A Review on Less Explored Plants with Anticancer Activity

By

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A thesis submitted to the Department of Pharmacy in partial fulfillment of the requirements for the degree of
Bachelor of Pharmacy (Hons.)

Department of Pharmacy
Brac University
March 2020

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Declaration

It is hereby declared that

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3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
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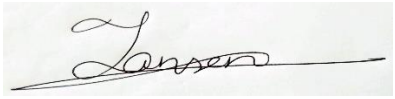

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Approval

The thesis titled “A review on less explored plants with anticancer activity” submitted by Mohammed Tansen Al Nahid (13146018) of Spring 2013, has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy (Hons.) on 2nd March, 2020.

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Ethics Statement

This study does not involve any kind of animal and human trials.

Abstract

Cancer is a disorder that is very complicated. Most tumors tend to be incurable. However, appropriate measures can reduce the risk of cancer. Cancer is a very costly illness to manage in a low-income nation such as Bangladesh. Many clinically effective plant-related compounds have been a key source of anticancer agents. Vinblastine, vincristine, derivatives of camptothecin, topotecan and irinotecan, etoposide and paclitaxel are among these. The planet also has so many plants that are less known or unexplored. We address in this review paper the less studied plants from which we can develop anticancer drugs. Detailed information about the part used, the use of the extract, the model type, the types of cancer cell lines tested, etc. of less explored plants are reported. These plants are still used for various cancer cell types. Such trees, as they have strong efficacy in anticancer activity, are all potential candidates for *in vivo* studies.

Keywords: Cancer; Anticancer activities; Plants; Less explored plants

Dedication

This work is dedicated to my parents for their continuous support and motivation.

Acknowledgement

All praise belongs to Allah (SWT) for giving me the strength, patience and good health to complete my project work and the courses necessary to complete a Bachelor of Pharmacy (B.Pharm) program.

I would like to express my heartiest gratitude to my respected research supervisor **Dr. Raushanara Akter**, Associate Professor, Department of Pharmacy, Brac University for her unconditional guidance, inspiration, caring, commitment to mentoring me in my research work. She has always encouraged me whenever I face problems.

After that, I would like to express my gratitude to my project supervisor **Md. Tanvir Kabir**, Senior Lecturer, Department of Pharmacy, Brac University for his instructions, guidance & supervising my work throughout the whole project. He provides effective feedback or comments on my research study.

I would also be grateful to **Dr. Hasina Yasmin,** Professor and Coordinator, Department of Pharmacy, BRAC University, for her willingness to give any kind of support to the project students and for giving me her invaluable comments and suggestion.

Then I would express my sincere & deepest gratitude to **Dr. Eva Rahman Kabir**, Professor and Chairperson, Department of Pharmacy, Brac University for her encouragement & support in every step of my work.

I would express my heartiest gratitude to my parents & family members for all of their support throughout my work & every person who helped me in any case while doing the research work.

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List of Acronyms

TP53	Tumor Protein 53
CRC	Colorectal Carcinoma
BRCA1	Breast Cancer Type 1
BRCA2	Breast Cancer Type 2
PTEN	Phosphatase and tensim
CASP8	Caspase protein
FGFR2	Fibroblast Growth Factor-2
MAP3K1	Mitogen Activated Protein Kinase 1
LSP1	Lymphocyte Specific Protein
CHEK2	Checkpoint Kinase 2
BRIP1	BRCA1 Interacting Protein
PALB2	Protein
PTPN12	Tyrosine Protein Phosphatase Non-receptor Type
LRP6	Low-Density Lipoprotein Receptor-Related Protein 6
MUTYH	MutY DNA Glycosylase
RB1	Retinoblastoma Protein
KS	Kaposi Sarcoma
AIDS	Acquired Immune Deficiency Syndrome
HIV	Human Immune-Deficiency Virus
KSHV	Kaposi's Sarcoma Associated Herpesvirus
HPV	Human Papillomavirus
PC	Pancreatic Cancer
VCM	Vinyl Chloride Monomar
PVC	Polyvinyl Chloride
HGSOC	High Grade Serous Ovarian Cancer
PARP	Poly-ADP-Ribose Polymerase
PAHs	Polycyclic Aromatic Hydrocarbons
ICDDRB	International Centre for Diarrhoeal Disease Research, Bangladesh
BSMMU	Bangabandhu Sheikh Mujib Medical University (Bangladesh)

DNA	Deoxyribonucleic Acid
ACT	Adoptive Cell Therapy
CTLA-4	Cytotoxic T-lymphocyte Associated Protein
PD-1	Programmed Cell Death Protein 1
CD152	Cytotoxic T-lymphocyte Associated Protein 4
T-VEC	Talimogene Laherparepvec
FDA	The Food and Drug Administration of the United States
IL-2	Interleukin-2
CRISPR	Clustered Regularly Interspaced Short Palindromic Repeats
WHO	World Health Organization
Hep-G2	Hepatoma G2
HeLa	Henrietta Lacks
MCF-7	Michigan Cancer Foundation-7
HL-60	Human Leukemia Cell
STAT	Signal Transduces and Activator
NF-KB	Nuclear Factor Kappa-Light-Chain-Enhancer of Activated B Cells
BRs	Brassinosteroids
ER	Estrogen Receptor
EGFR	Epidermal Factor Growth Receptor
HER2	Human Epidermal Growth Factor Receptor 2
AR	Androgen Receptor
LNCaP.	Lymph Node Carcinoma of the Prostate
Bcl-2	B-cell Lymphoma 2
HDAC	Histone Deacetylases
NPs	Nanoparticles
LC_{50}	Lethal Concentration 50
mTOR	Mammalian Target of Rapamycin
PSCs	Pancreatic Star Cells
GL1	Gliome Oncogene 1
HT29	Human Colon Adenocarcinoma Cells

HPLC	High Performance Liquid Chromatography
NCl-H460	Human Non Small Lung Cancer Cells
OVCAR-3	Ovarian Carcinoma Cell Line
BXPC-3	Pancreatic Cancer Cell Line
SK-N-SH	Human Neuroblastoma Cell Line
IMR-32	Human Neuroblastoma Cell Line
DLA	Dalton Lymphoma Ascites Cell
PBS	Phosphate Supported Saline
C2C12	Immortalized Mouse Myoblast Cell Line
FBS	Fasting Blood Sugar
DMSO	Dimethyl sulfoxide
HOCL	Hypochlorous Acid
MKN74	Stomach Cancer Cell Line

Chapter 1

Introduction

1.1 Cancer

Cancer is a threatened human disorder. It spreads through lifestyle shifts, survival and a dangerous environmental divergence. Cancer can cause excessive growth of human body cells. For this extreme proliferation, the organs are affected by cancer can't work properly and the patient can die from this serious condition. Cancer drugs are not well known as there are so many side effects of the medications currently available (Gennari et al., 2007). The World Health Organization has identified around 18 million new cases of cancer worldwide, which resulted in some 10 million deaths in 2018 (Bray F., Ferlay J., Soerjomataram I., Siegel R.L., Torre L.A., 2018). 26 million new cancer cases and 17 million cancer deaths are expected to rise each year by 2030 (Thun et al., 2009).

Bangladesh is the world's ninth-largest country, with a population of over 142 million. There are almost 15 lakhs of cancer patients in Bangladesh. However, every year around two lakh people are diagnosed with cancer. Males suffer most from lung cancer and cancer of the mouth called the oropharynx. The important aspect that is counted as the most prevalent cancer in women is cervical and breast cancer. Females may also undergo certain types of cancer, such as oropharyngeal or prostate, lung or esophageal cancer (SyedMd Akram Hussain, 2013).

The cell which we all know is the basic unit of life. Normally, the cells divide continuously in a healthy person's body and replace the dead ones in a controlled manner. Usually, the dead cells are replaced by shedding away (in case of skin). It can be buried inside the bone marrow. Additionally, it can be steered with the excreta. But it doesn't happen in the cancer cells. Cancer cells are not theoretically controlled and grow very fast every day. On average, a normal cell can live 7 to 10 years in a human. In comparison, cancer cells are larger than count. Cellular cancer is persistent. Moreover, they will not die. It's going to build up in our bodies. It then causes so many accidents that are dangerous and creates serious health risks (Wensink, 2016).

The term cancer was originally invented by Hippocrates, the "Father of Medicine." He named carcinos and carcinoma, which defined ulcer and non-ulcer causing tumors. A Roman doctor named Celsus changed the name instead and called it Cancer (Raichel Nivetha et al., 2019). Typically cancer is caused by mutations in two genes. Oncogenes that lead to cancer play an

important role in tumor suppression but other genes also suppress tumors. Cell cancer spreads across the body to metastasize blood vessels and lymph systems (Alfred G.Knudson, 2001).

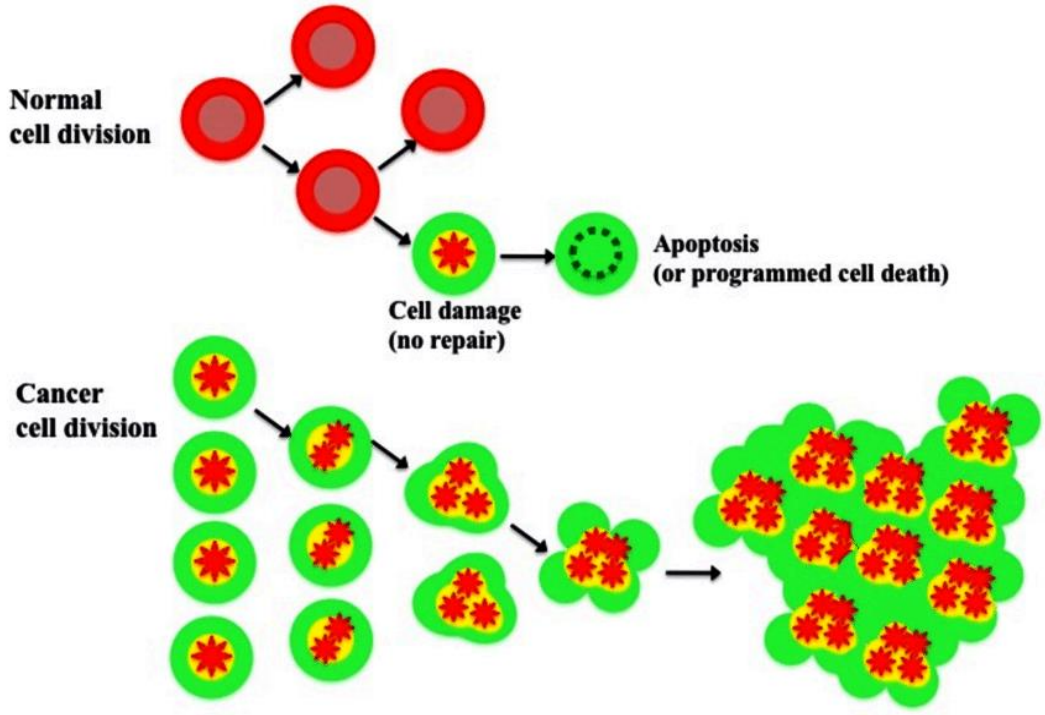


Figure 1: The difference between Normal cell vs Cancer cell division (Khamenehfar, 2015).

There's so much reason why cancer has developed and advanced. Human cells can proliferate by the "Hayflick Limit" definition. The Hayflick Limit describes the processes of cellular aging. The idea is that just replicating a traditional human cell. It breaks 40 to 60 times until it can no longer differentiate. Then, these cells grow old and gradually decompose through programmed cell death or apoptosis (Seluanov et al., 2009). Because of the loss of touch inhibition, it is a result of the loss of a function that typically preserves tissue equilibrium in our bodies (Hanahan & Weinberg, 2011). The control mechanism is inhibiting communication. Cells keep growing to form a substratum. When the cell occupies the whole substratum, the normal cells stop replicating. Unmanageable cancer cells can spread very quickly. However, that implies the possibility of uncontrollable cell division (Bartlett, 2014).

1.2 Cancer Types

Two ways of grouping cancer are: by the type of tissue in which the disease begins and by the essential place, or the area in the body in which the tumor originates.

1.2.1 Histological classification

From a histological angle, many diverse growths are gathered into six noteworthy classifications and the classification is as follows:

- Carcinoma
- Sarcoma
- Leukemia
- Lymphoma
- Melanocytes
- Mixed types

1.2.1.1 Carcinoma

The perilous neoplasm of the body's inside or outside coating is called an epithelial source or tumor's carcinoma. There are two types of carcinomas: adenocarcinoma that occurs in the organ and malignant growth in the squamous cells that begins on the epithelium scale. Adenocarcinoma happens in mucous films and is exhibited as a plaque-like thickened white mucosa. The delicate tissues, where they exist, are regularly proficiently disseminated. In any case, squamous cell carcinomas additionally happen in numerous pieces of the body. Numerous carcinomas can harm organs or organs from the emanations.

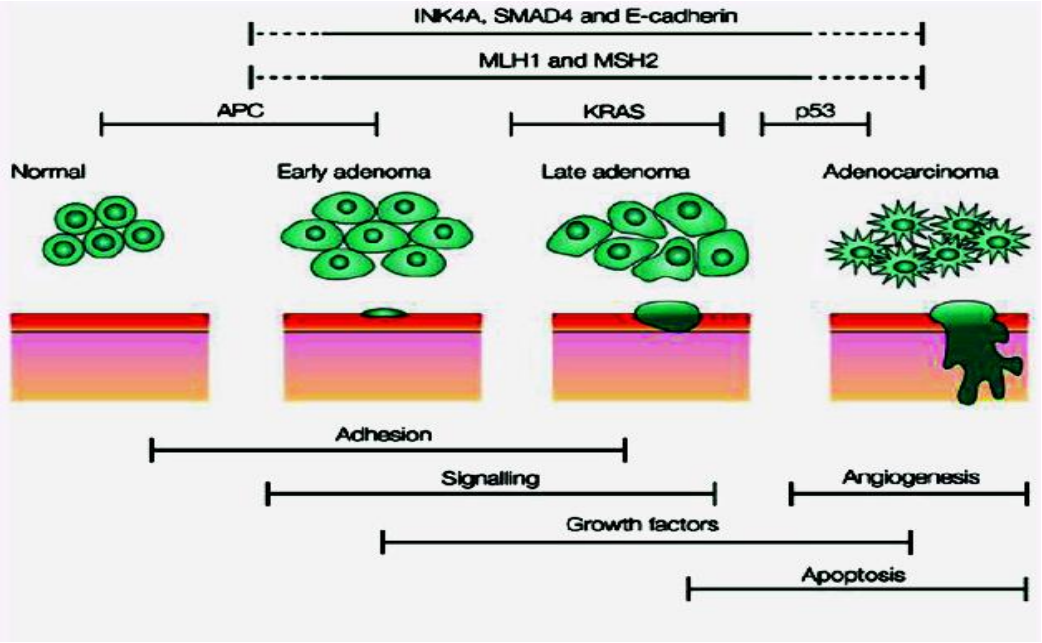


Figure 2: The sequence of Adenoma-carcinoma (Armaghany et al., 2012).

1.2.1.2 Sarcomas

The bone, muscle, and ligament are available in the connective tissue. Osteosarcoma is a disease of the bones related with sarcomas. Instances of sarcomas incorporate to mesothelial sarcomas or mesothelioma (membrane covering of the body hole), angiosarcomas or hemangioendothelioma (vein), chondrosarcoma (muscle skeleton), rhabdomyosarcoma (muscle skeleton), leiomyosarcoma (muscle smooth), liposarcoma (adiposis or greasy tissue), myxosarcoma (connective crude incipient organism tissue), astrocytoma or glioma (connective neurogenic tissue).

