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A Review on Natural Sources Use for Drug Discovery

Miss. Pooja Niranjan Kate, Dr. Chandrashekhar D. Khadse
Dr. Avinash S Jiddewar, Dhanashree Vijay Pingane, Dr. Avinash S Jiddewar
NSPM College of Pharmacy, Darwha, Yavatmal

Abstract: *Natural products have long served as a foundational resource for drug discovery,offering structurally diverse molecules that are difficult to replicate through synthetic chemistry alone. Their biological specificity, ecological relevance, and evolutionary refinement make them exceptionally valuable as lead compounds for modern therapeutics. This review summarizes the major classes of natural products derived from plants, animals, microorganisms, and marine organisms, emphasizing their roles in shaping landmark drugs across infectious disease, oncology, metabolic disorders, and cardiovascular medicine. Emerging technologies including genome mining, biosynthetic pathway engineering, and heterologous expression have further expanded access to rare or previously inaccessible metabolites, enabling scientists to generate new analogs and enhance pharmacological potential. By integrating historical insights, technological advancements, and notable examples such as morphine, quinine, epibatidine, and marine-derived anticancer agents, this review underscores the enduring and expanding relevance of natural products as indispensable templates in the development of future drug candidates.*

Keywords: Natural Product, Bioactive Compound, Watery world, Micro- Orgaisam, Venoms and Toxins

I. INTRODUCTION

Natural products have been foundational to drug discovery, serving as the basis for most early medicines and continuing to drive modern pharmaceutical development. These naturally derived compounds represent an invaluable reservoir of novel therapeutic agents, particularly for life-threatening diseases where effective treatments remain elusive or inadequate. Nature stands as an eminent and inexhaustible source of drug candidates, consistently affording medicinal chemists and researchers unprecedented opportunities to identify and optimize new lead compounds.[1]Even now, well into the second decade of the 21st century, there's still a massive interest in using molecules from living things what scientists call natural products or secondary metabolites to discover new drugs for all sorts of diseases[3,4].These compounds have naturally evolved to help the organisms that produce them survive [7]. When we look at the new, small-molecule drugs introduced in the last decade, most came from microbes on land, from plants, marine life, and land animals [5, 6]. A big advantage is that natural products are built in the perfect, biologically active [8].Although some big pharma companies aren't as keen on natural product research as they once were, newer, better testing a nd purification techniques have been developed [2,3,10,11]. It is perhaps unsurprising that natural sources continue to dominate pharmaceutical discovery, given that herbal medicine has been a pillar of healthcare since ancient times. Screening natural extracts has historically been a foundational practice in pharmacological research. This tradition has yielded numerous critical medicines, demonstrating the irreplaceable value of nature's chemical diversity.The impact of these compounds is quantified by their representation in current clinical use: approximately 80% of all medicines used to treat bacterial infections are either natural products or their derivatives. Similarly, about 60% of all anti-cancer agents are derived from natural products or are direct analogs [12] .

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Enhancing Natural Product Lead Discovery Through Biotechnology:

The integration of biotechnology, specifically genomics and the identification of natural product biosynthetic pathways (BPSs), represents a crucial strategic shift for natural product-based lead discovery. This approach addresses many long-standing limitations and significantly strengthens several key areas of the field:

1. Overcoming Supply and Synthesis Challenges:

Heterologous Expression and Over-production: Genomic information allows researchers to clone entire biosynthetic pathways and express them in easily culturable host organisms (e.g., E. coli or yeast). This overcomes the limitations of scarce natural sources, difficult cultivation, or

This focus on genomics transforms natural product research from a purely discovery-driven field to an engineering-driven discipline, offering unprecedented control over the production and structural modification of potential drug leads.[12,13]For centuries, people have been trying to figure out how to fight diseases and make life better. The journey really

took a major step back in 1806 when a German pharmacist named Friedrich Wilhelm Adam Serturner made a breakthrough. He managed to successfully isolate morphine 1, a powerful substance unsustainable harvesting, providing a reliable and scalable supply of natural products that are challenging or impossible to produce via total chemical synthesis.[15,16]

This crucial work essentially opened the door for discovering many other important compounds that come straight from nature. These include well-known substances like Strychnine 2, Atropine 3, Colchicine 4, and many others. [17]

2. Expanding Chemical Diversity and Drug Synthesis:

Accessing Intermediates and Novel Scaffolds: The identified biosynthetic pathways reveal the entire cascade of enzymatic reactions. This provides access to otherwise transient intermediates and unique, structurally complex scaffolds. These molecules can be isolated and utilized as starting points for chemical modification and the synthesis of natural product-like chemical libraries, broadening the chemical space for drug screening.

