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Impact and Challenges of Marine Medicine to Man and its Environment

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Abstract

Marine Medicine is a science of healing, maintaining and restoring health by prevention and treatment in relation to ocean derivatives. It has an associated corollary field called Dive Medicine. Marine ecosystem is a source of unique natural products which are mainly accumulated in living organism and serves as useful pharmacologically active substances. Marine Sponges, Molluscans, Algae, Corals, Ascidians, Bryozoans and Vertebrates are major sources of biomedical compounds. A few medical derived product such as Cytarabrine (Adenine arabinoside), Vidabrine (Cytosine arabinoside), Prialt and Trabectedin are approved by Food and Drug Administration (FDA); additionally several others are currently in preclinical and clinical pipeline. The main emphasis of marine drug discovery is given in search of cure for deadly disease. Divers are exposed to a number of physiological risks as a result of exposure to deep sea. Application of antihistamine drugs, pharmacotherapy and hyperbaric oxygen therapy are the curative method in the treatment of most disease and injuries in marine environment. The Marine environment is vast but not infinite and as a result there is a need for protection of this resource by conservation. Conservation of the marine environment provides enormous benefits for a sustainable future. Marine medicine has given hope to fight debilitating disease of man such as Osteoporosis, Alzheimer's disease, auto-immune disease and Cancer. To provide and sustain a high momentum of research in marine medicine, there is a need for advance conservation, increased research, more skilled divers, taxonomist, marine chemist and sufficient financial support to improve the benefits of marine medicine to man.

Keywords: Marine organisms; Diving illness; Treatment; Ocean; Ecosystem

Introduction

Medicines are medically recommended remedies intended for ameliorating disease conditions, restoring good health and vitality to man. Marine medicine is the restoring of health in relations to ocean derivatives. It encompasses a variety of practices using marine organisms to maintain health by prevention and treatment as medicine.

Marine medicine therefore is the science of healing, maintaining and restoring health by prevention and treatment in relation to the ocean derivatives. The Ocean which is called the 'mother of origin of life' is also the source of structurally unique natural products that are mainly accumulated in living organisms. Marine medicine is not separated from general medicine but rather the general medicine applied to the sea (Figure 1).

The history of marine medicine has started in the sixties with the inception of the Submarine Arm in the Navy when new dimensions of naval warfare were introduced. The undersea environment brought to the forefront new and unfamiliar health hazards and it was realised that medical officers would require specialised knowledge and equipment to tackle the new problems that would be faced. A new field, namely "marine medicine", was added to the spectrum of medical specialisations.

A subdivision of marine medicine is dive medicine also called Undersea and Hyperbaric Medicine (UHB). Dive medicine is the diagnosis, treatment and prevention of conditions caused by humans entering the undersea environment. It includes the effects on the body of pressure on gases, the diagnosis and treatment of conditions caused by marine hazards and how relationships of a diver's fitness to dive affect a diver's safety. Hyperbaric Medicine is a corollary field associated with diving, since recompression in a hyperbaric chamber is used as a treatment for two of the most significant diving related illnesses, decompression illness and arterial gas embolism.

The first two medical officers to volunteer for submarine service were Surgeon Lieutenants Abraham and Chatterji. Along with the rest of the submarine crew, they underwent training in the Soviet Union in the mid sixties. Following in their footsteps were other medical officers, some of whom were Madhwal, Idiculla and Gokulnath who received training in the United States and the USSR for varying durations on the subject of underwater medicine.

The efforts of these pioneers resulted in marine medicine being accorded the recognition due to it in India [1]. In 1978 a two – year course for a diploma in marine medicine was instituted in Bombay University, and the first two Indian – trained marine medicine specialists were available to the Submarine Arm in 1980. This number has risen considerably since then, and these specialists are engaged in a variety of tasks in submarines, ships, and on shore. They provide support for escape training, maintenance and development of submarine escape and rescue equipment, and for diving operations - all this in addition to their primary function as doctors. Dangers in the ocean that can affect divers include marine life, marine infections, polluted water, ocean currents, waves and surges and man-made hazards such as boats, fishing lines and underwater construction [2]. Diving medical personnel recognize and treat accidents from large and small predators and poisonous creatures appropriately diagnose and treat marine infections and illnesses from pollution as well

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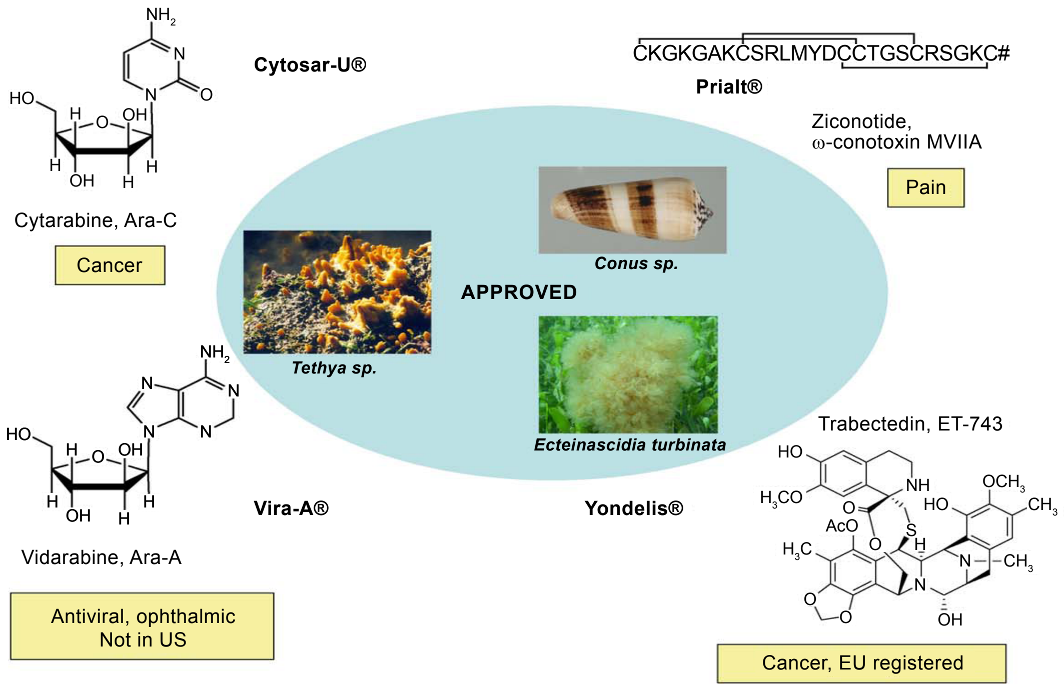

Figure 1: Schematic diagram of the approved marine derivatives.

as diverse maladies such as sea sickness, traveller's diarrhoea and malaria (Figure 2).

