A PLETHORA OF BENEFITS OF SEA CUCUMBER

Writer:
Dr. dr. Irena Ujianti, M.Biomed.
dr. Bety Semara Lakshmi, M.K.M.
Dr. Zahra Nurusshofa, Sp.PA.
Dr. Apt. Supandi

Penerbit Widina

A PLETHORA OF BENEFITS OF SEA CUCUMBER

Writer:
Dr. dr. Irena Ujianti, M.Biomed.
dr. Bety Semara Lakshmi, M.K.M.
Dr. Zahra Nurusshofa, Sp.PA.
Dr. Apt. Supandi

Cover Design:
Septian Maulana

Illustration Source:
www.freepik.com

Layout:
Handarini Rohana

Editor:
Dr. dr. Wawang S. Sukarya, Sp.OG(K)., MARS., M.H.Kes.

ISBN:

First Printing:
Juni, 2024

PUBLISHER:
WIDINA MEDIA UTAMA
Komplek Puri Melia Asri Blok C3 No. 17 Desa Bojong Emas
Kec. Solokan Jeruk Kabupaten Bandung, Provinsi Jawa Barat

Member of IKAPI No. 360/JBA/2020
Website: www.penerbitwidina.com
Instagram: @penerbitwidina
Telepon (022) 87355370

PREFACE

In the vast and diverse world of marine life, there exists a fascinating creature that has captured the attention of scientists, researchers, and enthusiasts alike - the sea cucumber. This humble marine invertebrate, often overlooked by many, harbors a treasure trove of advantages and potential that are yet to be fully realized. In this book, we delve into the remarkable world of sea cucumbers, exploring their biology, ecological importance, culinary delights, economic significance, and promising applications in various fields.

Sea cucumbers, despite their unassuming appearance, play a crucial role in maintaining the health and balance of marine ecosystems. Their ability to recycle nutrients, regulate sedimentation, and provide habitat for other marine organisms underscores their ecological importance. Furthermore, their bioactive compounds and unique physiological adaptations offer a myriad of potential benefits for human health and well-being.

One of the most intriguing aspects of sea cucumbers is their culinary value. Across different cultures and cuisines, sea cucumbers have been prized for their unique texture, flavor, and nutritional content. From traditional Asian delicacies to modern gourmet creations, sea cucumbers have found their way into a variety of culinary preparations, captivating the palates of food enthusiasts around the globe.

As we embark on this exploration of sea cucumbers, we invite readers to uncover the mysteries and wonders of these extraordinary creatures. Through scientific insights, cultural perspectives, culinary delights, and economic considerations, this book aims to showcase the multifaceted advantages of sea cucumbers and inspire a deeper appreciation for the treasures that lie beneath the ocean's surface.

TABLE OF CONTENTS

1

WHAT IS SEA CUCUMBER?

A. DEFINITION AND OVERVIEW

Sea cucumbers, scientifically known as Holothuroidea, are fascinating marine invertebrates belonging to the phylum Echinodermata. They are characterized by their elongated, cylindrical bodies with leathery skin and a soft, gelatinous interior. Unlike their close relatives such as sea stars and sea urchins, sea cucumbers lack spines and have a more cylindrical shape, ranging in size from a few centimeters to over a meter in length, depending on the species. These creatures inhabit various marine environments, from shallow coastal waters to deep-sea trenches, and can be found on sandy or muddy seabeds, rocky reefs, and coral reefs worldwide. Sea cucumbers play crucial ecological roles, contributing to nutrient recycling and sediment stability, and they are often referred to as "ecosystem engineers" due to their impact on marine ecosystems. These fascinating creatures play important roles in marine ecosystems. They are scavengers and detritivores, feeding on organic matter and helping to recycle nutrients on the ocean floor. Sea cucumbers also contribute to sediment turnover and assist in maintaining the health of coral reefs and other marine habitats.

Image 1.1 Sea Cucumber

In addition to their ecological significance, sea cucumbers have long been valued by humans for various purposes. They are harvested for food and have culinary importance in some cultures, especially in Asian cuisine where they are considered a delicacy. Sea cucumbers are also utilized in traditional medicine in several countries for their potential health benefits, including anti-inflammatory and immune-boosting properties.

B. SEA CUCUMBER AND ITS IMPORTANT ROLE IN MARINE ECOSYSTEM

Sea cucumbers play a crucial role in marine ecosystems due to their significant contributions to nutrient cycling, sediment dynamics, and biodiversity. One of their primary ecological functions is as detritivores, meaning they consume organic matter, detritus, and dead organisms on the ocean floor. By doing so, sea cucumbers help in recycling nutrients and breaking down organic material, which is vital for maintaining the health and productivity of marine ecosystems. Their feeding activities contribute to the decomposition process, releasing essential nutrients back into the water column, which supports the growth of phytoplankton and other primary producers, forming the base of marine food webs.

Another important aspect of sea cucumbers' role in marine ecosystems is their impact on sediment dynamics. As they move across the seabed, sea cucumbers ingest sediment particles along with organic matter. This process helps in bioturbation, which refers to the mixing of sediment layers by biological organisms. Bioturbation is crucial for nutrient cycling, oxygenation of sediments, and creating habitats for other benthic organisms. Sea cucumbers' burrowing activities also enhance water and nutrient exchange between the sediment and the overlying water, promoting overall ecosystem health.

Furthermore, sea cucumbers contribute to maintaining biodiversity in marine environments. They are an essential component of benthic communities, providing food and habitat for various organisms. Many species of fish, crustaceans, and other invertebrates rely on sea cucumbers as part of their diet, and some species use sea cucumbers' bodies for shelter and protection. Therefore, the presence of sea cucumbers influences the abundance and distribution of other marine species, contributing to the overall diversity and stability of marine ecosystems.

Sea cucumbers are ecologically significant organisms in marine ecosystems, playing key roles in nutrient recycling, sediment dynamics, and supporting biodiversity. Their activities contribute to the functioning and resilience of coastal and deep-sea environments, highlighting the importance of conserving and managing sea cucumber populations for the health and sustainability of marine ecosystems worldwide.

C. BIOLOGICAL FEATURES OF SEA CUCUMBER

Sea cucumbers, belonging to the class Holothuroidea within the phylum Echinodermata, exhibit a fascinating anatomy adapted to their benthic lifestyle and unique ecological roles. Their body structure is characterized by a cylindrical or elongated shape with a soft, leathery skin covering a flexible endoskeleton. Unlike other echinoderms such as sea stars and sea urchins, sea cucumbers lack spines and have a more streamlined appearance.

1. Anatomy

At the anterior end of a sea cucumber, there is a mouth surrounded by a ring of retractable tentacles used for feeding. These tentacles are equipped with specialized tube feet called podia that assist in capturing food particles and directing them towards the mouth. Sea cucumbers are detritivores, primarily feeding on organic matter, plankton, and sediment found on the ocean floor. Their feeding process involves the ingestion of sediment and organic material, which is then processed in their digestive system to extract nutrients.

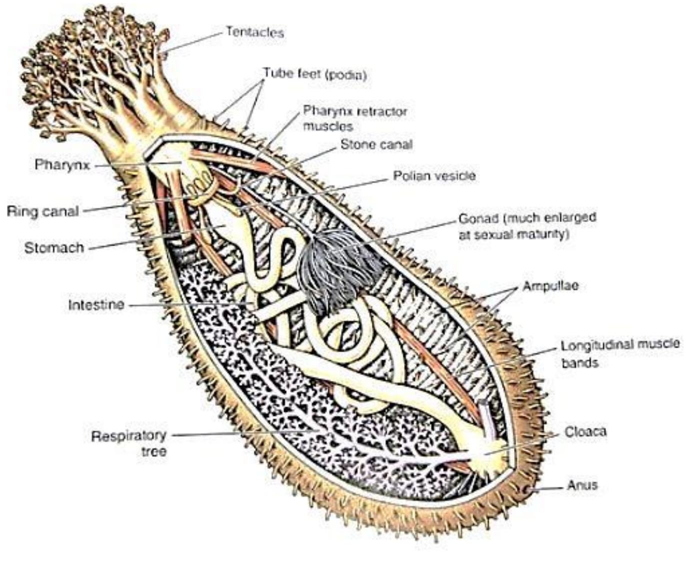

Image 1.2 Anatomy of Sea Cucumber

Internally, sea cucumbers possess a unique water vascular system, similar to other echinoderms, which helps in locomotion and respiration. This system consists of a series of water-filled canals and tube feet connected to a central ring canal around the mouth. By contracting and expanding their tube feet, sea cucumbers can move along the seabed and manipulate objects in their environment.

One of the most remarkable features of sea cucumbers is their ability to defend themselves from predators through a process called evisceration. When threatened, sea cucumbers can expel their internal organs, including the respiratory tree and part of the digestive tract, as a distraction or to deter predators. This remarkable defense mechanism allows them to survive and regenerate lost body parts over time.

In terms of reproduction, sea cucumbers can reproduce sexually by releasing eggs and sperm into the water for external fertilization. Some species also have the ability to regenerate lost body parts, such as their tentacles or even sections of their body, making them resilient and adaptable organisms in their marine habitats.

The anatomy of sea cucumbers reflects their specialized adaptations for feeding, locomotion, defense, and reproduction in diverse marine environments, showcasing the complexity and diversity of life within the oceans.

2. Physiology

The physiology of sea cucumbers is fascinating and reflects their unique adaptations to life in marine environments. These echinoderms possess a water vascular system that plays a crucial role in their physiology. This system consists of a network of fluid-filled canals and appendages called tube feet, which they use for locomotion, feeding, and respiration. Sea cucumbers can regulate the pressure within their water vascular system, allowing them to control the movement of their tube feet and adjust their body posture.

Respiration in sea cucumbers primarily occurs through their respiratory trees, specialized structures connected to the cloaca. These trees facilitate gas exchange, allowing sea cucumbers to take in oxygen and release carbon dioxide. The movement of seawater through their respiratory trees enables this respiratory process.

Digestion in sea cucumbers is aided by a unique feeding mechanism. They are detritivores, meaning they feed on organic matter and sediment particles. Sea cucumbers use their tentacles, which are equipped with sticky tube feet, to capture food particles and transport them to their mouth. Once ingested, the food passes through their digestive tract, where enzymes break down complex organic compounds into simpler nutrients for absorption.

Excretion in sea cucumbers involves the removal of metabolic wastes and excess water. Waste products are eliminated through the cloaca, which serves as a common opening for excretion and reproduction. Sea cucumbers also possess specialized structures called respiratory trees, which may play a role in excreting nitrogenous wastes, such as ammonia, produced during metabolism.

Sea cucumbers exhibit a remarkable ability to regenerate lost body parts. If a sea cucumber is injured or loses a portion of its body, it can regenerate the missing tissue over time. This regenerative capacity is facilitated by specialized cells and tissues within their bodies, allowing them to recover from damage and continue their life cycle in the marine environment.

3. Reproduction and Life Cycle

Sea cucumbers have a fascinating reproductive strategy and life cycle that contribute to their role in marine ecosystems. These echinoderms are typically dioecious, meaning individuals are either male or female. However, some species are hermaphroditic, possessing both male and female reproductive organs.

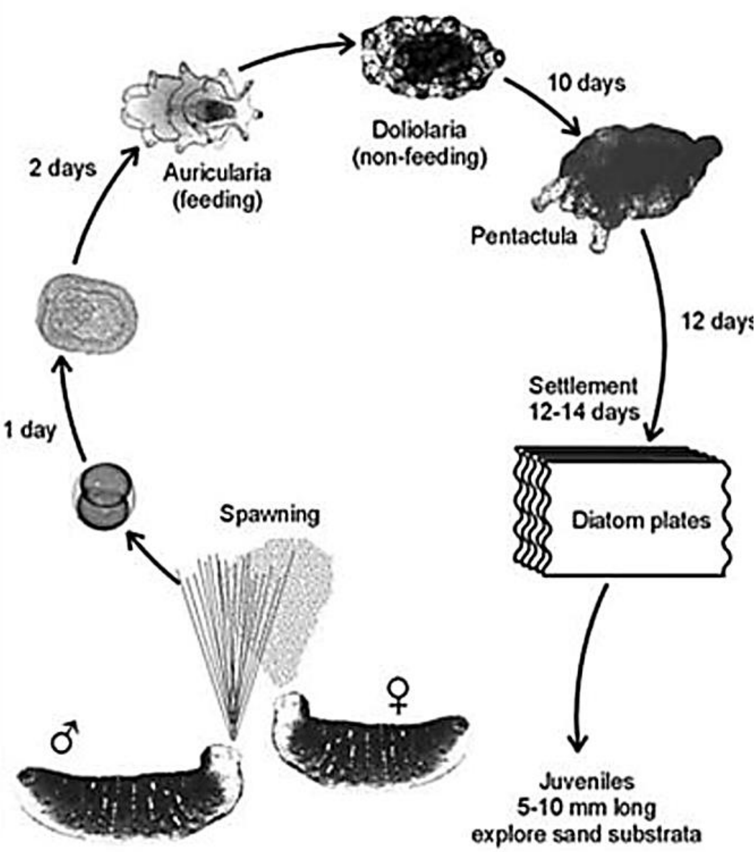

Image 1.3 Life Cycle of Sea Cucumber

The reproduction of sea cucumbers often involves external fertilization. During the breeding season, which varies among species, sea cucumbers release gametes into the water. The male sea cucumbers release sperm, while the females release eggs. Fertilization occurs when the sperm and eggs meet in the water, resulting in the formation of fertilized eggs.

Once fertilized, sea cucumber eggs develop into larvae through a process called embryonic development. The larvae are planktonic and drift with ocean currents. They undergo metamorphosis, transforming into juvenile sea cucumbers. These juveniles settle on the seafloor and begin their life as bottom-dwelling organisms.

The life cycle of sea cucumbers typically involves several stages: egg, larva, juvenile, and adult. The duration of each stage can vary depending on environmental factors, species-specific characteristics, and available food sources. Sea cucumbers can exhibit remarkable growth rates, with some species reaching maturity within a few years, while others may take longer.