1.2.1.3 Leukemia

The term leukemia is utilized to allude to bone marrow malignancy. In Greek, "white blood" signifies leukemia. This illness is to a great extent liable for the overproduction of youthful white platelets. Such youthful white platelets can't play out their work and can make the patient infectious. Leukemia may incorporate with granulocytic or myalgia leukemia (a myeloid and granulocytic white platelet arrangement), and polycythemia or erythema. Leukemia additionally influences red platelets and can prompt poor blood thickening and laziness.

1.2.1.4 Lymphomas

Lymphomas are delivered basically by lymph hubs, cylinders, centers, and bodies (strikingly tonsils, thymus, and spleen), which purge the body's common fluids and cause pathogenic battle against white platelets or lymphocytes. Indeed the lymphomas are arranged into two classes: the Hodgkin and the Non-Hodgkin. Reed-Sternberg cells are available in Hodgkin lymphoma which is missing from Hodgkin lymphoma.

1.2.1.5 Melanocytes

A phone called melanocytes starts from melanoma. Melanocytes are liable for the creation of melanin. Melanomas happen for the most part on the outside of the skin yet additionally in other pigmented tissues, for example the eyes.

1.2.1.6 Mixed types

These cancers may occur in one class or from individual overlapping classes. Several examples include carcinogenicity, teratocarcinoma, mixed mesodermal tumor, and adenosquamous carcinoma (Mandal et al., 2012).

1.3 Cancer risk factors

There are certain factors in the development of cancer, which are considered risk factors. Two risk factors lead to cancer growth, mostly genetic or hereditary and environmental risk factors.

1.3.1 Hereditary/Familial factors

1.3.1.1 Breast cancer

Breast cancer growth is a major risk factor: gene mutation (5-10%) and family history (20%) (Kwong et al., 2016). The risk of developing breast cancer among women carrying the genes BRCA1 and BRCA2 is reportedly increased 5 to 20 times (Kurian et al., 2011). The genes TP53 and PTEN also play an important part in breast cancer development. The CASP8, FGFR2, TNRCP, MAP3K1, rs4973768, LSP1 are some of the other genes that have been shown to contribute to breast cancer by the scientist. On the other hand, some rare genes may have defects, and may also increase breast cancer risk. They include ATM, CHEK2, BRIPI, PALB2 (Kwong et al., 2016).

1.3.1.2 Cervical Cancer

Cervical cancer can also occur because of genetic factors is the third most common cause of mortality in females and the second most common among certain developing countries. Among patients with one or two copies of p21gene polymorphism (rs1801270), the risk of cervical cancer was lower than that of the ancestral allele homozygotes (Martínez-Nava et al., 2016).

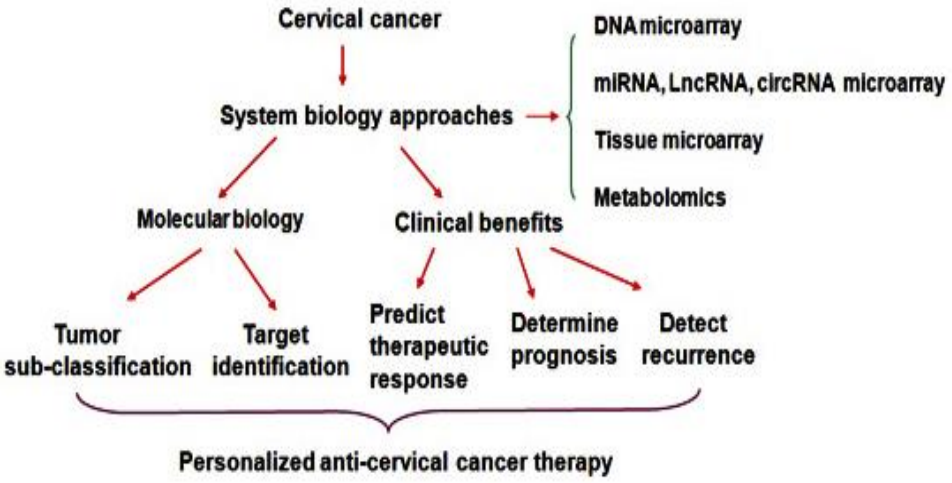


Figure 3: Systems biology approaches are utilized of cervical cancer (M. Lin et al., 2019).

1.3.1.3 Colorectal cancer

Approximately 25-30 percent of colorectal cancer with gene susceptibility occurs, 5-10 percent due to germline mutations, including Lynch syndrome, NTHL1-associated polyposis, family adenomatous polyposis, Peutz-Jeghers syndrome, MUTYH-associated polyposis, and certain hamartomatous polyposis condition. In all of these syndromes, the risk of developing CRC is high. Nonetheless, there is still no evidence of a significant part of colorectal cancer heritability. Some studies show that LRP6 and PTPN12 are new genes candidates for CRC susceptibility(de Voer et al., 2016; Jasperson et al., 2010).

1.3.1.4 Lung cancer

An important role in the occurrence of lung cancer is played by personal or family background as risk factors. Patients who bear germline mutation TP53 are three times more likely than non-smokers and also smokers who develop lung cancer. One report showed a lung cancer-associated chromosome 15 marker which has three genes in the acetylcholine receptor nicotine subunits. One copy of that marker is 30 percent, and the risk of lung cancer in those with two copies of that marker is 70-80 percent higher respectively (Zappa & Mousa, 2016).

1.3.1.5 Pancreatic cancer

While pancreatic cancer appears to be sporadic, the legacy of 5-10 percent of patients with pancreatic cancer has been found. In general, the tendency to inherited pancreatic cancer falls

into three classes. The key disorders are hereditary cancer, such as Lynch, syndrome of Petuz Jeghers, adenomatous polyposis of the brain, and atypical syndrome of multiple mole melanoma. All of these are expressed via germ mutations and lead to increased pancreatic risk. The second group is hereditary pancreatitis and cystic fibrosis, which are genetic to pancreatic cancer growth. The third group suggests that pancreatic cancer in the family has an increased risk of pancreas cancer which has not met some of the criteria for hereditary cancer problems (Q. J. Lin et al., 2015).

1.3.1.6 Cancer in children

Kids often have different cancer types than cancers found in adults. Childhood cancers are the result of changes in cell DNA that may occur before birth, whereas behavioral or environmental risk factors cause adult cancers and are not always recognized as a cause of childhood cancers. About 5 percent of all childhood cancers are predicted to be caused by genetic (inherited) mutation that can be transferred from parents to children. For example, 25 to 30 percent of eye cancers in children with retinoblastoma is caused by mutations in the RB1 gene, an inherited mutation. Retinoblastoma constitutes around 3 percent of all childhood cancer in all cases. Nevertheless, Fanconi, Noonan, Beckwith-Wiedemann Syndrome and Von-Hippel Syndrome are called a family syndrome, where the inherited mutation is observed and the risk of cancer in children is thus increased. The syndrome is also called a condition within the family.

Genetic mutations can occur in the development of the fetus in the womb. For example, one in every 100 children is created with a genetic mutation which increases the risk of leukemia. Ultimately, however, only one child in 8000 develops leukemia with that mutation (Ward et al., 2014). Children with Down's syndrome are expected to have an additional 21 chromosomes, for example, leukemia and testicular cancer, to develop malignancies. However, the purpose behind this is not surely known (Ross et al., 2005).

1.4 Genetic makeup

The genotype refers to the DNA sequence of an individual commonly called the hereditary code and transmitted from generation to generation.

1.4.1 Vascular Cancer

Kaposi sarcoma (KS) is a rare type of lymph or vascular cancer. It mainly affects the mouth's skin or mucous membrane, but it can occur in any part of the body such as the lymphatic glands,

lungs, and digestive tract. Different types of KS develop in different regions. For example, KS is the most common associated disease and AIDS in the US. Persons who are infected with AIDS-causing HIV viruses will be vulnerable to this type of KS. On the other hand, Classical KS grows mainly in the older Mediterranean, Western, and Middle Eastern cultures. Humans are more vulnerable to classical KS than women. One or more injuries occur in the soils of people's legs, ankles, or feet. Lesions do not grow as quickly as other forms of KS, so new injuries are required. There is another form of endemic (African) KS, most of which are present in the African Equatorial population and named after KS from Africa. In Africans infection with KSHV is more common than in people from other parts of the world. It is called herpesvirus (KSHV) linked to Kaposi's (American Cancer Society, 2016).

1.5 Environmental factors

1.5.1 Cancer in the Oral Cavity and Pharynx

Tobacco and alcohol consumption are the main risk factors for most mouth cancer. The risk of these cancers may also stem from a low-temperature diet of fruit, vegetables, food intake and drink (Shridhar et al., 2016). While their exact occurrence and clinical significance remain unclear, certain types of HPV (Human Papillomavirus) may also be a risk factor in oral cancer. The use of mouthwash with high alcohol, iron anemia, poor oral hygiene, and aerodynamics may be risk factors for mouth cancer. Mouth washing may reflect a risk factor. Locally khaini, mawa, mishri, gudakhu, nass, naswar, and gutkha are called substituent betel, oral snuff, and betel quid, and sweetened dry mixture of areca nut, catechu, all of which are more likely to cause oral cancer (Gelband et al., 2015; Lee et al., 2015).

1.5.2 Cancer in the Digestive system

1.5.2.1 Colorectal cancer

In addition to family or heritage risk factors, other dietary risk factors are correlated with colorectal cancer growth. Obesity and overweight are the principal risk factor for this cancer. Alcohol is less likely but it is not ignored. Physical inactivity, low fiber diets, and vegetables are also significant risk factors (Key et al., 2004). Additionally, with 30g of red and processed meat eaten each day, the risk of colorectal cancer increased by 10 percent. Several reports have shown that the possibility of colorectal cancer is linked to animal fats. Nonetheless, high

secondary bile acid levels in the large intestinal lumen will increase the risk of intestinal inflammation and other diseases because of high fat intake (Raskov et al., 2014).

1.5.2.2 Pancreatic cancer

One of the major risk factors for many cancers as well as pancreatic cancer is tobacco consumption. This reflects 9 percent of male smokers' cancer deaths, and 74 percent of male smokers' risk of pancreatic cancer. Overweight and certain dietary factors also increase the chances of pancreatic cancer. Apart from this Mellitus diabetes, the outcome is still ambiguous and thought to be a risk factor. Several studies have shown that PC cancers have a relationship with diabetes mellitus, 25% of patients diagnosed with diabetes mellitus, and 40% of patients diagnosed with pre-diabetes. Additionally, chronic pancreatitis, allergies, high-food diet, alcohol, and coffee or tea intake are potential risks for pancreatic cancer (Q. J. Lin et al., 2015).

1.5.2.3 Stomach cancer

One of the main risk factors for carcinoma or gastric cancer is helicobacter pylori. Dietary nitrates that can be found naturally and incorporated in foods such as cauliflower, celery, radish, carrot, cabbage, and spinach during restoration. One research examined the fact that the dietary nitrate was converted to N-carcinogenic compounds by gastric acid and increases the risk of stomach cancer. Moreover, high intakes of salted, poached or grilled food, dried fish, meat and carbohydrates are particularly susceptible to cancer. Tobacco use, smoked cigarettes, and ionizing radiation are important risk factors for carcinoma in the stomach and genetic factors (Compare et al., 2010; Saghier et al., 2013).

1.5.2.4 Liver Cancer

Hepatitis B or C infections are the most important risk factors for liver cancer. Aflatoxins present in unsuitable stored staples such as peanut, corn, maize, and seed, etc., are the major risk factor for liver cancer. Overweight and obesity considerably increase the risk of liver cancer. Excessive alcohol consumption is prevalent among risk factors linked to diet. Work-related exposure of vinyl chloride monomer (VCM), organic solvents polyvinyl chloride (PVC), thorium dioxide or vineyard chloride, chlorinated pesticides, arsenic can adversely affect the liver and cause cancer. (Janevska et al., 2015; Key et al., 2004; Rapisarda et al., 2016).

1.5.2.5 Esophageal cancer

The most significant risk factor for esophageal cancer is heavy alcohol and tobacco smoke, such as cigarettes, cigars, and pipes. Poor diet, obesity, folate deficiency, decreased levels of certain nutrients (thiamine, zin, riboflavin, carotene, and ascorbic acid), inadequate consumption of fruits and vegetables and high levels of sodium and animal fat may be the risk factors for this cancer (Key et al., 2004; Peng et al., 2016).

1.5.2.6 Gall bladder cancer

The principal risk factor is the development of gallstones for cancer of the gallbladder. The risk factors are amongst women's early marriage and the number of childbirths. Consumption of fatty / fried food, use of wood/coal, a long period between meals, use of tobacco and use of estrogen-containing pharmaceutical products are also considered significant risk factors (Jain et al., 2013).

1.5.3 Cancer in the Respiratory System

1.5.3.1 Lung cancer

Tobacco use is responsible for up to 80 percent to 90 percent of all lung cancers. The primary risk factor for lung cancer is passive smoking. It was also expected that the risk of developing lung cancer will increase occupational exposure to radon or various other toxins, such as vinyl chloride, asbestos, chloromethyl ethers or fossil fuel products, and high ionizing radiation dosages. Exposures to air pollution, including emissions of polycyclic aromatic hydrocarbons, considered a distinctive risk factor for lung cancer and associated with an eight percent increase in risk for all causes of lung cancer death. Lung cancer has also been linked to insufficient fruit and vegetable intake (J. R. Choi et al., 2016; Key et al., 2004; Zappa & Mousa, 2016).

1.5.3.2 Skin Cancer

1.5.3.2.1 Melanoma

Serious sunburn, fair skin, several or atypical moles (colored skin spots), personal or family history of melanoma and prolonged exposure to radiation occur key risk factors for melanoma cancer. Most melanomas are among white peoples (Lo & Fisher, 2014).

1.5.3.2.2 Non-melanoma

Long-term exposure to ultraviolet radiation (sunlight), fair skin, high doses of radiant ionizations and uncommon genetic disorders such as multiple basal cell carcinoma syndrome, xeroderma pigmentosum and albinism are key risk factors for non-melanoma cancer. Chronic diseases, poorly manufactured cosmetics, photosensitizers for the tanning aid, burn wounds and reduced immune function due to organ transplants or viral infection are potential risk factors (Preston & Stern, 1992).

1.5.3.3 Breast Cancer

A high dose of ionizing radiation is an identified risk factor for female breast cancer, long-term use of post-menopause estrogen and progestin, post-menopausal obesity and heavy use of alcohol, and also include a personal history of the ovary or odometer, family history, early monarchy, infertility and late pregnancy after age 30 (Weir et al., 2007). The risk factors for men are family history, aging and exposure to radiation, testicular disorders and Klinefelter syndrome. Possible risk factors include gynecomastia and obesity (Hsing et al., 1998).

1.5.4 Cancer in Reproductive Organs

1.5.4.1 Prostate cancer

Family history especially father or brother and ethnicity are the main risk factors for this cancer. Prostate cancer happens more to black males than in white males. Prostate cancer risk factors include obesity, high intake of animal fat, sexually transmitted agents, tobacco use, alcohol, and hormonal factors and a lack of physical activity. Infertility, obesity, hypertension, diabetes, and syndrome with Stein Leventhal are common risk factors (Gann, 2002; Key et al., 2004).

