Available online on 15.08.2023 at http://ajprd.com

Asian Journal of Pharmaceutical Research and Development

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Review Article

Marine Drugs: A Review

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A B S T R A C T

As all of usrecognizebecause ofbigimprovement of the sectorpopulacenumerouspresentreassets of the drug are diminishing and drug builders and producers are looking at for the brand newsources to increase new capsuleswhich aresecure and valuepowerful and effectively meet the growingcall for of world.Marine pharmacognosy gives the scope for studies on thosecapsules on marine origin. As we know marine monographs are very less compared to herbal monographs. Therefore an attempt has been made to explore knowledge on marine pharmacognosy. This assessmentspecializes in marine sources, type of drug molecule of marine organism, numerous marine tabletswith inside themarketplace and strategies to extract numerous biomolecules from seafood waste.

Key words- marine pharmacognosy, marine agents, pharmacology of marine source, under water study

A R T I C L E I N F O: Received 19 May 2023; Review Complete 23 June 2023; Accepted 09 July2023; Available online 15 Aug. 2023

Cite this article as:

Gupta M, Kumari A, Rankawat A, Rankawat G, Marine Drugs: A Review, Asian Journal of Pharmaceutical Research and Development. 2023; 11(4):155-161. DOI: http://dx.doi.org/10.22270/ajprd.v11i4.1301

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INTRODUCTION

Since primordial times the humans have been endeavouring to understand oceanic resource and how to use them. People of china and japan frequently ate variety of iodine rich seaweeds.These iodine wealthy seaweeds accounted for his or her little prevalence of goitre. Numerous disorders similar to pain, menstrual difficulties, abscesses and cancer are suggested by pharmacopoeia recipes.

Oceans shelters about 70% of earth's surface, in which earth's biosphere is 95%. Organismgive the idea in the sea for about 3500 million years ago. Over time, these organisms evolved numerous harsh environment like extreme high temperature, high salinity, high pressure, different level of aeration and radiations, effects of mutation and infections. To survive in different environment organism adapt themselves either physically or chemically. Those organism which do not have any physical defence like sessile organism these are evolved by chemical defence to protect themselves from predators. Predators also evolve themselves by chemicals weapons to paralyse or kill their pray. For example Conus magus, it is a cone snail that has a poisoned harpoon – like projectile that is used to moreover paralyse or kill the prey like small fishes in the ocean. Other organism like viperfish attract small fishes or preyby means of its photosphere [1,2].

Bioactives are the biologically active complex which are generated by marine organism. About 10% of known biologically active natural food stuff or products are obtained from microbial origin. Microbial resultant bioactive by the 20th century had turn out to be the basis of pharmaceuticals. Researches have confirmed us that 'living surface' symbolize an environment that synthesize bioactive, which is rich in epibiotic microorganism. Over the next eras drug development is contributed by the production of novel compounds which is produced by marine biotech development. Numerous natural food stuff and correlated drugs are used to treat 87% of human disease like anticancer, antibacterial, antiparasitic, anticoagulant, immunosuppressant [3,4,5,6].

Potent bioactive chemical substanceswhich can befashionedthrough marine bio-assets are peptide, proteins, polyether, fatty active, polysaccharides and enzymes. Due to marvellous richness, marine nutrients is a goldmine of progressivewholesomemeals stuff and numerousherbalcombos like bioactive peptides, fish oils,

microalgae, microalgae and fish proteins. Marine's nuraceuticals had been misused formeals uses [7,8].

MARINE DRUGS: Marine pharmacognosy is a department of pharmacognosy, it's milesspecificallyworried with the evidentlygoing on substance which incorporate medicinal fee from marine source. Those tabletswhich might bereceived from the marine species of bacteria, virus, algae, fungi and sponge are referred to as marine drug.

