# THE EFFECTIVENESS OF SEA CUCUMBER IN INHIBITING CANCER OF THE MOUTH: LITERATURE REVIEW

#### **THESIS**

Submitted to fulfill one of the requirements to achieve the degree

Bachelor of Dentistry



#### **ARRANGED BY:**

M Gibraltar Wansha Wibisono J011191111

DEPARTMENT OF ORAL DISEASES FACULTY OF DENTISTRY HASANUDDIN UNIVERSITY MAKASSAR 2022

### THE EFFECTIVENESS OF SEA CUCUMBER IN INHIBITING CANCER OF THE MOUTH: LITERATURE REVIEW

#### **SKRIPSI**

Submitted to fulfill one of the requirements to achieve the degree Bachelor of Dentistry

## M GIBRALTAR WANSHA WIBISONO J011191111

DEPARTMENT OF ORAL DISEASES STUDY PROGRAM OF DENTAL MEDICINE FACULTY OF DENTAL MEDICINE HASANUDDI UNIVERSITY 2022

#### HALAMAN PENGESAHAN

Judul: THE EFFECTIVENESS OF SEA CUCUMBER IN INHIBITING

CANCER OF THE MOUTH: LITERATURE RIVEIW

Oleh: M Gibraltar Wansha Wibisono/J011191111

Telah Diperiksa dan Disahkan

Pada Tanggal: 11 april 2023

Oleh:

Pembimbing

Prof. Dr. drg. Sumintarti, MS

NIP. 19540101 198301 2 001

Mengetahui,

Dekan Fakultas Kedokteran Gigi

Universitas Hasanuddin

Irfan Sugianto, drg., M. Med.Ed., Ph.D

NIP: 19810215 200801 1 009

#### SURAT PERNYATAAN

Dengan ini menyatakan mahasiswa yang tercantum di bawah ini:

Nama : M Gibraltar Wansha Wibisono

NIM : J011191111

Judul Skripsi: Efektifitas Teripang Dalam Menghambat Kanker Pada

Rongga Mulut

Menyatakan bahwa judul skripsi yang diajukan adalah judul yang baru dan tidak terdapat di perpustakaan Fakultas Kedokteran Gigi Universitas Hasanuddin.

Makassar, 14 Februari 2023 Koordinator Perpustakaan FKG UNHAS

661121 199201 1 003

PERNYATAAN

Yang bertandatangan dibawah ini:

Nama: M Gibraltar Wansha Wibisono

NIM: J011191111

Dengan ini menyatakan bahwa skripsi yang berjudul "Efektifitas Teripang Dalam Menghambat Kanker Pada Rongga Mulut: *Literature Review*" adalah benar merupakan karya sendiri dan tidak melakukan tindakan plagiat dalam penyusunannya. Adapun kutipan yang ada dalam penyusunan karya ini telah saya cantumkan sumber kutipannya dalam skripsi. Saya bersedia melakukan proses yang semestinya sesuai dengan peraturan perundang-undangan yang berlaku jika ternyata skripsi ini sebagian atau keseluruhannya merupakan plagiat dari orang lain.

Demikian pernyataan ini dibuat untuk dipergunakan semestinya.

Makassar, 14 Februari 2023

M Gibraltar Wansha Wibisono

NIM. J011191111

#### KATA PENGANTAR

Segala puji dan syukur penulis panjatkan kepada Tuhan yang Maha Esa atas rahmat dan karunia-Nya sehingga penulis dapat menyelesaikan skripsi yang berjudul "Efektifitas Teripang Dalam Menghambat Kanker Pada Rongga Mulut: Literature Review".

Penulisan skripsi ini dimaksudkan untuk memenuhi salah satu syarat mencapai gelar Sarjana Kedokteran Gigi pada Fakultas Kedokteran Gigi Universitas Hasanuddin. Selama proses penulisan dan penyusunan skripsi ini, penulis menyadari banyak hambatan, namun berkat dukungan dan bimbingan dari berbagai pihak sehingga penulisan skripsi ini dapat terselesaikan dengan baik.

Oleh karena itu, dengan segala kerendahan hati penulis ingin mengucapkan terima kasih yang sebesar-besarnya kepada:

- Irfan Sugianto, drg., M.Med.Ed., Ph.D selaku Dekan Fakultas Kedokteran Gigi Universitas Hasanuddin.
- 2. **Prof. Dr. drg. Sumintarti, MS** selaku dosen pembimbing skripsi yang telah meluangkan waktu, tenaga, dan pikiran untuk memberikan bimbingan, ilmu, arahan, nasihat serta dukungan kepada penulis selama penyusunan skripsi sehingga skripsi ini dapat terselesaikan dengan baik.
- Drg. Nur Asmin Usman, Sp.PM dan Drg. Andi Anggun Mauliana Putri, Sp.PM selaku dosen penguji yang telah meluangkan waktunya untuk memberikan arahan, bimbingan, dan masukan dalam proses penyusunan skripsi ini.
- 4. **drg. Nurhaeda H. Ghalib B., SKG., Sp.KGA** selaku Penasehat Akademik atas bimbingan dan dukungan yang diberikan kepada penulis selama perkuliahan.
- Orang tua tercinta drg. Gunawan Wibisono dan Santiadji Mustafa, SE., M.SA., AK., CA yang selalu mendoakan, serta memberikan bimbingan dan dukungan terbaik dan bentuk morel maupun materiil kepada penulis.
- 6. Kaka tersayang Indah Lestari Zakaria serta adik-adik terkasih Endah Wulandari Wansha Wibisono dan Tribuana Tungga Dewi Wansha

Wibisono atas segala doa dan dukungan yang selalu diberikan selama penulis

menempuh pendidikan.

7. Teruntuk sahabat-sahabat seperjuangan penulis Baiq Dhinda Aulia Hidayati,

Nury Azkiyah Hamid, Virly Medina Andalusia, Adnan Akram, Safira Yuni

Puspita yang senantiasa turut mendoakan kelancaran dan memberi dukungan

dari awal perkuliahan hingga penyusunan skripsi ini.

8. Teruntuk sahabat sesama pembimbing penulis Aprilia Renata Sitangga yang

telah mendoakan, membantu dan memberikan motivasi selama penyusunan

skripsi

9. Teman-teman seangkatan ALVEOLAR 2019 yang tidak dapat disebutkan satu

per satu atas segala dukungan dan motivasi yang telah diberikan selama ini.

10. Semua keluarga dan teman-teman yang tidak dapat disebutkan satu per satu atas

dukungan dalam proses penyelesaian skripsi maupun pendidikan.

11. Seluruh Dosen, Staf Akademik, Staf Perpustakaan FKG unhas, dan Staf

Bagian Ilmu Penyakit Mulut atas bantuannya dalam penyusunan skripsi ini.

Akhir kata, penulis menyadari bahwa skripsi ini masih jauh dari kata

sempurna. Oleh karena itu, dengan kerendahan hati, penulis sangat

mengharapkan saran dan kritik. Semoga penulisan skripsi ini dapat bermanfaat

bagi pembaca dan masyarakat luas serta berguna untuk perkembangan ilmu

kedokteran gigi.

Makassar, 14 Februari 2023

M Gibraltar Wansha WibisonO

vii

#### **ABSTRAK**

### Efektifitas Teripang Dalam Menghambat Kanker Pada Rongga Mulut Literature Review

M Gibraltar Wansha Wibisono, Sumintarti

Mahasiswa S1 Fakultas Kedokteran Gigi Universitas Hasanuddin, Indonesia

Departemen Ilmu Penyakit Mulut S1 Fakultas Kedokteran Gigi Universitas

Hasanuddin

gatar.876@gmail.com

Latar Belakang: Kanker adalah suatu kelainan yang ditandai dengan pertumbuhan cepat, menyerbu ke dalam jaringan yang berada di sekitarnya dan dapat menuju ke daerah organ lain yang lebih jauh atau dengan kata lain metastasis. Kanker di rongga mulut merupakan salah satu dari enam jenis tumor yang paling sering ditemukan di dunia. Di Indonesia berdasarkan sumber Kementerian Kesehatan Republik Indonesia 2018 jumlah kasus penderita kanker bibir, rongga mulut, dan tenggorokan sebesar 4,5%, sedangkan jaringan lunak 11,4%. Faktor penyebab kanker rongga mulut sangat kompleks antara lain bahan karsinogenik, seperti tembakau, sigaret termasuk asap rokok, selain itu virus EBV, HPV, pola makan dan minum serta gaya hidup yang tidak sehat. Banyak penelitian yang sedang mengembangkan obat-obat herbal dengan efektivitas tinggi dan toksisitas rendah juga penelitian yang mendalam terhadap supresor onkogen dan gen resistensi obat. Dalam penulisan ini akan dipaparkan obat alami berbahan teripang sebagai salah satu penanganan dalam kanker. salah satu senyawa yang dimanfaatkan dari teripang adalah Holothurin A. Bahan aktiftersebut diketahui memiliki fungsi mencegah metastasis kanker hingga membunuh sel kanker payudara dan kanker ovarium. Tujuan: Mengetahui keunggulan dan efektivitas teripang yang mengandung senyawa yang dapat digunakan sebagai penghambat kanker di rongga mulut. Metode: Jenis penulisan adalah literature review, yang berasal dari jurnal penelitian online, seperti PubMed, Researchgate, Google Scholar, Science Direct, MedScape, dan sumber relevan lainnya. Hasil: Penelitian ini menunjukkan adanya pengaruh percobaan terhadap efektifitas senyawa antikanker atau pada sel kanker dengan menggunakan sampel dari beberapa jenis teripang (Holothuria), sehingga menjanjikan sebagai kandidat antikanker. Kesimpulan: teripang memiliki komponen bioaktif yang dapat menghambat kanker di rongga mulut MPS, Lectin, Omega-3, triterpenoid, dan saponin yang memiliki penggunaan efektif dalam mengurangi gejala efek samping serta meningkatkan kualitas hidup manusia.