During their adult stage, sea cucumbers play essential roles in marine ecosystems. They contribute to nutrient cycling by consuming organic matter and recycling nutrients back into the environment. Sea cucumbers also serve as food sources for various marine organisms, including fish, crustaceans, and sea stars, forming part of the marine food web.

The reproduction and life cycle of sea cucumbers highlight their resilience, reproductive strategies, and importance in maintaining ecological balance in marine habitats. Their ability to reproduce and contribute to nutrient cycling underscores their significance in marine ecosystems worldwide.

4. Body Plan

The body of a holothurian is roughly cylindrical. It is radially symmetrical along its longitudinal axis, and has weak bilateral symmetry transversely with a dorsal and a ventral surface. As in other Echinozoans, there are five ambulacra separated by five ambulacral grooves, the interambulacra. The ambulacral grooves bear four rows of tube feet but these are diminished in size or absent in some holothurians, especially on the dorsal surface. The two dorsal ambulacra make up the bivium while the three ventral ones are known as the trivium.

At the anterior end, the mouth is surrounded by a ring of tentacles which are usually retractable into the mouth. These are modified tube feet and may be simple, branched or arborescent. They are known as the introvert and posterior to them there is an internal ring of large calcareous ossicles. Attached to this are five bands of muscle running internally longitudinally along the ambulacra. There are also circular muscles, contraction of which cause the animal to elongate and the introvert to extend. Anterior to the ossicles lie further muscles, contraction of which cause the introvert to retract.

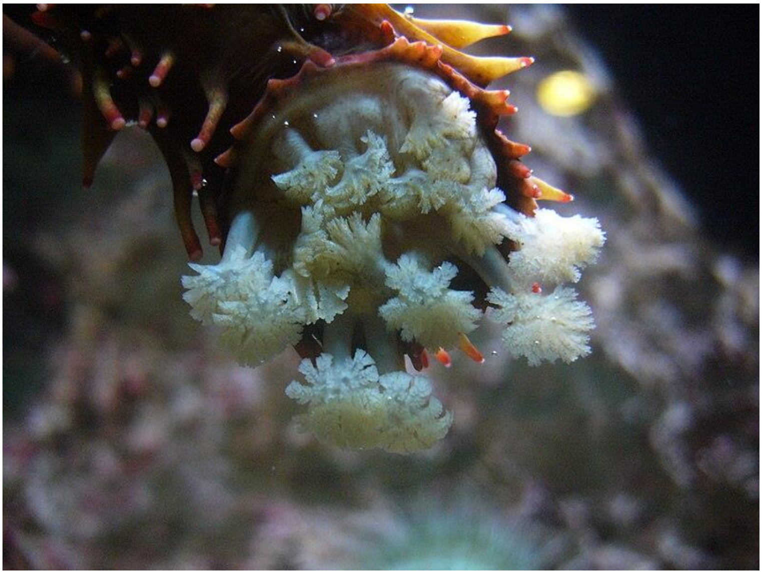

Image 1.4 Mouth and Tentacles of a Sea Cucumber

The body wall consists of an epidermis and a dermis and contains smaller calcareous ossicles, the types of which are characteristics which help to identify different species. Inside the body wall is the coelom which is divided by three longitudinal mesenteries which surround and support the internal organs.

5. Digestive system

A pharynx lies behind the mouth and is surrounded by a ring of ten calcareous plates. In most sea cucumbers, this is the only substantial part of the skeleton, and it forms the point of attachment for muscles that can retract the tentacles into the body for safety as for the main muscles of the body wall. Many species possess an oesophagus and stomach, but in some the pharynx opens directly into the intestine. The intestine is typically long and coiled, and loops through the body three times before terminating in a cloacal chamber, or directly as the anus.

6. Nervous system

Sea cucumbers have no true brain. A ring of neural tissue surrounds the oral cavity, and sends nerves to the tentacles and the pharynx. The animal is, however, quite capable of functioning and moving about if the nerve ring is surgically removed, demonstrating that it does not have a central role in nervous coordination. In addition, five major nerves run from the nerve ring down the length of the body beneath each of the ambulacral areas.

Most sea cucumbers have no distinct sensory organs, although there are various nerve endings scattered through the skin, giving the animal a sense of touch and a sensitivity to the presence of light. There are, however, a few exceptions: members of the Apodida order are known to possess statocysts, while some species possess small eye-spots near the bases of their tentacles.

7. Respiratory system

Sea cucumbers extract oxygen from water in a pair of "respiratory trees" that branch in the cloaca just inside the anus, so that they "breathe" by drawing water in through the anus and then expelling it.The trees consist of a series of narrow tubules branching from a common duct, and lie on either side of the digestive tract. Gas exchange occurs across the thin walls of the tubules, to and from the fluid of the main body cavity.

Together with the intestine, the respiratory trees also act as excretory organs, with nitrogenous waste diffusing across the tubule walls in the form of ammonia and phagocytic coelomocytes depositing particulate waste.

8. Circulatory systems

Like all echinoderms, sea cucumbers possess both a water vascular system that provides hydraulic pressure to the tentacles and tube feet, allowing them to move, and a haemal system. The latter is more complex than that in other echinoderms, and consists of well-developed vessels as well as open sinuses.

A central haemal ring surrounds the pharynx next to the ring canal of the water vascular system, and sends off additional vessels along the radial canals beneath the ambulacral areas. In the larger species, additional vessels run above and below the intestine and are connected by over a hundred small muscular ampullae, acting as miniature hearts to pump blood around the haemal system. Additional vessels surround the respiratory trees, although they contact them only indirectly, via the coelomic fluid.

Indeed, the blood itself is essentially identical with the coelomic fluid that bathes the organs directly, and also fills the water vascular system. Phagocytic coelomocytes, somewhat similar in function to the white blood cells of vertebrates, are formed within the haemal vessels, and travel throughout the body cavity as well as both circulatory systems. An additional form of coelomocyte, not found in other echinoderms, has a flattened discoid shape, and contains hemoglobin. As a result, in many (though not all) species, both the blood and the coelomic fluid are red in colour.

9. Locomotive organs

Like all echinoderms, sea cucumbers possess pentaradial symmetry, with their bodies divided into five nearly identical parts around a central axis. However, because of theirposture, they have secondarily evolved a degree of bilateral symmetry. For example, because one side of the body is typically pressed against the substratum, and the other is not, there is usually some difference between the two surfaces (except for Apodida). Like sea urchins, most sea cucumbers have five strip-like ambulacral areas running along the length of the body from the mouth to the anus. The three on the lower surface have numerous tube feet, often with suckers, that allow the animal to crawl along; they are called trivium. The two on the upper surface have under-developed or vestigial tube feet, and some species lack tube feet altogether; this face is called bivium.

In some species, the ambulacral areas can no longer be distinguished, with tube feet spread over a much wider area of the body. Those of the order Apodida have no tube feet or ambulacral areas at all, and burrow through sediment with muscular contractions of their body similar to that of worms, however five radial lines are generally still obvious along their body.

Even in those sea cucumbers that lack regular tube feet, those that are immediately around the mouth are always present. These are highly modified into retractile tentacles, much larger than the locomotive tube feet. Depending on the species, sea cucumbers have between ten and thirty such tentacles and these can have a wide variety of shapes depending on the diet of the animal and other conditions.

Many sea cucumbers have papillae, conical fleshy projections of the body wall with sensory tube feet at their apices. These can even evolve into long antennae-like structures, especially on the abyssal genus Scotoplanes.

10. Endoskeleton

Echinoderms typically possess an internal skeleton composed of plates of calcium carbonate. In most sea cucumbers, however, these have become reduced to microscopic ossicles embedded beneath the skin. A few genera, such as Sphaerothuria, retain relatively large plates, giving them a scaly armour.

D. LIFE AND BEHAVIOUR

1. Habitat

Sea cucumbers can be found in great numbers on the deep seafloor, where they often make up the majority of the animal biomass. At depths deeper than 8.9 km (5.5 mi), sea cucumbers comprise 90% of the total mass of the macrofauna. Sea cucumbers form large herds that move across the bathygraphic features of the ocean, hunting food. The body of some deep water holothurians, such as Enypniastes eximia, Peniagone leander and Paelopatides confundens, is made of a tough gelatinous tissue with unique properties that makes the animals able to control their own buoyancy, making it possible for them to either live on the ocean floor or to actively swim or float over it in order to move to new locations, in a manner similar to how the group Torquaratoridae floats through water.

Holothurians appear to be the echinoderms best adapted to extreme depths, and are still very diversified beyond 5,000 m deep: several species from the family Elpidiidae ("sea pigs") can be found deeper than 9,500 m, and the record seems to be some species of the genus Myriotrochus (in particular Myriotrochus bruuni), identified down to 10,687 meters deep. In more shallow waters, sea cucumbers can form dense populations. The strawberry sea cucumber (Squamocnus brevidentis) of New Zealand lives on rocky walls around the southern coast of the South Island where populations sometimes reach densities of 1,000 animals/m2 (93 animals/sq ft). For this reason, one such area in Fiordland is called the strawberry fields.

2. Locomotion

Some abyssal species in the abyssal order Elasipodida have evolved to a "benthopelagic" behaviour: their body is nearly the same density as the water around them, so they can make long jumps (up to 1,000 m (3,300 ft) high), before falling slowly back to the ocean floor. Most of them have specific swimming appendages, such as some kind of umbrella (like Enypniastes), or a long lobe on top of the body (Psychropotes). Only one species is known as a true completely pelagic species, that never comes close to the bottom: Pelagothuria natatrix.

3. Diet

Holothuroidea are generally scavengers, feeding on debris in the benthic zone of the ocean. Exceptions include some pelagic cucumbers and the species Rynkatorpa pawsoni, which has a commensal relationship with deep-sea anglerfish. The diet of most cucumbers consists of plankton and decaying organic matter found in the sea. Some sea cucumbers position themselves in currents and catch food that flows by with their open tentacles. They also sift through the bottom sediments using their tentacles. Other species can dig into bottom silt or sand until they are completely buried. They then extrude their feeding tentacles, ready to withdraw at any hint of danger.

In the South Pacific sea cucumbers may be found in densities of 40 individuals/m2 (3.7 individuals/sq ft). These populations can process 19 kilograms per square metre (3.9 lb/sq ft) of sediment per year.

The shape of the tentacles is generally adapted to the diet, and to the size of the particles to be ingested: the filter-feeding species mostly have complex arborescent tentacles, intended to maximize the surface area available for filtering, while the species feeding on the substratum will more often need digitate tentacles to sort out the nutritional material; the detritivore species living on fine sand or mud more often need shorter "peltate" tentacles, shaped like shovels. A single specimen can swallow more than 45 kg of sediment a year, and their excellent digestive capacities allow them to reject a finer, purer and homogeneous sediment. Therefore, sea cucumbers play a major role in the biological processing of the sea bed (bioturbation, purge, homogenization of the substratum etc.)

4. Development

In all other species, the egg develops into a free-swimming larva, typically after around three days of development. The first stage of larval development is known as an auricularia, and is only around 1 mm (39 mils) in length. This larva swims by means of a long band of cilia wrapped around its body, and somewhat resembles the bipinnaria larva of starfish. As the larva grows it transforms into the doliolaria, with a barrel-shaped body and three to five separate rings of cilia. The pentacularia is the third larval stage of sea cucumber, where the tentacles appear. The tentacles are usually the first adult features to appear, before the regular tube feet.

5. Symbiosis and commensalism

Some cleaner shrimps can live on the tegument of holothurians, in particular several species of the genus Periclimenes (genus which is specialized in echinoderms), in particular Periclimenes imperator. A variety of fish, most commonly pearl fish, have evolved a commensalistic symbiotic relationship with sea cucumbers in which the pearl fish will live in sea cucumber's cloaca using it for protection from predation, a source of food (the nutrients passing in and out of the anus from the water), and to develop into their adult stage of life. Many polychaete worms (family Polynoidae) and crabs (like Lissocarcinus orbicularis) have also specialized to use the mouth or the cloacal respiratory trees for protection by living inside the sea cucumber. Nevertheless, holothurians species of the genus Actinopyga have anal teeth that prevent visitors from penetrating their anus.

2

VARIETIES OF SEA CUCUMBER

There are so many varieties of sea cucumber around the globe, but there are just a few examples of the many species of sea cucumbers found worldwide. Each species has unique characteristics and adaptations that allow it to thrive in its specific habitat. Sea cucumbers play vital roles in marine ecosystems, including nutrient cycling, sediment bioturbation, and serving as prey for various marine animals. Their ecological importance, coupled with their economic and medicinal value, makes the study and conservation of sea cucumber species critical.

Sea cucumbers are diverse marine animals belonging to the class Holothuroidea. There are over 1,700 species of sea cucumbers distributed across the globe, inhabiting various marine environments from shallow coastal waters to deep ocean floors. Some of the well-known species include:

A. HOLOTHURIIDAE FAMILY

1. Holothuria Edulis - Edible Sea Cucumber

Holothuria edulis, commonly known as the edible sea cucumber, is a species found in shallow waters of the Indo-Pacific region.. This sea cucumber is usually a dark reddish-black colour on its upper side and a pinkish-mauve colour below, but can be grey or dark brown. This species can grow up to 30 cm in length and is often found in sandy or muddy substrates.

Holothuria edulis is usually soft and pliable with a smooth skin but, due to the special characteristics of its connective tissue, it can become firm and rigid. The body is lined with longitudinal rows of small tube feet which can be withdrawn into the body wall, leaving small hollows. About twenty tube feet in a ring round the mouth are modified into feeding tentacles

Image 2.1 Holothuria Edulis

Holothuria edulis is a common and widespread species in the Indo-Pacific Ocean. It lives on the seabed at depths down to 20 metres (66 ft). Its range extends from the Red Sea and East African coast to Sri Lanka, Japan, China, Indonesia, the Philippines, northern Australia and various Pacific islands. It is found in a number of different habitats including on sandy or muddy substrates, on coral rubble and in seagrass meadows. It can be found on inner and outer reef flats, on back reef slopes and in lagoons. It widely harvested for consumption, particularly in Asian cuisines where it is considered a delicacy.