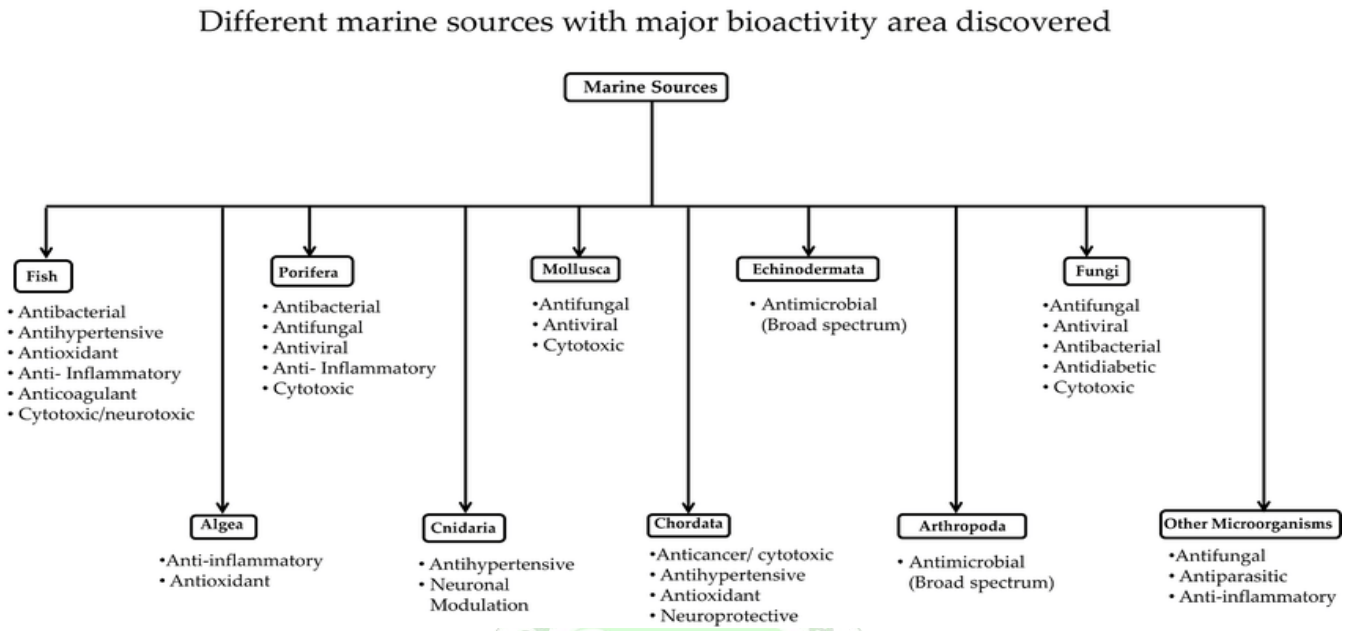

Figure 1: Different marine sources with major bioactivity area discovered

Classification of Drug Molecule of Marine Organism

Anti-Bacterial

A Polyunsaturated fatty acid Eicosapentaenoic Acid, it's far insulated from a diatom of marine beginning phaeodactylum tricornutum, it indicatesinterestopposite to an array of gram wonderful and gram bad bacteria, it comprise a multi- drug resistant style of staphylococcus arcus

Anti-Inflammatory

The anti-inflammatorycharacteristic on extracts and severadifferentquantities of the Mediterranean sponge species same spongia officinalis is used with inside theexamine on rat version of the carrageenan made paw edema assay

Neuroprotective

Neuroprotection is suppliedwith the aid of using the extracts of south Indian inexperienced seaweed like ulva reticulata. It do its motionwith the aid of using inhibiting acetyl and butyryl- cholinesterase. The efficacy has similarities to retailers and presentlyaccredited for Alzheimer's sickness treatment.

Anti-Parasitic

Tunisian sponge regardedbecause the extracts of sarcotragus species, it is ready in dichloromethane. It has been established in-vitro anti-leishmanial hobbythrough the demonstration of the related morphological alternation or variationswith inside the promastigotes of leishmanial major.