Semisynthesis of New Derivatives: Understanding the BPS facilitates rational semisynthesis. By identifying key enzymatic steps, new derivatives of known natural product-based drugs can be created, leading to compounds with modified pharmacological profiles (e.g., improved efficacy, reduced toxicity, or altered ADME properties).

3. Unlocking 'Silent' or Inaccessible Genetic Potential:

Isolation of Homologous Gene Clusters: Genomics provides the tools to scan the genomes of difficult-to-access or unculturable organisms (the "microbial dark matter") for homologous gene clusters. This bioinformatic approach allows for the discovery and isolation of novel BPSs and their cognate genes without the need for traditional, often challenging, whole-organism screening and cultivation.

Identification of Novel Biosynthetic Pathways: Advanced genomic mining techniques enable the discovery of entirely new biosynthetic pathways and, consequently, novel natural products whose chemical structures and activities have not been previously described, significantly accelerating the rate of new lead compound identification.

Ever since then, these natural products have continued to be an incredibly reliable source for finding new and medically significant compounds. They are constantly giving us new tools to improve human health.[14]

This piece is all about showing how incredibly powerful Nature is in helping us find new medicines. It turns out that for most people around the world, traditional treatments and folk remedies which come straight from natural sources are still a huge part of how they treat sickness, according to the World Health Organization (WHO).

We also know, scientifically, that natural compounds are brilliant at modulating, or tweaking, how our bodies work at a fundamental level.The big challenge today is bridging the gap: taking that ancient, traditional knowledge and combining it with all our advanced modern molecular technology. If we can figure out how to do this effectively, it could unlock a whole new generation of drugs.

When scientists look for drugs in nature, they follow a clear process:

i.Analyze the plant (phytochemical analysis).

ii.Identify the specific active ingredients (characterization).

iii.Test exactly what those ingredients do to the body (pharmacological analysis and biological effects).[18]

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A few well-known examples of natural product-based drugs include:
• Antibiotics: Penicillin, erythromycin, and rifampicin (for bacterial infections).
• Antimalarial : Quinine and artemisinin.
• Anticancer Agents: Paclitaxel, vinblastine, and vincristine.
• Cardiovascular Drugs: Statins (for cholesterol lowering/hyperlipidemia)
• Analgesics: Salicylic acid (the precursor to aspirin) and nonaddictive cocaine derivatives (for pain relief).

This review looks at natural medicines and things from nature our ancestors used for centuries to treat various illnesses. The core idea is that if we make a small change to the structure of these natural molecules in the lab, we might be able to turn them into even more powerful drugs. This process modifying a natural substance to create a better drug candidate is extremely valuable for pharmaceutical companies trying to discover and develop new medicine.

DIFFERENT NATURAL SOURCES AS FOLLOWS:

1] Drugs Obtained From Plants Source:

Bioactive compounds in plants are simply substances made by the plant that can have a noticeable effect either a beneficial (pharmacological) or harmful (toxicological) one when consumed by humans or animals. These compounds are generally produced as part of the plant's defense system or specialized processes, meaning they are classified as secondary metabolites (as opposed to primary ones like sugars or proteins, which are essential for basic life).

Bioactive Compounds :

A secondary plant metabolite that causes a pharmacological or toxicological response in people or animals. Pharmacological effects are generally what we seek out, such as the action of a drug or a beneficial health effect. Toxicological effects are the harmful or poisonous reactions we try to avoid.[19]several natural compounds, vitamins, and drugs, highlighting their sources, functions, and therapeutic applications in human health.

1. Biotin: The Essential Vitamin

Biotin is a common water-soluble B vitamin that's absolutely vital for mammals. Its primary job is to act as an essential helper molecule (coenzyme) for five different carboxylase enzymes in the body.[20]

• Source & Availability: It is an essential nutrient found naturally in some foods and is widely available as a dietary supplement.