Kata Kunci: Kanker, Teripang

#### **ABSTRACT**

### The Effectiveness of Sea Cucumbers In Inhibiting Cancer In The Oral Cavity Literature Review

M Gibraltar Wansha Wibisono, Sumintarti
Student of the Faculty of Dentistry, Hasanuddin University, Indonesia
Department of Oral Medicine, Faculty of Dentistry, Hasanuddin University
gatar.876@gmail.com

**Background:** Cancer is a disorder characterized by rapid growth, invaded into the surrounding tissue and can go to other organs that are more distant or in other words metastases. Cancer in the oral cavity is one of the six most common types of tumors in the world. In Indonesia, based on sources from the Ministry of Health of the Republic of Indonesia in 2018, the number of cases of cancer of the lips, oral cavity and throat was 4.5%, while soft tissue was 11.4%. The causative factors for oral cancer are very complex, including carcinogenic substances, such as tobacco, cigarettes including cigarette smoke, in addition to the EBV virus, HPV, eating and drinking patterns and an unhealthy lifestyle. Many studies are currently underway to develop herbal medicines with high effectiveness and low toxicity as well as indepth research on suppressor oncogenes and drug resistance genes. In this paper, a natural remedy made from sea cucumbers will be described as a treatment for cancer. One of the compounds used from sea cucumbers is Holothuria A. These active ingredients are known to have the function of preventing cancer metastasis to killing breast cancer cells and ovarian cancer. Objective: Knowing the advantages and effectiveness of sea cucumbers containing compounds that can be used as cancer inhibitors in the oral cavity. Methods: The type of writing is literature review, which comes from online research journals, such as PubMed, Researchgate, Google Scholar, Science Direct, MedScape, and other relevant sources. Hasil: This study shows the effect of experiments on the effectiveness of anticancer compounds or on cancer cells using samples from several types of sea cucumbers (Holothuria), so that they are promising as anticancer candidates. **Kesimpulan:** Sea cucumbers have bioactive components that can inhibit cancer in the oral cavity MPS, Lectin, Omega-3, triterpenoids, and saponins which have effective use in reducing symptoms of side effects and improving the quality of human life.

Keyword: Cancer, Sea Cucumber

#### **DAFTAR ISI**

TABLE Of CONTENTx
LIST OF TABLExi
LIST OF FIGURESxii
BAB I INTRODUCTION
1.1. Background
1.2. Probelm Statement
1.3. Objective
1.4. Benefits
BAB II. LITERATURE REVIEW
2.1. Sea cucumber4
2.1.1 Morphology4
2.1.2 Type of sea cucumber5
2.1.3 Components of bioactive substances6
2.1.3.1 Mucopolysacharida (MPS)8
2.1.3.2 Lectin8
2.1.3.3 Omega-38
2.1.3.4 Triterpenoid/steroid9
2.1.3.5 Saponin9
2.1.4 Benefits10
2.2 Cancer
2.2.1 Definition
2.2.2 Cancer in oral cavity12
2.2.2.1 Classification and staging of oral cancer12
2.2.2.2 Etiology of oral cavity cancer15
2.2.2.3 Pathomenchanism of oral cavity cancer16
Theoretical framework17

BAB III. WRITING METHOD	18
3.1. Writing method	18
3.2. Writing source	18
3.3. Method of data collection	18
3.4 Writing management procedures	19
BAB IV. DISCUSSION	20
4.1. Sythesis journal	20
4.2. Discussion sythesis journal	26
4.3 Analysis similarity and dissimilarity	32
BAB V. CLOSING	34
5.1. Conclusion.	34
5.2. Suggestion	34
BIBLIOGRAPHY	35

#### LIST OF TABLE

Tabel 3.1 Data source	18
Tabel 3.2 Criteria data collection	.19
Tabel 4.1 Synthesis journal	.20
Tabel 4.2 Yield of fraction hexane, fraction ethyl acetate and fraction methanol water ( <i>H. atra</i> )	.26
Tabel 4.3 Nilai IC50 Doxorubicin, fraksi heksan, fraksi etil asetat dan fraksi metanol-air terhadap sel HeLa (A) dan sel MCF-(B)	27
Tabel 4.4 Graphic of T47D cells viability after treatment	28
Tabel 4.5 Viability percentage of SP-C1 tested with extracts and fractions of black sea cucumber	30
Tabel 4.6 Cell absorbance average measured by using ELISA Reader on the wavelength of 550 nm	30