1.5.4.2 Ovarian cancer

In the gynecological division of cancers, ovarian cancer ranks among the worst. The US research firm said that 22,240 newly diagnosed ovarian cancer and 14,070 ovarian cancer fatalities are expected to be recorded in 2018 in the US (Torre et al., 2018). The fifth most frequent cause of death is identified among British women is ovarian cancer. Ovarian cancer was identified as 7,270 in 2015 and as many as 4,227 related to deaths in 2016 in the UK (Siegel et al., 2019). The classifications currently employed by pathologists for ovarian

epithelial tumors are based entirely on morphology of the tumor cells. There are five major types of epithelial tumors. They are:

- ✓ High-grade serous
- ✓ Low-grade serous
- ✓ Endometrioid
- ✓ Clear cell
- ✓ Mucinous (Jayson et al., 2014)

The most aggressive subtype of HGSOC (High-grade serous ovarian cancer), 70-80% of all ovarian cancer deaths, and for many decades the overall survival rate has not changed considerably (Bowtell et al., 2015; Jelovac & Armstrong, 2011). Generally, ovarian cancer is detected late and an appropriate screening technique is not available. A cycle that removes the majority of cancer cells in conjunction with chemotherapy, which sometimes contributes to several years of recovery, is the current standard ovarian cancer care (Jelovac & Armstrong, 2011). Three novelties of poly-ADP-ribose polymerase (PARP) inhibitors such as olaparib, rucaparib and niraparib have recently been licensed by the US Food and Drug Administration and the European Medicine Agency for the prevention of ovarian cancer triggered by the reparation mechanisms of DNA injuries (Franzese et al., 2019). The possibility of ovarian cancer allows it unsatisfied to conduct a study of new drugs that can give greater therapeutic benefits by resistance processes and the use of medicines to resolve ovarian cancer.

1.5.4.3 Cervix cancer

Long-term use of oral contraceptives, early puberty, a large number of sex partner parties, HPV infection is the risk factors for cervical cancer (Key et al., 2004; Natphopsuk et al., 2012).

1.5.5 Cancer in the Urinary System

1.5.5.1 Bladder cancer

Smoking is one of the key bladder cancer risk factors. The occupational risk of bladder cancer rises in the paint, leather or rubber sectors with aromatic amines and PAHs. Potential risk factors include the use of pain killers including phenacetin and genetic variations in arsenic, urinary tract infections, heavy coffee consumption (Janković & Radosavljević, 2007).

1.5.5.2 Kidney

Smoking is the main risk factor. Additionally, obesity, arsenic, and analgesic abuse (especially pain killers containing phenacetin) also contribute to kidney cancer. High levels of meat consumption and the use of prescribed diuretics are potential risk factors for kidney cancer (Chow et al., 2010).

1.6 Cancer Prevalence Worldwide

With this increasing number of incidences, cancer prevention is one of the most significant health problems of the 21st century. 17 million new cases of cancer were reported worldwide in 2018 (all composite cancers except skin cancer with no melanoma). Of those cases, 8.8 million (52 percent) were males, 8.2 million (48 percent) were females (Bray et al., 2018). A study showed that high-income countries have the highest incidence rate for the different cancer subgroups. In many high-income countries, the risk of cancer death is declining, while the risk is increasing in low and medium-income countries. Below middle-income countries have the highest cervical cancer rates (Torre et al., 2016). Across 114 countries, prostate cancer between men is a widely diagnosed disease. In Eastern Europe, lung cancer is the highest diagnosed disease amongst men. The leading cancers in Africa include thyroid, heart, liver, esophagus, leukemia, prostate, stomach, and non-Hodgkin lymphoma; the leading cancers in Asia are head, mouth, lung, liver, colorectal, prostate, and stomach. Breast cancer appears to be the most commonly seen among females in North America, Europe, and Oceania. In Latin America, and the Caribbean, Africa and most of Asia in women, breast and cervical cancers are most commonly diagnosed (The International Agency for Research on Cancer (IARC) report, 2018). Pulmonary, female, bowel and bowel cancer is found to be the four most common cancers in the world, and more than 4 out of 10 cancers diagnosed worldwide. By 2040, the number of cancer cases is set to be 27.5 million. Since 1975 the four most common causes of cancer death have been reported for heart, liver, stomach, and intestine cancer (Cancer Research UK, 2018).

1.7 Cancer Prevalence in Bangladesh

Cancer is counted as the sixth leading cause of mortality in Bangladesh according to the Bangladesh Bureau of Statistics. The primary causes of cancer death in Bangladesh vary according to the International Agency for Cancer Research. In Bangladesh, the most likely cases of oral, pharyngeal, and laryngeal cancer are those older than 30 years. In the latest World

Health Organization (WHO) report, 49,000 cases of oral cancers, 71,000 cases of laryngeal and 196,000 cases of lung cancer in Bangladesh have been identified. The most prevalent cancers in Bangladesh are men's oropharynx cancer and female's uterine cervix and breast cancer (Syed Akram Hussain & Sullivan, 2013).

About 150 trained oncologists and 16 pediatric oncologists are in different parts of the country. There are 19 hospitals for regular cancer treatment, and 465 hospital beds are provided as indoor or daycare in the oncology/radio therapeutic departments. There are currently approximately 15 linear accelerators and 12 brachytherapy. Around 56 chemotherapeutic cancer agents in Bangladesh can be collected.

Bangladesh has developed a unique National Strategy and Action Plan on Cancer Control 2009-2015 under the WHO integrated cancer management program to improve and expand the scope of cancer management services. Prevention measures taken to reduce cancer incidence involve decreasing tobacco smoking, improving diets and decreased food adulteration, maintaining sexual health, growing physical activity, and minimizing workplace harm. Publicity and advertising strategies are coordinated by the general public, opinion leaders and societies.

Besides these, Regarding Early Diagnosis such as breast cancer, cervical and oral cancer BANGLADESH Government and NG Officials such as the ICDDR'B, BRAC, BSMMU, Bangladesh Cancer Society, AK Khan Healthcare Trust, Oncological Club etc. have been introduced (SyedMd Akram Hussain, 2013).

1.8 Mechanism of carcinogenesis

Cancer refers to the uncontrolled proliferation of cells due to gene mutations that regulate cell growth and division, due to complex interactions between environmental factors and endogenous factors. Cancer has a broad group of genetically modified organisms, cells, and tissues and there are new improvements in its development (Arley & Eker, 1962). Genetic variation in chromosomes, proto-oncogenes, and the genes for tumor suppressor DNA repair leads primarily to cancer, known as cancer drivers.

Cells normally grow and divide by the oncogenes and suppressor genes of the tumors. However, genes or oncogenes that cause cancer may arise from alterations in these genes that permit uncontrollably proliferation and survival by cells (Shtivelman et al., 1985).

Genes identified as DNA repair genes are responsible for the stabilization of damaged DNA. In cells that carry DNA repair genes, it is a process of producing additional mutation genes of other origins. For all these mutations the cells are all transformed into cancer types (Wei et al., 2007).

Cancer progresses in 3 successive periods of initiation, promotion and progression.

1.8.1 Initiation

The initiators act directly or indirectly through the production of electrophile species. These species mix and alter DNA structures and influence DNA sequence. Initiation is intended to produce a long-lasting lesion (Van Duuren et al., 1975). An experimental survey showed that the skin of the mouse treated more than a year earlier was still very susceptible to tumor induction when it was a phorbol ester. Therefore it can be said that initiation is an irreversible step. In addition to this phenomenon, it has also been shown that repeated doses of initiators give rise to the development of additive tumors (BOUTWELL, 1964).

1.8.2 Promotion

The promoter causes carcinogenic responses when several doses are administered after one single dose of the sub carcinogenic initiator. By definition, promoters aren't carcinogenic. Only the laboratory can demonstrate that the promoter and the initiators have time-dependent administration. It is difficult to identify the appropriate procedures in humans as they take simultaneous environmental contamination from a range of chemical substances. Few promoters have demonstrated poor initiating potential at high doses. The electrophilic species are not known to form promoter species such as initiators. Symptoms caused by a developer identified as a first stage are assumed to be reversible. Once administered the second phase promoter causes permanent results. A total (full) carcinogen is classified as compounds that may be present on the same tissue as the initiator and promoter at the same time. Many initiators usually are carcinogenic (Weinstein et al., 1984).

1.8.3 Progression

The transformation process has multiple stages. It includes the activation of oncogenes chromosome aberration, interactions between tumor cells and host defenses, as well as the selection of different. Tumors can become highly malignant in development and heterogeneous and that is a dynamic process (Weinstein et al., 1984).

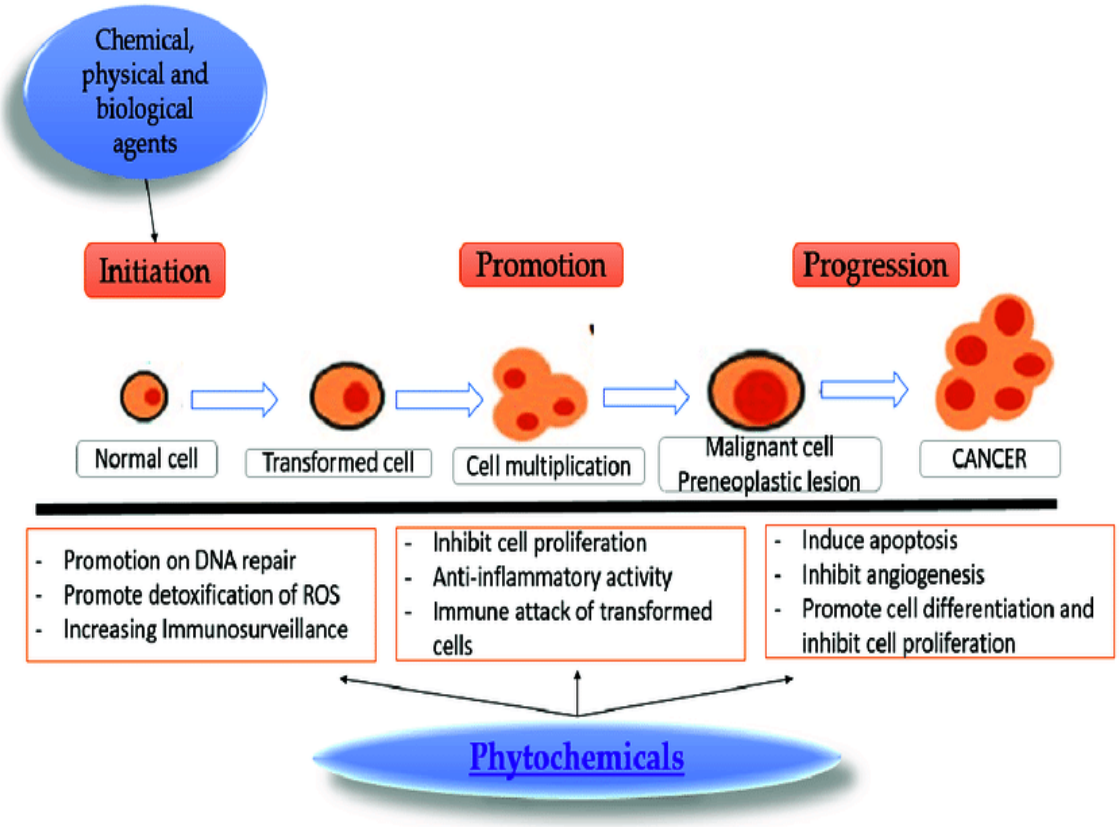


Figure 4: A multistep process of Carcinogenesis mechanism (Moga et al., 2018).

1.9 Cancer Immunotherapy

Immunotherapy helps our immune system remove malignancy from immune surveillance by overcoming the features of immune escape and flagging tumor cells and strengthening the immune system through the production of immune-removal substances (Beatty & Gladney, 2015; Oiseth & Aziz, 2017). Hence, cancer immunotherapy has become one of the most effective methods of cancer treatment. There are different types of immunotherapy that use different components of our immune system to cure cancer in different ways.

Adoptive cell therapy (ACT) is a subgroup of immunotherapy involving the isolated and *in-vitro* expansion of tumor-specific infiltrative T cells. Then, they have infused into their bodies again (Guillerey et al., 2016). Various forms of ACT include tumor infiltration, culture, and T-cell expansion, which identifies and attacks tumor cells. T-cells are also modified to contain receptors for the tumor cells. This is classified as an antigen receptor for chimeric T-cells (Oiseth & Aziz, 2017).

The extent and efficiency of the immune response depend on antigen recognition from the T-cell receptor and a balance between co-stimulating and inhibitory signals, known as immune

control points. Tumor cells may upregulate the expression of the inhibitory signals as part of their protective mechanism. These inhibitory moves also include CTLA4 and programmed protein 1 (PD1) for cell mortality, also known as CD152 (Pardoll, 2012). Immune control point inhibitors are used for speech suppression and immune system improvement. They use Immune control points. Monoclonal antibodies targeting CTLA4 and PD1 inhibit the negative blocking of T-cells. Those are Nivolumab and Ipilimumab antibodies (Postow et al., 2015).

Oncolytic virus, altered in normal cells due to lack of virulence, lyses the malignant cells and is further attacked due to the release of antigens after lysis (A. H. Choi et al., 2016). T-VEC, a herpes simplex-1 virus, is commonly licensed by the FDA for the treatment of advanced melanoma (Oiseth & Aziz, 2017).

One type of immunotherapy is the recombinant cytokines, including IL-2 (Proleukin), which were approved by the FDA for the treatment of melanoma and renal cancer. Interferon α is another such agent (Mellman et al., 2011).

The advancement in cancer immunotherapy has shifted the focus from treating a site of the disease to treating cancer cell biological traits. Immunotherapy's ability to memorize and identify malignant cells often offers inherent advantages over other therapies. The potential challenges to immunotherapy will be to identify the cause of success rate variability in care and change the immune system even when the micro-environmental tumor is completely blocked from infiltrating T-cells in patients that lack immunoassay to cancer cells (Hegde et al., 2016).

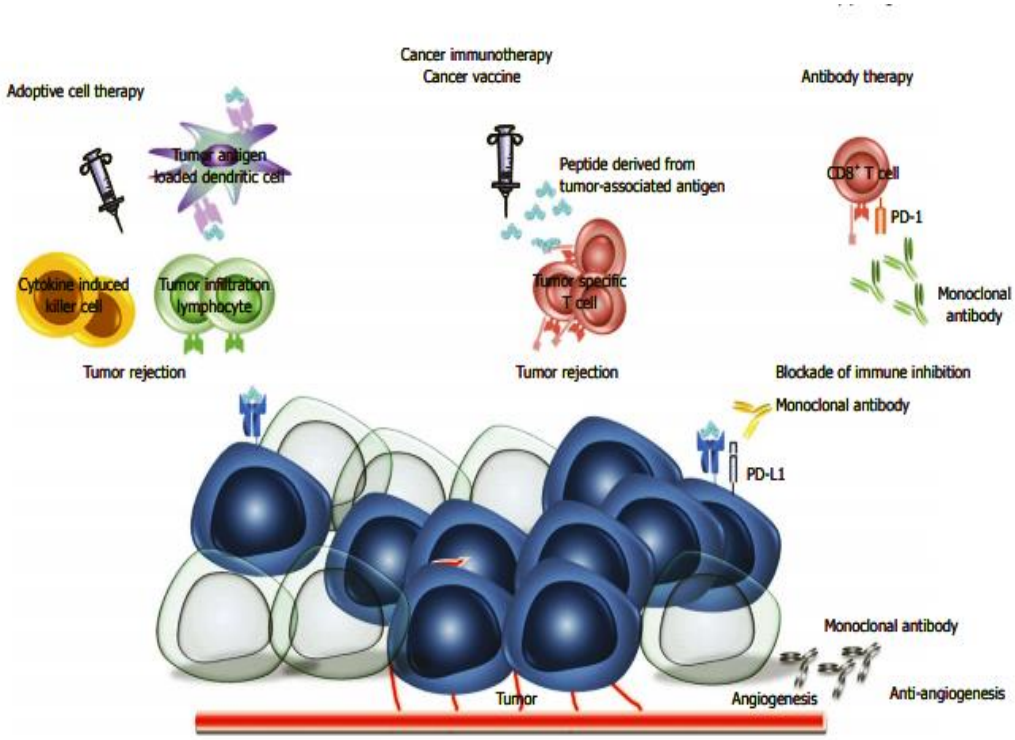


Figure 5: Immunological approaches to cancer therapy are based on the use of cancer vaccines, monoclonal antibodies etc. -Cancer immunotherapy (Matsueda & Graham, 2014).

