

Massetolides

There are two reports of in vitro anti-TB activity from marine origin. Massetolide A and viscosin are cyclic depsipeptides isolated from cultures of two Pseudomonas species isolated from a marine alga and tubeworm, respectively. When tested against M. tuberculosis, massetolide A and viscosin displayed MIC values of 5–10 and 10–20 mg/mL, respectively. When tested against M. avium-intracellulare, massetolide A and viscosin had MICs of 2.5–5 and 5–10 mg/mL, respectively. Pseudopteroxazole and seco-

pseudopteroxazole are new benzoxazole diterpene alkaloids isolated from the West Indian gorgonian Pseudopterogorgia elisabethae. Both compounds induced 97 and 66%, respectively, growth inhibition for M. tuberculosis H37Rv at a concentration of 12.5 mg/mL without significant cytotoxicity.[14]

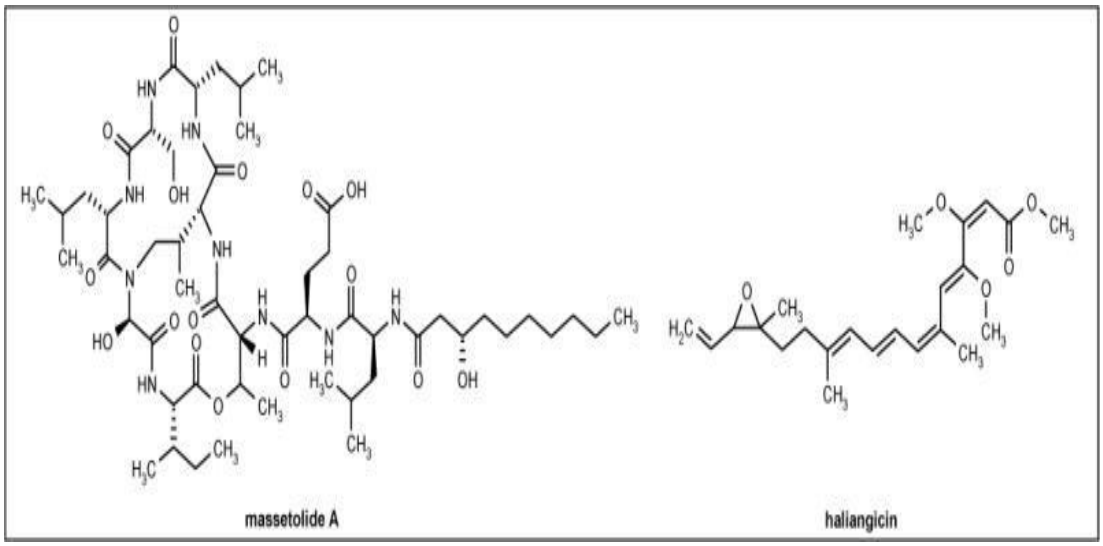


Figure No. 8: Structure of Massetolides and Haliangicin.

Testing For Antimicrobial[15]

The cells walls of "Gram positive" bacteria and not those of "Gram negative" bacteria ,are vividly stained by a crystal violet – iodine dye. The distinction has broader implications for antibacterial efficacy since cell wall permeability is an essential criterion for the inhibition of on intracellular target. An antibacterial or Antimicrobial is effectively transported across the thick peptidoglycan layer of gram positive bacteria (eg Staphylococcus aureus and Enterococcus faecium) lacks in many cases the appropriate chemical properties to cross the different glycolipid layer and membrane characteristics of gram negative bacteria (eg E .coli and Pseudomonas aeruginosa).

In discovery of Gram positive specific antibacterials has been successful, while the discovery of gram negative antibacterials has posed a greater challenge. There is two technique is widely used to in laboratory. In disc diffusion method a centralized paper disc is impregnated with the antimicrobialor antimicrobial compound and placed on lawn of test bacteria. The various study of antibacterial or antimicrobial natural product is to development of efficient assays to access antibacterial activity. In the microdilution method the compound of interest is serially diluted along each well of bacterium. The minimum inhibitory concentration (MIC) from the change in optical density in the well.