#### LIST OF FIGURE

Gambar 2.1 Sea cucumber	5
Gambar 2.2 Leukoplakia of the floor of the mouth	.14

### CHAPTER 1 INTRODUCTION

#### 1.1 Background

Various cases in the dental and oral field do not only discuss the teeth, but covers cavity mouth consisting of periodontitis and hard tissue mucosal soft. Diseases of the mucous tissue in oral cavity has become a necessary thing attention especially on the increase in the number of deaths caused by malignancy in cavity mouth. One of the malignancies in the oral cavity, namely cancer. Cancer is a disorder characterized by rapid growth, invade into the surrounding tissue and can go to the area of other organs Which more distant or in other words metastases. Metastases disease malignant the going to to organs other Can through various method, that is *hematogenous* and *lymphogen*. Cancer Biologically it can be caused by a failure in the process of apoptosis so that it can cause the cancer cells to survive autonomously in body. <sup>1</sup>

Cancer in cavity mouth is Wrong One from six type that tumor most often found in the world. In Indonesia based on Ministry sources Health of the Republic of Indonesia 2018 the number of cases of cancer of the lips, oral cavity and throat by 4.5%, while soft tissue 11.4%. Causes of cavity cancer mouth very complex, including carcinogenic substances, such as tobacco, cigarettes, including smoke smoking, in addition to the EBV virus, HPV, eating and drinking patterns and unhealthy lifestyles. Given the increasing number of oral cancers, it is estimated that the number of cases in Indonesia on which year will come increased. Even so, there have been many studies that are developing herbal medicines with high effectiveness and low toxicity as well as in-depth research on suppressors oncogene And gene resistance medicine. With Keep going emergence drug anti cancer new Also discovery of herbal medicines, such as ingredients sea cucumbers then this can make medicines herbs increasingly involved big. <sup>1</sup> In this paper, a natural remedy made from sea cucumbers will be described as Wrong One handling in cancer. As for definition from Sea cucumber is the name

given to the *Holothuroidea invertebrate*. There are about 1,400 species of sea cucumbers worldwide. Apart from being used as food, people in the country also have it use sea cucumbers as medicine because they are believed to have health benefits. Masteria said, one of the compounds utilized from sea cucumbers is *Holothurin* A. Active ingredientsIt is known to have the function of preventing cancer metastasis to killing cancer cells breast And cancer ovary. Head Hall Bio Industry Sea LIPI Ratih Pangestuti disclose active ingredients for cancer prevention by utilizing marine organisms intended to kill free radicals in the body. Thus, it can improve resilience body. <sup>2</sup>

So, it is known that sea cucumbers can be used as a drug in inhibiting cancer so that in this writing it refers to several references to research results regarding the superiority of sea cucumbers in inhibit cancer in cavity mouth.

#### 1.2 Problem statement

Based on this background, it appears that there is an alternative in treating cancer by utilizing marine life in this case, namely sea cucumbers. In its effectiveness in inhibiting cancer has been referred to several references, so the formulation of the problem from this *literature review*, namely the effectiveness sea cucumbers in inhibiting cancer in the oral cavity and how is the effectiveness of sea cucumbers in inhibiting cancer in the oral cavity?

#### 1.3 Objective

Based on the formulation of the problem, the purpose of writing this *literature review* is:

- 1. Know effectiveness sea cucumbers Which contain compound Which can used inhinder cancer in the oral cavity.
- 2. Knowing the effectiveness of deep sea cucumbers inhibit cancer in the oral cavity.

#### 1.4 Benefit

Based on the background of the problem, the benefits are: expected from this *literature review*, among others:

- 1. Add And expand study scientific results studies *literature reviews* about superiority sea cucumbers in inhibiting cancer in cavity mouth.
- 2. Give information to public about effectiveness sea cucumbers in inhibiting cancer in the cavity mouth.
- 3. Become a reference material for the development of knowledge on topics and problems related to the effectiveness of sea cucumbers in inhibiting cancer in cavity mouth .

#### **CHAPTER II**

#### LITERATURE REVIEW

#### 2.1 Sea cucumbers

#### 2.1.1 Morphology

Indonesia is an archipelagic country the world's largest with 17,504 islands with coastline length of 81,000 km with wide waters sea around 5.8 million km2 (75% of the total area of Indonesia), stretching on the equator , causing Indonesia to have source Power very rich and varied Good for land area nor sea , so known as a mega biodiversity country. Riches biological the need utilized the best For welfare of the Indonesian people.