Holothuria edulis is mainly nocturnal and tends to hide during the day under rocks or pieces of coral. It is a detritivore and feeds by ingesting sand and debris which has accumulated on the seabed which it picks up using its feeding tentacles. Sand is pushed into the mouth and any organic matter present, including the biofilm round the grains, is digested as the sand passes through the gut. The indigestible matter is expelled from the anus leaving a sand ridge as the animal moves around. During its feeding activities, the sea cucumber churns up the top few centimetres of seabed and aerates the sediment.

Locomotion in Holothuria edulis is very slow. It moves mainly by peristaltic action of its body wall, assisted to a limited extent by its tube feet. It can also anchor its feeding tentacles into the sand and haul itself along. If it gets overturned, it can use its feeding tentacles to help right itself.

Holothuria edulis has separate sexes and spawns at any time of year with gametes being liberated into the water column. The larvae are planktonic. This sea cucumber can also reproduce asexually by breaking into two parts, each of which then regrows the missing organs.

2. Holothuria Scabra – Sandfish

Holothuria scabra, known as sandfish, is a commercially important species in the sea cucumber trade. It has a thick body, gray to brown color with small dark spots, and can reach lengths of up to 40 cm. The sandfish has the same basic anatomy as most other species of sea cucumber. Their bodies are elongated and cylindric, and relatively stubby. Their dorsal side can range in color from a grey-brown to black, with darkened wrinkles across the body and small black papillae from end to end. They are counter shaded with a lighter ventral side, which is relatively flat. They have a mouth located on the ventral surface at one end of the body, considered the front end. Like other sea cucumbers, they use feeding tentacles which protrude from the mouth. Sandfish have around 20 short tentacles. On the opposite end the anus is found on the dorsal side. It reach maturity around 16 cm or 200 grams with some growing as much as 300 grams in one year. It is unknown how long they live undisturbed, but they can live to at least 10 years.

Their gonads are found through a single genital orifice on their dorsal anterior end. Their digestive system is made up of a mouth, an esophagus, a stomach, an intestine, a cloaca, and an anus. They extend respiratory trees from their cloaca in order to breathe. Their body wall is thick, making up a total of 56% of their weight. This body wall is filled with calcareous plates called spicules, and are used to ID species; the sandfish is identified by table and knobbed button shapes. Like other sea cucumbers, they can eviscerate their internal organs if they undergo stress, and can regenerate their organs; in sandfish this takes about 2 months.

The species can be found in the Indo-Pacific region, from east Africa to the eastern Pacific. Some have been found in the Persian Gulf, Iran. They are typically restricted to latitudes between 30° N to 30° S, due to it being a tropical species.

Image 2.2 Holothuria Scabra

The sandfish goes through 6 stages of growth before maturing into an adult. This starts when the adults spawn. After a day the fertilized eggs develop into a first planktonic phase, a gastrula, then after two days it becomes an auricularia, the feeding planktonic stage. Within the next 14 days the sandfish will enter a non-feeding doliolaria stage and a final planktonic pentactula stage, before becoming juveniles and settling into the sea grass meadows to mature.

They prefer shallow, sandy, or muddy seabeds and seagrass beds. They are highly valued for its meat, used in culinary dishes and traditional medicine. They do have a tolerance for lowered salinity, down to 20 ppt, such as that found in brackish water. Sandfish play a key role in the health of their habitat; like most sea cucumbers H. scabra are bioturbators and play a key role in reworking the sediment and ensuring that organic matter is evenly distributed for the ecosystem to function, and have a subsequent diet of detritus and other microorganisms.

The sandfish exhibits some distinct behaviors. Their burrowing behavior varies as they mature, with younger sandfish responding to changes in light and coming out in darkness. Older sandfish are more sensitive to changes in temperature and will burrow to escape the cold. Sandfish are particular about sediment size and type, settling in fine sand and muddy substrates high in nutrients. Like all sea cumbers, H. scabra exhibits defensive vomiting, where they expel their internal organs to distract predators while they escape. Male and females have distinct mating behaviors; when they spawn males erect their bodies and sway from side to side as they release sperm into the surrounding water. Shortly after, females will erect their bodies and send eggs into the water with the sperm in a short, forceful burst.

The sandfish has been eaten by man for over 1000 years. About twenty other species of sea cucumber are also consumed but the sandfish is the species most often used. In the 1990s it was being sold dried as beche-de-mer for up to US$100 per kilogram. Harvesting sandfish from the sea is known as trepanging in Indonesia. In many areas the fisheries have declined over the years because of over fishing, so ranching, aquaculture and hatchery rearing are being attempted.

The sandfish has a high value in Asian markets where they are sold as beche-de-mer for food. This makes them a key species for aquaculture production, where the species flourishes; one of the only tropical holothurian species to do so. They are also valuable in aquaculture for habitat restocking; juveniles are often grown in tanks and released into the wild with hopes of restocking the wild population and causing a spillover effect in protected areas. Broodstock is the population of adults that will be used for reproduction. These are gathered from wild stocks and since the sandfish is found in environments close to the equator, they can spawn year round. Peak season for spawning though is typically during the dry seasons, August to November. Approximately 30–45 adult sandfish are required to start a small batch of spawning individuals. Spawning for H. scabra is closely related to the lunar cycle, and will occur in the afternoon to early evening. Spawning can be induced using several methods: thermal stimulation involves increasing and decreasing water temperatures rapidly, dry treatment involves leaving the sandfish out of the water for 30–45 minutes before being returned to the tanks, and the food stimulant method involves providing a highly concentrated amount of algae to the water to overfeed the sandfish. Gonad extraction is also an option but requires the dissection of the animal. It is common in most aquaculture facilities to use a combination of the listed methods, in order to ensure spawning. The sandfish larvae are closely monitored in order to ensure survival, as they are temperamental and require specific conditions for success. Once the larvae develop into juveniles they must be moved into growout tanks, at a density of 200-500 individuals per square meter to ensure that each one is receiving proper space to grow and the required nutrients.

3. Holothuria Fuscogilva - White Teatfish

Holothuria fuscogilva, or white teatfish, is a large sea cucumber that can grow up to 60 cm. It is pale cream to white with darker patches and has prominent teats along its body.

Image 2.3 Holothuria Fuscogilva

It can be found in coral reef environments and sandy areas up to 30 meters deep. It is prized in the bêche-de-mer (dried sea cucumber) market for its high quality.

4. Holothuria Nobilis - Black Teatfish

Known as the black teatfish, Holothuria nobilis is similar in size to the white teatfish, often reaching up to 60 cm. It has a darker coloration, typically black or dark brown. The cucumber inhabits shallow waters near islands and reefs. Members of the species are blackish-brown and grey in colour, and mature adults can weight between 1.7 and 4 kilograms

Image 2.4 Holothuria Nobilis

It prefers coral reef habitats and is often found at depths of 10-40 meters.It’s highly valued for its thick body wall, used in the dried sea cucumber trade.

Like the related white teatfish, the black teatfish is part of a commercial fishery across its range and the cucumber is regularly consumed as a food. The species can be collected off the seafloor using diving suits or while skindiving, making the species very vulnerable to overfishing. The species is considered endangered in the Indian Ocean.

5. Holothuria Atra – Lollyfish

Holothuria atra, commonly known as lollyfish, has a smooth, black, or dark brown body and can grow up to 60 cm. It has a smooth, pliable, entirely black skin which often has sand adhering to it, especially in smaller individuals. The mouth is on the underside at one end and is surrounded by a fringe of 20 black, branched tentacles. The anus is at the other end. It is one of the most common sea cucumber species in shallow tropical waters. It was placed in the subgenus Halodeima by Pearson in 1914, making its full scientific name Holothuria (Halodeima) atra. It is the type species of the subgenus.

Image 2.5 Holothuria Atra - Lollyfish

Holothuria atra is found in the tropical Indo-Pacific region, its range extending from the Red Sea and East Africa to Australia. It is found on the seabed, in shallow waters on reefs and sand flats and in seagrass meadows at depths of up to 20 metres (66 ft). Its colouring makes it conspicuous but it is very often camouflaged by a coating of sand which may also serve to keep it cool by protecting it from the sun's rays. It favours reef flats where it is not fully exposed to the waves but the water is well aerated, and shallows beside slabs of rock from under which cool water wells out when the tide retreats. In such places it is often found in pools above the low tide mark which are warmed by the sun during the day. Holothuria atra seems to tolerate these high temperatures well and individuals appeared healthy and were feeding when the water temperature rose as high as 39 °C.

Holothuria atra is an omnivore, sifting through the sediment with its tentacles and feeding on detritus and other organic matter. As a defence against predators, Holothuria atra emits a toxic red fluid when its skin is rubbed or damaged. When attacked, it does not eject

Cuvierian tubules in the way that some sea cucumbers do, but instead extrudes its internal organs through its anus.

It is not possible to distinguish between male and female Holothuria atra externally. Maturity is reached at a body length of about 16 centimetres (6.3 in) and spawning mostly takes place during the summer and autumn although in equatorial waters it may take place all year round. It takes a minimum of 18-25 days for Holothuria atra to reach natural competence. Holothuria atra is also fissiparous, meaning that it can reproduce by transverse fission. It is mostly smaller individuals which divide in this way. A constriction appears, becomes deeper and deeper, and after some time the integument separates leaving two relatively wide but short individuals. No sand adheres to the newly separated surfaces as there are no tube feet present to retain the grains.

Holothuria atra, like many echinoderms, engage in sediment bioturbation—a process which plays an important role in the health of coral reefs. Holothuria atra is often found associated with the polychaete worm Gastrolepidia clavigera, a black worm which crawls about over the sea cucumber's skin. Holothuria atra seems to have few natural predators.

It is not commonly harvested due to its lower commercial value compared to other species. In the Pacific Islands, Holothuria atra is collected by diving or by wading at low tide, and used for human consumption. On Guam, the toxic red fluid that Holothuria atra releases is utilized to drive octopuses out of hiding holes. Compounds of potential biomedical importance are present in Holothuria atra, including lectin, steroidal sapogenins and triterpene glycoside.

6. Holothuria Mexicana - Donkey Dung Sea Cucumber

The donkey dung sea cucumber, Holothuria mexicana, is named for its appearance, with a dark, cylindrical body that can reach up to 50 cm in length. It has a rough texture with dark brown to black coloration.

It commonly be found throughout the Caribbean and reaches southern Brazil. It is a shallow or demersal water species most commonly found between 2 m (6 ft 7 in) to 10 m (33 ft) depth and up to 20 m (66 ft) depth. It inhabits sandy bottoms with calm waters including seagrass beds, offshore reefs or mangroves. It is occasionally harvested for food and traditional medicine.

This sea cucumber is transversely wrinkled and reaches 50 cm (20 in) in total length. It has a top surface that is dull brown or grey with occasional warts. The bottom surface is reddish, orange or pale and is uniformly covered in tube feet. Populations are unimodal and have a 1:1 male to female sex ratio.

Image 2.6 Holothuria Mexicana

7. **Holothuria Leucospilota - Black Sea Cucumber**

Holothuria leucospilota, or black sea cucumber, is a large species reaching up to 40 cm. It has a dark black or brown body with small white spots.

Image 2.7 Holothuria Leucospilota

It can be found in shallow reef environments and sandy substrates.It’s often collected for its medicinal properties in traditional practices. It is placed in the subgenus Mertensiothuria making its full scientific name Holothuria (Mertensiothuria) leucospilota. It is the type species of the subgenus and is found on the seabed in shallow water in the Indo-Pacific.

Holothuria leucospilota is a medium-sized sea cucumber reaching a length of up to 40 centimetres (16 in) when relaxed but it can stretch to about a metre (yard) when extended. It is roughly cylindrical, tapering towards the posterior end. At the anterior end, there are twenty oral tentacles with branched tips. These surround the mouth which is on the under side of the body. The animal is soft and pliable and is covered with fleshy papillae. The usual colour is charcoal grey or reddish-black with pale grey tube feet on the underside but off the African coast it is described as being bright or dark brown with white patches which are larger towards the posterior end.

Holothuria leucospilota is found in shallow water along the east coast of Africa and in much of the Indo-Pacific region. It is a common species on the north east coast of Australia where it is found on reefs and rocky coasts, often partly concealed under a boulder.

A study done near Singapore found that Holothuria leucospilota was more common near boulders, corals and seaweed clumps than it was on the open seabed. It found that this species is relatively tolerant of changes in salinity and temperature and continued to thrive in the laboratory when these parameters were changed. Under the same conditions, the Japanese sea cucumber (Apostichopus japonicus) shrank in size, eviscerated, and died within three days. In Singapore, Apostichopus japonicus is consumed as food and is becoming increasingly rare as a result of overexploitation.

Holothuria leucospilota is a scavenger and when feeding it usually has its posterior end anchored underneath a rock or in a crevice so that it can contract back out of sight if disturbed. It feeds by using its tentacles to shovel organic debris lying on the seabed into its mouth. In the process it swallows a significant quantity of sand, which passes through the gut.

If threatened, Holothuria leucospilota can emit a mass of fine sticky Cuvierian tubules from its anus which ensnare the potential predator allowing the sea cucumber to escape. It can regenerate these tubules in fifteen to eighteen days.

The worm pearlfish (Encheliophis vermicularis) is a parasite of this species and each parasitised H. leucospilota will host a male and female pair of the fish which live inside its body.

8. Holothuria Arguinensis

Holothuria Arguinensis is a species found in the Atlantic Ocean, particularly around the coasts of West Africa. It has a robust body with a light brown to yellowish coloration. According to some scholarly research, the species is actively expanding its range and colonizing the south-eastern coast of Spain.

Image 2.8 Holothuria Arguinensis

It prefers sandy and muddy bottoms up to 50 meters deep. It is limited commercial use, but studied for its potential nutritional and medicinal properties. It has a rigid and somewhat cylindrical body. A mature specimen can be 35 cm long and weigh 270 grams. Spawning is in summer to autumn. Reproduction success depends on environmental factors, primarily availability of daylight and water temperature – other likely factors include abundance of food, tidal flow and water salinity. The species is a fishery resource and in demand in Asian markets.