Chapter 2

Plants

2.1 Information

Herbal medicines have long been the main medical treatment method and tend to be used in developing countries. The plants were used for their antiseptic effects in pharmacy. The work has therefore identified the future characteristics and uses of terrestrial extracts for designing probable nanomaterial drugs for diseases such as cancer (Sivaraj et al., 2014). Many plant species are now being used for cure or cancer prevention. Most scientists classify species of plants with a strong focus on plant medicine that has anticancer characteristics in developing countries (Y. Z. Cai et al., 2006; Fouche et al., 2008).

In more than 400 000 species of plants on earth, only a very small percentage of these are examined in research studies, there is a huge reservoir of bioactive compounds. An important source of anti-cancer agents has been and is still being developed (Cragg & Newman, 1999; D. J. Newman et al., 2003; Pettit et al., 2000). Seeds are an effective anti-cancer vector and more than 60% of anti-cancers are derived from natural resources such as marine organisms and microorganisms (D. Newman et al., 2005). About 35,000 plant samples from 20 countries were obtained and nearly 114,000 extracts were tested for action in anticancer (Shoeb, 2006). In Asian patients, the incidence of plant-derived cancer products globally varies from 10% to 40% (Deng et al., 2004; Molassiotis et al., 2006; Tascilar et al., 2006). Europe alone is expected to invest 5 billion dollars annually on natural anti-cancer drugs (Tascilar et al., 2006).

2.2 Anticancer property substances in plants

For centuries, medicinal plants have been used in Asian and African cultures for herbal remedies and many plants in developed countries are used in their health benefits. According to the World Health Organization (WHO), many countries still use the benefits of natural products as an herbal medical source for therapeutic purposes (Desai et al., 2007). Polyphenols, brassinosteroids substances and taxols for their anticancer effects are compounds found and extracted from terrestrial plants.

2.2.1 Polyphenols

Certain polyphenolic chemicals such as flavonoids, tannins, curcumins, resveratrol, gallocatechin, are labeled cancer compounds (Azmi et al., 2006). In foods such as peanuts, grapes and red wine, resveratrol may be found. For green tea gallocatechins are available. Polyphenols in a diet are intended as natural antioxidants to improve health and minimize the risk of cancer (Apostolou et al., 2013; Azmi et al., 2006).

Polyphenols have shown cytotoxicity in several cancer cells and also have antioxidant properties (Heo et al., 2014; Siriwatanametanon et al., 2010). It is understood that polyphenols have properties that induce apoptosis and have characteristics of anticancer. The mechanism used to induce apoptosis in polyphenols is to control copper ion mobilization linked to chromatin, which contributes to the fragmentation of DNA. Resveratrol was shown to be able to degrade DNA at the presence of Cu (II) (Azmi et al., 2006). Certain plant polyphenols demonstrate their ability to interfere and promote the growth of proteins present in cancer cells. The polyphenol which regulates acetylation, methylation or phosphorylation can change cancer agents by direct bonding. For example, curcumin-treated cell lines have shown that the expression of the Tumor Necrosis Factor (TNF) is suppressed by associated stimuli (Gupta et al., 2014).

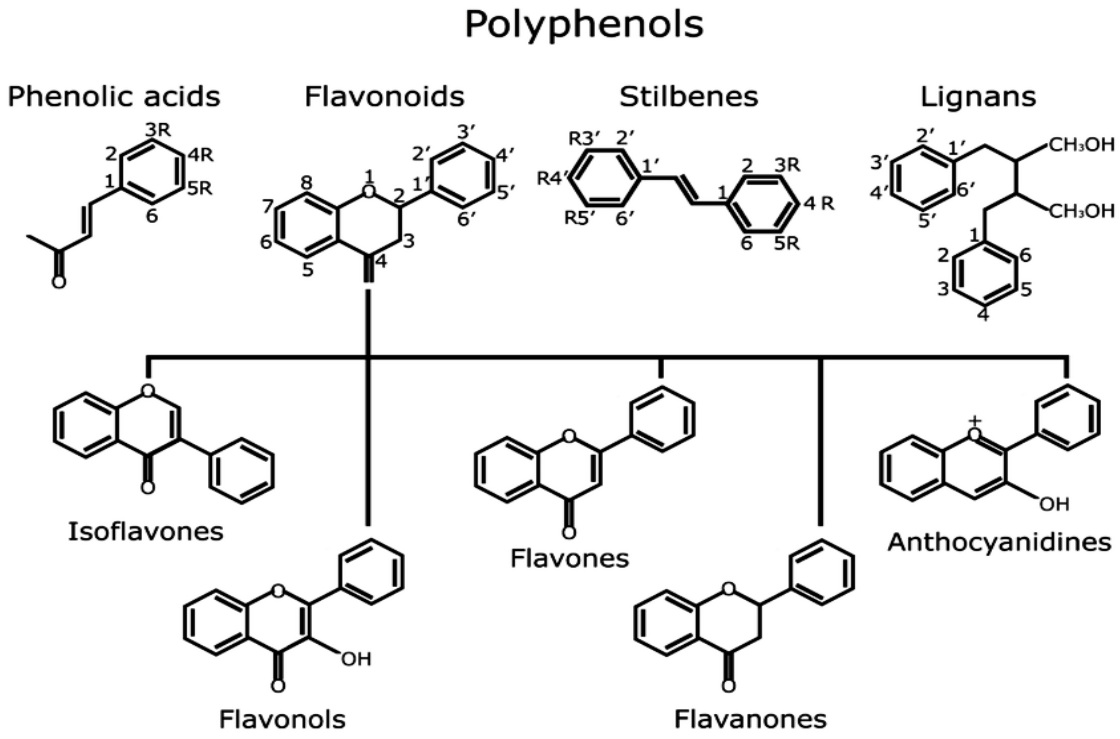


Figure 6: Deferent classes of polyphenols by structural classification (Pérez-Sánchez et al., 2018).

2.2.2 Flavonoids

Flavonoid polyphenols are a large group of secondary plant metabolites with 10,000 known structures. They are physiologically active agents in plants.

Different species, for example, fern and mushrooms, have also been researched in the conventional medicinal items of the Chinese languages such as litchi leaves. In a single structure such as seed, high levels of flavonoid compounds are stored: anthocyanins, flavones, flavonols, chalcones, and many more. *Dryopteris Erythrosora* has been shown to have anti-carcinogenic flavonoid activity in human lung cancer cells (A456 cell line). Cytotoxic for cells in cancer and with high free radical activity, flavonoids have been found. The activity of hepatoma (Hep-G2), cervical carcinoma (Hela) and breast cancer (MCF-7) were also demonstrated to be purified flavonoids. The cytotoxicity of *Erythrina suberosa* was shown in the cells HL-60 (human leukemia), stem bark extracted flavonoids (Wen et al., 2014). The cause of apoptosis has been the intrinsic and extrinsic pathways of MLF and AIF. The mitochondrial membrane potentials are significantly reduced with the activation of apoptotic proteins. Cancer cells cannot survive with cell damage from mitochondria (Sunil Kumar et al., 2013). Some studies also investigated flavonoid extracts from ferns and demonstrated a high percentage of anticancer activity even at low concentrations (Xia et al., 2014).

Polyphenols, as already described, can suppress or modify protein and other agents that can lead to cancer cell survival. Signal Transducer and Activator (STAT) proteins are anti-apoptotic and help the development of cancer cells. This protein band, necessary for cancer cells to live, has been blocked by MLF and AIF. The expression of NF-KB needed to live and angiogenesis and proliferate cells is also inhibited by these flavonoids (Sunil Kumar et al., 2013).

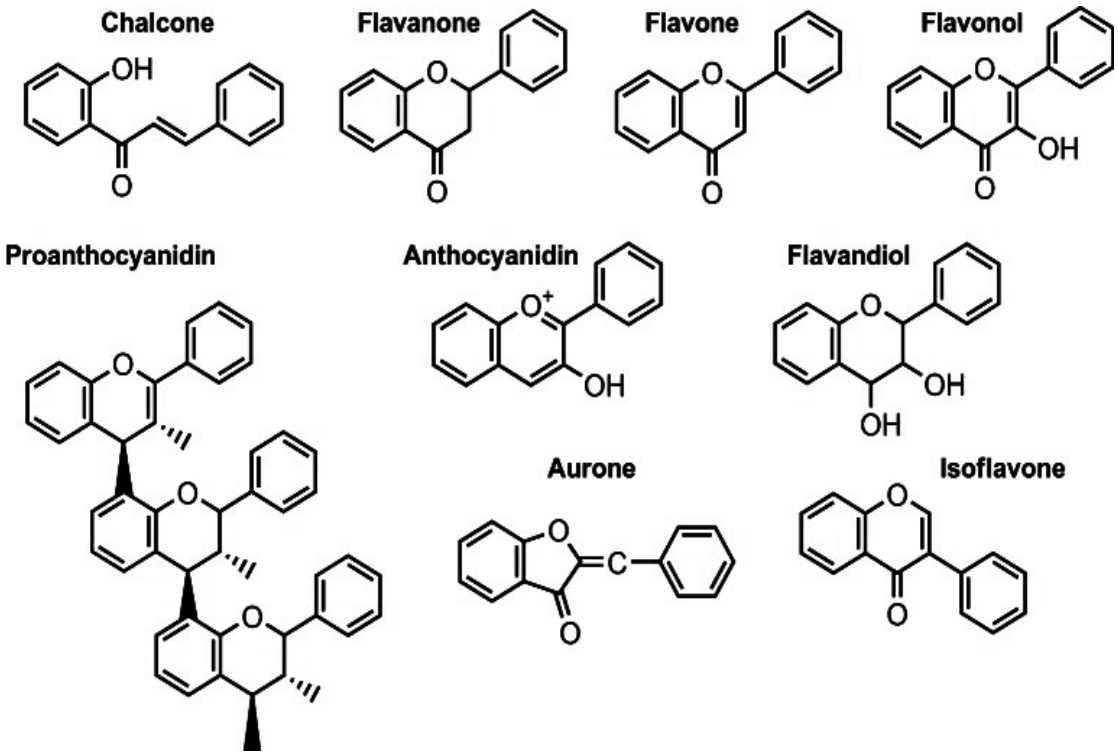


Figure 7: Structures of sub-classes of flavonoids. Six major subclasses: flavonols, flavanones, flavanols, flavones, anthocyanins and isoflavones (Falcone Ferreyra et al., 2012).

2.2.3 Brassinosteroids

Brassinosteroids (BR's) usually occur in plants that play roles in hormone motion to sustain cells' growth and differentiation, prolongation of the stem and root cells and different functions, such as tolerance and stress sensitivity. BRs are also used for plant senescence guidance (Bishop & Koncz, 2002). They are essential to the development and improvement of plants. BRs are other combinations that normally occur because of the illness and display remedial value.

The anticancer effects of these mixtures have been shown by two standard BRs in carcinogenic cell studies. The consequences for various malignant growth cell lines have been shown by 28-homocastasterone (28-homoCS) and 24-epibrassinolide (24-epiBL) (Malíková et al., 2008; Steigerová et al., 2010) and have demonstrated to be successful at micro molar concentration. An attribute of malignant growth cells is that they don't normally experience apoptosis and multiply uncertainly. In conjunction with the cell cycle, BRs will speed up critical reactions to an impediment to growth and instigate apoptosis. T-Lymphoblastic leukemia CEM, multiple myeloma RPMI 8226, cervical carcinoma HeLa and cell lines HOS have been used in exams to control the size of malignant growth cells.

Estrogen receptor (ER), epidermal factor growth receptor (EGFR) and human EGFR-2 (HER-2) are a portion of essential protein, for example, MCF-7, MDA-MB-468, T47D and MDA-MB-231 which are concentrated in the treatment of bosomal malignancy (Pledgie-Tracy et al., 2007). The androgen receptor (AR) is the basic protein associated with its progression and offers an ER comparative structure for prostate malignant cells (lncap and DU-145 cell lines). BRs will either work or tie these protein receptors and prevent hormone-sensitive and hormone-unfeeling cells from developing.

BRs may also trigger the blocking of the cell cycle. Treatment of the 28-homoCS and 24-epi bosom malignant cell lines showed a decrease in cyclin proteins linked to the G1 cell cycle stage. At this stage in the cells of the cell cycle, apoptosis is either set or added, and the BRs therapy in this process initiates apoptosis, which is usually not available without therapies for malignant growth cells. The equalization of apoptotic proteins that facilitate cell durability and which cause changed cell disappearance improvements in BR care in prostate malignant lines, LN CaP and DU-145. Bax expert's apoptotic protein levels have decreased after BRs and apoptotic proteins are processed, for example, Bcl-2 (Steigerová et al., 2012). BRs create various reactions in ordinary and malignant growth cells together with their anticancer properties. The manufacturer should not be cytotoxic to normal cells and specifically to malignant growth cells, which are the major specifics in the care of anticancer. BRs are experts here who are focused on correctional products (Malíková et al., 2008).

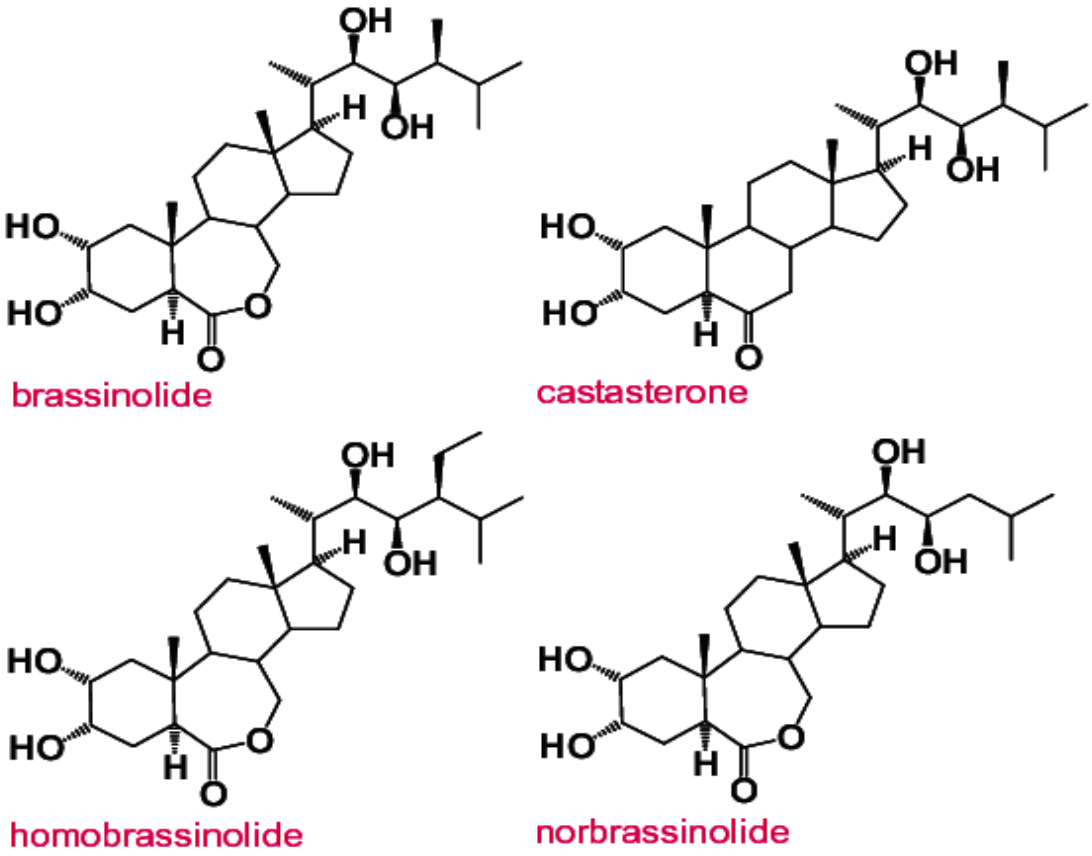


Figure 8: Structures of the different classes of Brassinosteroids (Zeferino-Diaz et al., 2017).