Ribosomal peptides

Ribosomal peptides are generally translated as "prepro- peptides" as composed of N terminal signalsequence, a "pro"segment and a C -terminal peptide.

Their proteolytic processing and other post translational modifications reveal the mature antibacterialpeptide classified six classes.

1) Linear peptides that fold into alpha- helices
2) Cyclic peptides that form beta sheet structure.
3) Peptides rich in one or more amino acid residues
4) Cyclic peptides with thio- ether
5) Lipopeptides
6) Macrocyclic knotted peptides.

There is also use of antibacterial ribosomal peptide to find therapeutic agents in humans depends on its ability to function physiological salt concentration. In ribosome produced AMPS are large, cationic, amphipathic molecules found among all classes of life. In prokaryotic cell membranethese peptides have broad spectrum antibacterial properties.

Physical, Chemical and biological characteristics is included but not limited the study of their three dimensional structure, biosynthesis and mechanism of action. Antibacterial secondary metabolites which are covalently strong carbon bonds to sulphur, nitrogen, oxygen and other carbon atoms, possess added stability that makes these molecule more likely effective as systemic drugs.

Non ribosomal peptides

These peptides are large multifunctional protein complexes called non ribosomal peptide synthetases (NRPSs). Adenylation (A), thiolation (T) and condensation (C) domains of NRPSs catalyze amide bond formation between amino acid residues. Also non- ribosomal peptide, bogarol A $C_{80}H_{24}O_{16}N_6$ was isolated from the marine bacterium Bacillus laterosporus PNG-276 collected near Lolata Island, papauNew Guinea.

Polyketides

These are natural products are constructed by polyketide synthases(PKS)that similar to non-ribosomal peptide synthetases. The building blocks of PKS are acetate and propionate. AN acyl transferase (AT)domain catalyzes thioester bond formation between an

acyl career protein (ACP) domain and coenzyme A(CoA) bound starter unit. ketoreductase (KS), dehydratase(DH), and enoyl reductase(ER) and diversity to the polyketides. PKS and NRPS molecules can co-operate to form hybrid PKS- NRPS likebogorol A.

Alkaloids

Alkaloids are basic nitrogen containing ring. The nitrogeneous character of these metabolites, often derived from amino acids such as lysine, tyrosine, tryptophan, histidine, nicotinic acid and anthranilic acid. These molecules generally basic or "alkaline".

Antibacterial alkaloid

8- hydroxymanzamine, C36H44N4O2 is a beta carboline alkaloid isolated from the marine sponge pachypellina sp. The molecule a derived manzamine A from an Okinawan sponge of the genus Haliclona, Contain 5,6-8 and 13- membered heterocyclic rings with beta carboline moity.8 – hydroxymanzamine showed an MIC=0.91 ugmL^-1 against the tuberculosis causing bacteriumMycobacterium tuberculosis.

Terpenes

Terpenes are diverse class of natural products from isoprene units. The biosynthetic terpene building blocks are dimethyl allyl pyrophosphate(DMAPP) and isopentyl pyrophosphate (IPP). These are both are five carbon compounds are derived from either from the mevalonate pathway or the deoxy-xylulose phosphate (non-mevalonate)pathway. The terpenes are classified monoterpenes (C10), sesquiterpenes(C15), diterpenes (C20), sesterpenes((C25) and so on. The rearrangement occurwhich distort the regular head to tail arrangement of the isoprene units and add diversity to the terpenoid structure.

Antibacterial terpenes

Haliconadin C, C16H25N is a sesquiterpenoid isolated from marine sponge Halichondria SP which was collected Okinawa, Japan. The Compounds ability to tightly complex copper may be linked to its antibacterial activity. Haliconadin C showed considerable activity against several bacteria against M. luteus the compound show antibacterial activity with MIC =0.52 ug/mL-1.

Classification of marine drugs[16]

1) Antibacterial

Eicosapentanoic acid, a PUFA, isolated from diatom of phaeodactylum tricornutum, against gram positive, gram negative, MDR and S.aureus.

2) Anti-inflammatory

Mediterranean sponge species spongia officinalis - invivo study on rat model of carragenan- inducedpaw edema.