9. Holothuria Cinerascens

Holothuria cinerascens is a species of sea cucumber in the family Holothuriidae. This sea cucumber is widely distributed in the Pacific and Indian ocean, being found from the Red Sea to Madagascar and from Japan to Australia. It was first described by Brandt in 1835. It is characterized by its grayish body, is a medium-sized sea cucumber that can grow up to 30 cm. It has a rough, leathery texture.

Image 2.9 Holothuria Cinerascens

This species can be found around coral reefs and rocks, in tide pools, in deeper waters, lagoons, and bays, often hiding in very tight spaces. Their movement and migration patterns depend on their depth of sea level they are located at, influence of light intensity, the temperature conditions and the amount of predators surrounding the area.

It is not widely harvested, but of interest for its ecological role in marine environments. These species play significant roles in their respective ecosystems and hold various degrees of commercial importance, especially in culinary and medicinal applications. The study and conservation of these species are crucial for maintaining marine biodiversity and ecosystem health.

B. STICHOPODIDAE FAMILY

1. Stichopus Chloronotus - Greenfish

Stichopus chloronotus, commonly known as greenfish, is notable for its vibrant green coloration and cylindrical body covered with small, soft papillae. This species can grow up to 30 cm in length.

The species Stichopus chloronotus is a dioecious species meaning the male and female reproductive parts are contained in separate individuals; however, the two sexes cannot be determined by external characteristics. For sexual reproduction within holothurians there is a single gonad located towards the anterior part of the coelom. Within the gonad reside either one or two tufts of tubules. Stichopus chloronotus has two tufts of tubules, one on each side of the mesentery.

Image 2.10 Stichopus Chloronotus

The tubules open up into a gonoduct which leads to a gonopore, or genital orifice, located on the top of the organism slightly behind the tentacles. This pore is wher e the gametes are released during spawning. While spawning, the sea cucumber lifts its anterior end vertically off the ground while leaving the posterior end on the ground. When the gametes are released, they are expelled from the genital orifice in a continuous flow, somewhat resembling a thin white thread. This spawning process only occurs two times per year, usually sometime around mid- November and late January, both of which are during the hot seasons of the Indo-Pacific region. After expulsion of the gametes occurs, fertilization takes place externally in the water. Following about three days of development the embryo becomes a free-swimming larva. Eventually the larva develops into a juvenile with tentacles and podia.

Not only is this species of sea cucumber able to produce sexually, it is capable, like a few other species in the Aspidochriotida, of performing asexual reproduction. Besides Stichopus chloronotus, seven other species of Aspidochirotida are capable of this unusual reproductive strategy. Asexual reproduction in these species is performed through the process of transverse fission. In most sea cucumber species capable of asexually reproducing, a method is used where the organism’s anterior and posterior end rotate in opposite directions. After a while, the two ends slowly move in different directions, eventually causing the body wall to tear and split the organism into two separate individuals. However, Stichopus chloronotus uses a different method of transverse fission in order to divide itself. More specifically, the organism starts by creating a constriction in the center of its body. While the posterior region of its body stays stati onary the anterior end begins to move forward. This results in a more intense constriction in the center of the body. As the anterior end moves further away from the posterior, the constriction in the center, or fission site, begins to turn in to almost nothing but a fluid like substance. Following this, the two halves separate with ease. Based on a study, this entire process only takes a few minutes. Following the fission, it takes around a day for the tissue at the fission site to heal. The body wall of Stichopus chloronotus is often referred to as “catch connective tissue” and it is very thin and fluid-like. It is believed that this tissue is the reason why it is possible for Stichopus chloronotus to undergo transverse fission with more ease than other species capable of the phenomenon. Furthermore, it is thought that this tissue also helps with the speedy recovery that Stichopus chloronotus is capable of after fission has occurred. Transverse fission usually occurs during cool portions of the year (around June in the Indo-Pacific region) and it is also thought that it mainly takes place a night.

It can be found in shallow waters of the Indo-Pacific region, particularly on coral reefs and sandy bottoms. It is harvested for food and used in traditional medicine. Its body wall contains bioactive compounds of interest for pharmaceutical research.

2. Stichopus Herrmanni – Curryfish

Stichopus herrmanni, known as curryfish, is a large sea cucumber species that can reach lengths of up to 50 cm. It has a robust body with a rough texture and coloration that ranges from brown to yellow with darker patches. The body is cylindrical with a flat sole. The body wall is rough and wrinkled, without large swellings but with orange-brown papillae (conical fleshy protuberances). The mouth is surrounded by eight to sixteen feeding tentacles and the sole bears short tube feet.

Image 2.11 Stichopus Herrmanni

Stichopus herrmanni, or Herrmann's sea cucumber, is a species of holothuroidean echinoderm in the family Stichopodidae. It is found in the tropical, western Indo-Pacific Ocean, at depths down to 20 m (66 ft). This and several other species are known as curryfish and are harvested commercially; it is called gama in Indonesia.

Stichopus herrmanni is found in the tropical west Indo-Pacific region. Its range extends from the east coast of Africa to Malaysia, Indonesia and Australia. It occurs on sand and mud substrates, seagrass meadows and rubble at depths down to about 25 m (80 ft). It prefers sandy and coral reef environments in the Indo-Pacific region.

Although the population of S. herrmanni is stable in Australia, elsewhere fishing pressure is causing declines in its populations over most of its range. As a result of overfishing of more desirable species, this species is likely to face greater exploitation, and the International Union for Conservation of Nature has assessed its conservation status as "vulnerable".

3. Stichopus Monotuberculatus – Snakefish

Stichopus monotuberculatus, commonly referred to as snakefish, has a distinctive elongated body with a series of large, rounded tubercles along its dorsal surface. The coloration is generally brownish with dark spots.

Image 2.12 Stichopus Monotuberculatus

Stichopus onotuberculatus is a tropical sea cucumber that is widely distributed in the coral reefs of the Indo-Pacific Ocean from the Red Sea and Madagascar to Easter Island and from Japan to Australia (Massin, 1996). S. monotuberculatus has been recorded in the coastal shallow of the Xisha Islands, Hainan Island and the Leizhou Peninsula in the South China Sea (Liao, 1997). S. monotuberculatus has high edible value since it has a thick body wall that is rich in collagen. S. monotuberculatus is a high-protein and low-fat food that is rich in essential amino acids, fatty acids (Chen, 2004), calcium, magnesium salts and other essential trace elements for the human body (Fan, 2001).

The morphologies of S. monotuberculatus in different regions vary greatly; for instance, two S. monotuberculatus morphologies with short verrucous feet were found in the Great Barrier Reef of Australia: one was yellowish-brown, and the other was greyish-white with black spots; S. monotuberculatus observed in the Samoa Islands was yellow and brown with long verrucous feet; S. monotuberculatus in Mauritius was cylindrical in shape and greyish-white in colour (Thandar, 2008; Byrne et al., 2010). S. monotuberculatus has recently been distinguished from similar species, such as Stichopus horrens and Stichopus herrmanni, by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) and forensically informative nucleotide sequencing (FINS) (Wen et al., 2010).

Sea cucumbers extract a variety of biologically active compounds, such as polysaccharides, saponins, brain glycosides and ganglioside, which have benefits such as immunity enhancement, anti-tumor, anti-cancer, anti-fungal features, and other physiological pharmacological activities; thus, these species can be widely used as medicinal drugs, cosmetics and other agents (Kumar et al., 2007; Guo, 2014; Su, 2003; Zhang et al., 2006). In addition, sea cucumbers are the most common invertebrates that can maintain a normal coral reef community (Bakus, 1973; Birkeland, 1989; Conand, 1993), and they maintain seawater acid-base balance to repair the coral reef ecosystems (Schneider et al., 2011). Sea cucumbers feed on submarine detritus, humus and sedimentary nutrients and thereby participate in coral material cycling (Rhoads, 1973). In this case, sea cucumbers accelerate bioturbation by ingesting organic matter on the sediment (Benavides-Serrato et al., 2013) and dissolve carbonate by feeding, which may promote the cycling of calcium carbonate (Jennings and Hunt, 2010; Birkeland, 2014).

Continuously increasing market demand have led to the overfishing of wild sea cumbers (Conand, 1997). Artificial culture has been considered as an effective approach to solve the risk of wild sea cucumber resources (Hu et al., 2013). Several tropical sea cucumber species have been successfully propagated by artificial methods, including the species in genus Bohadschia (Laxminarayana, 2005), Stichopus (Hu et al., 2010; Hu et al., 2013), Holothuria (Al-Rashdi et al., 2012; Huang et al., 2018; Rakaj et al., 2019; Laguerrea et al., 2020) and Isostichopus (Itzel et al., 2019). In aquaculture, however, the settlement and survival rates during the early developmental period of the larvae are low. Hence, it is considered that the production of sea cucumbers may be increased if their larval settlement and survival can be enhanced. However, limited information is known about the sea cucumber species in Stichopodidae, except for the studies that have shown that several potential neurotransmitters can increase the settlement, metamorphosis and survival rates of the sea cucumber Apostichopus japonicus (Matsuura et al., 2009; Sun et al., 2014). In the present study, the spawning of S. monotuberculatus was induced by a modified low-temperature stimulation method. Gonadal maturation and embryonic, larval and juvenile development were recorded in detail, and larval breeding was improved by diets supplemented with multiple digestive enzymes.

4. Stichopus Vastus

Stichopus vastus is a relatively large species of sea cucumber, characterized by its thick body and leathery texture. Its coloration varies but is typically a mix of brown and yellow tones with dark spots.

Image 2.13 Stichopus Vastus

Stichopus vastus, a species of sea cucumber, has been the subject of various studies focusing on different aspects of its biology and potential applications. Research has delved into the physicochemical properties of collagen extracted from Stichopus vastus, highlighting its potential protective effects against oxidative stress (Li et al., 2020). Additionally, studies have explored the biochemical properties of collagen hydrolysates from Stichopus vastus, emphasizing its radical-scavenging activity (Abedin et al., 2014). Furthermore, the isolation and characterization of collagen from Stichopus vastus have been investigated, shedding light on its potential applications in various industries (Karim et al., 2012).

Moreover, Stichopus vastus has been studied in the context of growth modeling, with research indicating slow growth and a long lifespan for this species, leading to informed decisions on catch quotas to aid in the recovery of natural populations (Lee et al., 2020). The species has also been identified in specific locations, such as Biau

Beach, highlighting its distribution and presence in certain habitats (Pangulimang, 2023). Additionally, studies have explored the amino acid and fatty acid compositions of Stichopus vastus, contributing to the understanding of its nutritional value (Rasyid, 2018).

Furthermore, Stichopus vastus has been associated with commercial exploitation, with its presence noted in areas like the Karimunjawa National Park (Mustagfirin et al., 2021). Studies have also aimed to explore the relationship between marine-associated bacteria and marine invertebrates like Stichopus vastus, uncovering compounds like valinomycin from Streptomyces associated with this species (Wibowo et al., 2023). Additionally, comparisons have been made between the collagen content of commercial sea cucumbers like Stichopus vastus and non-commercial species, providing insights into the collagen characteristics of different sea cucumber varieties (Yuniati & Sulardiono, 2019).

In conclusion, Stichopus vastus has been a subject of diverse research efforts, ranging from its biochemical properties to its distribution, growth patterns, and potential applications in various fields. These studies collectively contribute to a comprehensive understanding of this species of sea cucumber.

These species within the Stichopodidae family play crucial ecological roles in their habitats, contributing to the health of coral reef ecosystems and providing significant economic value through their use in culinary and medicinal contexts. Continued research and sustainable management practices are essential to preserve these valuable marine resources.

C. CUCUMARIIDAE FAMILY

1. Cucumaria Frondosa – Orange-Footed Sea Cucumber

A sea cucumber with a cylindrical, dark brown or bluish-purple body, and very tough, leathery skin. A large sea cucumber up to 50 cm long when fully grown. The tentacles and mouth region can be quite colourful, with areas of white or red. The contractile tube feet are present in five distinct rows. The ten equal-sized tentacles are black and bushy when extended. Fenestrate plates (microscopic calcareous plates containing small holes) present in younger animals but may be absent in larger specimens.

Image 2.14 Cucumaria Frondosa

Cucumaria frondosa, commonly known as the orange-footed sea cucumber, has been a subject of diverse research focusing on its biochemical composition, biological activities, and potential applications in various fields. Studies have highlighted the presence of bioactive compounds in Cucumaria frondosa, such as collagen, cerebrosides, glycosaminoglycan, chondroitin sulfate, saponins, phenols, and mucopolysaccharides, which exhibit unique biological and pharmacological properties.

Research has also explored the nutritional composition of Cucumaria frondosa, emphasizing its abundance in essential amino acids and polyunsaturated fatty acids, particularly eicosapentaenoic acid (EPA) (Liu et al., 2021). Furthermore, bioactive compounds derived from Cucumaria frondosa, such as frondoside A, have shown potential anti-cancer effects by inducing apoptosis and inhibiting cancer cell activity (Wargasetia et al., 2021; Ru et al., 2023).

Moreover, Cucumaria frondosa has been studied for its physiological and immunological parameters in comparison to other sea cucumber species, shedding light on its unique characteristics (Win, 2023). The species has also been investigated for its lectin content, which has demonstrated the ability to inhibit the growth of human cancer cells in vitro (Goel et al., 2021).

Additionally, the antioxidant properties of fresh and processed Cucumaria frondosa samples have been evaluated, providing insights into its potential health benefits (Zhong et al., 2007). Metabolomic studies have revealed the diverse composition of bioactive compounds in Cucumaria frondosa, expanding the understanding of its chemical constituents (Popov et al., 2022).

Overall, research on Cucumaria frondosa underscores its significance as a source of bioactive compounds with potential applications in functional foods, nutraceuticals, and pharmaceuticals, highlighting its importance in various scientific disciplines.