One of the major benefits of continued development in this field was the acceptance of Hyperbaric Oxygen Therapy (HBOT) as a means of supportive treatment for various ailments [3]. This facility has been gradually built up at the Institute of Naval Medicine in Bombay where presently a large number of service as well as civilian patients receive treatment.

However, Marine Medicine is still in infancy due to human capabilities and technological constraints limiting underwater activity for medicinal or commercial purposes [4]. Marine medicine specialists strive constantly to re-define these limitations and find means of coping to operate deeper and for longer durations in the ocean depth.

Marine plants and animals produce a wide variety of chemicals. These chemicals have allowed organisms to adapt to many different habitats in the sea by providing protection against other organisms and by aiding survival in harsh conditions [5-7]. Some chemicals are used in communication between organisms or for signalling when it is time to reproduce. These chemicals have been isolated and studied by marine scientist. In the past ten to twenty years, many new compounds have been discovered; which has chemical properties that make them useful to humans (Figure 3). As research continues, many more marine chemicals are found to have biomedical, industrial, or nutritional value. This remains an interesting and exciting area of research for scientists studying marine natural product chemistry and marine chemical ecology.

There's a medical gold rush going on the sea floor [8]. Marine scientists called bioprospectors are scouring the ocean for microorganisms and plants that naturally produce chemical compounds used for biological defense and health enhancement. These compounds are extracted, analysized and synthesized for potential human use. With literally billions of undersea life forms that are yet to be studied, scientists are finding that the oceans could become the biological mother load for deriving 21st century medicines [9-12]. The National Cancer Institute (NCI) estimates that 65 percent of all cancer drugs come from natural products. Drugs from the sea are without question one of the most promising new directions of marine science today.

Derivable Drugs from the Marine Environment

Marine derived drugs are pharmacologically active substances isolated from marine organism and developed into suitable forms for human use. The ocean has an enormous range of biodiversity which remains largely unexploited. The potential of marine organism as a new source of novel medicine was first discovered in the sixties. The isolation of soft corals was the first example to suggest that marine organisms might serve as an important source of novel chemical structure of high therapeutic value [13].

Marine organisms comprise approximately half of the total biodiversity on the earth and the marine ecosystem is the greatest source to discover useful therapeutics (Figure 4). The ever increasing resistance of wide variety of human pathogen to the existing drugs, the resurgence of otherwise eradicated infectious disease, the emergence of new infections, metabolic disorder and the rising incidence of ageing and life style related diseases amply justify the continuous search for more efficacious and highly selective drugs using both traditional and modern approaches to new drug design and development [14].

The lifesaving drugs are mainly found abundantly in microorganisms, algae and invertebrates. Modern technologies have opened vast areas of research for the extraction of biomedical compounds from oceans and seas [8]. Sessile marine invertebrates such as sponges, bryozoans, tunicates, mostly lacking morphological defense structures have developed the largest number of marine-derived secondary metabolites including some of the most interesting drug candidates (Figure 5). In recent years, a significant number of novel metabolites with potent

Figure 2: *Haliclona sp* (Purple encrusting sponge).

Figure 3: Anti-viral Eye drop.

Figure 4: *Tethya* sp.

pharmacological properties have been discovered from the marine organisms. Although, there are only few marine-derived products approved by the food and drug administration (FDA) and are currently in the market, several marine natural products are now in the pre-clinical and clinical pipeline, with more undergoing development [15]. Similar work has been conducted targeting uncultivable microbes of marine sediments and sponges using metagenomic-based techniques to develop recombinant secondary metabolites [16]. Marine bacteria are emerging as an exciting resource for the discovery of new classes of therapeutics. The promising anticancer clinical candidates like

Figure 5: Cytarabine intravenous drug.

salinosporamide A and bryostatin only hint at the incredible wealth of drug leads hidden just beneath the ocean surface. Salinosporamide A, which is isolated from marine bacteria that is currently in phase I clinical trials for the treatment of drug-resistant multiple myelomas and three other types of cancers [1].

Compared to the high degree of representation of terrestrial-derived bio products, the number of marine natural products that have found their way into hospitals, clinics and pharmacies is thus far small (Figure 6). This has more to do with the relative infancy of the field (compared to terrestrial bioprospecting) than any lack of potential for discovery. In fact, the natural products isolated from marine sources tend to be more highly bioactive than terrestrial counterparts. Below is a schematic drawing and table of drugs in the different clinical pipelines.

This is in part because they have to retain their potency despite dilution in surrounding seawater to be effective in the "chemical warfare" that allows organisms such as sponges to ward off would-be predators and animals that might attempt to grow over and mother them (Figure 7).

Despite lesser attention paid to marine natural products historically, there are notable marine-derived bioproducts that are commercially available [17]. These compounds were isolated by Bergmann and Feeney and are still prescribed today [3]. Marine organisms have some powerful toxins found in them which often have great medical and therapeutic benefits to humans. For example, okadaic acid found in dinoflagellates can kill cancer cells at extremely low concentrations (Figure 8). Several molecules are isolated from marine organisms using biotechnology into specific product useful to man.