• Deficiency Effects: If a person becomes deficient in Biotin, they can develop several concerning symptoms, including:

i. Hair loss (alopecia)
ii. An itchy, scaling skin rash (eczematous skin rash)
iii. Eye inflammation (conjunctivitis)
iv. Fungal infections (candidiasis)
(Rana, Mathur, Taneja, &Taneja, 2018)

2. Camphor: The Versatile Laurel Compound

Camphor is a substance extracted from the wood of the camphor laurel (Cinnamomumcamphora) and related trees in the laurel family. It has a remarkable range of pharmaceutical applications, often used topically:

• Pharmaceutical Uses :
i. Pain reliever (analgesic)
ii. Germ killer (antiseptic)
iii. Muscle relaxant (antispasmodic)
iv. Itch reliever (antipruritic)
v. Swelling reducer (anti-inflammatory)
vi. Skin reddener (which draws blood to the area rubefacient)
vii. Nasal congestion and cough relief (decongestant/suppressant).[21]

• Cancer Potential: Some components of the Cinnamomum camphora plant are also supported by literature as having antimutagenic properties, meaning they may help protect against cell mutations in human cancer cells.
(Chen, Vermaak, &Viljoen, 2013; Hamidpour, Hamidpour, Hamidpour, &Shahlari, 2013)

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3. Longifolene : The Aromatic Sesquiterpene Longifolene is a naturally occurring tricyclic sesquiterpene(a type of complex organic molecule) that is isolated from the longleaf pine (Pinuslongifolia).[23]

• Uses : It is commonly used in the aroma industry (for fragrances) and has also been found to have antibacterial properties.

(Swamy, Akhtar, &Sinniah, 2016)olecule)

4. Pilocarpine : Nature's Glaucoma Treatment . Nature offers a defense against the sight-threatening disease glaucoma through the alkaloid Pilocarpine.[24]

• Source & Action: This alkaloid is extracted from the plant Pilocarpus jaborandi and is used medically to treat glaucoma (a condition characterized by high pressure in the eye).

5. Estrane & Prostaglandin F2-alpha :

These two compounds represent critical signaling molecules in the body:

• Estrane [22]: This is the fundamental structure of the natural female hormones (like Estrogen).

• Prostaglandin F2-alpha [26]:This is a naturally occurring prostaglandin used in medicine primarily to induce labor. Due to this action, it can also be employed as an abortifacient (a substance used to terminate a pregnancy).

6. Epothilones (A & B) :The information on Epothilones (A & B). [25]

The journey of modern medicine owes a lot to compounds found in nature. Here are two groundbreaking historical examples:

The Isolation of Morphine:

In a significant early breakthrough, a chemist named Friedrich Wilhelm Sertürner managed to isolate a pure, crystalline substance from opium around 1803-1804 . [27]He named this substance morphine.

Morphine was quickly recognized for its importance. It became a commercially successful drug and was later marketed by E. Merck in 1826.[28]

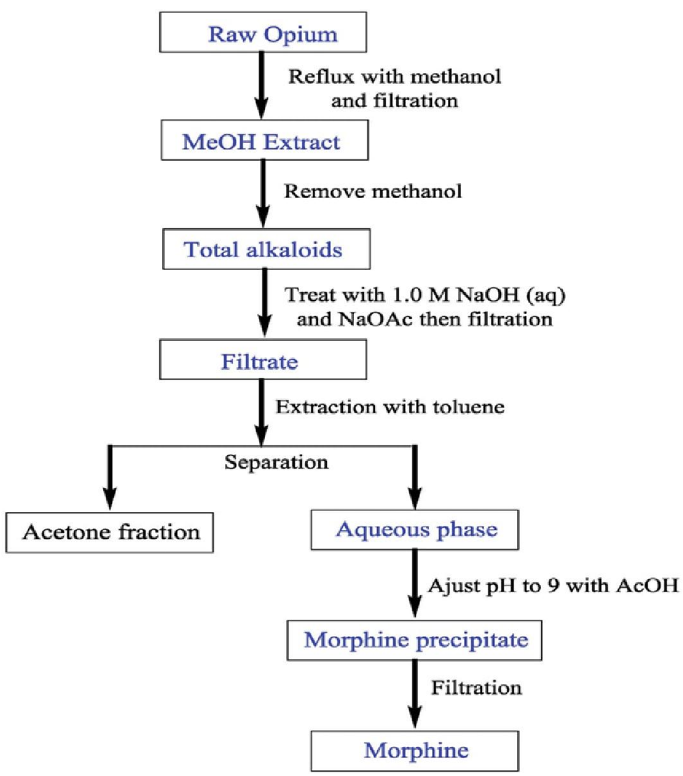


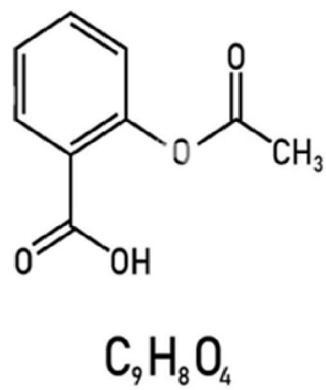
Fig.no.1 The Isolation Of Morphine From Opium