2. Cucumaria Miniata - Red Sea Cucumber

Cucumaria miniata is a species of sea cucumber. It is commonly known as the orange sea cucumber or red sea cucumber due to its striking color. This northeast Pacific species is often found wedged in between rocks or crevices at the coast or on docks and can generally be identified by its orange bushy tentacles protruding above the substrate.

Image 2.15 Cucumaria Miniata

Cucumaria miniata is generally orange or reddish brown. They are easily identifiable by their orange coloration and branching tentacles. The body is thick and has five rows of tube feet, separated by smooth, soft skin. Pentameric radial symmetry is present in the five equally spaced rows of feet. The ossicles, which are present in all echinoderms, are small and scarcely scattered throughout the dermis. Respiration occurs through two aborescent tubes known as respiratory trees that are located in the coelom.

They have fifteen sets of feeding arms that fan out into bushy tentacles when fully extended and feed into the mouth which is controlled by a sphincter muscle. Their mouth and anus are at separate ends of the body resulting in a full digestive tract. The lower part of the body is generally wedged in a crevice so often the tentacles are the main part of the organism visible.

3. Thelenota anax – Amberfish

Thelenota anax is a species of sea cucumber mostly found in the tropical, South Pacific Ocean. It is also commonly known as the amber fish. Some other names for T. anax are black teatfish, blackfish, brownfish, chief sea cucumber, curryfish, elephant trunk cucumber, lollyfish, tripang, and white-teat sea cucumber.T. anax is found on sandy ocean bottoms and often have ectocommensal relationships. They are commonly fished commercially and exported because of their medicinal properties and large size.

Image 2.16 Thelenota anax – Amberfish

The body of T. anax can be a creamy beige or light brown with dark brown or red spots. It usually has light colored bumps on the top of its body. T. anax also has large with papillae located laterally on its body. On its ventral surface there is long white podia. Its mouth is also located ventrally with 18-20 peltate tentacles. The anus is located on the dorsal side of the animal towards the terminal end. Their average length is about 69 cm long, but the longest recorded sea cucumber was 89 cm long. Some of the biggest sea cucumber can weigh up to 5 kg. It also has two gonads that are approximately 70-500mm long.

3

CULINARY USAGE OF SEA CUCUMBERS

A. HISTORICAL AND CULTURAL SIGNIFICANCE

The historical and cultural significance of sea cucumbers in culinary practices spans various cultures and regions, dating back centuries. In Asian cuisines, particularly Chinese, Japanese, and Southeast Asian cultures, sea cucumbers have been prized for their unique texture, flavor, and perceived health benefits.

Historically, sea cucumbers were considered a delicacy reserved for royalty and nobility in Chinese cuisine. They were often included in lavish banquets and special occasions due to their rarity and perceived medicinal properties. Sea cucumbers were also used in traditional Chinese medicine for their believed ability to promote health and vitality.

In Japanese cuisine, sea cucumbers, known as "namako," have been a part of culinary traditions for centuries. They are often served as sashimi or in hot pot dishes, prized for their gelatinous texture and umami flavor. In Japan, sea cucumbers are also associated with longevity and prosperity, making them a popular choice for celebratory meals and festivals.

Southeast Asian cuisines, including Indonesian, Malaysian, and Filipino cuisines, also feature sea cucumbers in various dishes. They are often used in soups, stir-fries, and braised dishes, adding a unique chewy texture and absorbing flavors from accompanying ingredients and spices.

Beyond Asia, sea cucumbers have historical significance in Pacific Islander cuisines, where they are considered a traditional food source and are often prepared using local cooking methods and flavors.

In modern times, the cultural significance of sea cucumbers in culinary practices continues, with chefs and home cooks incorporating them into innovative recipes and dishes. While their culinary appeal varies across cultures, sea cucumbers remain valued for their gastronomic qualities and symbolic associations with prosperity, health, and tradition.

B. CULINARY DELIGHTS FROM THE DEEP: SEA CUCUMBER RECIPES AROUND THE WORLD

Sea cucumbers, marine creatures known for their gelatinous texture and unique flavor, have long been prized in culinary traditions around the globe. From Asia to the Pacific Islands, sea cucumbers find their way into a variety of delectable dishes, each showcasing their versatility and delicate taste. Let's take a gastronomic journey to explore some popular sea cucumber recipes from different parts of the world.

1. **Chinese Sea Cucumber Stew (Braised Sea Cucumber)**

A classic Chinese dish, braised sea cucumber is often prepared during festive occasions and banquets. The sea cucumbers are first softened by soaking, then braised in a savory sauce made from soy sauce, oyster sauce, ginger, garlic, and sometimes Shaoxing wine. The result is a tender and flavorful delicacy that pairs well with steamed rice.

Image 3.1 Braised Sea Cucumber With Radish Chinese Mushroom

2. **Japanese Namako Sashimi (Sea Cucumber Sashimi)**

In Japan, sea cucumber, known as "namako," is enjoyed as sashimi, showcasing its delicate texture and mild taste. Thinly sliced and served raw with soy sauce, wasabi, and pickled ginger, namako sashimi is a refreshing and elegant appetizer often found in high-end sushi restaurants.

Image 3.2 Namako Sashimi

3. Korean Haesam Juk (Sea Cucumber Porridge)

Haesam juk is a traditional Korean porridge made with sea cucumber, rice, and various seasonings. The sea cucumber adds a subtle sea-flavor to the creamy porridge, creating a comforting and nourishing dish often served during the winter months or as a restorative meal.

Image 3.3 Haesam Juk

4. Malaysian Hoi Sum Sea Cucumber Soup

Hoi sum sea cucumber soup is a popular dish in Malaysian cuisine, featuring sea cucumbers simmered in a flavorful broth with chicken or fish, Chinese herbs, and vegetables. The soup is believed to have health benefits, making it a favorite choice for families and gatherings.

Image 3.4 Cucumber Soup

5. Pacific Island Lupea (Palauan Sea Cucumber Salad)

In Palau, sea cucumber is prepared in a refreshing salad called lupea. The sea cucumbers are cleaned, boiled, and sliced, then mixed with coconut milk, lime juice, onions, and spices. Lupea offers a balance of creamy, tangy, and savory flavors that reflect the tropical island's culinary heritage.

Image 3.5 Sea Cucumber Salad

6. Caribbean Sea Cucumber Fritters

In the Caribbean, sea cucumber fritters are a popular snack or appetizer. The sea cucumber flesh is mixed with spices, herbs, and batter, then deep-fried until golden and crispy. Served with a dipping sauce, these fritters showcase the sea cucumber's versatility and adaptability to different cooking styles.

Image 3.6 Cucumber Fritters

7. Mediterranean Sea Cucumber Pasta

In Mediterranean cuisine, sea cucumber is sometimes used in pasta dishes. Sautéed with garlic, tomatoes, olives, and fresh herbs, sea cucumber adds a unique seafood twist to pasta recipes, creating a delightful fusion of flavors from land and sea.

These culinary delights highlight the diverse ways sea cucumbers are enjoyed and celebrated in cuisines worldwide, showcasing their culinary versatility and importance in global gastronomy. Whether braised, stewed, fried, or served raw, sea cucumbers offer a unique dining experience that captivates the senses and honors the rich bounty of the ocean.

4

ECONOMIC AND ECOLOGICAL BENEFITS

A. COMMERCIAL IMPPORTANCE IN FISHERIES

The commercial importance of sea cucumbers in fisheries is multifaceted, driven by their high demand in Asian markets and their perceived medicinal and nutritional value. In many Asian cuisines, particularly in China, Japan, and Southeast Asia, sea cucumbers are considered a delicacy and are consumed fresh or dried. This culinary preference fuels a robust market for sea cucumbers, contributing significantly to the fishing industry's revenue streams.

Moreover, sea cucumbers hold a prominent place in traditional medicine, especially in traditional Chinese medicine (TCM). They are believed to possess various health benefits, including anti-inflammatory, immune-boosting, and anti-aging properties. As a result, there is a consistent demand for sea cucumber-derived products in the pharmaceutical and nutraceutical sectors, further enhancing their commercial importance.

The export market for sea cucumbers is also substantial, with many countries relying on the export of these marine creatures to meet the demand in Asian markets. This export trade not only brings in foreign exchange but also supports livelihoods in coastal communities, including fishermen, processors, and traders who are integral to the sea cucumber supply chain.

Additionally, the aquaculture of sea cucumbers has gained traction as a sustainable alternative to wild harvesting. Cultivating sea cucumbers allows for controlled production, reducing pressure on wild populations while meeting market demand. This shift towards aquaculture not only ensures the availability of sea cucumbers for commercial purposes but also promotes environmental conservation.

The commercial importance of sea cucumbers in fisheries extends beyond their value as a food item. Their significance lies in their contribution to culinary traditions, traditional medicine, export markets, aquaculture development, and the socioeconomic well-being of coastal communities involved in their harvesting, processing, and trade.

B. AQUACULTURE PRACTICES AND SUSTAINABILITY

Aquaculture practices related to sea cucumber farming have gained prominence due to the high demand for these marine creatures in various industries, including culinary and medicinal sectors. Sea cucumber aquaculture involves cultivating these echinoderms in controlled environments, offering several advantages in terms of sustainability and resource management.

One significant aspect of sea cucumber aquaculture is its potential contribution to environmental sustainability. Unlike some traditional fisheries that may deplete wild populations, aquaculture allows for controlled breeding and harvesting of sea cucumbers, reducing pressure on natural stocks. This approach helps conserve wild sea cucumber populations and promotes biodiversity in marine ecosystems.

Moreover, sea cucumber aquaculture often incorporates sustainable farming practices to minimize environmental impact. These practices include using eco-friendly feeds, optimizing water quality management, and implementing waste recycling systems. By adopting these sustainable methods, aquaculturists can reduce pollution, conserve resources, and maintain the ecological balance of marine habitats.

In addition to environmental sustainability, sea cucumber aquaculture also offers socioeconomic benefits to coastal communities and economies. Cultivating sea cucumbers provides livelihood opportunities for local farmers and fishermen, contributing to income generation and poverty alleviation. Furthermore, the market demand for sea cucumbers creates economic incentives for sustainable aquaculture practices and investment in research and development.

Sustainability in sea cucumber aquaculture extends beyond environmental and economic aspects to encompass social responsibility. Many aquaculture initiatives prioritize community engagement, knowledge sharing, and capacity building among stakeholders. These efforts promote responsible aquaculture practices, empower local communities, and foster collaborative partnerships for long-term sustainability.

Overall, the integration of sustainable aquaculture practices in sea cucumber farming plays a crucial role in enhancing environmental conservation, supporting socioeconomic development, and promoting responsible resource management. By embracing sustainability principles, sea cucumber aquaculture can contribute significantly to food security, ecosystem health, and the well-being of coastal communities.

C. ROLE IN MARINE BIODIVERSITY AND ECOSYSTEM SERVICES

Sea cucumbers play a vital role in maintaining marine biodiversity and providing essential ecosystem services within coral reef and coastal ecosystems. As key detritivores and nutrient recyclers, sea cucumbers contribute significantly to the health and functioning of marine habitats.

One of the primary roles of sea cucumbers is their function as detritivores. They feed on organic matter such as decaying plant material, plankton, and bacteria, helping to break down and recycle nutrients in marine sediments. By doing so, sea cucumbers facilitate nutrient cycling and promote nutrient availability for other organisms, supporting the productivity of marine ecosystems.

Moreover, sea cucumbers contribute to sediment bioturbation, a process essential for maintaining sediment stability and oxygenation. As they burrow and move through the substrate, sea cucumbers enhance sediment aeration, nutrient diffusion, and microbial activity. These activities improve sediment quality, prevent anoxic conditions, and support the growth of benthic organisms, including seagrasses and coral reefs.

In addition to their ecological roles, sea cucumbers provide several ecosystem services that benefit both marine life and human communities. For instance, their feeding habits help regulate nutrient levels and water quality, contributing to the overall health and resilience of marine environments. Sea cucumbers also play a role in carbon sequestration, as they absorb and store organic carbon in their tissues and fecal pellets, potentially mitigating carbon dioxide levels in coastal waters.

Furthermore, sea cucumbers serve as prey for various marine predators, contributing to the trophic dynamics and food webs of marine ecosystems. Their presence supports the biodiversity of coral reef and coastal habitats, fostering ecological balance and species interactions.

Overall, sea cucumbers play a multifaceted role in marine biodiversity and ecosystem functioning. Their contributions to nutrient cycling, sediment stability, carbon sequestration, and trophic interactions highlight their significance in sustaining healthy and resilient marine ecosystems. Protecting and conserving sea cucumber populations is crucial for preserving marine biodiversity and ensuring the continued provision of essential ecosystem services.

5

POTENTIAL MEDICAL APLICATIONS

A. BIOACTIVE COMPOUNDS AND PHARMACOLOGICAL PROPERTIES

The usage of sea cucumbers as a potential therapeutic option begins by highlighting the intriguing nature of these marine creatures. Sea cucumbers, also known as holothurians, are echinoderms that play essential roles in marine ecosystems. They have long been recognized in traditional medicine for their diverse array of bioactive compounds, ranging from antioxidants and anti-inflammatory agents to antimicrobial and anticancer properties.

Recent scientific investigations have shed light on the therapeutic potential of sea cucumbers, particularly in the realm of cancer treatment. Studies have identified specific compounds within sea cucumbers that exhibit promising anticancer activities, including the ability to inhibit tumor growth, induce apoptosis (cell death) in cancer cells, and modulate immune responses.

B. RESEARCH AND DEVELOPMENT IN MEDICINE

Furthermore, sea cucumbers are considered a valuable source of novel molecules that may offer unique mechanisms of action compared to conventional cancer therapies. Their bioactive compounds have shown potential in targeting various hallmarks of cancer, such as angiogenesis (blood vessel formation within tumors), metastasis (spread of cancer cells), and resistance to chemotherapy.

Image 5.1 Medicine from Sea

As researchers delve deeper into understanding the molecular pathways and therapeutic mechanisms of sea cucumber-derived compounds, the prospect of incorporating these natural substances into cancer treatment strategies becomes increasingly compelling. However, challenges such as standardization of extracts, dosage optimization, and clinical validation remain significant hurdles that require concerted efforts from the scientific community.