Anti- Cancer

Bryostatin, it's farby and largeobtained from the bryozoan, buegula neritina. Some paperworkadditionallyhad been extracted from tunicates and sponges. Sorbicillin spinoff alkaloids sorbicillactone A and its analog 2', 3'- dihydro sorbicillactone B has proven its interest in contradiction of leukaemia cells that'sunfastened from any cytotoxicity. Sorbicillactone-B has been derived from the salt water way of life of the bacterial stress penicillium chrysogenum. Penicillium chrysogenum has been insulated from a sponge ircinia fasciculata, that's a Mediterranean sponge specimen.KLH (keyhole limpet hemocyanin) it is alternative anti- cancer drug which is used as immunotherapeutic agent. KLH comprise copper and it is extracellular respiratory protein. It is present in megathura crenulata. Megathura crenulata is a marine gastropod species typically found at pacific coast of California and Mexico in large numbers. The 2 isoforms of KLH are KLH1 and KLH2. KLH has immunostimulatory properties in numerous experimental animals and several humans which are used in experimental immunology and as an immunotherapeutic agent. KLH is used for the treatment of bladder carcinoma. Its efficacy is due to the cross-reacting carbohydrates epitode.

Anti – Viral Agents

Anti – herpes simplex virus-1 (HSV) activity is establish in the higher molecular weight exopolysaccharides which is extracted from the celtodoryx giradae which is a French marine sponge and it has stated its associated symbiotic bacteria.

Analgesic

In 2004 to the tract pain U.S Food and drug administration (USFDA) has accepted Ziconotide which was the first drug of marine origin. It was extracted from the marine snail conus magus and it is also acknowledged as prialt. Ziconotide acts by blocking nerves of the spinal cord.

Anti- Microbial

Well known anti-microbial agents are cephalosporin, which have marine source of origin. From marine fungus cephalosporin C was firstly extracted and purified marine fungus was from which it has been extracted was cephalosporin acremonium [9,10,11,12].

Marine Drugs

CYTARABINE (cytosine arabinoside or arabinosyl .cytosine, ara-c)

Cytarabine (aka Ara-C, cytosar-U) was insulated from marine sponge. It is used to kill cancer cell by blocking DNA polymerase function.Cytarabine is also named as cytosine arabinoside it is a chemotherapy medication used for the treatment of acute myeloid leukaemia, chronic myelogenous leukaemia and non-Hodgkin's lymphoma.

Figure: 2

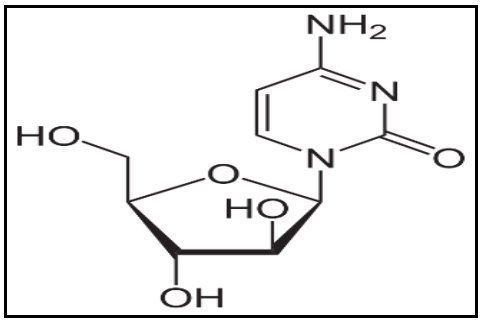

Figure: 3

Molar Mass*:* 243.217 G/Mol

Formula*:* $C_9H_{13}N_3O$

Routes of Administration: Injectable (Intravenous or infusion or intrathecal or subcutaneous)

MOA: It is converted into the triphosphate form with in the cell and complete with cytidine to combine itself into DNA. The sugar moiety of Cytarabine hampers the rotation of the molecule in the DNA.

Excretion: Kidney

Protein Binding: 13%

Metabolism: Liver

Class*:* anti metabolites

Dosing: In the induction therapy of acute non- lymphocytic leukaemia, the usual Cytarabine dose in combination with other anti-cancer drug is 100mg/m^2/day by constant IV infusion (day 1-7) or 100 mg/m^2 IV every 12 hours (day 1-7).

Side Effects: Bone marrow suppression with leukopenia thrombocytopenia and anaemia, nausea, vomiting, diarrhea, abdominal pain.

VIDARABINE (adenine arabinoside, Ara-A or arabinofuranosyladenine)

The most significant antiviral lead of marine origin reported is nucleoside ara-A (vidarabine) insulated from sponge tethya crypta. Vidarabine is an antiviral, active against herpes virus, pox virus, rhabdoviruses, hepadnaviruses and some RNA tumour viruses. A 3% ophthalmic vira-A is used in the treatment of acute keratoconjuntivitis and recurring superficial keratitis initiated by HSV-1 and HSV-2.