A few of the marine organisms and isolated metabolites are discussed below.

Sponge

Sponge (Phylum Porifera) is the most primitive of multicellular animal that have existed for 700-800 million years. Approximately 10,000 sponges have been described in the world and most of them live in marine waters. A range of bioactive metabolites has been found in about 11 sponge genera. Three of these genera (Haliclona, Petrosia and Discodemia) produce powerful anti-cancer, anti-inflammatory agents. They produce toxic compounds to repel or deter their predators compete for space and for communication and protection against infection. They are studied because of their wealth of metabolites which display biological activity [18-20].

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Sponges are known to be rich source of terpenoids which has shown strong antibiotic activity. Terpenoids is an active ingredient in drugs like Variabilins and Hydroquinone with both analgesic and anti-inflammatory properties. Chloroquine, mefloquine, quinine and sulfadoxinpyrimethamine once were effective drugs in treating malaria caused by the protozoan, Plasmodium falciparum. However, the efficacy of these drugs has met rising cases of developed resistance by the protozoan itself (Figure 9). Manzamine type alkaloids have been isolated from an Indonesian sponge and have shown its effects against malaria, in addition to tuberculosis and leishmania. They can be cultivated from cutting parent and planted in the sea or an aquarium [21]. There are number of drugs derivable from the marine sponge but only two have been approved by Food and drug administration (FDA) namely; Vidarabine (Ara-A) and Cytarabine (Ara-C).

Ara-A (Vidarabine®, Vidarabin®, Thilo®)

The family of antiviral drug, based on a group of compounds (arabinosides) extracted from the sponge Tethya crypta . Vidarabine ophthalmic is a drug derived from a marine sponge; the preparations are used to treat viral infections of the eye (Figure 10) [22].

Ara-C (Cytarabine, Alexan®, Udicil®)

(Patrzykat and Douglas, 2003) Cytarabine is an antineoplastic drug also derived from marine sponge. It slows down the growth and spread of the cancer cells in the body to effectively cure certain types of cancer. It is used in the treatment of several forms of leukemia including acute myelogenous leukemia and meningeal leukemia. Anti-

Figure 6: Cone snail (*Conus magnus*).

Figure 7: Prialt ziconotide intravenious drug.

Figure 8: *Ecteinascidia turbinate*.

Figure 9: Trabectedin drug.

Figure 10: Soft Coral (*Pseudopterogorgia elisabethae*).

metabolites masquerade as purine or pyrimidine which becomes the building blocks of DNA [23]. They prevent these substances becoming incorporated into DNA during the "S" phase (of the cell cycle), stopping normal development and division (Figure 11). This medicine is a type of chemotherapy for treating cancers of the blood and certain other cancers.

Cone snail

Conus: Conus is a large genus of small to large predatory sea snails, marine gastropod molluscs, with the common names of cone snails, cone shells or cones [24]. This genus is placed in the subfamily Coninae within the family ConidaeIs, Phylum Gastropoda which injects potent cocktail of peptide toxins into their prey to immobilise them. They are

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not culturable because they are planktonic at some stages of their life cycle (Figure 12).

Ziconotide: Ziconotide known by its trade name Prialt® is a synthetic form of a compound extracted from the toxin/venom of predatory cone snails (Conus magus). Scientists have been intrigued by the effects of the thousands of chemicals in marine snail toxins since the initial investigations in the late 1960s by Baldomero Olivera. Ziconotide was discovered in the early 1980s by University of Utah research scientist Michael McIntosh, when he was barely out of high school and working with Baldomero Olivera. Ziconotide was developed into an artificially manufactured drug by Elan Corporation. It was approved for sale under the name Prialt® by the U.S. Food and Drug Administration on December 28, 2004, and by the European Commission on February 22, 2005. Azur Pharma acquired worldwide rights (except Europe) to Prialt in 2010. It has since been used as treatment for severe cases of chronic pain in patients with conditions such as cancer and AIDS (Figure 13). Current clinical results suggest that Prialt is a powerful, non-addictive alternative to drugs such as morphine [25,26].

Ziconotide is a non-narcotic pain reliever that works by blocking pain signals from the nerves to the brain. It is used to treat severe chronic pain in people who cannot use or do not respond to standard pain-relieving medications. Prialt® offers 1,000 times the analgesic power of opiates but without the addiction and waning potency.

Tunicates

The tunicates are commonly known as sea squirts. They are sessile as adults and hermaphrodites. The name arises from the existence of tunics typically this tunic is attached to substratum by a small holdfast and stands upright. They are a rich source of chemical metabolite with remarkable biological activity. These compounds are simple amino-acid or complex alkaloids (Figure 14). These compounds have shown various biological activities like antifungal, antibacterial, cytotoxicity, antimalarial activity, inhibition of protein kinase C.

Didemnin B: Didemnins are cyclic depsipeptide compounds isolated from a tunicate (sea-squirt).They were first isolated in 1978 at the University of Illinois. Although more than nine didemnins (didemnins A-E, G, X and Y) have been isolated from the extract of Trididemnum solidum, didemnin B is the one that possesses the most potent biological activities. It is a strong antiviral agent against

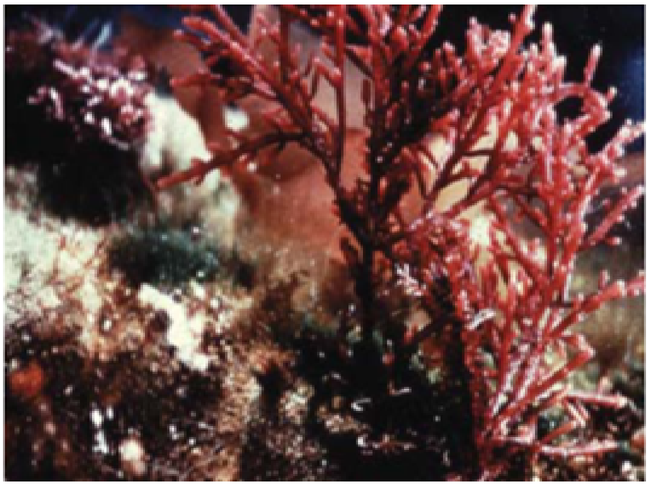

Figure 11a: Seaweed (Laurencia sp).