2.3 Plant-derived anticancer drugs

For the treatment of anticancer, plant-inferred medicines are tried since they are inexpensive and available quickly. They can be handled quickly orally for the diet of a patient (Amin et al., 2009; Cornblatt et al., 2007). Moreover, since mixtures have usually been obtained from plants, they are usually harder and less lethal to ordinary human cells. Specific cases, such as cyanogenic glycosides, lectins, saponins, lignans, lectin and some taxanes exist in any case (Shah et al., 2014). If selectiveness of plant determined drugs can be tested, non-lethal to typical cell lines, and cytotoxicity in malignant cell lines, these medications can lead to further improvement in the clinical preliminary stage. Plants may fall into four classes of accompanying exercises; inhibitors of methyltransferase, preventative DNA drugs, histone deacetylases (HDAC) inhibitors and mitotic disruptors (Amin et al., 2009).

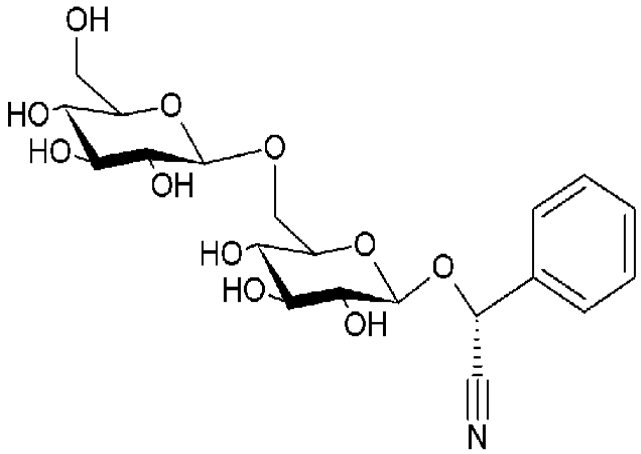
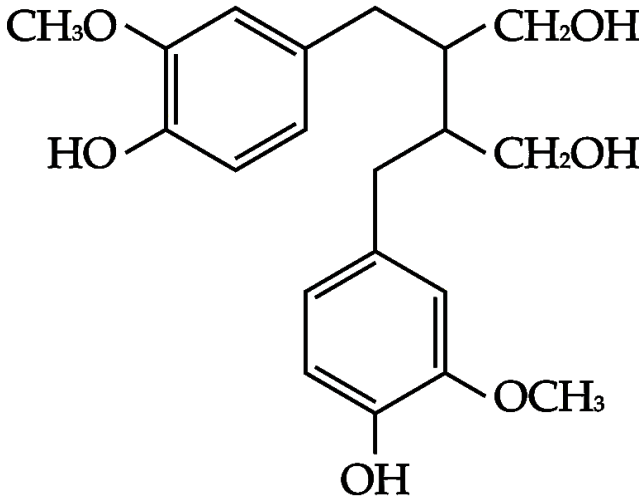
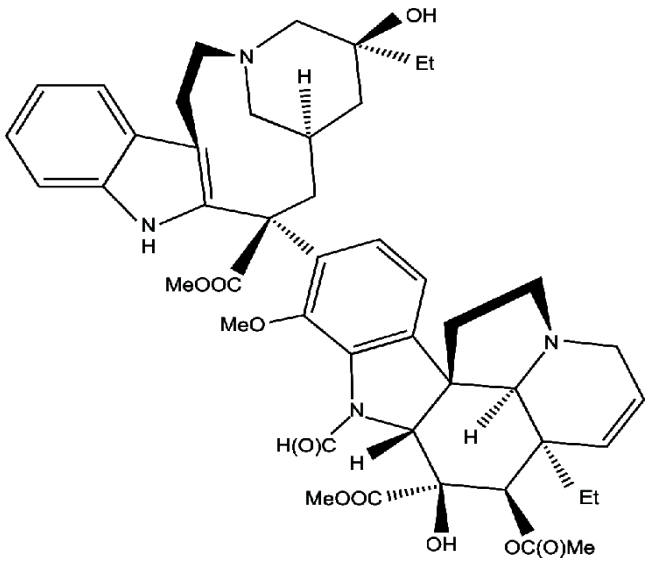
The HDAC-inhibitors are considered to include mixtures such as sulforaphane, isothiocyanates, isoflavones and pomiferin. It prevents the movement of proteins that cause cancer. For instance, the concentrations of sulforaphan on malignant bosom growth have been

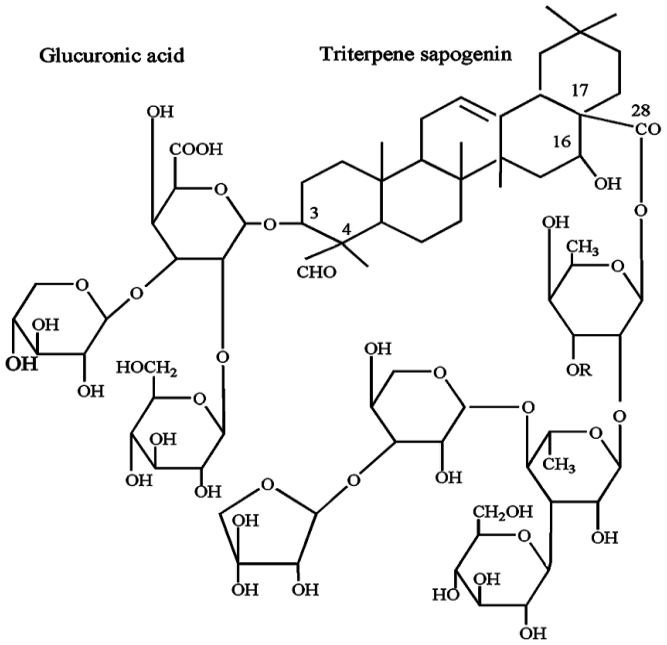
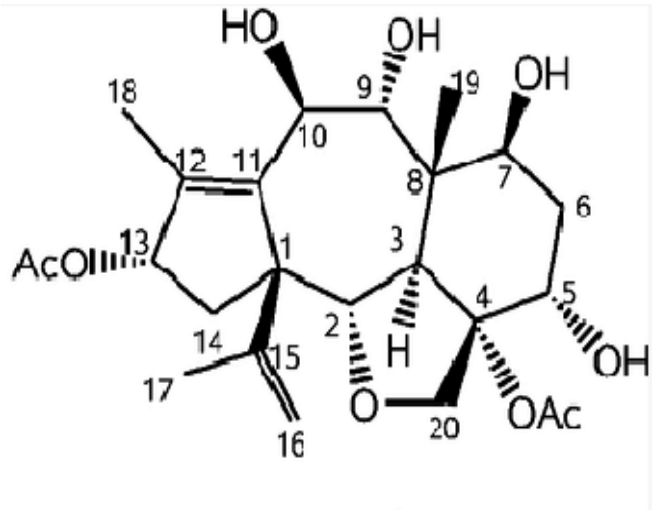
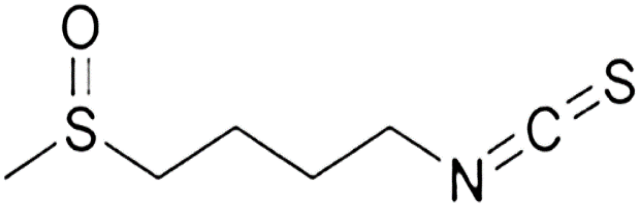
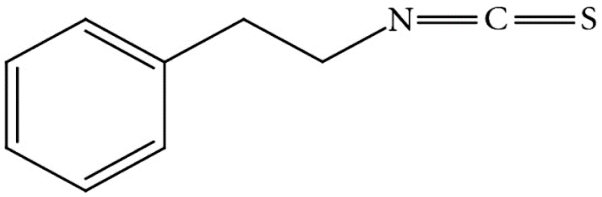
obstructed. Diminished articulation of ER, EGFR and HER-2 came about because of HDAC hindrance by sulforaphane treatment in bosom malignancy cell lines (Pledgie-Tracy et al., 2007). Disease cells are reactivated by HDAC inhibitors and malignant cells can then enter modified cell demises (apoptosis) in epigenetically-requited characteristics that are practical for chromatin acetylation. Plant-determined blends showing restraint of HDAC will enhance chemotherapy in humans (Amin et al., 2009; Pledgie-Tracy et al., 2007).

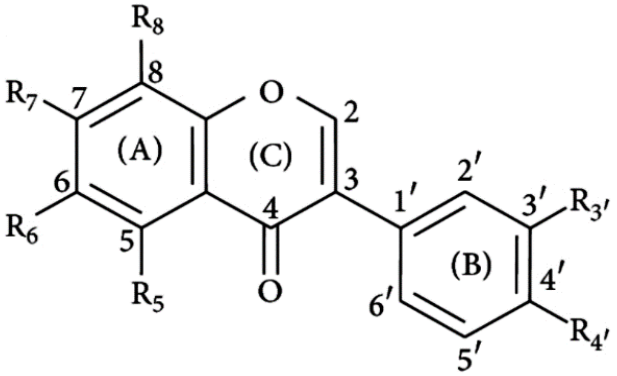
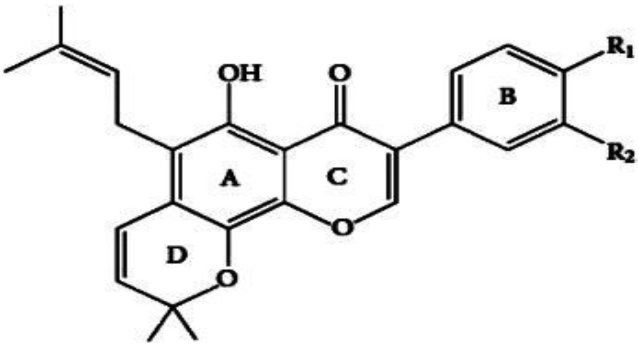
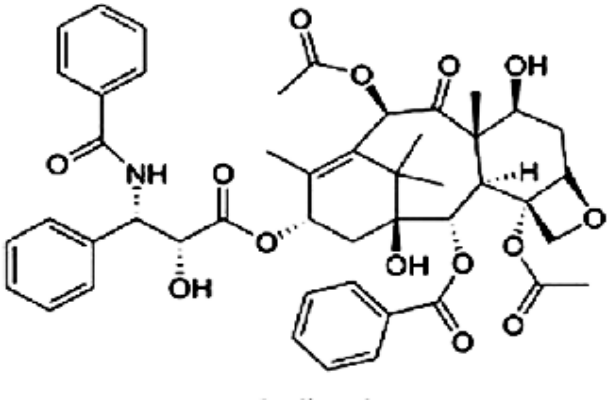
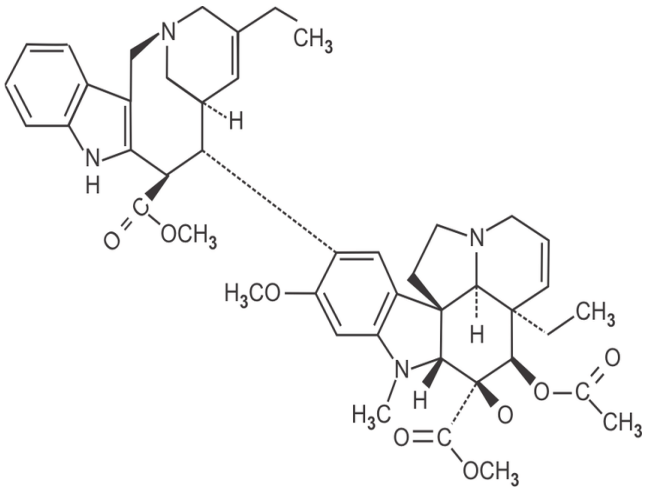
Vinca alkaloids, vincristine, vinblastine, vinorelbine, vindesine, and vinflunine subordinates are drugs which are authoritative of the β-tubulin and prevent micro tubulin elements. Texans are also micro tube disruptors, for instance, paclitaxel and its basic docetaxel. These mixes limit the phase of the cell cycle from metaphase to anaphase causing capture and apoptosis. Replication of malignant growth cells is reduced with paclitaxel because it replaces or polymerizes cellular microtubules. Paclitaxel was one of the key treatments for managing vincristine and vinblastine with a huge effect, two of the underlying medicines were separated (Khazir et al., 2014).

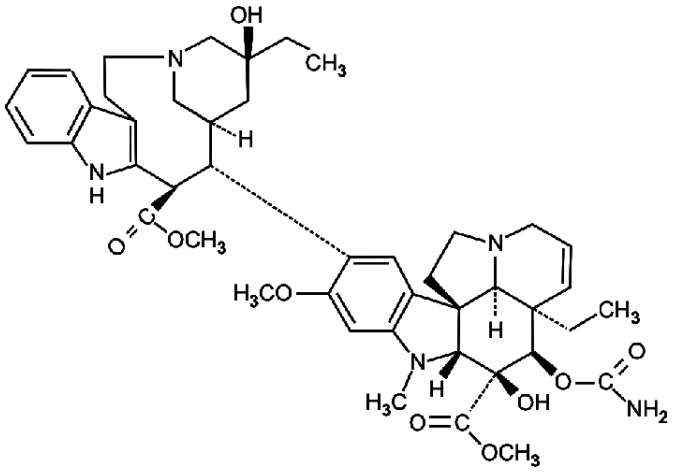
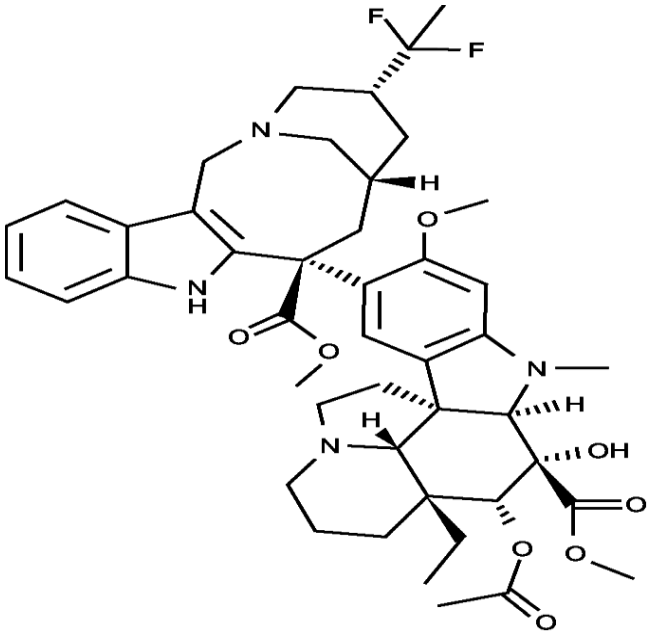
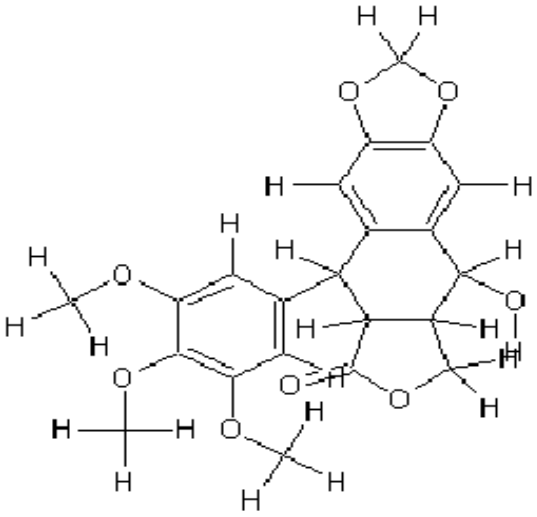
Blends of medications got from vinca alkaloids, Taxus diterpenes, Podophyllum lignans and in-plant concentrates, camptotheca alkaloids can improve their anti-cancer effects and improve their viability as remediation operators (Khazir et al., 2014; Solowey et al., 2014). Concentrates from *Urtica membranaceous*, *Artemesia monosperma* and *Origanum dayi* have been explored to test their impacts on a wide scope of malignant growth cell lines from lung, bosom, colon and prostate tumors. The analysis found that the plant segregated by a mixture of cancer mixtures had the possibility of slaughter activity specifically for malignant growth cells and that they did not affect the typical human lymphocytes and fibroblasts. This makes plants more appealing than treatments artificially assumed that cause dangerous complications in the malignant treatment of development. Initiated apoptosis was separated by a growing cell population of cells with a lower DNA substance and chromate accumulation in the sub-G1 stage. Likewise, after concentrate therapy, a major stage in the apoptotic cell passage, an expansion in caspase 3 has been observed (Solowey et al., 2014).