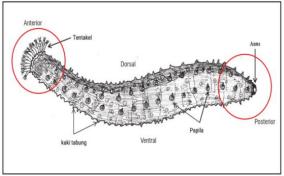
one \_ results sea that has mark economical important is sea cucumbers or also called \_ sea cucumber , teat fish and sea ginseng . A number of factor important cause \_ in a manner economy sea cucumbers own mark important that is as source biopharmaceuticals potential from results sea and as food health that is material raw various industry in various countries. Sea cucumbers is one \_ commodity subsector exports enough fishing \_ potential . Utilization sea cucumbers in Indonesia as material food compared product fishery other belong low and less popular , caused sea cucumbers own mark low aesthetics \_ seen from form physique impressed sea cucumbers disgusting , however thereby sea cucumbers indeed contains sufficient protein high .

Sea cucumbers is animal No boned behind with body shaped cylinder elongated with oral and aboral lines as connecting axis \_ anterior and posterior parts . Form the resemble cucumber so that sea cucumbers known with Name cucumber sea ( *sea cucumber* ).

The mouth and anus are located at the ends axis opposite, ie mouth anteriorly and anus posteriorly, at around mouth sea cucumbers there is tentacles that can

extended and pulled with fast . Tentacle is leg modification working tube  $\_$  For catch food .  $^{3,4}$ 





Morfologi teripang secara umum

Figure 2.1 Sea cucumbers

Surface body sea cucumbers No ciliated and enveloped layer thick chalk \_ influenced age . Condition elongated mouth \_ to the anus there are five rows of tube feet ( <code>ambulaceral</code> ), three tube feet \_ suckers ( <code>trivium</code> ) are in the stomach role in movement and attachment . Two rows of tube feet found on the back ( <code>bivium</code> ) as tool respiration . Layer lower skin own one layer of muscle circular and five layers of muscle . on layers lower muscle there is cavity body that contains organs \_ such as gonads and intestines. <sup>5,6</sup>

#### 2.1.2 Type sea cucumbers

Amount species Sea cucumbers in the world about 2000 species with area deployment very broad sea cucumbers. Color sea cucumbers different, ie white, black, brown greenish, yellow, gray, orange, purple even some are striped. From several type sea cucumbers the only three genera of sea cucumbers found in Indonesia, namely the genera *Holothuria*, *Muelleria* and *Sticopus*. Species found \_ are 23 species and only five species (from the genus *Holothuria*) have been exploited and exploited as well as have mark economical important. Fifth type sea cucumbers the is sea cucumbers black (*Holoturia edulis*), sea cucumber sap or rivet (*Holothuria vacabunda*), sea cucumbers red (*Holoturia vatiensis*), sea cucumbers brown (*Holoturia marmorata*), and sea cucumbers sand (*Holothuria scabra*) which is most species \_ cultivated and traded in Indonesia.

#### 2.1.3 Components of Bioactive Substances

Sea cucumbers are a bioactive source which has antibacterial, antifungal, anticancer, antihypertensive, antithrombotic, antinociceptive and anti-inflammatory properties. Sea cucumbers are detritus-eating animals, that is, they eat by sweeping sand into their mouths. The slow movement of sea cucumbers causes these animals to have an efficient body defense mechanism, namely by releasing *holothurin* which is toxic and can paralyze small animals. *Holothurin* is secreted by special glands known as *cuviers*. Research on *holothurin* began in the early 1920s and began intensively in the 1950s. One of the main types *of holothurin* from sea cucumbers which is efficacious in wound healing, postpartum care and as an antifungal are saponins.

Sea cucumber bioactive ingredients are also known as antioxidants which help reduce damage to cells and body tissues. The antibacterial and antifungal properties of sea cucumbers can enhance their ability for treatment purposes skin. Sea cucumbers are also known to have antinociceptive (painkilling) and anti-inflammatory (against inflammation and reduce swelling) effects. Research

that has been conducted in several areas, especially in Malaysia on residents in Kudat, Semporna, Setiu, Kuantan, Pekan, and Pangkor Island proves the efficacy of sea cucumbers as an antihypertensive agent. Kaswandi and Lian reported the active ingredients produced by *Holothuria* sp. As antibacterial and antifungal. <sup>8</sup>, <sup>9</sup>Based on the results of this study it was concluded that the active ingredient from the sea cucumber *Holothuriatubolosa* can inhibit the growth of *Saccharomyces cerevisiae*.