Figure 11b: Red seaweed.

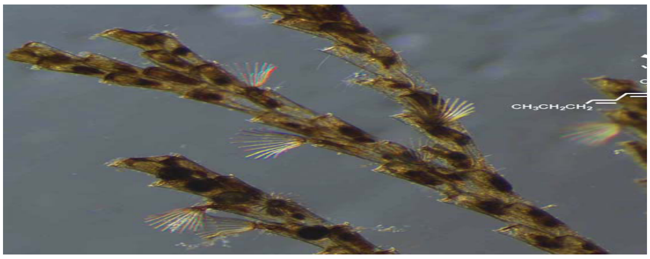

Figure 12: Bryozoan (*Bugula neritina*).

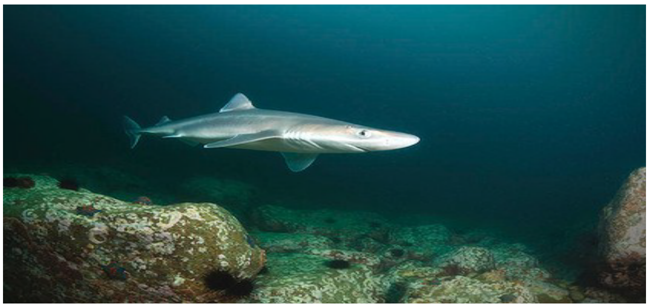

Figure 13: Dog fish shark.

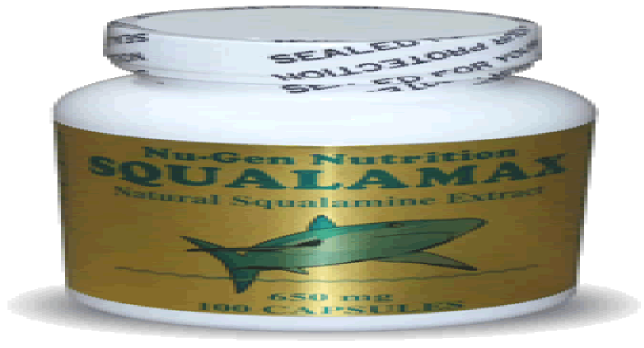

Figure 14: Nutritional supplement.

both DNA and RNA viruses such as herpes simplex virus type 1, a strong immunosuppressant that shows some potential in skin graft and is also very cytotoxic. It shows strong activity against murine leukemia cells.

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There are variety of other marine natural products that have potential medicinal value such as anticancer agent, anti-inflammatory agent and pain-killers.

Trabectedin: Trabectedin is a naturally occurring compound that is derived from a marine organism, Ecteinascidia turbinate. It is tetrahydroisoquinoline alkaloid with trade name Yondelis®. It's the first type of chemotherapy medicine accepted in the European Union for cancer known as an anti-neoplastic.

Corals

These are marine animals in class Anthozoa of phylum Cnidaria typically living in compact colonies of many identical individual polyps. The group includes the important reef builders that coral head is a colony of myriad genetically identical polyps. Each polyp is a spineless animal typically only a few millimeters in diameter and a few centimeters in length. A set of tentacles surround a central mouth opening. An exoskeleton is excreted near the base. Over many generations, the colony thus creates a large skeleton that is characteristic of the species. Individual heads grow by asexual reproduction of polyps (Figure 15). Corals also breed sexually by spawning: polyps of the same species release gametes simultaneously over a period of one to several nights around a full moon. There are two main types of corals; hard corals composed of stony calcium carbonate, and soft corals made up of a protien/calcium carbonate material. Scleractinians, or hard corals such as brain, star, staghorn, elkhorn and pillar corals have rigid exoskeletons, or corallites, that protect their soft delicate bodies. Gorgonians, or soft corals such as sea fans, sea whips and sea rods, sway with the currents and lack an exoskeleton. inhabit tropical oceans and secrete calcium carbonate to form a hard skeleton.

Gorgonians (pseudoterigorgia elisabethae)

Gorgonacea is an order of sessile colonial cnidarian found throughout the oceans of the world, especially in the tropics and subtropics. Gorgonians are also known as sea whips or sea fans and are similar to the sea pen, another soft coral. Individual tiny polyps form colonies that are normally erect, flattened, branching, and reminiscent of a fan. Others may be whiplike, bushy, or even encrusting. A colony can be several feet high and across but only a few inches thick. They may be brightly coloured, often purple, red, or yellow. Photosynthetic gorgonians can be successfully kept in captive reef aquariums. The name "Gorgonacea" is no longer considered valid and Alcyonacea is now the accepted name for the order.

Pseudopterosins: The pseudopterosins were isolated from a Caribbean soft coral species called a sea whip (Pseudopterogorgia elisabethae). They belong to a class of compounds known as tricyclic diterpene glycosides. Pseudopterosins have been shown to possess potent anti-inflammatory and analgesic (pain relief) properties. They appear to work by inhibiting the synthesis of eicosanoids, (locally functioning hormone-like substances) in specific white blood cells called polymorphonuclear leukocytes. The extreme selectivity with which the pseudopterosins target their activity is intriguing to researchers. They appear to be pharmacologically distinct from other non-steroidal anti-inflammatory drugs (NSAIDs) and their mechanism of action appears to be novel as well. The pseudopterosins have been licensed to a pharmaceutical firm for medical use as anti-inflammatory drugs (Figure 16). At least one of the pseudopterosins has been brought through preclinical tests and an Investigational New Drug (IND) application has been filed with the U.S. Food and Drug Administration. A pseudopterosin extract has found its way to the non-pharmaceutical marketplace as an additive to prevent skin irritation in a line of Estèe Lauder cosmetic skin care.The anti-inflammatory and analgesic pseudopterosins isolated from a Bahamian soft coral. This led to the development of bioproducts now used in Estee Lauder skin care and cosmetics lines and currently worth $3-4 million a year.