3) Neuroprotective

Green seaweed Ulva reticulata-neuroprotection by inhibiting acetyl and butyryl cholinesterase, in treatment of Alzheimer's.

4) Antiparasitic

Extracts of Sarcotragus sp- tunisian sponge experimented in in-vitro for anti-leshmanial activity.

5) Antiviral

Fresh marine sponge- Celtodoryx girardae for anti – HSV activity.

6) Anticancer

Bryostatin from Bryozoan bugula neritina against leukemia cells KLH (keyhole limpet hemocyanin)from Megathura crenulata(gastropod sp.) for Bladder ca.

7) Analgesic

Ziconotide – 1st FDA approved drug in treatment of pain extracted from marine snail Conus magus.

8) Antimicrobial

Cephalosporin C derived from marine fungus Cephalosporium acremonium.

9) Antimalarial

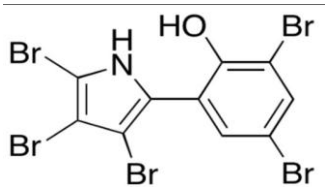
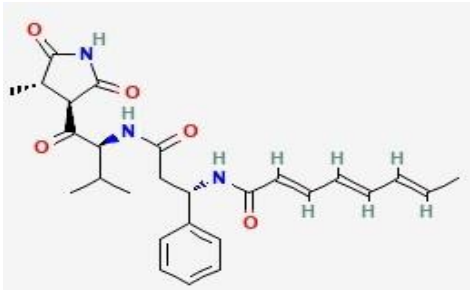
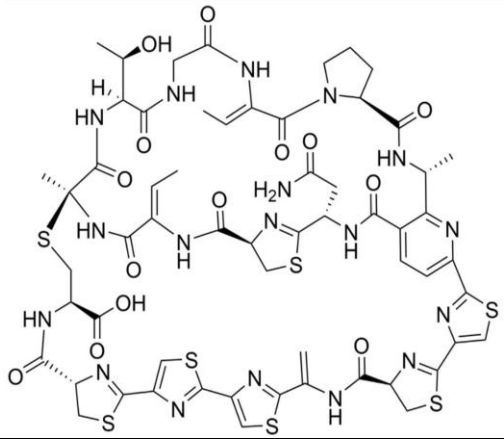
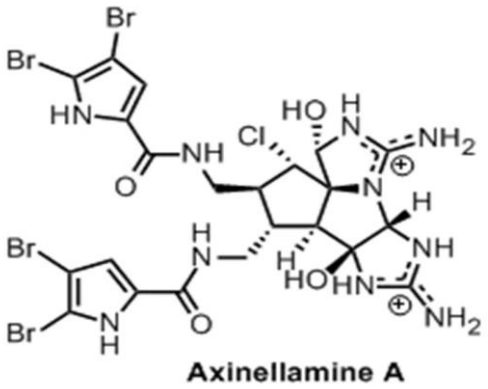
Isonitrile containing Acanthella sp.(Japanese sponge).