C. HEALTH BENEFITS AND THERAPEUTIC USES

Sea cucumbers, known for their potential health benefits, have been used in traditional medicine for centuries. One of the key therapeutic uses of sea cucumbers is their anti-inflammatory properties. Compounds found in sea cucumbers can help reduce inflammation and alleviate symptoms associated with conditions like arthritis, rheumatism, and asthma. Additionally, they may aid in wound healing due to their ability to promote tissue regeneration and collagen production.

Another significant health benefit of sea cucumbers is their potential to boost the immune system. They contain bioactive compounds such as polysaccharides and peptides that have immunomodulatory effects, helping to enhance immune responses and defend against infections. Some studies suggest that sea cucumbers may also possess antiviral and anticancer properties, although further research is needed to validate these claims.

Sea cucumbers are also valued for their potential cardiovascular benefits. They are a good source of omega-3 fatty acids, which are known for their heart-healthy effects. Consuming sea cucumbers as part of a balanced diet may help lower cholesterol levels, reduce blood pressure, and improve overall cardiovascular health.

In traditional Chinese medicine, sea cucumbers are often used to promote overall well-being and vitality. They are believed to nourish the kidneys, improve blood circulation, and enhance energy levels. Moreover, sea cucumbers are considered a natural aphrodisiac and may support reproductive health in both men and women.

Image 5.2 Dried Sea Cucumber in Chinese Medicine

Overall, sea cucumbers offer a range of health benefits and therapeutic uses, making them a valuable addition to a healthy diet and lifestyle. However, it's essential to consult with a healthcare professional before incorporating sea cucumbers or sea cucumber supplements into your routine, especially if you have any underlying health conditions or are taking medications.

D. SEA CUCUMBER COMPOUNDS FOR CERVICAL CANCER THERAPY

Cervical cancer is a leading cause of death among women in many countries, and finding effective anticancer treatments for this type of cancer is challenging due to high rates of HPV infection and low vaccination rates among women of childbearing age. Studies have shown that protein oncogenes produced by HPV stimulate cell growth, promoting tumor development and treatment resistance. It explores the potential therapeutic mechanisms of Scitophus hermanii in treating cervical cancer using network pharmacology, identifying PTGS2, EGFR, and NFE2L2 as targets. Bioactive compounds in sea cucumbers, such as Gangliosides, Stichoposide and variegatuside have the potential to prevent cancer cell proliferation by inhibiting the epidermal growth factor receptor expression. The review suggests that targeting pathways could be a promising strategy for the treatment of cervical cancer. SwissADME also predicted the drug-like properties of the active chemicals in sea cucumbers. This discussion sheds new light on the potential use of marine natural products for the treatment of various types of cervical cancers.

Cervical cancer is a significant public health issue worldwide, with an estimated 604,000 new cases anticipated in 2020, according to the World Health Organisation (WHO).1 Unfortunately, the majority of cervical cancer-related deaths (approximately 90%) are expected to occur in low- and middle-income countries, with an estimated 342,000 deaths projected for 2020.1,2 This highlights the urgent need for increased awareness, prevention, and treatment strategies to address this problem. In Indonesia, cervical cancer is the third most common cancer in women, with 36,633 new cases reported in 2020.3 Human papillomavirus (HPV) is the main risk factor for cervical cancer, with types 16, 18, and 45 being the most common.4 HPV has several signalling pathways that are involved in signalling pathway transmission via active molecules such as MEK, ERK, and Akt.5 The virus has several oncoproteins, including E6 and E7, that play a significant role in cancer development. In early stages of cancer, the HPV genome suppresses viral oncoproteins E6 and E7, which maintain Akt phosphorylation status. E6 and E7 activate the Akt/mTOR signalling pathway, promoting viral cap-dependent protein synthesis and leading to carcinogenesis. HPV16 oncoprotein E7 increases keratinocyte migration.6 E5 plays a role in HPV-related cancer proliferation by regulating myogenic signalling pathways and stimulating VEGF expression through ERK activation, which is involved in angiogenesis.7 Cancer eventually develops through these pathways.8

While various treatment modalities are available, there is still a need for further investigation into the effects of these treatments. The Surveillance, Epidemiology, and End Results (SEER) programme estimates the overall 5-year relative survival rate for cervical cancer to be 67.2%. Therefore, there is a need for continued research to develop more effective treatment strategies. Natural chemicals originating from plants and animals that have potential anti-cancer effects are being researched for new cancer treatments. Teripang, also known as Sea cucumber, is a marine natural product that has shown efficacy in medical treatments. Researchers have demonstrated the anti-cancer properties of seacucumber in previous studies, but its exact mechanism of action remains unclear. Sea cucumber, is a marine natural product that has shown efficacy in medical treatments. According to current research, a specific group of Sea cucumbers has many promising pharmacological properties. This substance is composed of a diverse range of compounds, including various types of polysaccharides, such as glycosaminoglycans, neutral glycans, fucosylated chondroitin sulfates, and sulfated fucans. Studies have shown that Sea cucumber-derived compounds can exhibit cytotoxic activity, induce apoptosis, arrest cell cycle, reduce tumor growth, inhibit metastasis, and prevent drug resistance. Cytotoxic activity prevents cancer cell growth. Bioactive carbohydrate compounds from Holothuria scabra species, such as holothurine A3 and A4, are cytotoxic in Hep-G2 and KB cell lines. Frondanol A5, derived from Cucumaria frondosa extract, induced apoptosis in pancreatic cancer cells S2013 and AsPC. Echinoside A and echonoside A from Pearsonothuria graeffei disrupt the G0/G1 cell cycle of Hep-G2 liver carcinoma cells, preventing DNA replication. Saponins from Pentacta quadrangulari, particularly Philinopsides E and A, inhibit tumour growth in sarcoma and hepatoma mouse models.

Pearsonothuria graeffei bioactive's compound, Ds-echinoside A, inhibits hepatocellular carcinoma (Hep-G2) cell migration, invasion, and adhesion, thereby reducing cancer cell metastasis. The bioactive compounds, potential targets, and underlying mechanisms of Sea cucumber in cervical cancer are not well understood.

This chapter aims to investigate the potential of natural products, specifically sea cucumber, as a novel therapeutic strategy for the treatment of cervical cancer. A network pharmacology analysis of S. hermanii, will be presented to identify the active ingredients and targets of S. hermani. The findings of this study may provide a better understanding of the bioactive compounds, potential targets, and underlying mechanisms of S. hermanii, which may be useful for the development of novel therapies for cancer treatment.

1. Screening Methods of Potentially Active Compounds of Sea Cucumber

The search for bioactive compounds in Sea cucumbers (Sticophus sp.) was conducted using the CMNPD database. Each compound was then searched for its SMILE (simplified molecular-input line-entry system) profile and 3D structure using the PubChem database.

a. Quantitative Structure-Activity Relationship (QSAR) Analysis

Based on the information provided, the bioactive compounds found in Sea cucumbers or Schistocopus hermani, were analyzed for their potential using the WAY2DRUG PASS prediction tool as an anticancer treatment. The WAY2- DRUG Pass Prediction tool uses

Structure Activity Relationship (SAR) analysis to compare input compounds 2with known compounds that have specific potential. The greater the similarity of the structure of the compounds, the higher the prediction value obtained. Compounds with similar structures can be predicted to have similar potential. The Pa value (Probability to be Active) is the output prediction value of the WAY2DRUG PASS, which describes the potential of a tested compound. If the Pa value is greater than 0.7, it indicates that the compound is predicted to have high potential as an anti-inflammatory, for example, because it has a high similarity to compounds in the database.

A score of 0.5 is recommended as the cut-off score. The Pa value provides the accuracy of the obtained prediction function, the higher the Pa value of a function, the better the accuracy.

b. Toxicity Analysis of Compounds

The toxicity of bioactive compounds of Sea cucumbers can be predicted using the Protox II database. The parameters analyzed include Hepatotoxicity, Carcinogenicity, Immunotoxicity, Mutagenicity, and Cytotoxicity, as described by Banerjee et al. (2018).

- **Prediction of proteine targets**

  The targets of teripang were obtained from SuperPred (with score accuracy and probability > 80%). The target prediction was obtained by entering the SMILES found in step 1. Genes and proteins related to cervical cancer were obtained from the Open

Target database (with overall score prediction ≥ 0.1). The Open Target database was chosen because it includes information from other databases and is the most up-to-date (last update February 2023 (Version 23.02)). The targets related to the disease and the teripang target were then mapped using a Venn diagram to determine the intersection target. The function of each target from the best compound (Variegatusdie) was then mapped using the Database for Annotation, Visualization, and Integrated Discovery version 2021. The R package gplot2 was used to visualize the results of functional annotation from DAVID.

c. Network analysis

The protein target of Variegatuside from teripang was further analyzed using Search Tool for the Retrieval of Interacting Genes/Proteins (STRING DB V.12.0). The following parameters were used: Organism: Homo sapiens; Network type: Full STRING network; Required core: medium confidence (0.4). The data format TSV from STRING was then further processed using CytoScape V.10.0 for network analysis.

2. Results

a. Screening of Potentially Active Compounds of Scitophus Hermanii

Bioactive profile of seacucumber from Comprehensive Marine Natural Products Database (CMNPD). In general, this study extracted

16 compounds from the CMNPD database, which were obtained from samples of sea cucumbers in Table 5.1.

Table 5.1 Profile of Bioactive Compounds in Sea Cucumber.

Name	Compound ID
SCG-1	CMNPD13820
SCG-2	CMNPD13821
SCG-3	CMNPD13822
Stichoposide A	CMNPD1722
Stichoposide B	CMNPD1723
Stichoposide C	CMNPD1724
Stichoposide D	CMNPD1725
Variegatuside C	CMNPD25648
Variegatuside D	CMNPD25649
Variegatuside E	CMNPD25650
Variegatuside F	CMNPD25651
Stichorrenoside A	CMNPD29857
Stichorrenoside B	CMNPD29858
Stichorrenoside C	CMNPD29859
Stichorrenoside D	CMNPD29860
Stichorrenoside E	CMNPD31481

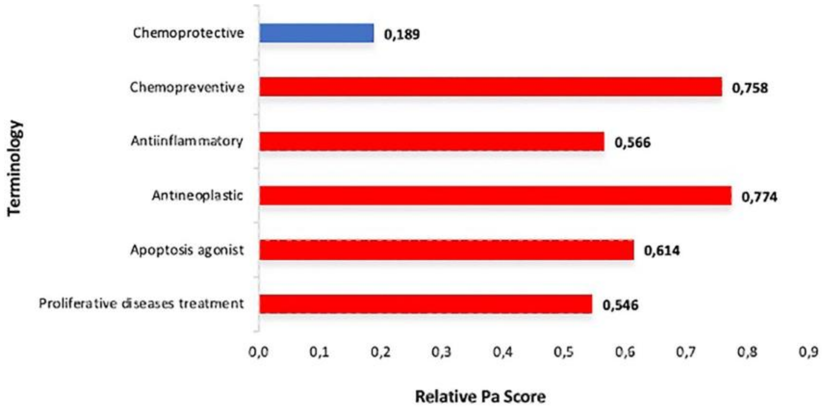

Image 5.3 SAR-based Prediction of Sea Cucumber's Potential as an Anticancer Agent

b. Quantitative Structure-Activity Relationship (QSAR) analysis

Based on SAR analysis using Way2Drug Pass Online, it is found that bioactive compounds in Sea cucumber have a good potential as Chemopreventive (Pa Score: 0.758), Anti-inflammatory (0.566), Antineoplastic (0.774), Apoptosis Agonist (0.614), and Proliferative diseases treatment (0.546). Chemopreventive is the use of natural or synthetic compounds to prevent cancer. Compounds included in chemopreventive can be used to prevent the occurrence of cancer, for someone with a high risk, and can be used to prevent relapse in patients undergoing treatment. The parameters of anti-inflammatory, antineoplastic, apoptosis agonist, and proliferative diseases treatment are used to see the potential as anticancer based on Hallmarks of cancer. Sea cucumber has the highest potential as Chemopreventive and Antineo- plastic toxicity in Image 5.3.

c. Analysis of Compound Toxicity

Analysis of each Sea cucumber sample using the Protox II webserver demonstrated that all compounds analyzed were predicted to exhibit immunotoxicity, with some also displaying cytotoxic effects. The Protox II immunotoxicity model assesses their ability to inhibit B cell growth. Additionally, mutagens are compounds with the potential to induce changes in an organism's genetic material, while carcinogens can cause cells to become cancerous by altering their genetic structure, leading to uncontrolled cell proliferation. Hepatotoxicity refers to kidney dysfunction or damage associated with an overload of drugs or xenobiotics. Based on the comparison with QSAR data, Variegatuside C and Variegatuside D were identified as potential candidate compounds falling into the toxicity class 4 (range 1 – 6, with lower values indicating higher toxicity), signifying the need for further investigation and evaluation of these compounds as presented in Table 2. Meanwhile, Table 3 displays the profile of the most promising predicted compounds.