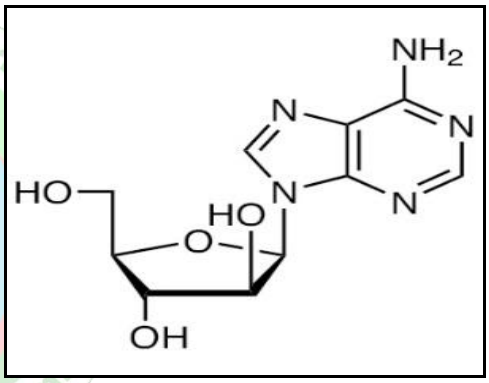

Figure: 4

Figure: 5

Molar Mass: 267.24

Formula: $C_{10}H_{13}N_5O_4$

Route of Administration: Eyes

Excretion: Kidney

Protein Binding: 24-38%

MOA: Vidarabine work by snooping with the production of viral DNA. It is nucleoside analog and therefore has to be phosphorylated to be active. Vidarabine is consecutively

phosphorylated by kinases to the triphosphate ara-ATP by 3 step process.

Side Effects: Burning, pain, irritation, itching, redness, swelling, blurred vision.

ZICONOTIDE

Ziconotide is also named as SNX-111. It is a non-opioid analgesic drug. It is a synthetic form of conotoxin MVIIA. Conotoxin is a peptide that is found in the venom of fish eating marine snail, conus magus. It has low ability to cross BBB, therefore it is administered intrathecally topatients. Intra thecal administration permits Ziconotide to reach its maximum local concentration in short time which encourages rapid onset of analgesia.

Figure: 6

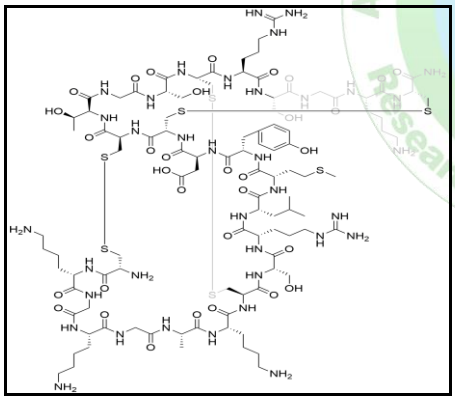

Figure: 7

Molar Mass: 2639.14

Formula: $C_{102}H_{172}N_{36}O_{32}S_7$

Route Of Administration: Intra thecal

Excretion:<1% urine

MOA: Its binding blocks N-type calcium channels, which lead to a barrier of excitatory neurotransmitter release from the primary afferent nerve terminal and antinociception.

Side Effects: Dizziness, drowsiness, nausea, headache, weakness.

TRABECTEDIN

Trabectedin, is solid under the brand name Yodelis. It is an alkylating cytostatic drug derivative from Caribbean tunicate. Trabectedin injection is used to treat liposarcoma (a cancer that begins in fat cells) or leiomyosarcoma (a cancer that begins in smooth muscle tissue) that has spread to other parts of the body and cannot be treated with surgery in those people who have been already treated with chemotherapy medications.

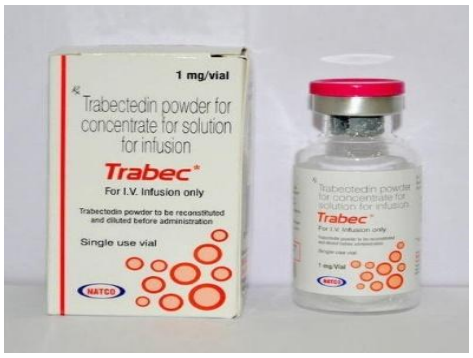

Figure: 8

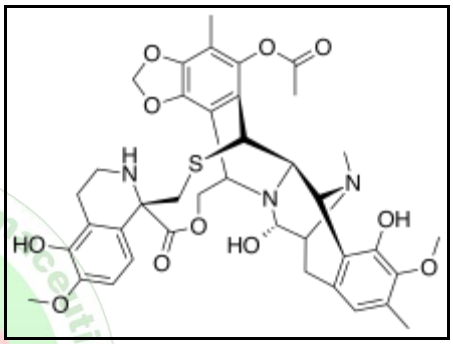

Figure: 9

Molar Mass: 761.84 g/mol

Formula: $C_{39}H_{43}N_3O_{11}S$

Protein Binding: 94-98%

Other Names: ecteimascidin 743, ET-743

Metabolism: Liver

MOA: Binds to the minor groove of DNA interfacing with the cell division and genetic transcription process and DNA repair machinery.