Fig.no.2 Opium

The Introduction of Aspirin:

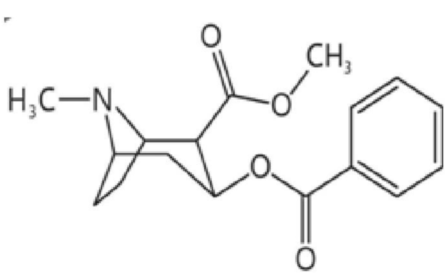
The well-known pain reliever, aspirin, also has natural roots.The first semi-synthetic pure drug aspirin was developed based on salicin, a natural compound originally isolated from the White Willow (Salix alba).The drug was successfully introduced by the company Bayer in 1899.

Fig.no.3 Willow Tree

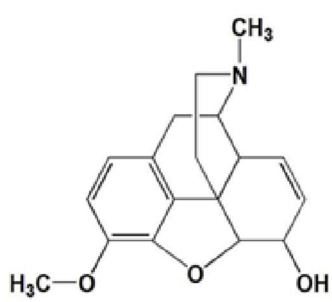


Aspirin[1]

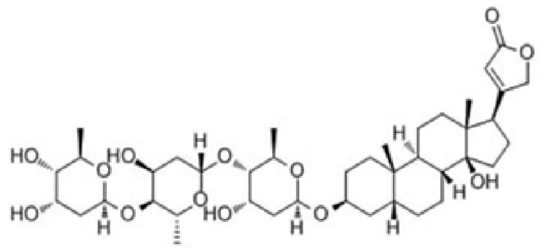
This success with aspirin fueled a wave of new discoveries and led to the subsequent isolation of other early, powerful drugs from natural sources.These include:



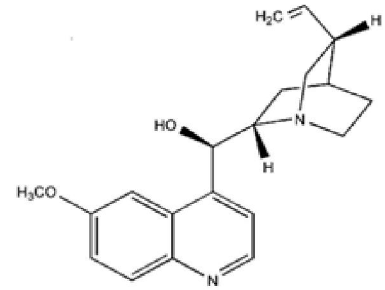
Cocaine [2]



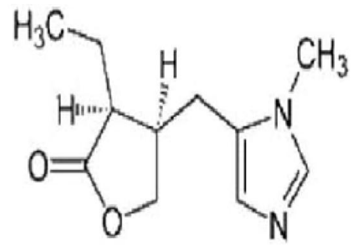
Codeine[3]



Digitoxin[4]



Quinine[5]



Pilocarpine[6]

Many of these compounds, even after decades, are still in use today.[27,28, 29,30]Studies of traditional medicinal practices reveal that out of 122 identified compounds, a massive 80% were sourced from just 94 different plant species. This shows that nature is an incredible source of therapeutic agents.

Examples of Modern Drugs with Plant Origins: (many drugs we use today started as natural compounds)

1) Sodium Cromoglycate (used to treat asthma) was developed from Khellin, which comes from the plant Ammi\ Visnaga (Bishop's Weed).

2) Metformin (a primary drug for Type 2 diabetes) has its roots in Galegine, a compound found in the plant Galega\ officinale (French Lilac).

3) Verapamil (used to treat high blood pressure) is related to Papaverine, which is derived from the Opium Poppy (Papaver\ somnifera).

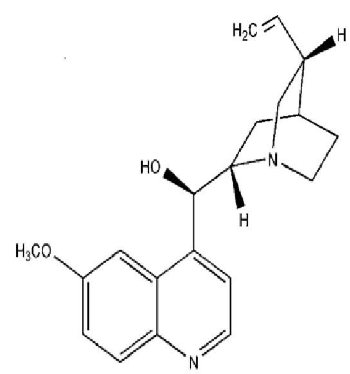
4) Aspirin (a common pain reliever) traces its lineage back to Salicin, a compound isolated from Willow bark.