Seaweeds

The term seaweed refers to the large marine algae that grow almost exclusively in the shallow waters at the edge of the world's oceans. They provide home and food for many different sea animals, lend beauty to the underwater landscape, and are directly valuable to man as a food and industrial raw material. Seaweeds are plants because they use the sun's energy to produce carbohydrates from carbon dioxide and water. They are simpler than the land plants mainly because they absorb the nutrients that they require from the surrounding water and have no need for roots or complex conducting tissues. Many seaweed have hollow, gas-filled structures called floats or pneumatocyst. These help to keep the photosynthetic structures of the seaweed buoyant so they are able to absorb energy from the sun (Figure 17). Seaweed draws an extraordinary wealth of mineral elements from the sea which includes sodium, calcium, magnesium, potassium, chlorine,

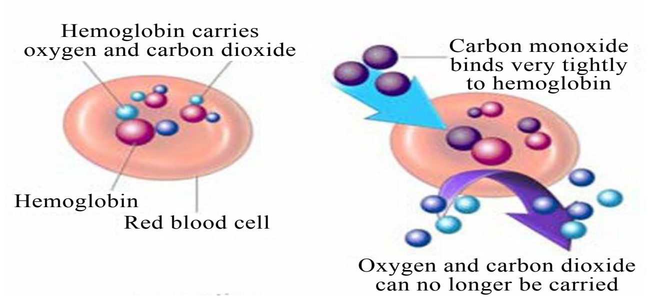

Figure 15: Schematic representation of decompression disease.

Figure 16: Divers' Suffering DCS.

Figure 17: Decompression oxygen.

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sulfur and phosphorus; the micronutrients include iodine, iron, zinc, copper, selenium, molybdenum, fluoride, manganese, boron, nickel and cobalt. It also contains several vitamins like carotenes (provitamin A); vitamin C, B12 along with higher proportion of essential fatty acids than land plants. Seaweeds provide a rich source of structurally diverse secondary metabolites which includes terpenes, acetogenins, alkaloids and polyphenolics, with many of these compounds being halogenated. Nwankwo, 2004 and Onyema, 2009 also confirms the use of seaweeds for medicinal purposes.

Bryozoans: Bryozoans sometimes referred to as moss animals or ectoprocts are tiny, colonial organisms. Their development does not follow either a true protostome or true deuterostome pattern. They, along with the Phoronids (worm-like animals) and the Brachiopods (bivalve-like animals sometimes referred to as lampshells) are thus classified based on the presence of a specialized feeding structure called a lophophore, an extension of the body wall into a tentacled structure that surrounds the mouth and is either horseshoe-shaped or circular. Bryozoan colonies can be encrusting, arborescent (branching, and tree-like), or even free living. Individuals within colonies may be referred to as either zooids, or polypides. The term polypide refers to the contents of each zooid (gut, lophophore, muscles, etc.) within the body wall (Figure 18).

Bryostatin-1: Bryostatin-1 is another anti-cancer compound that works by binding to the same receptors as phorbol esters (which actually promote tumor formation). However, bryostatin-1 is found to down regulate the production of protein kinase C which leads to inhibition of cell growth, alteration, or differentiation and ultimately may lead to cell death. Bryostatin-1 has also been described many other properties including T-cell activation, immunomodulation, and haematopoietic progenitor cell stimulation through its down regulation of protein kinase C. It is currently in the Phase II clinical trials for the treatment of melanoma, non-Hodgkin's lymphoma, renal cancer, and colorectal cancer.

Squalamine

This is an essential ingredient which may be derived from various sources of nature but predominantly found in the liver of dogfish sharks (Squalus acanthias). It was discovered in 1993 but a new study has found potential uses against human viruses (Smh, 2011). Squalamine is an aminosterol compound which the body readily uses to carry out its normal anti-angiogenesis function. It is safe for humans and has been considered a potential tool against cancer and eye diseases. According to Zasloff, 1993 Squalamine has shown significant and promising activity in certain forms of cancer and diabetic retinopathy.

Figure 18: Decompression oxygen chamber (Interior).

An example of a product which contains a highly concentrated form/extract of squalamine is a remarkable dietary supplement on the market by the name of Squalamax™. It has an extremely high bio-availability of these active compounds and as a result is very important to be ingested as a supplement to the human diet.

Drugs from the sea are one of the most promising new directions of marine science. Sea has got plenty of metabolites and other resources in living or dead form. Sponges (37%), coelenterates (21%) and microorganisms (18%) are the major sources of biomedical compounds followed by algae (9%), echinoderms (6%), tunicates (6%), molluscs (2%) bryozoans (1%), etc. The main emphasis is given in the search of drugs for deadly human diseases as cancer and AIDS. The scientists at different parts of the world have extracted various drugs for such diseases in recent years.

Further, many chemical compounds isolated from marine organisms have great potential as antimicrobials or cytotoxic compounds due to the reliance of marine organisms on antimicrobial compounds or cytotoxic molecules as their innate defence mechanisms. There are currently over 3000 new substances identified from marine organisms in the past three decades, giving researchers a large pool of novel molecules from which to find new compounds to develop. However, not all derived drugs from marine sources have been approved for treatment as some are still in different phase of clinical approval (Table 1).

