International Journal of Research in Engineering, Science and Management
Volume-2, Issue-11, November-2019
www.ijresm.com | ISSN (Online): 2581-5792

Treatment of Cancer by Using Sea Cucumber

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***Abstract*: Sea cucumbers and their extracts have gained immense popularity and interest among researchers and nutritionists due to their nutritive value, potential health benefits, and use in the treatment of chronic inflammatory diseases. Many areas of the world use sea cucumbers in traditional foods and folk medicine. Though the actual 6vcomponents and their specific functions still remain to be investigated, most sea cucumber extracts are being studied for their anti-inflammatory functions, immune stimulatory properties, and for cancer prevention and treatment. There is large scope for the discovery of additional bioactive, valuable compounds from this natural source. Sea cucumber extracts contain unique components, such as modified triterpene glycosides, sulfated polysaccharides,glycosphingolipids, and esterified phospholipids. Frondanol A5, an isopropyl alcohol/water extract of the enzymatically hydrolyzed epithelia of the edible North Atlantic sea cucumber, *Cucumaria frondosa*, contains mono sulfated triterpenoid glycoside Frondoside A, the disulfated glycoside Frondoside B, the trisulfated glycoside Frondoside C, 12-methyltetradecanoic acid, eicosapentaenoic acid, and fucosylated chondroitin sulfate. We have extensively studied the efficacy of this extract in preventing colon cancer in rodent models. In this review, we discuss the anti-inflammatory, immune stimulatory, and anti-tumor properties of sea cucumber extracts.**

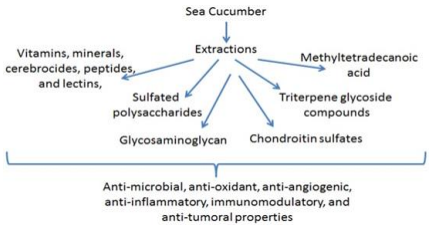
***Keywords*: Sea cucumbers, Triterpene glycosides, Anti-cancer, apoptosis, metastasis.**

1. Introduction

At the present time, ~60% of approved cancer treatment drugs are of natural origin [1]. Natural products that exist in marine animals and plants function as anti-mutagenic and anti-carcinogenic and may inhibit one or more stages of carcinogenesis by preventing or delaying cancer development. An estimated 14,000 pharmacologically active compounds have been isolated from marine plants and animals, suggesting an existence of immense diversity within this environment. The marine environment is therefore a rich source for discovering novel lead compounds for the development of new anti-cancer drugs and cancer-preventive nutraceuticals. A comprehensive survey of pharmacologic activity was conducted over a period of 15 years by the U.S. National Cancer Institute and found that 4% of the marine species (mainly animals) examined contained anti-tumor compounds. Potential sources of new types of biologically active compounds isolated from marine echinoderms are being applied in biomedical field.

In recent years, attention has been devoted to developing bioactive agents from natural food sources to produce pharmaceutical grade anti-inflammatory supplements. Sea cucumbers are nutrient-rich, invertebrate deep-sea dwellers that have been used for centuries as an anti-inflammatory and anti-disease food source and for treating ailments in Korea, Japan, Indonesia, and China [2]. Sea cucumbers are usually soft-bodied echinoderms, looking like a cucumber, and they are a diverse group of flexible, elongated, worm-like organisms, with a leathery skin and gelatinous body. Habitually, they tend to live on the sea floor in deep seas. Sea cucumbers are reported in Chinese and Malaysian literature as they are recognized as a tonic and traditional remedy for various diseases. The export and consumption of bioactive components extracted from marine sea cucumbers has increased in western markets as these components become available in supplements for various diseases. Hence, a comprehensive approach to utilizing biologically active agents derived from natural foods for wellness and towards disease prevention and treatment is necessary.

Sea cucumbers consist of vitamins, minerals, cerebrocides, peptides, and lectins, and also contain unique molecules, such as sulfated polysaccharides, 12-methyltetradecanoic acid (12-MTA), philinopside E, triterpene glycoside compounds, glycosaminoglycan, and chondroitin sulfates [3,4]. In sufficient quantities, these unique compounds are known to possess anti-microbial, anti-oxidant, anti-angiogenic, anti-inflammatory, immunomodulatory, and anti-tumoral properties [5]. As supplements, these sea cucumber extracts have been shown to suppress inflammation and increase innate immune responses. In this review, we will discuss the anti-inflammatory, anti-tumorigenic, and immune properties of bioactive agents extracted from sea cucumbers.



2. History

In the 16th and 17th centuries, it became more acceptable for doctors to dissect bodies to discover the cause of death. The German professor Wilhelm fabry believed that breast cancer was caused by a milk clot in a mammary duct. The Dutch professor francois de la boe sylvius, a follower of descartes,

believed that all disease was the outcome of chemical processes, and that acidic lymph fluid was the cause of cancer. His contemporary nicolaes tulp believed that cancer was a poison that slowly spreads, and concluded that it was contagious

The first cause of cancer was identified by British surgeon percivall pott, who discovered in 1775 that cancer of the scrotum was a common disease among chimney sweeps. The work of other individual physicians led to various insights, but when physicians started working Together they could draw firmer conclusions.