Historical and Lifesaving Discoveries:

Plants have given us some of the most essential medicines, particularly for infectious diseases.

In 1820, a French pharmacist successfully isolated quinine from Cinchona bark. This compound became a key antimalarial drug and its chemical structure later served as a blueprint for synthesizing other effective antimalarial medicines.

Fig.no.4 Cinchona bark



Quinine [7]

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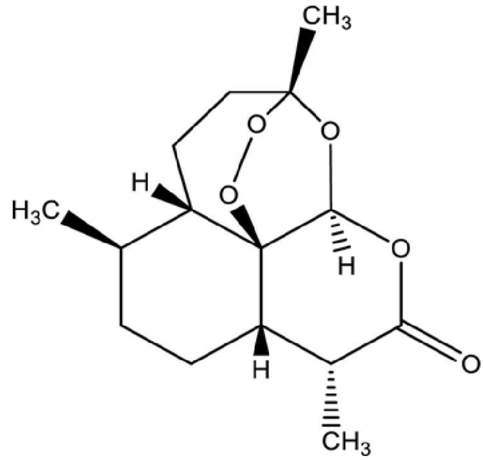
Another vital antimalarial, Artemisinin, was developed from the plant Artemisia\ annua (Sweet Wormwood)

Fig.no.5 Artemisia (Sweet Wormwood)



Artemisinin [8]

Foundation for New Medicines:

Plant-derived compounds don't just become drugs; they often provide the chemical foundation for entirely new synthetic drugs:

Reserpine, an antihypertensive drug, comes from the Rauwolfia\ serpentina (Indian Snakeroot) plant.

Ephedrine, sourced from Ephedra\ sinica, was used as a starting material (or lead compound) to create effective anti-asthmatic drugs like Salbutamol and Salmeterol.[33]

Fig.no.6 Ephedra\ sinica

Fig.no.7 Rauwolfia /serpentina

2] Drugs Obtained From Animals:

Animals are a fascinating source for developing potent and unique drug compounds.

Epibatidine

• Source :This compound is extracted from the skin of the Ecuadorian poison frog.

• Potency: Epibatidine is remarkably powerful it is ten times more potent than morphine as a pain reliever. [31]

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Venoms and Toxins

• Role in Medicine: Toxins and venoms produced by various animals have become vital in the pharmaceutical world.

• Application: They have been instrumental in the development and design of a wide range of cures for several different diseases.

• Animal-Derived Drugs: From Venom to Relief ,Many important medications have been developed by studying compounds isolated from the skin and venoms of amphibians and reptiles.

1. The Poison Frog and a Powerful Painkiller:

Fig.no.8 Poison Frog

• Source: The skin of the Poison Frog (Epipedobates tricolor).

• Compound/Lead Drug: Epibatidine.

• Key Insight: This compound is a powerful analgesic (painkiller), with an activity much greater than Morphine.

• Challenge: Unfortunately, the dose needed for pain relief is too close to the dose that is toxic, making it unsafe to use directly as a drug.

• Significance: Because of its potent activity, Epibatidine has become an important lead compound a blueprint for scientists working to synthesize novel, safer painkillers.

2. The Pit Viper and a Blood Pressure Drug:

• Source: The venom of the Brazilian Pit Viper (Bothropsjararaca).

• Compound/Lead Drug: Teprotide.

• Key Insight: Teprotide, a component of the snake's venom, was studied and used as the foundation for synthesizing the life-saving drug Captopril.

• Significance: Captopril is an antihypertensive drug (used to lower high blood pressure) that works as an ACE inhibitor (Angiotensin-Converting Enzyme inhibitor).

DOI: 10.48175/568

Fig.no.10 Pit Viper

3. The Gila Monster and a Diabetes Treatment:

• Source: The venom of the GilaMonster (Helodermasuspectum).
• Compound/Lead Drug: Exendin-4.
• Key Insight: This compound was the basis for developing the injectable anti-diabetic drug Byetta,\.
• Significance: Byetta is a medication used to help control Type 2 diabetes mellitus. [32]

Fig.no.11 Gila Monster

3] Drug Obtained From Micro-Orgaisam:

Microbial Revolution in MedicineThe discovery of penicillin by Alexander Fleming in 1929 from the mold Penicilliumnotatum launched what's often called the "Golden Era of Antibiotics. This single event changed the world, proving that nature holds powerful medicines and triggering an intense search for other bioactive agents substances that have an effect on living organisms from the microbial world.