Concentration: 0.25 mg and 1 mg of Trabectedin per vial.

Indications: Yomdelis is specified for the treatment of adult's patients with advance soft tissue sarcoma, after disappointment of anthracyclines and ifosfamide or who are unsuited to receive these agents.

Side Effects: Headache, weakness, tiredness, constipation, diarrhea, body ache, skin darkening or trouble sleeping.

Eribulin Mesylate (E7389) Or Halichondrin

Eribulin is an anticancer drug used for the treatment of breast cancer and for the treatment of other solid malignancies. Eribulin mesylate is a synthetic analogue of halichondrin B. which are bulky polyether macrolide derived from natural mitotic tubule inhibitor. Eribulin is solid under the brand name halaven, correspondingly used for the treatment of liposarcoma.

Figure: 10

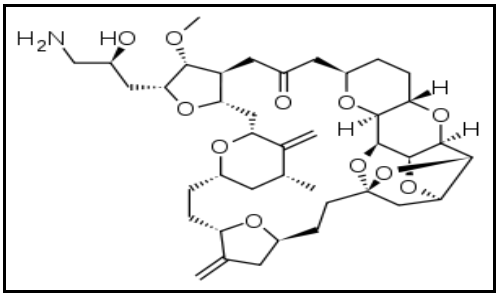

Figure: 11

Molar Mass: 826.0 g/mol

Formula: $C_{14}H_{69}NO_{14}S$

Other Names: E7389, ER-086526, NSC- 707389, Eribulin mesylate (JANJP), Eribulin mesylate (USAN US).

Class: Anti- neoplastic drug

MOA: Inhibition of the growth phase of the microtubule without any corresponding inhibition of the shortening phase.

Indications: HALAVEN is indicated for the treatment of patients with metastatic breast cancer who have earlier received at least 2 chemotherapeutic regiment for the treatment of metastatic disease.

Side Effect: Nausea, constipation, loss of appetite, weight loss, headache, weakness, tiredness, bone-back pain or joint pain.

SOBLIDOTIN

Soblidotin is a tetra peptide derivative of dolastatin 10. It is an inhibitor of tubulin polymerisation which shows potent anti-tumour activity. It has a role as a microtubule destabilising agent, an antineoplastic agent and an apoptosis inducer. It is functionally correlated to phenyl ethylamine and L-valine.

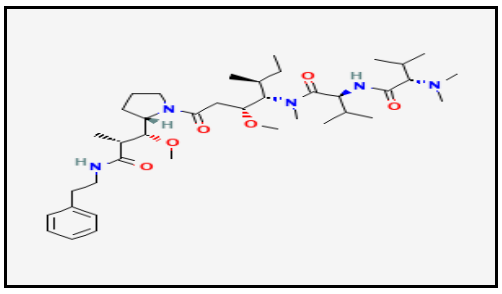

Figure: 12

Molar Mass: 702.0 g/mol

Formula: $C_{39}H_{67}N_5O_6$

MOA: Inhibits tubulin polymerisation, resuliting in cell cycle arrest and induction of apoptosis.

Side Effects: Severe cumulative neuropathy, neutropenia and fatigue , alopecia, diarrhea and nausea.

Tetrodotoxin

Trtrodotoxin (TTX) is a potent neurotoxin. Its name is derived from tetraodontiformes an order that includes puffer fish, porcupinefish, ocean sunfish, trigger fish, severel of these species carry toxin.Tetrodotoxin (TTX) is a selective sodium channel blocker non-protein toxin. The consumption of an organism containing TTX can cause neurological and gastrointestinal symptoms .