With the widespread use of the microscope in the 18th century, it was discovered that the 'cancer poison' eventually spreads from the primary tumor through the lymph nodes to other sites ("metastasis"). This view of the disease was first formulated by the English surgeon campbell De Morgan between 1871 and 1874. [6] The use of surgery to treat cancer had poor results due to problems with hygiene. The renowned Scottish surgeon Alexander Monro saw only 2 breast tumor patients out of 60 surviving surgery for two years. In the 19th century, asepsis improved surgical hygiene and as the survival statistics went up, surgical removal of the tumor became the primary treatment for cancer. With the exception of William Coley who in the late 19th century felt that the rate of cure after surgery had been higher before asepsis (and who injected bacteria into tumors with mixed results), cancer treatment became dependent on the individual art of the surgeon at removing a tumor. The underlying cause of his results might be that infection stimulates the immune system to destroy left tumor cells. During the same period, the idea that the body was made up of various tissus. that in turn were made up of millions of cells, laid rest the humor-theories about chemical imbalances in the body.

3. Cancer causes

Pain: Pain can be caused by cancer or by cancer treatment, though not all cancer is painful

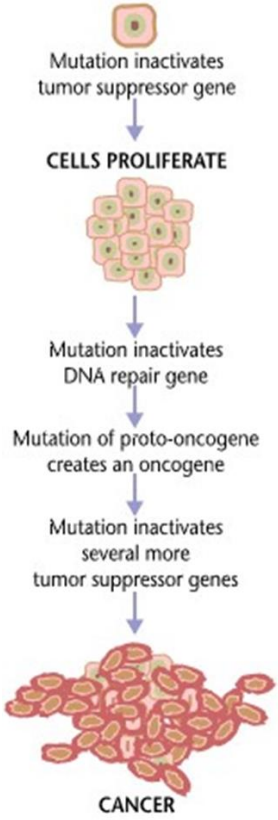
Fatigue

Difficulty breathing

Nausea

- Diarrhea or constipation
- Weight loss
- Chemical changes in your body

Pathogenesis



A. Cancer epidemiology

Cancer is second only to heart disease as the leading cause of death in the United States. One-half of all men and one-third of all women will develop cancer at some time in their lives. Although prostate cancer is the most common form of cancer in males, and breast cancer is the most common form in females, lung cancer causes the highest mortality rates for either gender (American Cancer Society, 2007). African-Americans have lower survival rates for most cancers compared with other groups of people. This may be due to a variety of factors, including limited access to health care, little or no medical insurance, lack of a primary health care provider, homelessness,

poverty, lack of knowledge on early diagnosis and treatment, and greater exposure to carcinogens (McCance & Roberts, 1998).

The five-year survival rate from all cancers is currently estimated at 58% (American Cancer Society, 2000). Generally, if there is no detectable recurrence of cancer for five years following the initial diagnosis, a person is considered to be in remission or cured. However, many people considered cured continue to demonstrate limitations or disabilities from their cancer or its treatment. These disabilities include movement dysfunctions, limited physical activity levels, chronic fatigue, and depression. These limitations and disabilities can be improved through rehabilitation and physical training (Gerber & Augustine, 2000, Pinto & Maruyama, 1999, Dimeo, et al., 1998, Segar, et al., 1998, Dimeo, et al., 1997, Friendenreich Courneya, 1996).

Ethnic lines include nasopharyngeal cancers in the Chinese, gallbladder cancer in American Indians and some Hispanic groups, and skin cancers in ethnic groups that lack protective skin pigmentation (McCance & Roberts, 1998, Fraumeni, 1982).

Types of cancer

- Breast cancer
- Prostate cancer

A cancer in a man's prostate, a small walnut-sized gland that produces semin

- Basal cell cancer

A type of skin cancer that begins in the basal cells.

- Skin cancer (melanoma)

The most serious type of skin cancer.

- Colon cancer

A cancer of the colon or rectum, located at the digestive tract's lower end.

- Lung cancer

A cancer that begins in the lungs and most often occurs in people who smoke.

- Leukemia

A cancer of blood-forming tissues, hindering the body's ability to fight infection.

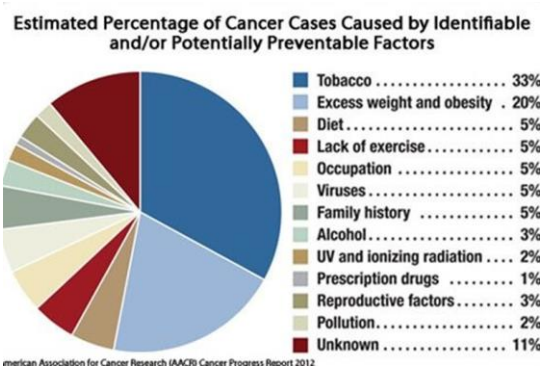
- Lymphoma

A cancer of the lymphatic system.