Nature's Pharmacy Key Drug Discoveries:Microorganisms like molds (fungi) and bacteria have become an indispensable source of life-saving drugs for the pharmaceutical industry

• Antibiotics (Fighting Infections)

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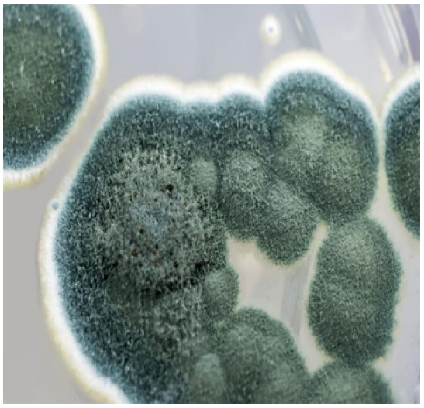
1) Penicillin (from Penicilliumnotatum mold).



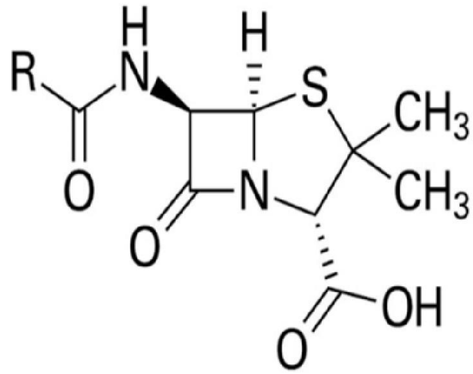
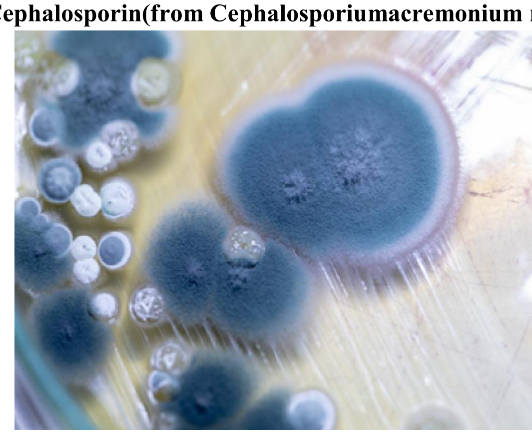


Fig.no.12 Penicillium notatum

Penicilli [9]

2) Cephalosporin(from Cephalosporiumacremonium mold).



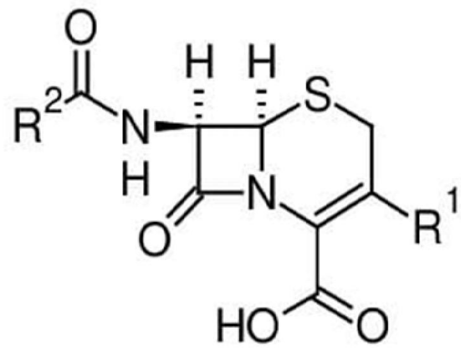
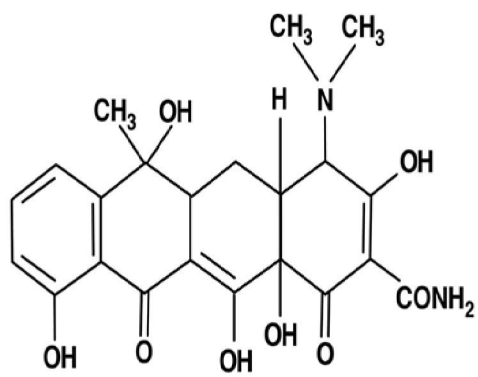


Fig.no.13 Cephalosporiumacremonium mold

Cephalosporin [10]

3) Tetracycline(from Streptomyces genus):



Fig,no14 Streptomyces genus

Tetracycline[11]

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Immunosuppressants (Managing the Immune System):

• Cyclosporin (from Trichoderma mold), a crucial drug that prevents the body fromrejecting transplanted organs.

Cholesterol-Lowering Agents (Heart Health):

• Mevastatin (from Penicillium species)

• Lovastatin (from Aspergillus species) were among the first statins, which are now widely used to control high cholesterol and reduce the risk of heart disease.