Kustiariyah reported that the bioactive of sea cucumber ( *Holoturia scabra* ) can inhibit the growth of *Candida maltosa*. <sup>9</sup> Besides containing antibacterial and antifungal properties, sea cucumbers are also reported to contain various unsaturated fatty acids such as linoleic, oleic, eicose pentaenoic (EPA), and docosahexaenoic (DHA). Several studies also show the potential of sea cucumbers as anti- cancer. Sea cucumbers also contain antioxidants in the form of saponin glycosides. This component has a structure similar to the active compounds of ginseng and ganoderma. Anticancer compounds in the form of terperoids, proteins, saponins, and polysaccharides are also found in sea cucumbers. The results showed that sea cucumbers contain the active compound triterpene glycosides which can inhibit cancer growth in lymphoid cells, human lung cancer cells, cervical cancer cells , and mouse melanoma at a concentration range of 0.38–0.46 mg/ml. <sup>10</sup>

Sea cucumbers are also reported to contain lectins, which are non-immunogenic proteins or glycoproteins Which can inhibit cancer growth. The compound at a concentration of 50 µg can agglomerate and kill cancer cells . Research results medical lately this is on sea cucumbers *Stichopus japonicus* show that almost in all part her body contain a number of type of " *mucopolysaccharida* " acid that has effect special to growth , recovery ( *recovery* ) of sick , anti-imflammation , formation bones , and prevention / delay to aging tissue , as well as " *arteriosclerosis* ". *Mucopolysaccharide* is also powerless anticancer drug . <sup>1</sup>

#### **2.1.1.1 Mucopolysaccharides (MPS)**

Body and skin sea cucumbers *stichopus japonicus* a lot contain sour mucopolysaccharide one \_ useful content \_ For healing disease kidney , anemia, diabetes, lung wet , anticancer , anti- inflammatory , prevention aging network body as well as prevent arteriosclerosis. <sup>12</sup>

#### **2.1.1.2** Lectins

Lectin is a sugar with activity normal anticancer \_ We find inside \_ plant . In chemical assays , the lectins are isolated from wall body sea cucumbers is a Type Non - Blood - specific Lectin that agglutinates blood type A, B, AB, and O. besides that , No - Blood - Lectin classified as a complete lectin , no need more testing formerly with trypsin for know activity lectins . Lectins are also found effective oppose cancer muscle mice and cancer lungs humans at levels of 5 and 50 micrograms, respectively. 12

#### 2.1.1.3 Omega-3

Sea cucumbers as one \_ product <code>seafood</code> has content Omega-3 fatty acids are needed by the body . Deep omega-3 fatty acids matter This These are EPA ( <code>eicosapentanoic acid</code> ) and DHA ( <code>docosahexaenoic acid</code> ). Relative content of EPA and DHA high , respectively 25.69% and 3.69%. EPA value high \_ shows speed \_ \_ sea cucumbers in repair network damaged and obstructed causative prostaglandin formation inflammation high . While DHA, fatty acids in sperm and brain , and the retina of the eye . When DHA intake is high can lower

triglycerides blood reason disease heart. However, can cause

decreased brain serotonin trigger disease Alzheimer's and depression. 12

#### 2.1.1.4 Triterpenoids/ steroids

Triterpenoids and terpenoids were also detected in the extracts rough  $\it{H.atra}$  . Triterpenoid positive test results are marked with exists formation color red until orange . Triterpenoids and terpenoids in sea cucumbers own benefit as anti- inflammatory , anticancer , sedative , and insecticide.  $^{20}$  Compound active sea cucumbers triterpenoid / steroid group can hinder growth cancer in cells cancer lungs humans and cells cancer cervix with IC50 2.38 and 2.46  $\mu g/$  mL.  $^{13}$ 

#### **2.1.1.5 Saponins**

Saponins (triterpenes glycosides) is glycosides complex triterpenes with molecule lots of carbohydrates Found in plants, bacteria nor organism lots of sea own activity biologics, like antifungal, antibacterial and anticancer. Saponin content in sea cucumbers *H. atra* Lots found in the wall body with a number of saponins (triterpenes glycosides) that have identified, including: (1) holothurin B1 (2) holothurin B2 (3) holothurin B3 and (4) holothurin B/B4 which have activity as anticancer. 14,15

#### 2.1.3 Benefits

Since ancient times sea cucumbers has known nutritious as medicine . this \_ No not only trust a number of public such as Korean and Chinese , but also various nation in the world. One of them is public Malaysian fishermen who are common drink essence sea cucumbers before go to sea this \_ done Because essence sea cucumbers the effect the tonic can strengthen the body. Beside In addition , sea cucumbers are also used as drug wound light , sick joints , inflammation , asthma , lungs , pressure blood height , and pee sweet . As source of protein, sea cucumbers speed up healing wound in after surgery , normal delivery , and caesarean section. Sea cucumbers can too function For strengthen bones and joints . Content chondroitin sulfate prevent thinning joints maker inflammation . Compound That fix and build return bone prone , forming eroded joints \_ consequence accidents , collisions , and excesses body weight without effect side .