Compound Name	Source	Status	Disease
Bryostatin 1	Bryozoan *Bugula neritina*	Phase II	Cancer
TZT–1027	Synthetic Dolastatin	Phase II	Cancer
Cematodin	Synthetic derivative of Dolastatin 15	Phase I /II	Cancer
ILX 651, Synthatodin	Synthetic derivative of Dolastatin 15	Phase I/II	Cancer
Ecteinascidin 743	Ascidian *Ecteinascidia turbinate*	Phase II/III	Cancer in 2003-2005
Aplidine	Ascidian *Aplidium albicans*	Phase II	Cancer
E7389	Sponge *Lissodendoryx* sp.	Phase II	Cancer
Discodermolide	Sponge Discodermia dissolute	Phase I	Cancer
Kahalalide F	Mollusk Eylsia rufescens and Alga Bryopsis sp.	Phase II	Cancer
Zalypsis	Synthetic Safracin B derivative	Phase I	Cancer
ES-285	Spisula polynyma	Phase I	Cancer
Squalamine	Shark *Squalus acanthias*	Phase II	Cancer
Æ-941 (Neovastat)	Shark	Phase II/III	Cancer
Okadaic acid	Dinoflagellates	Phase I	Cancer
E-7974 (Eisai)	Synthetic	Phase I	Cancer
Salinosporamide A (NPI-0052)	Bacterium *Salinispora tropica*	Phase I	Cancer
GTS-21 (aka DMBX)	Marine worm	Phase I	Alzheimer's
IPL-576,092 (aka HMR-4011A)	Sponge *Petrosia contignata*	Phase II	anti-asthmatic
CGX-1160	*Conus geographus*	Phase I	Pain
ACV1	*Conus victoriae*	Phase I	Pain
Didemin B	Sea squirts	Phase I	Anti-inflammatory

Table 1: Status of Marine-Derived Natural Products in Clinical and Preclinical Trials.

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Effects of Diving in the Marine Environment

Exposure to the underwater environment is increasing as a result of the medical gold rush going on the sea floor. Bioprospectors are scouring the ocean for microorganisms and plants that naturally produce chemical compounds used for biological defense and health enhancement. These compounds are extracted, analyzed and synthesized for potential human use. As a result disease and injuries from marine environment are inevitable which leads damages and disorder of structure or function in human. Diving related illnesses are consequently increasing as divers are exposed to a number of physiological risks as a result of the underwater environment including: bites/envenomation, the toxic effects of hyperbaric gases, the respiratory effects of increased gas density, drowning, hypothermia and bubble related pathophysiology. Some of which are discussed below;

1. Bites/Envenomation
2. Decompression disease
3. Arterial Gas Embolism
4. Nitrogen narcosis
5. Pneumothorax
6. Hypothermia

Bites/Envenomation

As man takes increasing advantage of the waters of the world for recreational, commercial and scientific purposes, the hazards of human contact with inhabitants must be appreciated. Abrasions, bites, and lacerations are usually the result of a marine creature's instinct to protect itself against a perceived danger. Many invertebrate and vertebrate animal species have developed natural defense mechanisms, some of which involve envenomation, with a few species posing the threat of serious injury or death. Coral scrap is one of the most common injuries to divers as they spend significant amounts of time around the marvellous communities of corals (Figure 19). The mechanism of a coral injury involves the depositing of living organisms into the wound caused by the contact with the rigid limestone structure. Coral poisoning is a more toxic version of coral infection as the symptom includes chills, fever, swollen lymph glands and putrid discharge from the wound.

Decompression disease

Decompression sickness occurs when a sufficiently large gas phase forms within the tissues of the body after a reduction in ambient pressure. The physiological problems associated with decompression from elevated atmospheric pressures have been known for over 100 years. These problems can generally be divided into two broad categories:

1) Those due to physical injury as a result of an expansion of gas

2) Those due to liberation of a gas phase in tissues. Some of the best clinical descriptions of the latter were published almost a century ago

As an underwater diver descends in the water column, the increasing barometric pressure (0.445 psi/ft of descent) has two major effects. The first is entirely mechanical: any gas-containing space in the body is reduced in volume according to Boyle's law (P1V1=P2V2). Thus, if one starts off with a volume V in the lungs on the surface and one swims to a depth of 10 m without breathing any additional gas, the volume of gas in the lungs (V) will be reduced to 1/2 V. If one should breathe from a gas source while at that depth (for example, from SCUBA equipment), the lungs will then return to V. Should the diver then swim back to the surface, the volume of gas in the lungs will then expand to 2V. This enlarging volume of gas is usually exhaled, but should there be some reason that the gas is not exhaled (i.e., breath holding), then mechanical forces can result in disruption of lung parenchyma, causing one of the pulmonary over-inflation syndromes (Figure 20).

The second major category of physiological problems associated with decompression is based on a different physical principle. As a diver descends in the water column, the partial pressure of the constituent gases he breathes is increased. This then is reflected in alveolar gas, then arterial blood, and eventually increasing amounts of gas are driven into solution in the tissues of the body. Should a diver be using air as the breathing medium, the most important component gas driven into solution is nitrogen. Depending on the amount of gas driven into solution (which is basically a function of depth and time), a varying number or volume of bubbles (gas phase) will form during decompression as a consequence of the reduction in ambient pressure. It is this gas phase that causes the signs and symptoms collectively referred to as "decompression sickness" (DCS).

Decompression disease can produce many symptoms, and its effects may vary from joint pain and rashes to paralysis and death. Individual susceptibility can vary from day to day, and different individuals under the same conditions may be affected differently or not at all. Although DCS is not a common event, its potential severity is such that much research has gone into preventing it, and underwater divers use dive

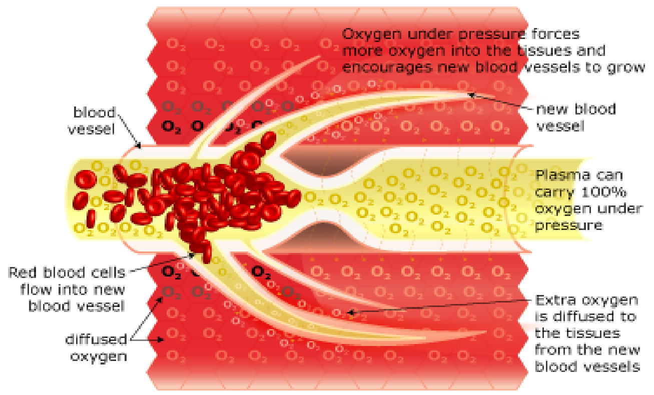

Figure 19: Schematic representation of hyperbaric oxygen therapy.