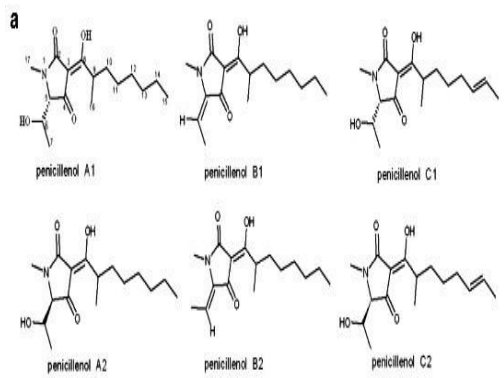
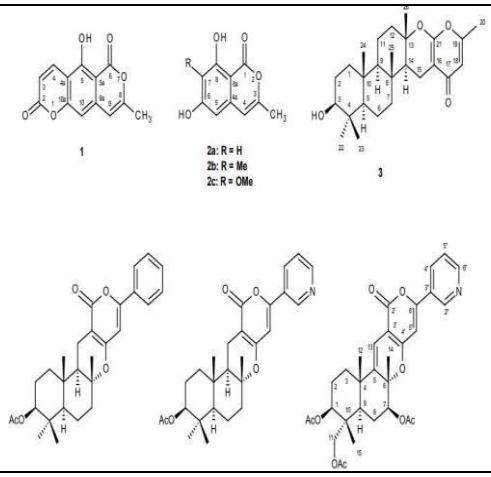
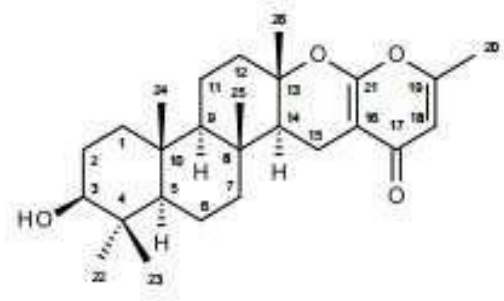
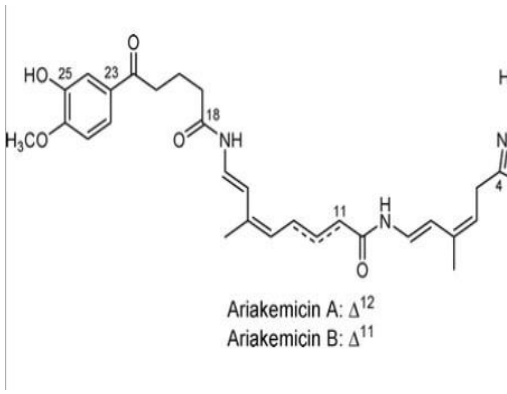
Matrine Antibiotics

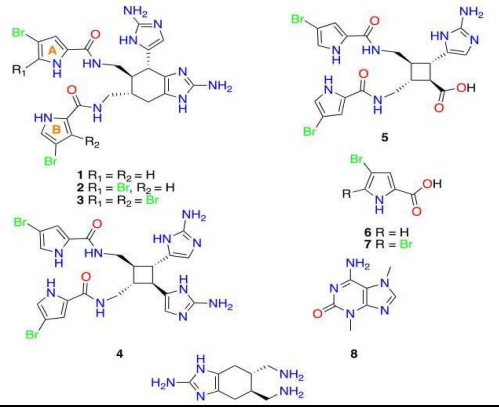
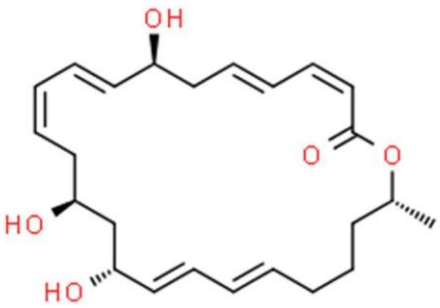
In this review paper after literature study important drugs compiled with their chemical structures. This gives thorough information of different antibiotics that are isolated from

marineplant and animal sources.

Table No. 1: Marine Antimicrobial Agents.

Sr.No	Name of antibiotic	Chemical structure	Description	Ref
1	Pentabromopseudilin		A rare actinomyeetegenus belonging to family of Micromonosporacceae namely verrucosispora. Which is a marine was recently isolated from a new anti-folate scaffold, termed abyssomicin	[17]
2	Andrimid		The hybrid NRPS-PKS peptide antibiotics andrimid is probably the best studied antibiotic produced by vibiriouas. The compond is effective against a wide range of bacteria and interfers with fatty acid biosynthesis	[18]
3	Cyclothaiazomycin		Thiopeptides were recently isolated and characterised and were named after the parent compound which have a very similar structure to cyclothioazomyein B1 was found to inhibit transcription by bacteriophage RNA polymerase. Such result might serve to further understand transcription at the molecular level.	[19]
4	Axinellamines	 Axinellamine A	complex polycyclic skeleton isolatedfrom the sponge Axinella sp. They exhibit activity against several Gram-positive and Gram negative bacteria. Moreover, axinellamines cause membrane destabilization in E. coli. synthesis method.	[20]