Table 1: Structure of Plant-derived Anticancer Drugs

Serial No.	Name	Structure	References
1	Cyanogenetic glycosides		(Ordoudi et al., 2018)
2	Lignans		(Mrduljaš et al., 2017)
3	Vincristine		(Arora et al., 2010)

4	Saponins		(Tang et al., 2017)
5	Taxanes		(M. Zhang et al., 2008)
6	Sulforaphane		(Joozdani et al., 2015)
7	Phenethyl Isothiocyanate		(Morris et al., 2011)

8	Isoflavones		(Karlíčková et al., 2015)
9	Pomiferin		(Gruber et al., 2014)
10	Paclitaxel		(Sharma et al., 2014)
11	Vinorelbine		(Arora et al., 2010)

12	Vindesine		(Arora et al., 2010)
13	Vinflunine		(More & Talbot, 2010)
14	Podophyllum lignans		(Bagchi et al., 2011)

2.4 Enhancing drug administration

Innovations for the application and measurement of these anticancer mixes are increasing due to progressions and disclosures in normally inferred medications. The use of nanoparticles (NPS) as a transport framework for drugs to reach destinations is established through nanotechnology. Many exacerbate of anticancer workouts may be minimized in their clinical development owing to the need for large measures. Bromelain, which is isolated from *Ananas comosus,* has proved to be more effective than free bromelain as a NPs anticancer provider. (Bhatnagar et al., 2015). This exploration exhibited a sheltered and biocompatible technique utilizing bromelain NPs to support the arrival of the medication at the objective site while likewise ensuring the medication. This polylactic co-glycolic corrosive NPs (BL–PLCG NPs) stacked bromelain seemed to trigger more than free bromelain apoptosis of child-hearted cells by checking out the outflow of apoptotic genial and apoptotic proteins in mice. Various blundered NPs have also been investigated, e.g., *Antigono leptopus* gold powdered and *Acalypha indica* copper oxide NPs (Balasubramani et al., 2015). This results in the focus of the plant and NPS revealed the development of cell lines of the bosom MCF-7.

Paclitaxel has experienced early treatment and clinical preliminary procedures. The innovative work means using NPs to control medicine arrival by using attractive mesoporous silica NPs with a gelatin film and upgrading target particularities; Paclitaxel can be remotely controlled using an attractive field. This has demonstrated to be fruitful in expanding the medication's capacity to restrain the development of tumors and diminish undesirable impacts of other tissue regions as the medication's circulation is controlled (Che et al., 2015). The successes were also seen with the use of QMPs against BMPs (MCF 7) of cell lines (Rajesh Kumar et al., 2014). NPs creates confidence in their use for cancer treatments and is a product choice, as opposed to existing medicines.

Again, research using nanocochleate and nanoliposomes shows successful completion by oral or inhalable admission in anticancer exercises. Taken orally, Paclitaxel is extremely knowledgeable and pleasurable to the patient. Controlled drug discharge and viable exercises against lung, ovarian and bosom malignant cell lines can be used to manage orally a description of paclitaxel-stacked nanochleates (Pawar et al., 2014). Likewise, noscapine was restricted in clinical preliminaries because of insoluble properties until inferred analogs have been created (Jyoti et al., 2015). The noscapine clear nanostructured lipid fragments, 9-Bromo-noscapine, have been investigated. Here, improved cytotoxicity and apoptosis were demonstrated in the

pulmonary growth cell lines, expanded drug use into cancerous noscapine cells in contrast to a free drug (Henary et al., 2014).

2.5 Demands of medicinal plants

Medicines from the beginning of the plants are well established for healthy development of successful scientific preliminaries. They were found to have non-toxic effects on ordinary cells and their cytotoxic effects on disease cells. Most study organisms are selected from the development of countries in Africa and Asia with drilled natural treatments and regenerative plants (Fouche et al., 2008; Kamatou et al., 2008). In 2007, the World Health Organization estimated the benefit of 100 billion dollars for plant-inferred medicines. By 2050, the exchange will reach 5 trillion dollars (Desai et al., 2007).

There is a colossal interest for therapeutic plants in creating nations squeezing the plant populaces. Numerous therapeutic plants are developed from wild populaces for casual exchange however this development isn't controlled. The preservation of medicinal plants is becoming a matter of urgency with increasing population growth, erosion, and growing urbanization. With a steady increase, highly valued restaurant plants become compromised by eradication if abuse takes place. It is imperative to preserve these plants. At the time of the harvesting of wild plants, only explicit plant parts, like the bark of a tree or bulbs and tubers from bulbous and tuberous plants are used for treatment. Separation of only sections of a plant is likely to damage and reduce its longevity (Zschocke et al., 2000).

The use of all plant parts including the stem, leaf, root and bark should be remembered for treatment to increase the maintainability of restorative plants in developing countries. Specific preventive methods include the storage of germplasm; elimination of appropriate seed, cryopreservation; defense of natural material from fluid nitrogen and tissue cultivation; replication and distribution of sterile plant conditions and quick production of plant clones of rare organisms. These techniques of conservation also consider mechanical use in created countries (Parveen et al., 2013).

For starters, certain restorative plants were grown to an enormous degree in developed regions, Europe and parts of India and China, to remain conscious of increasing applications for electro regular medicine (Zschocke et al., 2000). Reasonable species growth can exert pressure on wild species and plant biodiversity loss. Mass production could however easily spill over offshore accessible for numerous horticultural properties.

Fodder with medicinal qualities, cruciferous vegetables and herbal crop berries are included in these food sources (Huntley, 2009). Crude side-effects from enterprises could be used to remove anticancer specialists from sources that have these operators. For instance, probably the greatest yield developed universally are grapes (*Vitis vinifera*) and 'grape seed extricate' is frequently included elements of nourishment items because of its human medical advantages. The grape stems are a harsh side effect for the viticulture in the winery industry. The Earth containing the winery will acidize this high natural pressure. However, its high polyphenolic substance can improve anticancer drug usefulness and make a useful plan for understanding natural problems. Grape stem removals have shown cancer prevention, forestalling DNA disruption from reactive oxygen-causing bacteria and shown cancer potential enemies against different vaginal, thyroid and increasingly diseased cell lines (Sahpazidou et al., 2014).

Although several anticancer agents are derived from medicinal plants, other species do remain, but they have not yet been thoroughly studied. It is therefore important to determine whether these extracts are the cause of anticancer action or whether they are used to prevent cancer or reverse human body results.

Chapter 3

Less Explored Plants

3.1 Combretum albidum

Combretum albidum (C. albidum), a member of the Combretaceae family, commonly referred to as Piluki, "buffalo calf" in English, “karalankody” in Malayalam and “vragay” in Tamil. This family is made up of a variety of genus commonly used for around 90 pharmaceutical items in the conventional medicines method. Many of them tackle different infectious diseases including anti-microbial diseases, anti-bacterial diseases and anti-fungal diseases. Most Combretum organisms have anthelmintic, antibacterial and anti-fungal properties such as *Combretum molle* (Ademola & Eloff, 2010; Asres et al., 2006). In fact, several plants such as *Combretum imberbe* also have anticancer effects against human cell lines in conjunction with antimicrobial and anti-inflammatory action (Angeh et al., 2007). So, *Combretum albidum*, an unexplored genus of Combretum and an important topic for research.

Combretum albidum is a 3-10m thick shrub. Leaves are ovate or elliptical, unstable or somewhat sharp, roundish on the root, flat below. Flowers are panicle, narrower, oblong, or almost globe-like at the end of limbs and yellowish-white colors. The limb of the sepal cup arm with a rough rim underneath the stamens penetration. The triangular-ovate of Sepal is bent down. It has elliptical-oblong petals, around sepal length and semicircular fruit arms. It is blossoming in February-April (Raja & Babu, 2011).

The foliage of the host tree is large. It is only found along the banks of the river in semi-evergreen and dry lagoon woods (Bokhad M. N and Rothe S. P, 2012). The fruit of this plant is used for diarrhea and dysentery (Karuppusamy, 2007), the stem barks for Jaundice (Sreedhar et al., 2012) and skin diseases (Ramamoorthy, 2011) and leaf for a peptic ulcer (Raja & Babu, 2011).

The Kalrayan and Shervaarayan hill tribal societies use a wiry device, seed oil and root to cure eye problems, eczema and malaria which is found by an ethnobotanical survey of the woody species (Kadavul & Dixit, 2009). Antibacterial activity against various bacterial strains have been reported to be present in *C. albidum* crude extract (Mahida & Mohan, 2006).

3.1.1 Anticancer Activity

Cytotoxic behavior has been measured using a brine shrimp motility assay (Rao et al., 2012). Brine shrimp assay has shown a good correlation with the cytotoxic potential in several medicinal plants such as *Zeyheria tuberculosa* and a large number of medicinal plants of amazon making it a suitable model for the cytotoxic activity (QUIGNARD et al., 2003). Cytotoxic activity of leaf and bark extracts of *Combretum albidum* from wild and cultivated samples show the presence of tannins, flavonoids, triterpenes, saponins and glycosides. *Combretum albidum* has 5 types of flavonoids and they are Myricetin, Quercetin, Kaempferol, Orientin and Vitexin. Total flavonoids content (mg rutin equivalent/g DW) is 92.30±0.05 (Manipal et al., 2017).

The association with phase I metabolizing enzymes (eg, cytochrome P450), Flavonoids stimulates metabolically a large number of procarcinogens which is one of the most important ingredients for reactivating medial that are capable of interacting with cell nucleophiles and eventually of triggering carcinogens. Flavonoids are known to be a shielding agent against the development of cellular damages through the stimulation of carcinogens, inhibiting behaviors of certain P450 isozymes, such as CYP1A1 and CYP1A2 (Le Marchand et al., 2000; Tsyrlov et al., 1994).

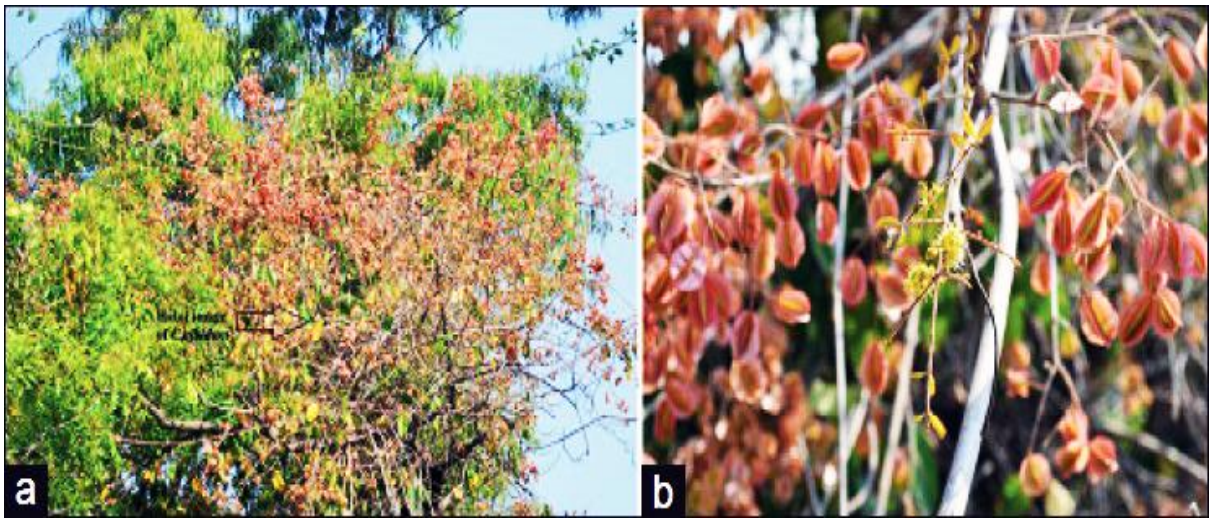


Figure 9: (a) C. albidum plant (b) Flowers and fruit of C. albidum (Zalke et al., 2013).

In conclusion, *Combretum albidum* has shown cytotoxic activity against cancer cells. This unexplored plant has been extracted and established and given Tannins, flavonoids, triterpenes, saponins and glycosides, offering a new source of cancer drugs. In the future, it needs more

accurate experiments, especially on stem and roots. Besides, there is not so much experiment on cancer cell lines which is needed more.

3.2 *Rutidea Parviflora*

Rutidea parviflora D.C. (RP) in the Rubiaceae family belongs in the Rutidea genus. The fourth-biggest class of angiosperm is the rubiaceae called the coffee family or bedstraw family. Rubiaceae has roughly 611 genera and around 13500 species in several parts of the globe but in sub-tropical areas of greater diversity. *Cinchona L*, the medication used in the treatment of malaria, and *Coffea L*, are two main genera in the company, which provided the best in class caffeine coffee in the world. Certain forms of shades include the *Rubia, Pavetta L*., *Uncaria schreb*, *Oldenlandia L.*, *Tarenna Gaertn* and *Galium L*. (Phylogeny Angiosperm) (Johnson-Ajinwo et al., 2015).

R. Parviflora was used for anti-inflammatory and anticancer practices by indigenous communities in the State of Delta, Nigeria. The fruits are used for vomiting and curing hallucinations (Burkill & others, 1985). This thesis explains *R.parviflora* cytotoxic palmatine and its activation of apoptosis that results in the death of the ovarian cancer cells.

The characterization of phytochemical and pharmacological in *R.parviflora* has been performed in this study. In ovarian cancer cells, significant cytotoxic activities have been shown, both inorganic and aquatic extracts. Two cytotoxic compounds have been extracted from the organic extract: palmatine (1), the quaternary alkaloid protoberberine and urs-12-ene-24-oic-acid, 3-oxo, methyl ester (2), the triterpenoid. In the cell growth test, palmatine shows significant inhibitory activity (Whitacre et al., 1999).

3.2.1 Anticancer activity

Palmatine has shown preferential selective cytotoxicity to the cancer cells, and the growth of HOE cells is slightly less efficient. Testing of cancer cells by the compound will probably take place through apoptosis, evidenced by a significant increase in activity of Caspase 3/7, PARP cleavage, cellular annexin V / propidium iodide labeling PARP Cleavage is a proven apoptosis process since PARP is caspase 3 and 7, separated into two apoptosis fragments (Trucco et al., 1998). PARP is a nuclear DNA restoration enzyme which detects DNA fragmentation (D'Amours et al., 1998). The cleavage of PARP-1 is an apoptosis confirmation.

The medicament target for this enzyme was verified by the production in the treatment of ovarian cancer of effective PARP inhibitors (Johnson-Ajinwo et al., 2015). It is worth noting that palmatine shows higher strength and selectivity than carboplatin. Especially in the cisplatin-resistant A2780 cells (IC_{50}=6.6 μM for A2780 and 5.5 ′ M for A2780cis cells), there is a lack of cross-resistance. The results are particularly relevant (Binju et al., 2019).