- **Prediction of Proteine Targets**

  Image 2 shows the Functional Analysis Target of Variegatuside in Sea cucumber, while in Image 3, it is described that there are 11 overlapping targets between cervical cancer and Sea cucumber, namely MTOR, PDGFRA, PIK3R1, KLF5, NTRK3, HIF1A, CCNE1, AR, TRIM24, HSP90AB1, and TOP2A. MTOR is an oncogene that plays a role in promoting proliferative signalling. It is also involved in triggering invasion, metastasis, angiogenesis, evasion of programmed cell death, and altering cellular energetics (Hallmarks of Cancer: Cosmic Database).

d. Network analysis

MTOR is considered as a potential target because it has the highest values in terms of betweenness centrality, closeness centrality, degree, and cervical cancer overall score compared to other targets (Table 4, Image 4). Classic centrality calculations such as degree, closeness, and betweenness centrality are used to identify influential nodes (proteins) in biological networks. Degree provides an indication of how many proteins interact with a protein node. Closeness centrality is useful for estimating how quickly information flows through a node, or in other words, how short the fastest path is from node x to all other nodes. Meanwhile, betweenness centrality is based on communication flow. Nodes with high betweenness centrality values play a role in controlling information flow (Scardoni & Laudanna, 2009) Based on these analyses, it is predicted that Sea cucumber, specifically through the MTOR pathway, may be effective in targeting cervical cancer

Table 5.2 Profile sea cucumber bioactive compounds in toxicity analysis

Name	Hepatotoxicity	Probability	Carcinogenicity	Probability	Immunotoxicity	Probability	Mutagenicity	Probability	Cytotoxicity	Probability
SCG-1	Inactive	0.84	Inactive	0.72	Active	0.97	Inactive	0.88	Inactive	0.77
SCG-3	Inactive	0.84	Inactive	0.72	Active	0.98	Inactive	0.88	Inactive	0.77
Stichoposide A	Inactive	0.96	Inactive	0.61	Active	0.99	Inactive	0.91	Inactive	0.58
Stichoposide B	Inactive	0.97	Inactive	0.66	Active	0.99	Inactive	0.93	Active	0.7
Variegatuside C	Active	0.69	Inactive	0.62	Active	0.96	Inactive	0.97	Inactive	0.93
Variegatuside D	Active	0.69	Inactive	0.62	Active	0.96	Inactive	0.97	Inactive	0.93
Stichorrenoside A	Inactive	0.95	Inactive	0.69	Active	0.99	Inactive	0.92	Active	0.56
Stichorrenoside C	Inactive	0.96	Inactive	0.68	Active	0.99	Inactive	0.9	Active	0.79
Stichorrenoside D	Inactive	0.95	Inactive	0.59	Active	0.99	Inactive	0.91	Active	0.69
Stichorrenoside E	Inactive	0.95	Inactive	0.69	Active	0.99	Inactive	0.89	Active	0.71

Table 5.3 Profile of the most potential predicted compounds.

Name	Hepatotoxicity	Probability	Carcinogenicity	Probability	Immunotoxicity	Probability	Mutagenicity	Probability	Cytotoxicity	Probability
Variegatuside C	Active	0.69	Inactive	0.62	Active	0.96	Inactive	0.97	Inactive	0.93
Variegatuside D	Active	0.69	Inactive	0.62	Active	0.96	Inactive	0.97	Inactive	0.93

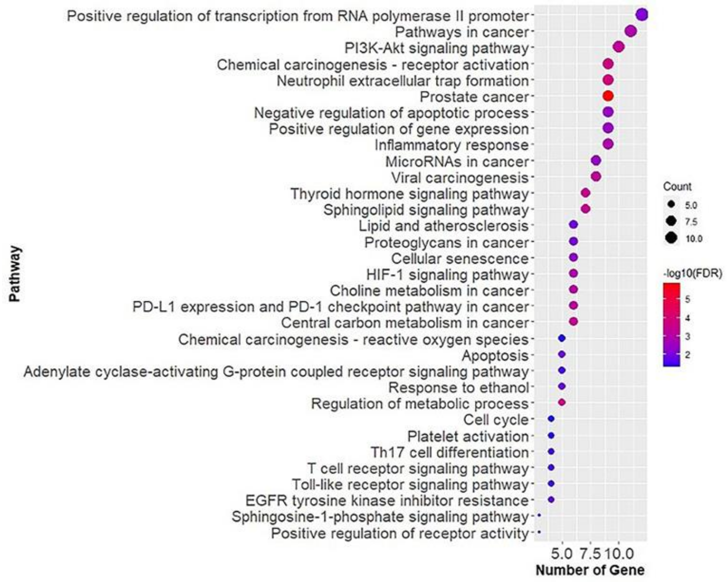

Image 5.4 Functional Analysys Target of Variegatuside in Seacucumber

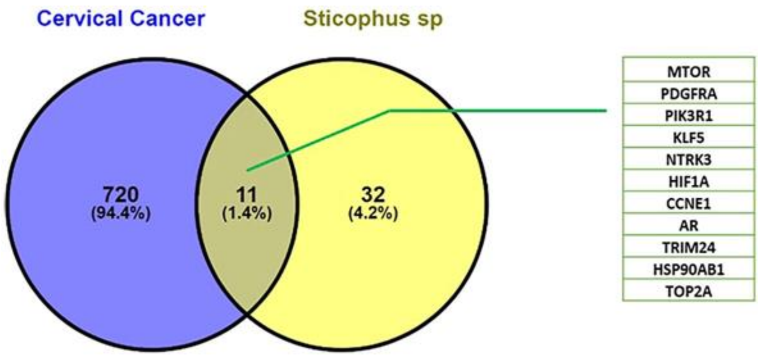

Image 5.5 Venn Diagram, Intersection Cervical Cancer and *Sticophus* sp.

3. Investigation

Our investigation revealed that Variegatuside C and Variegatuside D were the crucial components responsible for its anti-cancer effects. Recent study findings have identified 11 overlapping targets between cervical cancer and Seacu- cumber. mammalian Target of Rapamycin (MTOR), Platelet-Derived Growth Factor Receptor Alpha (PDGFRA), Phosphoinositide-3-Kinase Regulatory Subunit 1 (PIK3R1), Krüppel-like Factor 5 (KLF5), Neurotrophic Receptor Tyrosine Kinase 3 (NTRK3), Hypoxia-Inducible Factor 1 Alpha (HIF1A), Cyclin E1 (CCNE1), Androgen Receptor (AR), Tripartite Motif Containing 24 (TRIM24), Heat Shock Protein 90 Alpha Family Class B Member 1 (HSP90AB1), and Topoisomerase II Alpha (TOP2A), are crucial proteins with unique roles in promoting cancer growth and progression. PDGFRA is a protein that promotes cell proliferation and survival in several types of cancer. The study conducted by Chang et al. regarding miRNA-487a and its role in promoting proliferation and metastasis in hepatocellular carcinoma, demonstrated that PIK3R1 is a fundamental factor in facilitating cellular survival, growth, and proliferation. According to the review conducted by Luo et al., the transcription factor protein KLF5, which is implicated in various cancer types, plays a role in promoting cellular proliferation, growth, and survival. Similarly, NTRK3, a receptor tyrosine kinase protein involved in cell survival, proliferation, and differentiation, plays a significant role in cancer.

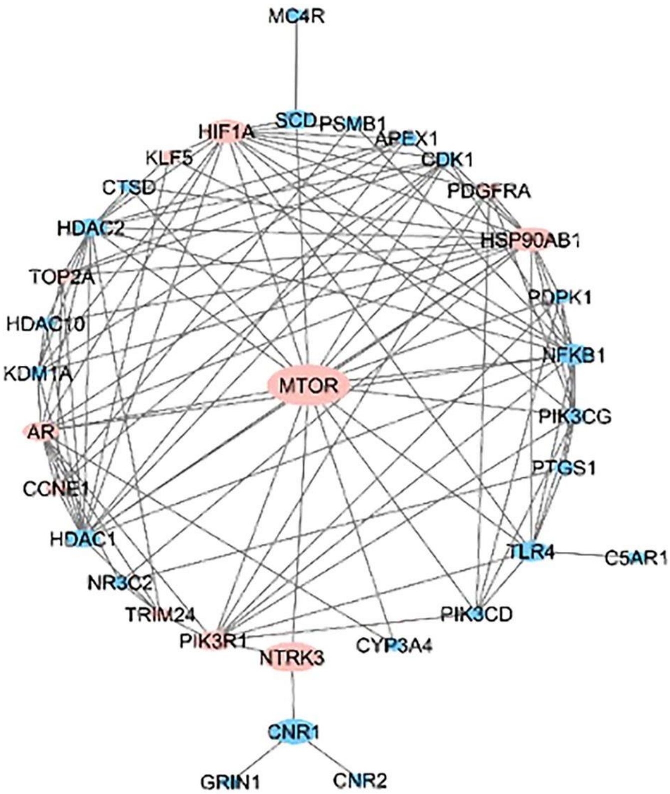

Image 5.6 Target pathway network of Sea cucumber (Variegatuside C and Variegatuside D) for treating cervical cancer

The blue nodes represent Sea cucumber targets, while the red nodes represent targets of both Sea cucumber and cervical cancer. The diameter of each node indicates its betweenness centrality score, with larger diameters indicating higher scores.

Table 5.4 Betweenness centrality score of network analysis

Name	Degree	Betweenness centrality	Closeness centrality	Cervical cancer overall score
MTOR	17	0.288	0.653	0.486
NTRK3	3	0.175	0.444	0.323
CNR1	3	0.123	0.323	0.001
HSP90AB1	17	0.122	0.604	0.185
HIF1A	15	0.113	0.593	0.298
NFKB1	14	0.079	0.571	0.031
PIK3R1	10	0.078	0.533	0.362
TLR4	9	0.077	0.516	0.010
AR	13	0.072	0.552	0.456
SCD	3	0.063	0.438	n/a

HIF1A is a protein that plays a crucial role in cancer cells' adaptation to low-oxygen environments, promoting the survival and growth of cancer cells even in challenging conditions. CCNE1 is a regulatory protein that contributes to cell cycle progression and is frequently overexpressed in various cancers, leading to the uncontrolled growth of cancer cells. Meanwhile, AR is a transcription factor protein that is crucial in the development and progression of prostate cancer, promoting cell growth and survival of androgen-dependent cancer cells. TRIM24 is an oncogenic transcriptional activator that regulates gene expression and promotes cancer cell growth. Recent studies have shown that HSP90AB1 is a chaperone protein that plays a critical role in cell signalling pathways related to the growth and survival of cancer cells. This is consistent with the findings of Ujianti et al., which suggest that endoplasmic reticulum stress conditions involving HSP90 as a marker for UPR may contribute to the development of liver carcinoma. These insights help us better understand the complex role that HSP90AB1 plays in cancer biology and could lead to new potential therapeutic targets for the treatment of liver cancer and other cancers in which this protein is involved. Finally,

TOP2A is an enzyme that is often overexpressed in cancer and plays a role in DNA replication and repair, contributing to the proliferation of cancer cells. Understanding the functions of these proteins can help researchers develop targeted therapies for cancer treatment develop targeted therapies for cancer treatment.

The discussion brings attention to the significant potential of MTOR (mammalian target of rapamycin) as a target for cervical cancer treatment. Network analysis, which includes parameters like betweenness centrality, closeness centrality, degree, and cervical cancer overall score, reveals that MTOR possesses the highest values among other targets. These network properties are fundamental in identifying influential nodes or proteins within biological networks. These findings align with the study conducted by Ji et al., which found that MTOR is one of the factors influencing the growth of various cancers, particularly cervical cancer. Degree centrality defines the number of proteins interacting with a protein node, while closeness centrality estimates the efficiency of information flow through a node.

On the other hand, betweenness centrality is based on controlling the flow of information. Considering these network properties, the analysis indicates that targeting MTOR may prove effective in the treatment of cervical cancer. MTOR, a serine/threonine kinase, plays a critical role in cell growth, metabolism, and proliferation. It is well-established that mTOR signalling is involved in multiple cancer characteristics, such as cell growth, survival, metabolism, angiogenesis, and metastasis. The activation of mTOR is frequently observed in cancer cells, contributing to their uncontrolled growth. Activation of mTOR signalling can enhance mRNA translation and increase the production of proteins involved in cell cycle progression, thus promoting cancer cell proliferation. Additionally, mTOR activation induces metabolic reprogram- ming in cancer cells, enabling them to adapt to nutrient-deprived and hypoxic conditions. The mTOR signalling pathway is also involved in regulating essential cellular processes for cancer progression, including angiogenesis and metastasis. By stimulating the production of vascular endothelial growth factor (VEGF), mTOR signalling promotes the formation of new blood vessels (angiogenesis). Furthermore, mTOR signalling facilitates cancer cell migration and invasion, facilitating the spread of cancer throughout the body. Consequently, targeting the mTOR pathway has emerged as a potential therapeutic strategy for cancer treatment. Several mTOR inhibitors, such as rapamycin have been developed and assessed in preclinical and clinical studies. The results are consistent with the SAR analysis conducted in this study using Way2Drug Pass Online, which demonstrated that bioactive compounds found in Sea cucumbers have promising potential as agents for cancer prevention, anti-inflammatory, antineoplastic, apoptosis agonist, and treatment of proliferative diseases. Toxicity analysis using the Protox II webserver showed that Variegatuside C and Variegatuside D are potential candidates, as they belong to toxicity class 4.

a. **The use of Protox II as a tool in toxicity analysis is explained in a review study conducted by Benarjee et al.**

The study suggests that Variegatuside C and Variegatuside D, active ingredients found in seacucumber, show potential as treatment options for cervical cancer. These compounds have the ability to regulate targets associated with the disease, opening up avenues for further exploration and the development of novel therapeutic interventions. However, it is important to consider the limitations of the study. The findings were based on network pharmacology analysis, which relies on computational predictions and may not fully capture the complexities of biological systems. Therefore, further experimental studies, such as in vitro and in vivo experiments on cervical cancer cells and animal models, are needed to validate these findings and provide more concrete evidence. This will help strengthen the evidence presented in the study and provide a more robust understanding of the therapeutic efficacy of Sea cucumber and its active ingredients.

6

CONCLUSION AND FUTURE PERSPECTIVES

A. SUMARRY OF KEY POINTS

Sea cucumbers are marine invertebrates with a cylindrical shape and soft body, belonging to the class Holothuroidea. They play an essential role in marine ecosystems due to their unique biological features and ecological functions. Sea cucumbers have a simple anatomy, consisting of a mouth surrounded by tentacles, a muscular body wall, and a digestive system with respiratory structures called respiratory trees. Their physiology allows them to filter feed and recycle nutrients in coastal waters, contributing to nutrient cycling and sediment stability. In addition to their ecological importance, sea cucumbers have been utilized in culinary practices for centuries, especially in Asian cuisines. They hold historical and cultural significance, with traditional recipes showcasing their delicate flavor and texture. Sea cucumbers are also valued for their nutritional content, being rich in protein, vitamins, and minerals, which contribute to their potential health benefits.