Besides being able to cure various diseases, sea cucumbers also have the ability to regenerate cells and this is the main reason sea cucumbers are used to cure various diseases. Besides capable regenerate sel, sea cucumbers are also rich in content nutrition. Compound active the most form excellent antioxidant \_ For repair cell body human. efficacy sea cucumbers chase away cancer has proved Tong Y, et al, from the Pharmacology Division Anticancer, State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, China. Tong isolate sulfated saponins from sea cucumbers Pentancta the so-called quadrangulari philinopside A. With inject 2-10 microliters philinopside A in rat aorta, able prevent formation

vessels blood micro new cells (angiogenesis). cancer . As a result , cell cancer No get supply nutrition so that cell fail growing and finally die . That result prove that philinopside A on sea cucumbers potentially as anticancer .  $^{12,15,16}$ 

#### 2.2 Cancer

#### 2.2.1 Definition

Cancer or carcinoma (Greek *karsinomos* ) is any formation of new tissue that is abnormal and malignant ( malignant ). The cancer cells will infiltrate into the surrounding tissues and destroy them. <sup>17</sup> Cancer is a disease caused by the growth of body tissue cells that are not normal, develop quickly, are uncontrollable and continue to divide. Cancer is also disease No marked infectious \_ with growth cell in a manner constantly and no under control so that can damage network surrounding as well as can metastasize. Cell cancer characteristic fierce and can grow from every type cells in the body human. <sup>18</sup> Cancer or malignant tumors happen consequence exists growth cells network abnormal body, caused by neoplasia, dysplasia, and hyperplasia. Neoplasia is condition cells present in the tissue proliferate in a manner abnormal and invasive, dysplasia that is condition cells that don't develop normally with indication exists changes in the nucleus (cell nucleus ), and hyperplasia is condition normal cells in the tissue experience growth excessive. 19

#### 2.2.2 Cancer in the Oral Cavity

The oral cavity is a cavity in the mouth that is bounded by the red border of the lips, tongue, lining of the inner cheek called the cheek mucosa, palate, and gums. Cancer that occurs in the oral cavity is a growth of cancer cells in the oral cavity including the lips, tongue, salivary glands, and other parts of the mouth. Oral cavity cancer is also a serious problem and when combined with throat cancer, it is the sixth most reported case in the world. <sup>3</sup> Oral cavity cancer is a chronic multifactorial disease caused by interactions between internal factors, namely nutrition and genetics, and external factors, including chronic exposure to sunlight and *human papilloma virus* and factors such as smoking, excessive alcohol consumption, chewing betel nut, and delays in diagnosis. dentist. Cases of oral cancer in Indonesia are still high followed by increasing mortality from cancer.

There are also cancers of the oral cavity that start from untreated teeth or chronic wounds due to improperly positioned dentures. So that constant irritation due to the sharp edges of the teeth that will break can cause an additional risk of developing malignant tumors in the oral cavity. <sup>20,21,22,23</sup>

#### 2.2.2.1 Classification and Staging of Oral Cavity Cancer

Based on abnormal cell growth, oral cancer is divided into; <sup>24</sup>

a) Benign Tumors of the Oral Cavity
 Benign tumors of the oral cavity can originate from various cells, namely;

- 1. Eosinophilic granuloma 9. Neurofibromas
- 2. Fibromas 10. Papillomas
- 3. Granular cell tumors 11. Condyloma acuminatum
- 4. Keratoacanthoma 12. Verruciform xanthoma

5. Leiomyomas

- 13. Pyogenic granuloma
- 6. Osteochondroma
- 14. Rhabdomoma

7. Lipomas

- 15. Odontogenic tumors
- 8. Schwannomas

#### b) Pre-cancerous Lesion of the Oral Cavity

#### 1) Leukoplakia

Leukoplakia is a lesion in the form of white plaque attached to the oral mucosa. These lesions are difficult to distinguish from other white plaque lesions caused by other factors, such as infection, inflammation, or other causes. This lesion can develop into oral cancer depending on the causative factors, such as the degree of dysplasia, the size of the leukoplakia, and the progression of the lesion. <sup>25</sup>

Dysplasia in the basal third of the epithelium is mild dysplasia, more than half of the epithelium is moderate dysplasia, and severe dysplasia covers the entire depth of the epithelium. Severe dysplasia with

carcinoma *in situ* has a 43% ratio to squamous cell carcinoma. <sup>26</sup>



Figure 2.2 Mouth Floor Leukoplakia

#### 2) Erythroplakia

Erythroplakia are bright red plaques on the oral mucosa, which may or may not be raised. These lesions may not appear in all parts of the oral cavity, often on the floor of the mouth, soft palate, ventral tongue, and *tonsillar fauces*. Erythroplakia has an atrophic epithelium and a less keratinized layer, which can lead to hyperplasia. The reddish color in erythroplakia is caused by the thin layer of the epithelium so that *microvasculature structures appear*. Erythroplakia needs to be treated immediately because of the risk of malignancy. <sup>24</sup>