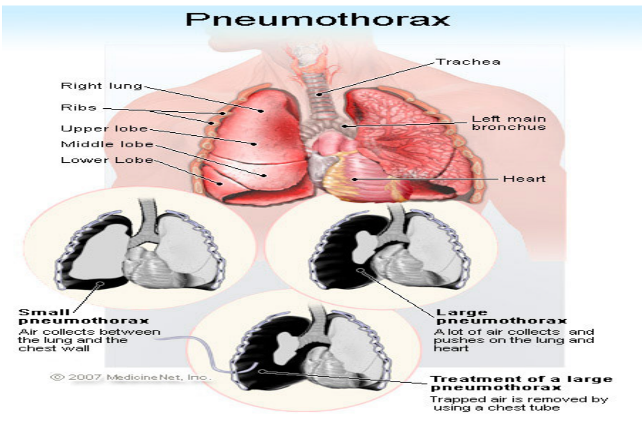

Figure 20: Schematic representation of Pneumonax treatment.

tables or dive computers to set limits on their exposure to pressure and their ascent speed.

Arterial gas embolism (AGE)

Arterial gas embolism occur secondary to pulmonary barotrauma when gas is forced into the pulmonary vasculature Arterial gas embolism is a major cause of death in diving and the initiating cause (pulmonary barotrauma) usually goes undetected. Caused most often by the expansion of respiratory gases during ascent, it also occurs when the breath is held during ascent from a dive, when there is local pulmonary pathology, when there is dynamic airway collapse in the non-cartilaginous airways and if there is low pulmonary compliance, particularly if this is not distributed evenly throughout the lungs. In most severe form, AGE presents catastrophically (~4% of victims) with collapse, loss of consciousness, apnea, and cardiac arrest. Various theories have been advanced to explain the mechanism of cardiac arrest in these victims. Animal models of carotid artery embolization with gas result in ventricular arrhythmias, and dog models of coronary artery air embolization have also resulted in cardiac arrest. Unfortunately, the course and nature of the ventricular arrhythmias produced by carotid artery embolization does not duplicate the clinical situation in humans, and accidental coronary artery air embolization in humans (in catheter lab misadventures) does not result in sudden cardiac arrest as is seen in victims of AGE. The earliest hypothesized mechanism was "vapor lock" due to filling of the central vascular bed with gas. Unfortunately, injecting gas into a compliant balloon placed into the left ventricle of a dog does not produce cardiac arrest. Thus the exact mechanism by which AGE causes sudden death in humans remains unclear.

In victims who do not die suddenly, the signs and symptoms of AGE can be quite varied. Sudden unconsciousness, hemiparesis, marked confusion, and loss of coordination are all consequences of gas embolization to the brain. Frequently, patients will to some degree recover spontaneously from the early and often more dramatic initial signs and symptoms of AGE. Other varied and more subtle signs of the gas embolization may remain, such as abnormalities of the mental status examination. If the initial signs and symptoms are minor and transient, they may be missed entirely.

In the remaining victims of AGE, if the initial signs and symptoms do not resolve spontaneously, neurological deficits of varying severity tend to persist. As noted above, the vast majority of victims will survive the initial insult, and it is only a small percentage who died in the hospital. With treatment, those who survive tend to have a reasonably good prognosis.

Although the initial and most obvious signs and symptoms of AGE are due to the distribution of gas emboli to the brain, it is now fairly well accepted that gas bubbles are distributed throughout the entire systemic vascular bed.

Nitrogen narcosis

Nitrogen Narcosis also known as nitrogen euphoria or raptures from the deep is a reversible alteration in consciousness that occurs while scuba diving at depth. The Greek word ναρκωσις (narcosis) is derived from narke, which means temporary decline or loss of senses and movement, numbness. Nitrogen under pressure affects the brain by acting as an anesthetic agent producing a state similar to alcohol intoxication or nitrous oxide inhalation, and can occur during shallow dives, but usually does not become noticeable until greater depths, beyond 30 meters (100 ft).

Apart from helium and neon, all gases that can be breathed have a narcotic effect. This effect is consistently greater for gases with a higher lipid solubility and there is good evidence that the two properties are mechanistically related. As depth increases, the mental impairment may become hazardous. Although divers can learn to cope with some of these effects, it is not possible to develop a tolerance. While narcosis affects all divers, predicting the depth at which narcosis will affect a diver is difficult, as susceptibility varies widely from dive to dive, and between individuals.

When narcosis appears, it may be completely reversed in a few minutes by ascending to a shallower depth with no long-term effects. For this reason, narcosis while diving in open water rarely develops into a serious problem as long as the divers are aware of its symptoms, and may ascend to manage it. Diving beyond 40 m (130 ft) is generally considered outside the scope of recreational diving: as narcosis and oxygen toxicity become critical factors, specialist training is required in the use of various gas mixtures such as trimix. Nitrogen narcosis can cause death among experienced scuba divers (Table 2).

Hypothermia

Hypothermia (from Greek υποθερμία) is a condition in which core temperature drops below the required temperature for normal metabolism and body functions which is defined as 35.0°C (95.0°F). Body temperature is usually maintained near a constant level of 36.5–37.5°C (98–100°F) through biologic homeostasis or thermoregulation. If exposed to cold and the internal mechanisms are unable to replenish the heat that is being lost, a drop in core temperature occurs. As body temperature decreases, characteristic symptoms occur such as shivering and mental confusion.

Hypothermia is the opposite of hyperthermia which is present in heat exhaustion and heat stroke. One of the lowest documented body temperature from which anyone has recovered was 13.0°C (55.4°F), in a drowning incident involving a 7-year-old girl in Sweden in December 2010.