5	Penicillenols		S. aureus and C. albicans Penicillenols (A1, A2, B1, B2, C1 and C2) finds fromthe deep-sea-derived fungus A. Previous studies reported that the six penicillenolsexhibits cytotoxic activities againstseveral cell lines, and penicillenols B1 andB2 also showed dose-dependent antimicrobial activity against S. aureus.	[21]
6	Similanpyrone B		Similanpyrone B **1**, **2a-c** and **3-6** exhibittheir antimicrobial activity against both Gram-positive and Gram-negativebacteria, *Candida albicans* , and multidrug-resistant isolates from the environment.	[22]
7	Chevalone E		Fungi species named Aspergillus similanensis is related with other marineorganism such as sponges. This metabolite does not present activityagainst E. coli, S. aureus, and E. faecalis,.Chevalone E is coactive when used withoxacillin against MRSA. Othercompounds of chevalone E exerts weak activity for *mycobacterium tuberculosis*and tumour cell lines.	[22]
8	Ariakemicins A andB		Ariakemicins A and B unusual linear hybrid polyketide-nonribosomal peptide antibiotics, were discovered from the fermented extract of the marine bacterium *Rapidithrix* sp. The ariakemicins composed of threonine, two ω-amino-(ω-3)-methyl carboxylicacids with diene or triene units, and δ-isovanilloylbutyric acid. The antibiotics selectively inhibited the growth of Gram-positive bacteria.	[23]

9	Bromoageliferin		Bromoageliferin displayed significantactivity against *P. aeruginosa*. This inhibits growth of *P. aeruginosa* byin vitro assays. Moreover,increases the survival time in an in vivo *Galleria mellonella*. The findingsshows bromoageliferin as apotential lead for scheming new antibacterial drugs.	[24]
10	macrolactin A		Macrolactin were isolated from the culture broth of the bacterium Bacillus marinus, Macrolactins are a large group of macrolide antibiotics, e.g., macrolactins T (3), B (4), and O (5) show inhibitoryactivity against gram pssitive and gram negative bacteria like *S. aureus* and two species of fungi, *Pyricularia oryzae* and *Alternaria solani.*	[25]

- **CONCLUSION**

The marine diversity is the largest ecosystem of the earth because, it is covered 70 % surface of the earth. So, marine ecosystem gives new research opportunities. Marine diversity provides large source of antibiotic for bacterial infection.

Marine antibiotics having potent pharmacological activities. There are many marine natural products are developed with their many biological and pharmacological activities. Antibiotics are important weapon to fight against infectious diseases. But, there is problem of antibiotic resistance. Antimicrobial agents are not beneficial with chemotherapy in cancer treatment. The growth of antibiotic resistant pathogens , increases the risk in cancer patient.

The demand of novel antibiotics from marine source increased because they are beneficial to fight against infectious diseases.

- **DISCUSSION**

The various compounds isolated to date were recently reviewed and reported natural products are alkaloids, polyketides and peptides. The bacteria are frequently associated with macro-

organisms and therefore it can be expected that the chemical molecule as an important role as a signalling and defence molecule.[2] These bacteria are mostly associated with healthy animals and plants, only few reports exit that these strains act opportunistic or pathogenic. The analysis of this talented antimicrobial producers as probiotics in aquaculture and the analysisof produced molecule as potential lead structures for medicinal drugs will be subject for future studies. The threat by antibiotic resistance bacteria, new treatment options and new bioactive compounds must be identified.[6] This is proven by the fact that about 80% of all antimicrobial drugs in current use are natural products or are based on their structures. Another approach is reinvestigation of known antibiotic compounds, which were not developed further in the goldenage of antibiotic research where enough treatment options had been available. Hence it became clear that nature is still the most promising resource for novel compounds with antibiotical activity.[22]

Recent efforts by diverse groups including scientists, medical doctors, and even in some cases politicians, have shared light on this predicament. However the approval of the five new classes of antibiotics since the turn of the century to combat the emergent resistance gram positive pathogen of the 1990s was step in right direction. Advanced scientific technology have provided the necessary for the discovery of new antibiotic classes and improvement of already established ones to combat the largely unchecked rise of resistance gram negative[23] In this review, there is a basic introduction of marine drugs bacteria, antibiotic, antibacterial activity and also AMA (chemotherapy). There are various types of marine bacteria is very useful to prepare a new antibiotic in recent years.[14] Also there is member of each class of metabolite- ribosomal and non- ribosomal peptides, alkaloids, polyketides and terpenes. Also they show antibacterial an activity. It is marine that will provide the Pharmaceutical industry with the next generation of antibiotics. Definition of antibiotics, also its classification, problem arises due to use of antimicrobial agents (AMAs), Relationship between antibiotic use and antibiotic resistance. Therefore the potential of antimicrobial drugs for production of natural products and also inherent potential to be developed into drug leads must be judged is very high.