Anti-Parasitic Agents (Fighting Worms and Pests):

• Ivermectin (from Streptomyces bacteria) is an incredibly important drug used to treat a wide range of parasitic diseases in both humans and animals, including river blindness.In essence, simple organisms often overlooked molds and bacteria are the source of some of the most vital medications we use today, controlling everything from common infections to complex organ transplants and chronic heart conditions.[32]

4] Drug Obtained From Marine Sources:

The ocean covers 75% of the Earth's surface and is a vast, diverse environment. This huge, watery world is a treasure trove of resources that can potentially lead to new drugs to fight some of the most serious diseases, like malaria and cancer. In fact, marine (aquaticc) organisms are already being studied all over the world to develop these new medicines.

Future Research in Marine Pharmacology ,The field of marine pharmacology (the study of drugs from the sea) has a lot of potential for future research based on these key areas:

i.Engineering Marine Organisms: Scientists can use genetic engineering to modify marine organisms. This might help them produce high amounts of a specific compound needed for a drug.

ii.Marine-Based Health Products: The ocean can be a source for manufacturing both pharmaceuticals (medicines) and nutraceuticals (food-derived products that provide health benefits, like supplements).Harnessing Natural Marine

iii.Chemicals: Many chemicals naturally produced by or found within marine organisms have been shown to have a wide range of uses as potential medicines.[34]

iv.Naturally Derived Anti-Cancer Agents: This section describes two significant anti-cancer compounds originally found in marine organisms, along with their modified, synthetic versions.

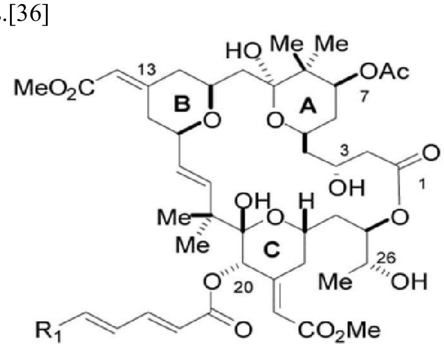
1)Bryostatin1 and its Bryologs:

• Original Compound: Bryostatin1.[35]

• Source: This compound was originally isolated from a marine invertebrate called a bryozoan, specifically the species Bulgulaneritina.

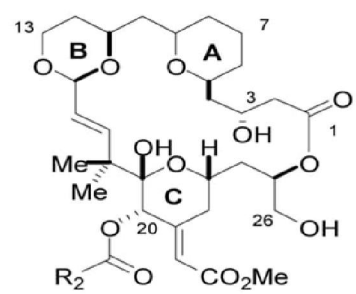
• Function: It is known for its anti-neoplastic (anti-cancer) properties

• Synthetic Derivatives: Scientists created synthetic derivatives, or modified versions, of Bryostatin1, which are known as the bryologs.[36]



$R_1 = C_3H_7$ **1**

Bryostatin1 [12]



$R_2 = C_7H_{15}$ **2**

Bryologs 2 [13]

2) Halichondrin B

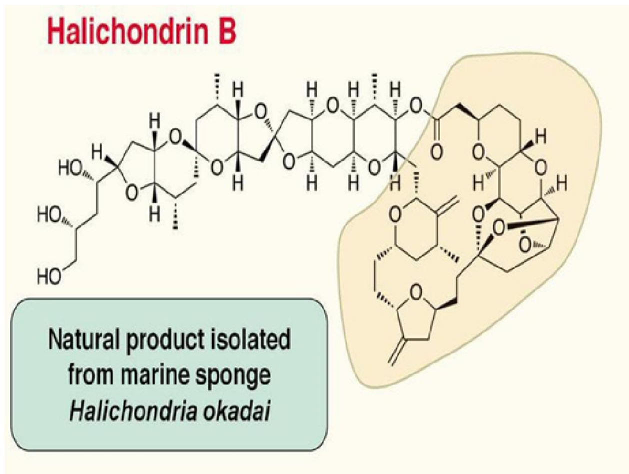
• Original Compound: Halichondrin. [37]

• Source: This compound has been isolated from several different types of sponges found across various global marine locations:

o Halichondriaokadai Species of Axinella from the Western Pacific.

o Phakelliacarteri from the Eastern Indian Ocean.

o Lissodendoryx sp., found off the East Coast of the South Island of New Zealand.