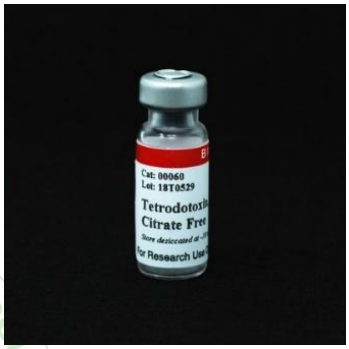

Figure :13

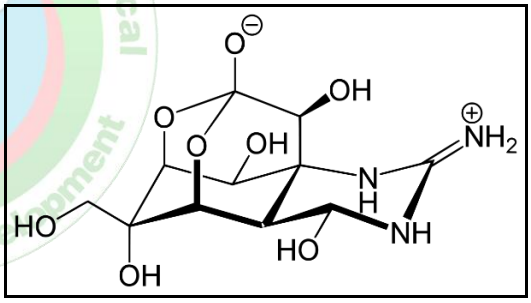

Figure : 14

Molar Mass: 319.27 g/mol

Formula : $C_{11}H_{17}N_3O_8$

MOA: Inhibits voltage gated sodium channels, preventing cell membreane from depolarising. Thisin turn inhibit action potential propagation and prevents neurons and myocytes from functioning.

Side Effects:

Headache, diaphoresis, body numbness, dysantheria, dysphagia, nausea, vomitting, abdominal pain, generalised malaisc, weakness [9,10,11,12].

Methods To Extract Various Biomolecules From Seafood Waste

By- product are produced when sea food processing takes place. It has a substantial economic and environmental consequenses[12,13]. For the recovery of biomolecules from by product from sea food industry , green extraction techniques are very powerful method. These technique increase extraction yield by reducing time for processing

and resources needed. By the use of combination of green approches, some problems can be resolved like the extraction procedures and the operating conditions that were used are very crucial for manufacture of green extraction yield and more target substance quality. This is because of the diversity of seafood by product and due to the variances in the characteristics of sea food biomolecules[14].

Traditional Method

Some common traditionalextraction method are Maceration, Percolotion and Soxhlet. These type of extraction are common process that are found through out the world. Most commonly used solvents that are choosen depending on the polarity the molecules to be extracted are ethly ethanoate, ethanol, acetone, water and methanolin various combinations. Hydroalcoholic mixtures are appropriate for this technique because phenolic compounds arehydrophilic. According to research , combining the solvent with acids or instance like citric acid, tartaric acid or hydrochloric acid can enhance the extraction efficiency of various substance. Among various extraction methods the Soxhlet extraction procedure show better results as compared to the others. Although it have many demerits like degradation of thermolabile substance (for example anthocynanis, hydrolyzable tannins) the use of large volumes of solvents and more processing time. For the extraction of lipophilic compounds, the soxhlet technique is commonly used[15,16].

Emerging Methods

Pulse Electric Field- Assisted Method

Pulse electric filed (PEF) processing is more acceptable because it uses less specific energy per processed product and due to its cost effective and environmental benefits. From the last previous decade, several food bussiness have confirmed the use of PEF-based extraction. PEF based technology are more sustainable than the present procedure of the food industry. Various different researches have discovered that when combined with other technique like osmotic shocks and the mechanical press, this developing PEF technology is very efficient in the process of extraction. As we know by the use of exixting methods wastage of food is more but the combination of PEF and solid/liquid extraction produces fewer wastage of food.the moderate PEF therapy used 0.5-1.0 Kv/cmfield strength with the treatment of period of 100-10000 sec or 1-10Kv/cm field strenght and treatment time of 5-100sec. Irreversible pores are required for the extraction of bioactive substance from natural material. Treatment using 1-20 kJ/kg specific energy and 0.7-3 kV/cm electric field intensity are commonly used[17,18].