ACKNOWLEDGMENT

The authors extend their sincere thanks to Hon. Nilesh Nalwade, CEO of Agricultural Development Trust (ADT), Shardanagar, Baramati and Shardabai Pawar institute of Pharmaceutical Sciences and Research, Shardanagar Baramati for timely support, motivation

and guidance.

REFERENCES

1. Bhattacharjee M. K., Introduction to Antibiotics, Chemistry of Antibiotics and Related Drugs, Springer International Publishing Switzerland, chap-1, 2016.
2. Tripathi K.D., Essential of Medical Pharmacology seventh edition, Antimicrobial Drugs:General Considerations, Sec-12,Chap-49, 2013; 688-691.
3. Teresa M. Barbosa, Stuart B. Levy, The impact of antibiotic use on resistance development and persistence, 2000; 3: 303-311.
4. Lito E. Papanicolas, David L, Gordon, Steve L. Wesselingh, and Geraint B. Rogers, Not Just Antibiotics :Is a Cancer Chemotherapy Driving Antimicrobial Resistance?, 2017.
5. Doshi G.M, Aggarwal G. V, Martis A.E., Shanbhag P.P, Novel Antibiotics from marine sources, International Journal of Pharmaceutical Sciences and Nanotechnology, 4[3], October- December 2011.
6. Stonik1,a* V.A, Makarieva1 T.N, Shubina1 L.K,1Elyakov Pacific Institute of Bioorganic Chemistry, Antibiotics From Marine Bacteria, Far Eastern Branch of the Russian Academy of Sciences (PIBOC), 690022 Vladivostok, Russia aemail: stonik@piboc.dvo.ru, 2020; 85: No.11.
7. Tripathi K. D, Essential of medical pharmacology sixth edition, JAYPEE BROTHERS MEDICAL PUBLISHERS (P), Ltd section-12, chap-49, Antimicrobial drugs, page no - 667.
8. Noer K. microorganisms and Mark T. H.Department of Pharmacognosy, Development of antibiotics and the future of marine microorganisms to stem the tide of antibiotic resistance, Center for Natural Product Research, School of Pharmacy, The University of Mississippi, MS 38677, USA.
9. Nobutaka I. , Miyuki N., Takahide T., Kyoko A., Miho S., Hiroshi S., New anticancer antibiotics Pelagiomicins, Produced by New Marine Bacterium pelagiobacter variabilis Marine Biotechnology Institute, Shimizu Laboratories, 1900 Sodeshi, Shimizu, Shizuoka 424, Japan, The Journal of antibiotics, 1997; 50(1): 8-12.
10. Fusao T., Tamaoki T., Shirahata K., Kasai M., Morimoto M., Ohkubo S., Mineura K., Ishii K., Novel antitumor antibiotics, tetracarcins, The Journal of antibiotics, 1980; 33(6): 668-670.
11. Jun'ichi S., Ryuzi S., Yoshiharu W., Kenzo K., Mikao M., Shinzo M., Koichi M., Isolation Of A New Antibiotic, Laterosporamine (Studies On Antibiotics From The

Genus Bacillus. Xiiv), Shionogi Research Laboratory, Shionogi & Co., Ltd., Fukushima-ku, Osaka 553, Japan, APR, 1976.