A probable palmatine receptor was established with prostate cancer cells as the ribosomal protein S6, an endogenous p70S6 K target, and the Akt / mTOR signaling cascade. Palmatine has been also reported to be selectively cytotoxic to prostate cancer cells (Hambright et al., 2015). Palmatinum production is inhibited by pancreatic star cells (PSCs) or cancer cells alone or with gemcitabine. This suppression of the development and movement of pancreatic cancer cells is attributed to blocking the signaling modifications in apoptosis-associated glioma oncogene 1 (GL1) due to glutamine-mediated shifts. Palmatine has been found primarily in the endoplasmic reticulum and MCF-7 mitochondria (Chakravarthy et al., 2018). Photo cytotoxicity of normal photosensitizer palmatine in breast cancer has been shown by more photodynamic therapy.

The cause of major cell apoptosis and increased intracellular reactive oxygen concentrations is MCF-7 and HT-29 colon adenocarcinoma cells (Wu et al., 2016). Palmatine is also shown to be an inhibitor of telomere elongation and oncogene production in humans, which means that it is binding and stabilizing parallel G-Q4 DNA (Padmapriya Kumar & Barthwal, 2018).

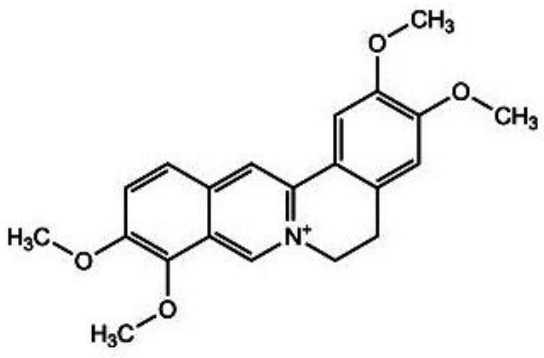


Figure 10: Chemical structure of Palmatine (Long et al., 2019)

In conclusion, *R. parviflora* has shown cytotoxic activity against cancer cells. Palmatine has been extracted and established as a new palmatine source from that unexplored farm. The root and bark are not checked yet. For potential, anticancer behavior should be checked. The

cytotoxicity of palmatine with apoptosis as the path of cell death is also shown in this study. Thus, palmatine is a potential lead agent in the treatment of ovarian cancer.

3.3 *Schleichera oleosa*

S.oleosa belongs to the class of Sapindaceae. *Schleichera oleosa* is an evergreen tree up to 30m high and 3 m diameter. The leaves are 20-40 cm long, paripinnate. The leaflets are 2 to 4 set, elliptical or elliptical-oblong, coriaceous, maximum edge, and rounded apex. The flowers are minute bulbs, yellowish-white, male or female, spiked like an axillary raceme of approximately 7.5 and 12.5 cm in length (Gandhi et al., 2011). The seeds of a succulent aril are dark, irregularly elliptical, tightly pressed and sticky (Bhatia et al., 2013).

In Central and South Asia, *S.oleosa* is widely distributed in sub-Himalayas, Burma, Ceylon, Indonesia and Timor. Kusum oil or macassar oil is the oil obtained from its seeds and is widely used for the treatment of pain, acne, burns, other diseases of the scalp, rheumatism (external massage), hair-dressing and hair development (Gandhi et al., 2011). It is commonly used to treat dysentery, analgesics and antibiotics in Thailand (Rout et al., 2009). Southern, North-east, South-east, South-west and Central areas are reported to have the *S.oleosa* called Ta-Khro. It is a popular nectar bee plant in parts of southern India (Meshram et al., 2015). The feeds are fed to animals with seeds, roots, and seed-cake. The wood of *S.oleosa* is ideal as firewood and produces good charcoal (Palanuvej & Vipunngeun, 2008).

The presence of lupeol, pipeol acetate, betulin, beta-sitosterol and scopoletin has been identified in its bark through phytochemical studies (Sipra et al., 1986). In an upcoming study, taraxerone and tricadenic acid have also been detected in its outer bark. Bark also contains tannin and anti-tumor isolates including betulin and betulinic acid, which is around 10% (P. Ghosh et al., 2011).

3.3.1 Anticancer activity

S.oleosa's phytochemical tests have shown the existence of triterpene derived lupeol and betulinic acid with anti-neoplastic activity (Sipra et al., 1986). Against cancer, *S.oleosa* works as a chemo preventive agent. Several studies show that phytochemicals have their cancer effects, either through the suppressive cellular signaling pathways or through the development of free radical tums, such as reactive oxygen/nitrogen cells, to inhibit tumor cell proliferation and to cause apoptotic death (Bharti et al., 2003; Estrov et al., 2003).

A study on the removal from the bark of the Sri Lankan tree *S.oleosa* of an extract, Scheicherastins (1e7) and 2 corresponding sterols 8 and 9 referred to as Schleicheols (1 and 2) are isolated (Bhaumik et al., 1999). The isolated Scheicherastins had inhibitory characteristics of cancer cell growth. The sample was treated by 1:1 dichloromethane methanol solution. Andhexane was used for the resulting partitioning of dichloromethane and ethyl acetate solutions. The different fractions have been tested against the cell line P-388. The dichloromethane fraction against the P-388 cell line is involved. Chromatographical isolation using Sephadex LH-20 and Si gel board, accompanied by HPLC purification and recrystallization procedures isolated this dichloromethane portion.

The insulated Scheicherastins showed significant inhibition activity of CNSSF-295, colon 20L2, lung NCI-H460, ovary OVCAR-3, pancreatic BXPC-3 and prostate cell lines against P-388 cells and Schleicheols demonstrated minimal activity of CNSSF-298. The new set of sterols is an important inhibitor of cancer cell development. Several reports show that antioxidants are included in carcinogenesis prevention (Ki et al., 2005; Nemeikaite-Čeniene et al., 2005). The phytochemicals induce tumor cell toxicity by either scavenging or producing an accumulation of free radicals, paradoxically leading to cellular oxidative instability, repression of cell proliferation, and eventually cell death (Loo, 2003; Sakagami et al., 2000). In a report, 20 bark extracts of *S.olenoesa's* CT-13 (colon), A-549(lungs) and HEP-2 were evaluated against different cell lines, such as 502713 (colon) and SW-520(column) for SK-NS-H (center nervous) as well as IMR-32 (neuroblastoma).

In all cell lines except the IMR-32 cell line, heavy cytotoxicity was observed for ethyl acetate, methanol and water extract, while a hexane and chloroform extract didn't have major cell line inhibition. The cytotoxic potential was attributed to the hydroxyl scavenge's radical powers. The less hydroxylic radical scavenging ability, the less cytotoxic towards different cell lines has been demonstrated in the hexane and chloroform extracts (Skehan et al., 1990; Thind et al., 2010).

Besides, Taraxerone and tricadenic acid are obtained from *Schleichera oleosa* which are mainly triterpenoids (P. Ghosh et al., 2011). Triterpenoids drugs are used as anticancer (Petronellia et al., 2009).

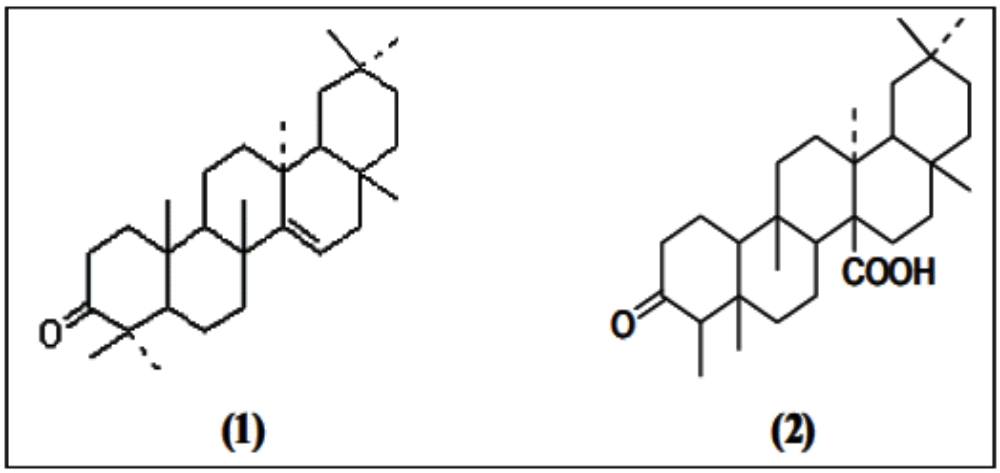


Figure 11: Triterpenoids from S. oleosa (1) taraxerone (2) tricadenic (P. Ghosh et al., 2011).

In conclusion, *S. oleosa* has shown cytotoxic activity against cancer cells. This unexplored plant has extracted taraxerone and tricadenic acid that is a new source of taraxerone and tricadenic acid. Tests on the leaves and the root of these plants are also needed to know that this plant has anticancer activity or not.

3.4 *Aporosa wallichii*

Aporosa wallichii Hook.f, is a dry evergreen plant of Meghalaya and Tripura which is found in India, Bangladesh, Myanmar & Thailand (Schot, 2004). Kokra in Bangladesh commonly referred to as Castoma is the local name for this herb (Hossain et al., 2015). It can be up to 15m high and about 15cm in diameter. The texture of the bark is dark, rugged, fresh, and gray. The stipulations of the plants are thinly upper and about 5-7 mm per 1.5-2.8 mm in thickness. The shape of the basal glands is large and narrow and dark in color. Leaves' narrowly egg-shaped form is thin and elliptical and the scale is up to 9-17.5 cm × 3.5-6.5 cm. Irregular small dots are found on the surface of the leaf of the plant. Either one or two seeds are in each fruit (Schot, 2004).

*Aporosa wallichii Hook.f.*is one of the families of Phyllanthaceae. The numerous medicinal plants include a range of therapeutic activities, including tumors, disorders of the scalp, vomiting, nausea, dysentery, icing, and headaches. *Aporosa lindleyana* also has antioxidant, anti-amylase and lipid-reducing properties and is of the same kind of *Aporosa wallichii Hook.f* (Kathirgamanathar et al., 2018). Antimicrobial, analgesic (Vagdevi et al., 2008) and antidiuretic (Ganegamage et al., 2014) activity are also found in this vine. There is also an appropriate anti-plasmodia operation threshold for *Crotron gratissimus. Croton argyratus*, on

the other side, *Aporosa wallichii* has very good anti-protozoan behaviors (Noor Rain et al., 2007).

There are also good prospects at *Aporosa wallichii Hook.f* with different pharmacological characteristics. Free radicals are blamed not only for aging but also for a variety of age-related diseases (Harman, 2009). Different sources suggest that free radicals contribute to cell death processes in the body such as apoptosis and necrosis (Chatterjee et al., 2011). Blocking of the veins is a thrombosis affecting multiple species, which can contribute to various diseases (Bekker et al., 2009).

3.4.1 Anticancer activity

Antithrombotic and thrombolytic treatments are of major importance in the management of thromboembolic diseases and they are effective (Hirsh et al., 2008). To kill cancer cells, cytotoxic activity is very necessary. Therefore, *Aporosa wallichii Hook.f* plant may be a possible source of medicinal properties. In this analysis, the cytotoxicity function of the plant was calculated.

The cytotoxic properties of methanol extract were tested using the brine shrimp lethality assay. Different levels of mortality were given from the extract at different concentrations. Vincristine sulfate was used as normal (positive control) in the present experiment, where 2.0 μg/ml was obtained as the LC_{50} value compared to the *Aporosa wallichii Hook.f* reference methanol sample. The leaves have LC_{50} content of 26.7 μg/mL. With rising amounts of vincristine sulfate and methanol extract, the mortality rate has increased. The methanol extract from the leaves *Aporosa wallichii Hook* had cytotoxic activity in this analysis (Runa et al., 2013).

In conclusion, *Aporosa wallichii Hook.* has shown cytotoxic activity against cancer cells. Hope that in the near future, the mechanism of this plant will be discovered and the drugs can be made from this plant. Besides, the cancer cell line is still not tested and there is also needed test on stem, root and bark of *Aporosa wallichii Hook.f.*

3.5 *Atuna indica* and *Atuna travancorica*

Atuna indica (Bedd.) Kosterm and *Atuna travancorica* (Bedd.) Kosterm are both forms expressed in the Southern Western Ghats that are the two types of Atuna. Sources of *Atuna indica* from Nadukani (Nilambur North Forest Division, State of Kerala, India) have been identified and in Beddomei from Wayanad carcoorghats. In comparison, *Atuna Travancorica*

has been shown in the surrounding valara cascading field of Munnar Forest Division, Kerala State, India, according to Hooker's collection. The genus is clearly described both by the taxonomy and the morphology (Sasidharan & Sujanapal, 2011).

Atuna indica, a 20 m high tree with an elliptic-oval, smooth, thin, black and white flowers. On the other hand, a description of *Atuna travocorica*, the lanceolate leaves with 7-16.5 cm long and 1.7-4.5 cm broad with yellow or white lavender blooms, are a 25 m high tree with smooth grayish darker bark. One kind of family component (Chrysobalanaceae) is seen as clearly squatting (VT & Gopal, 2018). On account of *Atuna indica* (Bedd.) Kosterm, Flowering and fruiting are happened from November to February and habitat are West Coast tropical evergreen backwoods (the Western Ghats in India) while on account of *Atuna travancorica* (Bedd.) Kosterm, flowering and fruiting happen from January to May and habitat are West Coast tropical evergreen woodlands, typically riparian (Southern India, Travancore region) Both the species are having a place with the endangered class (Puyravaud et al., 2003; Reddy et al., 2007; Sasidharan, 2002).

Superficial medical goods such as Digitalis, Atropine, Morphine, Ergot and Quinine have been the starting point for plants, and pharmaceutical scientists obtain beneficial plants in their remediation. It has been observed that the affected human population is in misery because of serious disorders such as Advanced Cancer (Metastatic Cancer) (Jorge et al., 2016). In *Atuna indica* types, Umbelliferone, an active coumarin with various advertised pathways found to have improved movement of reinforcement cells as specified (Asish et al., 2013).

3.5.1 Anticancer activity

Dalton's lymphoma ascites cell (DLA) line secured from ACI, Chennai and kept up in the peritoneal hole of tumor-bearing mice from which it is suctioned during the examination suitable cell suspension (1x 106 cells in 0.1 ml) was added to tubes containing different convergences of the test mixes of leaf concentrates of *Atuna indica* and *Atuna travancorica* and the volume was made up to 1 ml utilizing phosphate supported saline (PBS). Cell practicality was controlled by trypan blue rejection technique. Such blends were washed at a temperature of 370°C for 3 hours. More suspension of the cell had to be mixed into the hemocytometer with 0.1 mL, 1% trypan blue, holding for 2-3 minutes. The blue shade of trypan blue brings in dead cells, whereas living cells do not get color. Colored and sterile cell volumes were separately counted.

The findings indicated that the leaves of the two plants, for example, have an anticancer activity, especially leaves of *A. Travancorica* displays noticeable anticancer behavior, as compared to the various parts of the two studied plants, and the present research shows that the leaves of the threatened tree species *Atuna travancorica* have striking anticancer effects on a useful edge which can be correlated with the cell reinforcement intensity observed in connection with the effects of DPPH Assay (VT & Gopal, 2018).

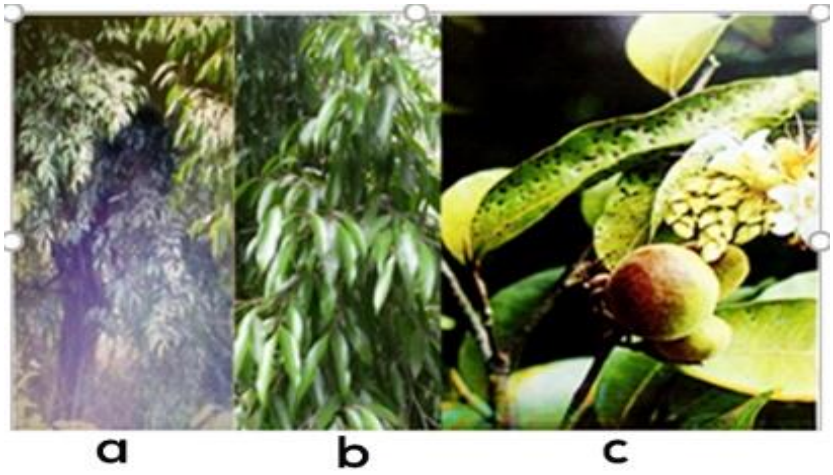


Figure 12: Picture of Atuna indica (Bedd.) Kosterm (a) Whole Plant (b) Leaf and (c) Flowering twig with flower and leaf (VT & Gopal, 2018).