Microwave Assisted Method

Microwave radiation are non ionising radiations that increases the molecular mobolity while keeping the structure of the molecule intact. Microwave wavelengh ranges from 0.03-30 cm and frequency ranging from 300 MHz. MAE (microwave assisted extraction) is a combination two technique that work in a synergistic way. The two technique are namely energy and mass transfer. The high pressyre of the all is due to the evapouration of moisture as the temperature rises during the microwave process. Porosity of the cell is improved by fracturing of cell wall. Due to this physical alternation the matrix improves its porosity. The efficacy of MAE process is affected by the sample moisture, the microwave power output, processing duration, sample viscosity, frequency, extraction cycle, pressure, sample size, and solvent nature[14].

Ultrasound Assisted Method

To improve the extraction efficiently ultasonic waves in the range of 20-1000 KHz are commonly used. Ultrasonic waves the mechanical waves that travel through target matrices by compressing them and rarefying them. When the ultrasonic waves propagates through the solvent, they create negative pressure . ultrasonic waves with the frequency ranging from 20-100KHz are generally used for this method, due to pressure difference that is created, bubbles are formed. These bubbles burst and cavitation occurs due to which triggering particle break up along with liquid – solid interface and release of the bioactive chemicals into matrix takes place. To extract phenolic compounds chemicals from algae . some key advantages of using ultrasound assisted method (UAE) are low temperature , short duration and small volume of solvent. To optimise this type of extraction frequency power and temperature are parameters to optimise. Two type of ultrasound equipment used are ultrasonic bath(inderict sonification) or an ultrasonic probe(direct sonification). These 2 have different operating conditions and how ultrasonic waves affects the sample. Ultrasonic probe is inserted into the sample when the sample has been immersed in the ultrasonic bath. Compared to other extraction method this device is less expensive and it can be used with a variety of solvents. UAE operates at low temperature allowing for the preservation of thermolabile compounds[19,20,21].

Supercritical Fluid Extraction

This technique is dependent on the supercritical fluid extraction principle which includes in raising temperature and pressure above their critical points by maintaining liquid and gas charactersticts. The density of fluid is similar to gases. CO_2 Carbon dioxide is most common used solvent for supercritical fluid extraction (SFE) because it is non toxic , safe and has low cost. In terms of mass transfer supercritical fluid have substantial advantage because of their low viscosity and enhanced diffusion coefficient. Supercritical carbon dioxide CO_2 can only extract non polar and low polarity molecule only because it is a non polar solvent , though it can also extract polar chemicals[19,22].

High Hydrostatic Pressure

For refining the photochemical extraction from the red macroalgae, a non thermal high hydrostatic pressure (HHP) technology which is joined with polysaccharides is proposed as novel method. Two macroalgae species specifically palmaria palmata and solieria chordalis were hydrolysed with hemicellulose and cellulose under the HHP conditions there were at 400MPa for 20 minutes. The extraction of assured components alike proteins, polyphenols and polysaccharide were improved by HHP assisted enzymatic treatment. The benefits vary depending upon the macroalgae species. The activity of antioxidants fractions is increased by over 2.8 time by the use of HHP and hemicellulose

treatment. A non thermal processing methodthat is high hydrostatic pressure is used to reduce the microbial population and inactivate the enzymes in the marine food and for the treatment of marine food, dairy, fruits and vegetable. Under very high pressure of 100-1000 MPa and temperature of 5-35degree C T the charged particles were deprotonated and salt bridges were shattered due to which cell permeability were increased[23,24].

CONCLUSION

In conclusion, marine-derived compounds hold immense potential as valuable resources for the development of novel drugs and therapeutic agents. The unique biodiversity of marine environments offers a plethora of bioactive compounds with diverse chemical structures and biological activities. Through extensive research and investigation, numerous marine-derived compounds have demonstrated promising results in various preclinical and clinical studies. These compounds have exhibited a wide range of pharmacological activities, including anticancer, anti-inflammatory, anti-microbial, anti-viral, and neuroprotective properties, among others. The rich source of marine organisms, such as marine bacteria, algae, sponges, and corals, has enabled scientists to isolate and characterize these bioactive compounds, paving the way for potential breakthroughs in drug discovery. Furthermore, the exploration of marine ecosystems has not only led to the discovery of bioactive molecules but has also provided insights into their unique mechanisms of action. Many marine-derived compounds have shown novel modes of interaction with biological targets, which can contribute to the diversification of drug development strategie

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