Curative Methods and Marine Medicine Procedures

Hyperbaric Oxygen Therapy (HBOT) is a major curative method in the treatment of most marine diseases and injuries. It is a procedure where a patient is placed into a module called a hyperbaric chamber and subjected to high pressure 100% oxygen, with the intention of stimulating healing for certain medical problems. Using atmospheric pressure to treat patients isn't new. The process was actually introduced in the 1600s by a British clergyman. Oxygen didn't become the gas of choice until the 1930s. It was found that oxygen saturates the haemoglobin in the blood, and can help patients with routine wounds heal faster.

The overall issue with hyperbaric oxygen therapy is that there aren't a lot of medical schools that actually teach physicians about it because the equipment is too expensive.

Gas		Relative Narcotic Potency		Molecular Weight
He	Helium	4.26	Least narcotic	4
Ne	Neon	3.58		20
H	Hydrogen	1.83		2
N	Nitrogen	1		28
A	Argon	0.43		40
Kr	Krypton	0.14		83.7
Xe	Xenon	0.039	Most Narcotic	131.3

Table 2: Various gas of mixtures.

The major disadvantage of Hyperbaric Oxygen Therapy is that it's not 100% safe, as with any medical procedure, there are risks involved such as oxygen toxicity, temporary nearsightedness and middle ear injuries. Some people have suffered minor injury to their lungs, their eyes, and their nasal airways; most of the time, the injuries are temporary. On rare occasions, patients suffer temporary blindness.

Hyperbaric Oxygen Therapy is recommended to be used on patients with Air or gas embolism, Carbon Monoxide poisoning, Acute traumatic ischemia, Exceptional blood loss, Cyanide poisoning, Decompression sickness, Some non-healing wounds, Gas gangrene, Necrotizing infections, Some cases of osteomyelitis, Radiation effects, Compromised skin flaps and Burns.

There are also some maladies that hyperbaric oxygen therapy has been said to help with such as autism, diabetic neuropathy, inflammatory bowel disease, and multiple sclerosis. While hyperbaric oxygen therapy is by no means a new treatment, doctors and health professionals have only recently begun to see the many benefits associated with it.

Preservation of Life in the Marine Environment

Marine environment is an amazing part of our planet, covering more than seventy percent of Earth's surface, containing ninety-nine percent of the planet's living space and supports nearly fifty percent of all species on Earth. Marine environment is enormous but not infinite; various human activities are impacting its health. Our lives require healthy marine environment for oxygen, food, jobs, medicines and more. The availability of these resource calls for conservation and protection of the marine environment.

Marine conservation is the study of conserving physical and biological marine resources and ecosystem functions. Conservation of marine life provides enormous benefits for a sustainable future. Coral reefs are the epicentre for immense amounts of biodiversity, and are a key player in the survival of an entire ecosystem. They provide various marine animals with food, protection, and shelter which keep generations of species alive. Furthermore, coral reefs are an integral part of sustaining human life through serving as a food source (i.e. fish, mollusc, etc), medicine, as well as a marine space for eco-tourism which provides economic benefits. Unfortunately, because of human impact of coral reefs, these ecosystems are becoming increasingly degraded and in need of conservation. The biggest threats include over- exploitation, destructive fishing practices, dredging, sedimentation and pollution from land-based sources. This in conjunction with increased carbon in oceans, coral bleaching, and diseases; there are no pristine reefs anywhere in the world. In fact, a very high percentage of coral reefs in Southeast Asia are now threatened, with fifty percent of those reefs at either "high" or "very high" risk of disappearing which directly effects biodiversity and survival of species dependent on coral.

The marine environment is also threatened by climatic change resulting in sea level rise and acidification due to an increase in CO_2 levels. This is a most serious threat to societies relying heavily upon oceanic natural resources. A concern is that the majority of all marine species will not be able to evolve or acclimate in response to the changes in the ocean chemistry.

The prospects of averting mass extinction seems unlikely given current trends

For oceans to keep sustaining us, we must find a way to sustain them. Man owes the sea a debt he can never repay as it holds the hope for continued life. Sustainability has become one of the ever broadening fate of the ocean Millions of people around the world depend upon the oceans for a diverse array of resources and services. The sustainable provision of these materials is determined by a diversity of complex ecological interactions between a variety of different living and non-living factors. Global warming acts in synergy with other anthropogenic factors, such as pollution and over exploitation, of negatively impact upon these complex ecosystems driving changes in the marine environment with important socio-economic consequences.

These menace can be curbed by intervention of Governments, organizations, communities and individuals working together to protect more of the ocean, restore habitats and make wise decisions about ocean use. We all have a shared responsibility to protect our oceans: to use only what we need, make smarter choices about what we use, and pass on healthy oceans that will continue to support future generations.

Conclusion

The benefit of marine medicine is that the work of allopathic practitioners is subject to rigorous safety and effectiveness protocols. Treatments and medications pass a strict review before a patient can receive them. Marine medicine treatments have been the subject of clinical trials and long-term studies with an history of safety to back up treatment protocols. Before a new treatment or drug is approved for use on the public, it goes through an extensive testing process, first in the laboratory, and then through several layers of patient testing. The ocean has an enormous range of biodiversity which remains largely unexploited. Drugs from marine sources give hope as novel mechanisms to fight some of the most debilitating disease of man such as: HIV, osteoporosis, Alzheimer's disease and cancer. Although, the cost of developing these drugs from marine sources have been prohibitive in the past, the development of new technology and a greater understanding of marine organisms and their ecosystem are allowing research in this area. Therefore there is a dire need for sustainability in the ever broadening fate of the ocean To provide and sustain a high momentum of research in marine medicine, there's a need for more skilled divers who can make collections from the deep sea, taxonomist for identification of new species and marine chemist for rapid isolation and characterization of pure compounds in sufficient quantities. Sufficient financial support is needed to sustain the various activities for smooth and rapid implementation.

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