12. Tomokazu N., Kyoko A., Miho S., Miyuki N., Hiroshi S., Novel Macrolactins as Antibiotic Lactones from a Marine Bacterium, The Journal of antibiotics, 2001; 54(4): 333-339.
13. Fudou, Takashi L. and Shigeru Y., Haliangicin, a Novel Antifungal Metabolite Producedby a Marine Myxobacterium, 2001; 54(2): FEB.
14. Khalid A. E. S., Piotr B., Xiaoyu S., Tony L. P., Jordan K. Z., Mark T. H., Department of Pharmacognosy, NCNPR School of Pharmacy, The University of Mississippi, MS 38677, USA, Marine Natural Products as Antituberculosis Agents, Tetrahedron, 2000; 56: 949-953.
15. Dr.Chambers C. H., William F., Antibacterials from the sea, centre of marine biotechnology and biomedicine, Scripps institution of oceanography, UCSD, 9500 Gilman Dr. La Jolla CA 92093-0204 (USA).
16. Vadlakonda S., Nagur S. G., Monica N., Valishetti Manoj Kumar, Marine pharmacology:an ocean to explore novel drugs, 2020 may; 9(5): 822-828.
17. Hafizur R., Brian A., Wilfrid J. M., Peter C. M., Derek J. J., Darid R. A., Andrew M. S.,Michael S. Novel Anti-Infective Compound from Marine Bacteria Mar. Drug, 2010; 8: 498-518.
18. Mansson, Lone G., Thomas O. L., Production of Bioactive Secondary Metabolites byMarine Vibrionaceae Mar. Drug, 2011; 9: 1440-1468.
19. Xavier J. B., Fernando A., Mercedes A., Thiopeptide Antibiotics: Retrospective and RecentAdvances Mar. Drug, 2014; 12: 317-351.
20. Yuly L., Virginio C., Sara M. S., The Marine Ecosystem as a Source of Antibiotics, Chapter1,https://www.springer.com,https://www.springer.com/cda/content/document/cda_do wnloaddo…
21. Jie W, Qi-Feng Y., Muhammad A., Xu-Hua N., Xiao-Y. Z., Shu-H. Q., Penicillenols froma deep-sea fungus Aspergillus restrictus inhibit Candida albicans biofilm formation and hyphal growth, The Journal of Antibiotics, 2017; 70: 763–770.
22. Chandaporn P., Tida D., Lucida J. B., Madalena M. M., Luis G., Paulo M. C., Artur M. S. S., Anake K., New isocoumarin derivatives and meroterpenoids from the marine sponge-associated fungus Aspergillus similanensis sp. nov. KUFA 0013, 2014 Oct 14; 12(10): 5160-73. doi: 10.3390/md12105160.
23. Naoya O., Kyoko A., Satoru M., Hiroaki K, Akira T. Yoshikazu S., Ariakemicins A and

B, Novel Polyketide-peptide Antibiotics from a Marine Gliding Bacterium of the Genus Rapidithrix, ACS pulications, 2008 Jun 19; 10(12): 2481-4, doi: 10.1021/ol8007292.

24. Dawrin P., Mar P., Marta M. G., Cristina L. M., Juan C., Germán B. , Jaime R.,* , Alejandro B., Carlos J., In Vitro and In Vivo Assessment of the Efficacy of Bromoageliferin, an Alkaloid Isolated from the Sponge Agelas dilatata, against Pseudomonas aeruginosa, Mar. Drugs, 2020; 18: 326; doi:10.3390/md18060326.
25. Dong H. K., Hye K. K., Chun K. K., Min H. J., Chan Y. K., Kyung H. M., Jae S. K., Antibacterial activities of macrolactin A and 7-O-succinyl macrolactin A from Bacillus polyfermenticus KJS-2 against vancomycin-resistant enterococci and methicillin-resistant Staphylococcus aureus, 2011 Jan; 34(1): 147-52, doi: 10.1007/s12272-011-0117-0.
26. North S., Indonesia. Nils Bohringer, katja M. Fisch, Dorothee schillo, Robert Bara, Cora Hertzer, Fabian Grein, Jan Hendrik Eisenbarth, Fontje Kaligis, Tanja Schneider, Heike Wagele Gabriele M. Konig and Till F. Schaberle, Antimicrobial potential Of Bacteria Associated with marine sea slugs.
27. Richard J Fair and Yitzhak Tor, Antibiotics and Bacterial Resistance in the 21st Century.