Consult a doctor for medical advice

Signs and symptoms of cancer

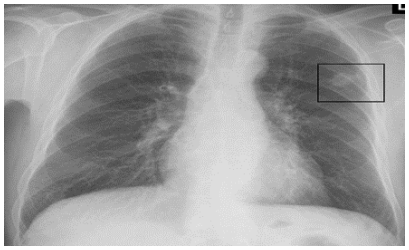
- More Cancer Signs and Symptoms
- Blood in the urine. ...
- Hoarseness. ...
- Persistent lumps or swollen glands.
- Obvious change in a wart or a mole.
- Indigestion or difficulty swallowing.
- Unusual vaginal bleeding or discharge.
- Unexpected weight loss, night sweats, or fever.
- Continued itching in the anal or genital area.



Percentage causes of cancer

4. Cancer diagnosis

Cancer diagnosis can be simple or complex depending on the type, location, and the extent of the disease. Early detection offers the best opportunity for recovery. Early detection requires knowledge of an individual's risk factors for developing cancer, regular cancer screening, and attention to subtle symptoms that might signal cancer. Risk factors for cancer include environmental exposures, lifestyle practices, occupational hazards, and a family history of cancer. Some of the early symptoms of cancer are fatigue, weakness, weight loss, depression, headache, pain, changes in bowel habits, and a persistent cough or hoarseness (American Cancer Society, 2000). Timely screenings, such as breast self-examinations, mammography, prostate screenings, chest X-rays, and colonoscopy, have markedly improved early detection and survival rates from cancer. Physicians may also use evidence from laboratory tests, X-rays, CT scans, ultrasound examinations, bone scans, liver and spleen scans, and biopsy analysis to confirm a diagnosis of cancer.



5. Treatment of cancer by using sea cucumber

Triterpene glycosides isolated from sea cucumbers (Mensamaria intercedens) were evaluated for their anti-tumorigenic properties in a mouse model of S180 sarcoma and mouse Lewis lung cancer cell line.A hot water extract of sea cucumber (Stichopus japonicus) was reported to significantly inhibit proliferation and produce concentration-dependent cytotoxicity in human colon cancer Caco-2 cells.Isolated sphingoid bases of sea cucumber (Stichopus variegatus) showed profound cytotoxic effects and decreased cell viability, and induced apoptosis via caspase 3 activity in DLD-1, WiDr, and Caco-2 human colon cancer cells. These in vitro studies of

Table 1

Compound	Sea cucumber	Effects	Type of cancer
Triterpene glycosides	*Mensamaria intercedens*	Anti-tumorigenic	mouse model of S180 sarcoma and mouse Lewis lung cancer cell lines
Hot water extract	*Stichopus japonicas*	Anti-proliferation cytotoxic	Human colon cancer CaCo2 cells
Organic extracts	*Holothuria leucospilota, Holothuria scabra, Stichopus chloronotus*	Anti-proliferation	human A549 non-small lung cancer cells and C33A cervical cancer cells
sulfated triterpene glycosides	*Pearsonothuria graeffei*	Invasion, migration, decreased VEGF, MMP9, increased TIMP-1, decreased NF-κB	human hepatocellular liver carcinoma cells (HepG2) and human endothelial cells (ECV-304)
Frondoside A	*Cucumaria frondosa*	Anti-proliferation	Pancreatic cancer cells
Frondoside A	*Cucumaria frondosa*	Tumor inhibition, anti-proliferation, apoptosis, increased p21	Pancreatic cancer xenografts

human colon cancer cells suggest that glycosides extracted from sea cucumbers may be good anti-tumor agents for the prevention and treatment of human colon cancer. Sea cucumber extracts and their effects on various cancers in in vitro and in *vivo* models.

6. Conclusions

The isolation and use of bioactive compounds from sea cucumber extracts has received increasing attention for their potential anti-inflammatory and anti-tumorigenic properties and the possibility of applications to the treatment and prevention of human diseases, including cancers. These compounds are appealing because of their natural origin, long history of use as food, and lack of toxic effects. Although sea cucumber extracts are used for food and medicinal purposes, their exact functions have not yet been studied in detail. There is a need to develop methods to isolate and purify individual compounds and study their medicinal values, which could be applied to the pharmaceutical, cosmetic, and nutraceutical industries.

These compounds must be explored in appropriate animal models to provide empirical evidence of their functionality. The available data suggest the sea cucumber as a rich source of bioactive compounds, which makes it an ideal source for drug discovery, although much future analysis is necessary. Most isolated agents have been tested in small amounts and in combination with various components. Still, there is the potential to identify novel individual anti-cancer agents from various species of sea cucumbers.

Sea cucumber extracts have a promising future to be developed as functional foods. These extracts could be potential candidates for the prevention and treatment of cancers. The compositions and doses of sea cucumber extracts must be standardized for human clinical use, and individual agent analysis must be performed to determine the potential benefits for the prevention and treatment of inflammatory diseases and cancer.

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