Halichondrin B[14]

Marine creatures and plants like tiny invertebrates (animals without backbones) and algae (seaweed) are proving to be a treasure trove for modern medicine. They have already given us many powerful natural compounds that are helping to treat diseases today, but experts believe there is still huge untapped potential waiting to be discovered and used in new ways.

The specialized, potent chemicals produced by these ocean resources are incredibly diverse. They include:

• Peptides and Proteins: Complex molecules essential for life and function.

• Polyethers: Large organic compounds often noted for their antimicrobial properties.

• Fatty Acids: Basic building blocks, some with potent anti-inflammatory effects.

• Polysaccharides: Large sugar molecules (like those found in some seaweeds).

• Enzymes: Biological catalysts that speed up chemical reactions.

In short, the ocean is a source of specialized, highly active substances that could significantly diversify our current medical treatments.

(Reference: Sigwart et al., 2021). [38]

Most promising MNPs are mycosporine-like amino acid(MAAs), which have been obtained from a variety of marinemicroorganisms with UV absorption properties (Rosic, 2021).

Bioactive substances and secondary metabolites generatedfrom sponges, crabs, seaweed, algae, fungi, fish, bacteria, andother marine species provide a huge source of healthful. The principal functional constituents having biologicalqualities from marine sources applied as functional foods arepigments, polysaccharides, proteins, lipids, vitamins, minerals, and phenolic compounds. Seaweeds have antioxidant, anticancer, anti-inflammatory, anticoagulant, anti-obesity, and antibacterialfunctions making them a promising crop.

Fig.no.15 Potential Bioactive Compounds Obtained From Different Marine Source.

Name of marine species	Byproduct	Bioactive component	Biological role	References
Bluefin leatherjacket (Navodonseptentrionalis)	Skin	Bioactive peptides	Antioxidant activity	Chi et al., 2015
Atlantic salmon (SalmosalarL.)	Skin	Collagen hydrolysates	Antioxidant and antihypertensive activities	Subin et al., 2018

Salmon (Oncorhynchusketa)	Skin	Oligopeptides	Antidiabetic Properties and Protein recovery	Lapeña et al., 2018
Indian mackerel (Rastrelligerkanagurta)	Bone	Bioactive peptides	Antioxidant activity	Al Khawl et al., 2020
Rainbow trout (Oncorhynchusmykiss)	Viscera	Bioactive peptides	Antibacterial Activity	Nikoo et al., 2019
Tuna (Thunnusalalonga)	Bone	Bioactive peptides	Antioxidant activity	Saïdi et al., 2014
Sardinella (Sardinellaaurita)	Head	Bioactive peptides	Antioxidant activity	Ozogul et al., 2021
Chum Salmon (Oncorhynchusketa)	Skin	Collagen peptide	Antioxidant activity	Al Khawli et al., 2020
Tilapia (Oreochromisniloticus)	Head	Bioactive peptides	Antimicrobial activity	Hemker et al., 2020
Rain bow trout (Oncorhynchusmykiss)	Viscera	Protein hydrolysate	Antimicrobial activity	Yaghoubzadeh et al., 2020
Pacific cod (Gadusmacrocephalus)	Skin	Gelatin hydrolysate	Angiotensin converting enzyme inhibitors	Vásquez et al., 2021
Red snapper (Lutjanuscampechanus)	Viscera	Protease	Proteolytic activity	Rodgers et al., 2018

TABLE [1] Various By Products With Biological Activities Extracted From Different Species

II. CONCLUSION

Natural products continue to stand at the forefront of drug discovery due to their unique chemical diversity, evolutionary optimization, and proven therapeutic value. Their contributions span centuries from early plant-derived medicines to modern breakthroughs inspired by microbial and marine metabolites. As demonstrated throughout this review, compounds sourced from nature have yielded essential drugs and remain unmatched in their ability to inspire innovative pharmaceutical design. The integration of biotechnology, especially genomics-based exploration of biosynthetic pathways, is opening unprecedented opportunities to uncover new molecular scaffolds, revive overlooked species, and create derivatives with improved safety and efficacy. Although challenges such as limited availability and structural complexity persist, current scientific tools are rapidly overcoming these barriers. Ultimately, the combination of traditional knowledge, natural diversity, and advanced molecular technologies positions natural products as a limitless reservoir for next-generation therapeutics, reaffirming their critical role in global healthcare advancement.

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