#### 3) Erythroleukoplakia

Erythroleukoplakia is a combination of oral mucosal plaques marked with red and white areas. Erythroleukoplakia is rare, but has the potential to become malignant. <sup>24</sup>

#### c) Oral Cavity Cancer

a) Squamous Cell Carcinoma of the Oral Cavity (SCCRM)

As much as 90% of oral cancers are KSSRM which develop from squamous cells with characteristic flat, scaly appearance that lines the oral cavity and pharynx. The development of squamous cells can go through several stages, from metaplastic, displaced, to carcinoma in situ. Named *carcinoma in situ*, which means cancer cells are only present in the outer layer of the epithelium. Position lesion carcinoma cell squamous get on the lips bottom (30%-40%), tongue (25%), and base mouth (20%). Carcinoma on the tongue, 75% in section frequent tongue \_ move especially on the edges tongue and 25% occurs at the base tongue. Expansion KSSRM invasion can contralateral and bilateral. carcinoma cell squamous on the lips bottom and bottom mouth will invade the submental nodes, whereas carcinoma in the posterior region of the mouth will invade the superior iugular node. <sup>24,26</sup>

#### b) Minor Salivary Glandular Carcinoma

This cancer develops from the glands that line the skin of the mouth and pharynx. The types of cancer are adenoid cystic carcinoma, mucoepidermoid carcinoma, and *polymorphous low-grade adenocarcinoma*. <sup>24</sup>

#### 2.2.2.2 Oral Cavity Cancer Etiology

The causes that can trigger oral cancer, namely tobacco, alcohol, iron deficiency Plummer-Vinson syndrome, UV light, AIDS, radiation, chemotherapy, and chronic irritation. Of these various causes, tobacco causes a significant risk of developing oral cancer. Intensity

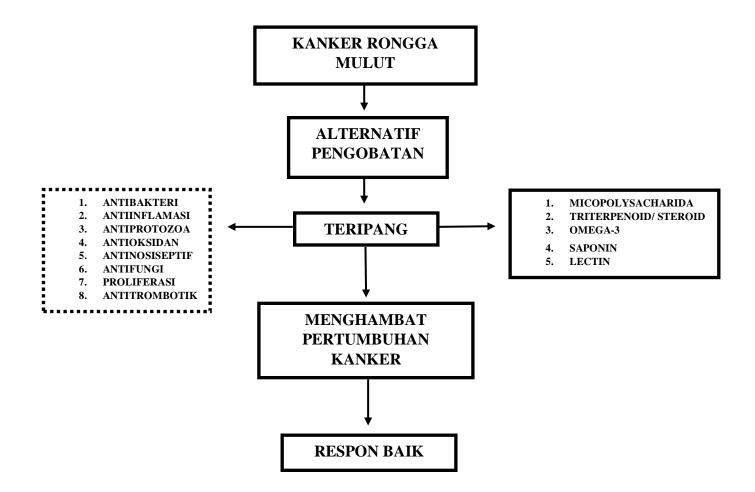
Tobacco use due to smoking affects the palatal and lingual parts of the oral cavity. In cigarettes there are doses of carcinogens that greatly affect the cause of oral cancer. Tobacco use, whether it produces smoke or not, still poses a risk of developing oral cancer. Another cause of oral cancer that has been tested by research, namely alcohol, although it does not contain carcinogens, can increase the risk of developing oral cancer. Research showing the existence of Human Papilloma Virus (HPV) subtypes 16 and 16 in squamous cells of oral cancer indicates a potential role for viruses in oral cancer. <sup>27</sup>

#### 2.2.2.3 Pathomechanism of Oral Cavity Cancer

Cancer grows and develops gradually. The growth of cancer begins when one cell out of many normal cells suddenly develops a genetic mutation. Then the cell will undergo another mutation to cause the cell size to become abnormal, this condition is called the *dysplasia phase*. Dysplasia will continue to develop from mild, moderate, severe dysplasia, and eventually become cancer *in situ*, namely cancer that has not penetrated the boundaries of the tissue where the cancer grows. Several years later, cancer cells will penetrate the basal tissue and infiltrate the surrounding tissue, this condition is known as *invasive cancer*. Cancer cells can also penetrate blood vessels or lymph vessels, then along with the bloodstream the cancer is carried to other parts of the body. Cancer cells that spread to new places have the same characteristics as their parent cancer cells. The cause of cancer to other tissues is called spread

or metastases. It is usually difficult to avoid the risk of death when metastases have occurred. <sup>28</sup>

#### **Theoretical framework**



Note:

: reviewed

: not reviewed