The economic significance of sea cucumbers extends to commercial fisheries and aquaculture practices. They are harvested for their high market value and are subject to sustainable management to ensure their continued availability. Aquaculture techniques have been developed to cultivate sea cucumbers, promoting their economic viability while reducing pressure on wild populations.

Furthermore, sea cucumbers play a crucial role in marine biodiversity and ecosystem services. They contribute to biodiversity by serving as prey for various predators and enhancing sediment bioturbation. Their presence helps maintain healthy coastal ecosystems and supports fisheries productivity.

In terms of potential medical applications, sea cucumbers contain bioactive compounds with pharmacological properties that have shown promise in research and development for therapeutic uses. These compounds have been studied for their anti-inflammatory, antioxidant, and anticancer properties, including their potential in cervical cancer therapy.

B. CHALLENGES AND OPPORTUNITIES

Addressing the challenges and opportunities associated with sea cucumbers spans various aspects, from their ecological importance to their culinary, economic, and medical potential.

1. **Sea Cucumber and Its Ecological Role**

Challenges: One of the challenges is the vulnerability of sea cucumber populations to overfishing due to high demand in Asian markets. Unsustainable harvesting practices can lead to population declines and ecosystem imbalances.

Opportunities: Implementing sustainable fisheries management practices, such as quotas and protected areas, presents an opportunity to conserve sea cucumber populations and maintain their ecological functions in marine ecosystems.

2. **Culinary Usage and Nutritional Benefits**

Challenges: Limited culinary diversity and awareness outside of Asian cultures can hinder the global appreciation and market demand for sea cucumbers as a culinary delicacy.

Opportunities: Promoting sea cucumber recipes and educating consumers about their nutritional value, such as high protein content and potential health benefits, can create new culinary markets and opportunities for seafood industries.

3. **Economic and Ecological Contributions**

Challenges: Balancing the economic importance of sea cucumbers in fisheries with sustainable harvesting practices is a challenge, especially in regions where they are heavily exploited.

Opportunities: Developing aquaculture technologies and practices for sea cucumbers can reduce pressure on wild populations while creating economic opportunities for coastal communities and seafood industries. Furthermore, recognizing their role in maintaining marine biodiversity and ecosystem services highlights their value beyond commercial exploitation.

4. Potential Medical Applications

Challenges: Research and development in harnessing sea cucumber bioactive compounds for medical applications face challenges such as identifying and isolating specific compounds, understanding their mechanisms of action, and ensuring safety and efficacy in therapeutic uses.

Opportunities: Advances in biotechnology and pharmacology offer opportunities to explore the full potential of sea cucumber compounds in medicine, including their use in cancer therapies like cervical cancer. Collaborative efforts between researchers, industry, and regulatory bodies can accelerate the translation of sea cucumber-based medicines from lab to clinical practice.

Overall, addressing these challenges and seizing opportunities requires a holistic approach that integrates scientific research, sustainable practices, market development, and regulatory frameworks to maximize the benefits of sea cucumbers while ensuring their long-term viability and conservation.

C. FUTURE DIRECTIONS IN SEA CUCUMBER RESEARCH AND UTILIZATION

Future directions in sea cucumber research and utilization encompass a wide range of areas, from conservation and sustainable management to biotechnological advancements and innovative uses in various industries.

1. Conservation and Sustainable Management

The future of sea cucumber research involves a strong focus on conservation and sustainable management practices. This includes developing and implementing effective fisheries management strategies, such as quotas, closed seasons, and marine protected areas, to prevent overexploitation and ensure the long-term viability of sea cucumber populations. Collaborative efforts between scientists, policymakers, and local communities are essential for designing and implementing these conservation measures.

2. Biotechnological Applications

Advances in biotechnology offer promising avenues for the utilization of sea cucumbers. Future research may explore the bioactive compounds found in sea cucumbers and their potential applications in pharmaceuticals, nutraceuticals, and cosmeceuticals. This includes studying the mechanisms of action of these compounds, their therapeutic properties, and their safety profiles for human use.

Bioprospecting efforts can lead to the discovery of novel compounds with diverse biological activities.

3. Aquaculture and Mariculture

The future of sea cucumber utilization also lies in the development of sustainable aquaculture and mariculture practices. Research in this area may focus on optimizing breeding and rearing techniques, enhancing feed formulations for optimal growth and health, and mitigating disease risks in aquaculture settings. Sustainable aquaculture of sea cucumbers can reduce pressure on wild populations while meeting the growing demand for these organisms in various markets.

4. Innovative Uses and Value-Added Products

As awareness of sea cucumbers' nutritional and bioactive properties grows, there is potential for the development of innovative uses and value-added products. This includes exploring new culinary preparations and recipes, creating functional food products enriched with sea cucumber extracts, and developing novel applications in industries such as biomedicine, biotechnology, and cosmetics. Collaborative research and development efforts between academia, industry, and government entities can drive innovation in sea cucumber utilization.

5. Climate Change Resilience

With the ongoing impacts of climate change on marine ecosystems, future research may also focus on understanding how sea cucumbers respond to environmental stressors and their role in ecosystem resilience. Studying their adaptive mechanisms, reproductive strategies, and interactions with other species can provide valuable insights into their resilience to changing environmental conditions and inform conservation and management strategies.

In conclusion, future directions in sea cucumber research and utilization involve interdisciplinary collaborations, technological innovations, sustainable practices, and a deeper understanding of their ecological, biological, and economic importance. By addressing these areas, researchers and stakeholders can unlock the full potential of sea cucumbers while ensuring their conservation and sustainable utilization for generations to come.

BIBLIOGRAPHY

24-Dehydroechinoside A, on Antimetastasic Activity via Regulation of the MMP-9 Signal Pathway. *J. Food Sci.* 2010; 75(9): H280–H288.

Albakova Z, Mangasarova Y, Albakov A, *et al*.: HSP70 and HSP90 in Cancer: Cytosolic, Endoplasmic Reticulum and Mitochondrial Chaperones of Tumorigenesis. *Front. Oncol.* 2022; 12(January): 1–14.

Banerjee P, Eckert AO, Schrey AK, *et al*.: ProTox-II: A webserver for the prediction of toxicity of chemicals. *Nucleic Acids Res.* 2018; 46(W1): W257–W263.

Bonab FR, Baghbanzadeh A, Ghaseminia M, *et al*.: Molecular pathways in the development of hpv-induced cervical cancer. *EXCLI J.* 2021; 20: 320–337.

Castanon A, Tataru D, Sasieni P: Survival from cervical cancer diagnosed aged 20–29 years by age at first invitation to screening in England: Population-based study. *Cancers (Basel).* 2020; 12(8): 1–9.

Chang R-M, Xiao S, Lei X, *et al*.: miRNA-487a Promotes Proliferation and Metastasis in Hepatocellular Carcinoma. *Clin. Cancer Res.* 2017 May 14; 23(10): 2593–2604.

Chen Z, Huang Z, Luo Y, *et al*.: Genome-wide analysis identifies critical DNA methylations within NTRKs genes in colorectal cancer. *J. Transl. Med.* 2021; 19(1): 13–73.

Choudhari AS, Mandave PC, Deshpande M, *et al*.: Phytochemicals in cancer treatment: From preclinical studies to clinical practice. *Front. Pharmacol.* 2020; 10(January): 1–17.

Filimonov DA, Laqunin AA, Gloriozova TA, *et al*.: Prediction of the Biological Activity Spectra of Organic Compounds Using the PASS online Web Resource. *Chem. Heterocycl. Comp.* 2014; 50: 444–457.

Gorski JW, Ueland FR, Kolesar JM: CCNE1 amplification as a predictive biomarker of chemotherapy resistance in epithelial ovarian cancer. *Diagnostics.* 2020; 10(5): 1–14.

Hoang DT, Iczkowski KA, Kilari D, *et al*.: Androgen receptor- dependent and -independent mechanisms driving prostate cancer progression: Opportunities for therapeutic targeting from multiple angles. *Oncotarget.* 2017; 8(2): 3724–3745. PubMed Abstract|Publisher Full Text|Free Full Text

Hossain A, Dave D, Shahidi F: Northern sea cucumber (Cucumaria frondosa): A potential candidate for functional food, nutraceutical, and pharmaceutical sector. *Mar. Drugs.* 2020; 18(5).

Ilahi NE, Bhatti A: Impact of HPV E5 on viral life cycle via EGFR signaling. *Microb. Pathog.* 2020; 139: 103923.

Irena U: CMNPD-database. 2023 [cited 2023 Jul 19].

Irena U: DAVID. 2023 Jul 21 [cited 2023 Jul 21].

Irena U: Protox-II. 2023 Jul 21 [cited 2023 Jul 21].

Irena U: PubChem. 2023 Jul 22 [cited 2023 Jul 22].

Irena U: String_DB. 2023 Jul 21 [cited 2023 Jul 21].

Irena U: superPred. 2023 Jul 21 [cited 2023 Jul 21].

Irena U: WAY2DRUG PASS. 2023 Jul [cited 2023 Jul 21].

Ji J, Zheng PS: Activation of mTOR signaling pathway contributes to survival of cervical cancer cells. *Gynecol. Oncol.* 2010; 117(1): 103–108.

Lachs L, Oñate-Casado J: Fisheries and Tourism: Social, Economic, and Ecological Trade-offs in Coral Reef Systems. *YOUMARES 9 - The Oceans: Our Research, Our Future.* 2020; pp. 243–260.

Liu G-J, Wang Y-J, Yue M, *et al*.: High expression of TCN1 is a negative prognostic biomarker and can predict neoadjuvant chemosensitivity of colon cancer. *Sci. Rep.* 2020; 10(1).

Lotfimehr H, Mardi N, Narimani S, *et al*.: mTOR signalling pathway in stem cell bioactivities and angiogenesis potential. *Cell Prolif.* 2023; e13499.

Luo Y, Chen C: The roles and regulation of the KLF5 transcription factor in cancers. *Cancer Sci.* 2021; 112(6): 2097–2117.

Magaway C, Kim E, Jacinto E: Targeting mTOR and metabolism in cancer: Lessons and innovations. *Cells.* 2019; 8(12).

Mahendra INB, Prayudi PKA, Dwija IBNP, *et al*.: HPV16-E6/E7 Oncogene Mutation and p53 Expression among Indonesian Women with Cervical Cancer. *Asian Pac. J. Cancer Prev.* 2022; 23(8): 2705–2711.

Marine Biotechnology: Applications in Food, Drugs and Energy. Shah MD, Ransangan J, Venmathi Maran BA, editors. Singapore: Springer Nature Singapore; 2023; pp. 171–188.

Masoud GN, Li W: HIF-1*α* pathway: Role, regulation and intervention for cancer therapy. *Acta Pharm. Sin. B.* 2015; 5(5): 378–389.

Mazlan NB, Abd Rahman NNB, Shukhairi SSB, *et al*.: *Sea Cucumbers: Source of Nutritional, Medicinal, and Cosmeceutical Products BT -*

Papadopoli D, Boulay K, Kazak L, *et al*.: mTOR as a central regulator of lifespan and aging. *F1000Res.* 2019; 8(998).

Papadopoulos N, Lennartsson J: The PDGF/PDGFR pathway as a drug target. *Mol. Asp. Med.* 2018; 62: 75–88.

Pommier Y, Nussenzweig A, Takeda S, *et al*.: Human topoisomerases and their roles in genome stability and organization. *Nat. Rev. Mol. Cell Biol.* 2022; 23(6): 407–427.

Roginsky A, Ding X-Z, Singh B, *et al*.: Frondanol-A5 from cucumaria frondosa induces cell cycle arrest and apoptosis in pancreatic cancer cells. *J. Am. Coll. Surg. - J. AMER. COLL. Surg.*

Salindeho N, Nurkolis F, Ben GW, *et al*.: Anticancer and anticholesterol attributes of sea cucumbers: An opinion in terms of functional food applications. *Front. Nutr.* 2022; 9(1).

scabra Cultured in the Open Pond System. *J. Aquat.* 2022; 31: 599–614.

Scardoni G, Tosadori G, Faizan M, *et al*.: Biological network analysis with CentiScaPe: centralities and experimental dataset integration. *F1000Res.* 2015; 3(139).

Strickland SW, Vande Pol S: The Human Papillomavirus 16 E7 Oncoprotein Attenuates AKT Signaling To Promote Internal Ribosome Entry Site-Dependent Translation and Expression of c-MYC. *J. Virol.* 2016; 90(12): 5611–5621.

Ujianti I, Semara Lakshmi B, Nurushoffa Z, *et al*.: cmnpd_teripang_final.csv. Dataset. *figshare.* 2023.

Ujianti I, Sianipar IR, Prijanti AR, *et al*.: Effect of Roselle Flower Extract (Hibiscus sabdariffa Linn.) on Reducing Steatosis and Steatohepatitis in Vitamin B12 Deficiency Rat Model. *Med.* 2023; 59: 1044.

Ujianti, I., Semara Lakshmi, B., Nurusshofa, Z., Sukarya, W., & Indriyanti, L. (2023). Network Pharmacology Analysis Reveals Bioactive Compounds and Potential Targets of Sea cucumber for Cervical Cancer Therapy. F1000Research, 12, 1358.

Wargasetia TL, Widodo.: Mechanisms of cancer cell killing by sea cucumber-derived compounds. *Investig. New Drugs.* 2017; 35(6): 820–826.

WHO: *Cervical Cancer Profile.* World Health Organization; 2021.

WHO: WHO Mortality Database. 2023.

Wulandari DA, Gustini N, Murniasih T: Nutritional Value and Biological Activities of Sea Cucumber Holothuria

Yang M, Lu Y, Piao W, *et al*.: The Translational Regulation in mTOR Pathway. *Biomolecules.* 2022; 12(6).

Zhang L, Wu J, Ling MT, *et al*.: The role of the PI3K/Akt/mTOR signalling pathway in human cancers induced by infection with human papillomaviruses. *Mol. Cancer.* 2015; 14(1): 13–87. Zhao Q, Xue Y, Liu ZD, *et al*.: Differential Effects of Sulfated Triterpene Glycosides, Holothurin A1, and