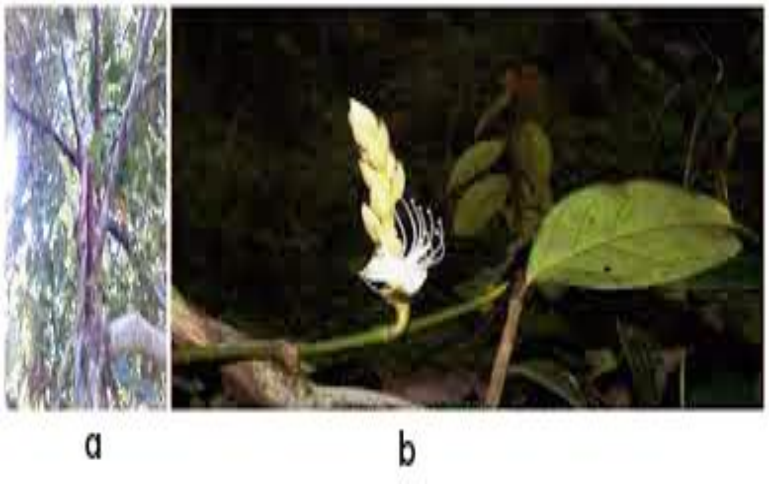


Figure 13: Picture of Atuna travancorica (Bedd.) Kosterm (a) Whole Plant and (b) Flowering twig with flower and leaf (VT & Gopal, 2018).

In conclusion, *Atuna indica* (Bedd.) Kosterm and *Atuna travancorica* (Bedd.) Kosterm has shown cytotoxic activity against cancer cells. There is no study on the stem, bark and root of *Atuna indica* (Bedd.) Kosterm and *Atuna travancorica* (Bedd.) Kosterm about the anticancer activity. It needs more study.

3.6 *Phoenix pusilla*

The family Phoenix has been accounted for to contain 13 species. Various pieces of the plant Phoenix are utilized to treat different metabolic aggravations and illnesses like fever, loss of motion, irritation, anxious clutters, loss of awareness, memory unsettling influences, cystitis, gonorrhea, stomach issues and in balancing liquor inebriation (Barrow, 1998). The vast majority of the species are utilized for decorative purposes. The fruits of the plant known as dates, from around 80% of the species are eatable and are regularly devoured as nourishment and drug all through the world (Barh & Mazumdar, 2008). *Phoenix pusilla* (Little date palm) a firmly related type of the date palm is found in India and Sri Lanka. It is a wonderful shrubby suckering palm with a short stem wrapped in constant leaf sheaths. A crown of around 15-17 leaves is delivered each year. It has been distinguished that this palm can withstand low (4°C) to high (48°C) temperatures. In Sri Lanka, it is generally known as indigaha. It is appropriated in the dry woods of Kerala, Karnataka and Eastern Ghats of Tamilnadu in India, at low rises, edges and slopes. At the hours of nourishment lack, trunk fills in as the significant wellspring of palatable starch (Gamble, 1972).

P. pusilla is an evergreen, singular or grouping, shrubby palm tree with an exceptionally short unbranched stem up to 3-6 meters tall and 30 cm in distance across that is thickly dressed with old leaf sheaths (Bharathi & Anuradha, 2019). The leaves are 3 meters long pinnate. The Leaf-sheath is stringy and rosy dark-colored. The Rachis is with at least one set of spines. Handouts pretty much sporadically masterminded, on each side of the rachis, sword-molded with sharp needle-like apices, inflexible, pale dark with an orange-red at the intersection with the rachis.

Pistillate blossoms are greenish for the most part in the distal portion of rachilla. Organic products are moderately meaty, sweet with a kind of chestnut, ovoid, 11-15 x 5-8 mm, dull purple, dark when ready in the long periods of July and August (Livingstone & Henry, 1994). Seeds are ovoid 8-12 x 6 mm with round apices, pinkish-dark colored when crisp. They are cartilaginous, scored longitudinally with a little height in the center of the back. Endosperm is homogeneous. Phoenix is engendered by pre-drenching seeds for 24 hours before planting. The ideal temperature for seed germination is 21-27^{0}C (Griffiths & Huxley, 1992). The blooming season is from November to January. The Palm creates a tangle of stringy roots that grapples it immovably to the substratum.

Polyphenols are distinguished as a compelling cell reinforcement operator to battle against infection like diabetes, malignancy, neurodegenerative maladies (E Obrenovich et al., 2011).

Flavonoids go about as a cancer prevention agent by repressing the compounds of free extreme age and lipid oxidation. It likewise demonstrated calming, antibacterial, anticancer, antiviral exercises (Shashank Kumar & Pandey, 2013). The other auxiliary metabolites like carotenoid, stilbenes and tannins additionally found to have cell reinforcement potential (Y. J. Zhang et al., 2015).

Different types of Phoenix are known to have against microbial, hostile to oxidant, antidiabetic, antitumor and hepatoprotective exercises (Bh, 2017). Consequently right now, *in vitro* cancer prevention agent action, of ethanolic concentrate of *Phoenix pusilla* root was exhibited utilizing different *in-vitro* techniques. Standard medications are utilized to look at the movement of the concentrate.

3.6.1 Anticancer activity

Numerous medical advantages are related to flavonoids like cell reinforcement and free radical rummaging movement, decrease and avoidance of cardiovascular and chronic diseases (M. P. Das et al., 2016). It has been accounted for that oral organization of ethanoic unripe natural product concentrate of *P.pusilla* (PFE) in rodents showed cancer prevention agent action by expanding the movement of compounds diminished glutathione and superoxide dismutase that go about as free extreme scroungers (Sankar & Shoba, 2017).

It has been accounted for that ethanol concentrate of dried root powder likewise have a potential rummaging property and hostile to tumor action that may be credited to the nearness of most extreme auxiliary metabolites like alkaloids, saponins, flavonoids, triterpenoids, tannin, phenolic mixes, glycosides and essential metabolites (Bharathi & Anuradha, 2019). Flavonoids are known to have anticancer activities (Susmita Das et al., 2012).

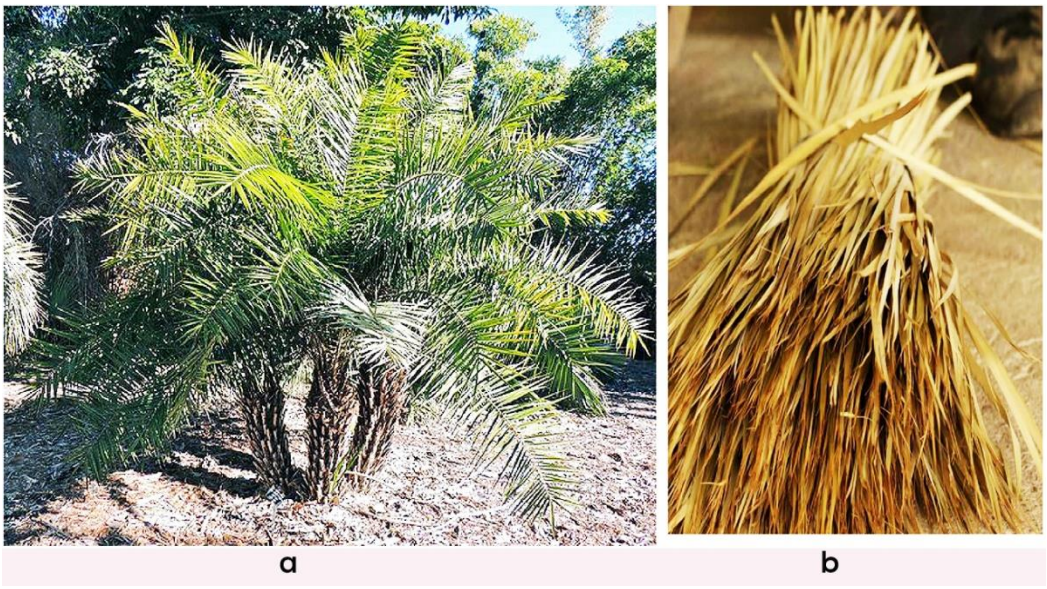


Figure 14: Picture of P. pusilla (a) Plant and (b) Leaf Fibres (Madhu et al., 2019)

In conclusion, *Phoenix pusilla* has shown cytotoxic activity against cancer cells. Tannins, flavonoids, triterpenes, saponins and glycosides have been isolated and identified from this unexplored plant. But cancer cell line test or any other test is still not happened. Even, there is not a study about stem and bark of *Phoenix pusilla* that have an anticancer activity or not.

3.7 *Lasiosiphon eriocephalus Decne*

Lasiosiphon eriocephalus Decne usually known as Raamethaa (Family: Thymelaeaceae) is generally utilized in the treatment of numerous ailments. It has generally circulated all over India, for the most part in Maharashtra, Kerala, Karnataka, and all through the Western Ghats. Phytochemical examines on a few types of family Thymelaeaceae indicated the nearness wide range of classes of normal items including auxiliary metabolites, for example, tannins, glycosides, coumarins, and flavonoids straightly disseminated in plant parts, for example, leaves, stem bark, roots, and natural products (Cottiglia et al., 2001; Liang et al., 2008). There are barely any reports on phytochemicals and their pharmacological exercises in various plant portions of these plants (Borris et al., 1988). Prior, a few genera of Thymelaeaceae are considered for their organic exercises, for example, anticancer (Rajwar et al., 2011), anti-leukemic (He et al., 2002), antidiabetic (S. Ghosh et al., 2012), anti-plasmodia (Kraft et al., 2003) and cytotoxicity (S. Y. Zhang et al., 2012) exercises. Likewise, phytochemicals from various types of Thymelaeaceae have been accounted for to show cell reinforcement action in *Gnidia stenophylla*, antibacterial in *Gonia capitata* (Nasser et al., 2010), antifungal in *G. kraussianus* and antiparasitic in *G. cuneata* exercises (Clarkson et al., 2004).

L. eriocephalus is utilized in traditional African drugs for malignant growth, sore throat, stomach torment, wounds, consumes and snake chomps (Amarajeewa et al., 2007). Leaves have been applied to treat wounds, expanding, spinal pain and joint hurts (Kareru, P. G., Kenji, G. M., Gachanja, A. N., Keriko, J. M., & Mungai, 2007). It is considered as a force full vesicant. The underlying foundations of this plant are utilized as an antiviral operators against rabies in Ethiopia. It likewise has agrochemical applications as a molluscicide, bug spray, pesticide and even larvicidal operators (Naik & others, 2007).

3.7.1 Anticancer activity

Cytotoxicity of the plant portions of *L. eriocephalus* leaves, stem, bark, and blossoms has been researched on MCF-7 and HeLa cells. Examinations of the cytotoxicity of the ethanol concentrate of blossoms and leaves showed extensive action as displayed by an IC_{50} estimation of 0.033 mg/mL and 0.061 mg/mL, trailed by the action of ethanol concentrate of stem bark with IC_{50} 0.084 mg/ml. The methanol concentrate of blossoms indicated solid cytotoxic movement with IC_{50} 0.05 mg/mL while the cytotoxic impacts of methanol concentrates of leaves and stem bark demonstrated relatively lower cytotoxic consequences for MCF-7 cells with IC_{50} valves of 0.150 mg/mL and 0.108 mg/mL, separately. Relatively, the portions of watery concentrates of leaves, stem bark, and blossoms required to murder both HeLa and MCF-7 cells are higher with IC_{50} Leaves: 0.523 mg/mL, Stem bark: 0.327 mg/mL, and Flowers: 0.128 mg/mL for HeLa cells and IC_{50} Leaves: 0.313 mg/mL, Stem bark: 0.210 mg/mL, and Flowers: 0.144 mg/mL for MCF-7 cells. The unrefined ethanol concentrate of the leaves gave the most noteworthy adequacy toward HeLa cells with a half-maximal inhibitory convergence of 0.024 mg/mL, which was trailed by the blossoms and stem bark extricates which gave IC_{50} estimations of 0.034 and 0.083 mg/mL, individually. The methanol concentrate of blossoms and leaves was modestly cytotoxic and had the option to diminish cell feasibility by half at 0.047 mg/mL and 0.066 mg/mL, separately, while methanol concentrate of stem bark demonstrated relatively lower portions for cytotoxicity for HeLa cells. The outcomes unmistakably demonstrated that both methanol, just as ethanol concentrates of leaves, stem bark, and blossoms, indicated critical inhibitory consequences for the tried HeLa just as MCF-7 cells at nearly lower fixations than the fluid concentrates. Right now, MCF-7 and HeLa cells when treated with both watery concentrates, methanol, and ethanol removes for 48 h, the outcomes demonstrated portion subordinate cytotoxicity of leaves, stem bark, and blossom separates against tried cells. Further examination of the DNA fracture, considered as

one of the signs of cell apoptosis was affirmed settling DNA separated from MCF-7 and HeLa cells presented to IC_{50} and IC_{90} centralizations of fluid, methanol just as ethanol concentrates of leaves, stem bark, and blossoms on agarose gels. Broad DNA twofold strand breaks showed up from MCF-7 and HeLa cells presented to plant removes which fill in as the ground-breaking genotoxic capability of *L. eriocephalus*. Along these lines, this investigation gives conceivable proof supporting *L. eriocephalus* plant separate showed solid cytotoxic and apoptotic potential against chose malignancy cells. Further point by point contemplates are important to improve the atomic component answerable for cytotoxicity and apoptotic impacts of genotoxic mixes right now (Durgawale et al., 2019).

All in all, the cytotoxicity of *L. eriocephalus* removes on malignant growth cell lines has indicated solid cytotoxic and genotoxic impacts. The outcomes can make a decent essential for additional examination in the potential revelation of new characteristic bioactive mixes and sub-atomic systems engaged with cytotoxicity and genotoxicity of those bioactive mixes from this conventional plant with therapeutic worth. The root of *L. eriocephalus* is still not tested.

3.8 *Elephantorrhiza elephantina*

The medicinal plants *Elephantorrhiza elephantina* (Ee) are commonly used as therapies for different illnesses in South Africa. Elandsbean or mupangara (in Shona), intolwane (in Xhosa and Zulu) and mositsane (in Sotho and Tswana) are the terms that are referred to as *E. elephantina* (Phillips, 1917). In the society of Sotho, "Red medicines" are linked to blood and great health. *E. elephantina* has a rosy origin. San's citizens also cure the iron deficiency, deficiencies (e.g., hardened blood) and fevers with red plant parts (Laidler, 1928).

E. elephantina, a species from the family of Fabaceae or Leguminosae, is a permanently low bush with stalks up to 90 cm tall in ground level and a persistent, sometimes dense rhizome up to 8 m long from the woody surface (Maroyi, 2017). Elephantorrhiza is a genus and is the most commonly found species of *E.elephantina* in southern Angola, Namibia, Botswana, Tanzania, Mozambique and many regions of South Africa (McGaw & Eloff, 2008).

Mixes identified from *E.elephantina* contains have been shown to include 5.8 to 22.3 percent of tannins that explain root redness (Watt et al., 1962). Furthermore, there are some portions of this plant's concoction framework which include phenolic mixtures such as flavonoids such as Kaempferol, Dihydrokaempferol, and Ethyl-β-D-Galactopyranoside, Quercetin 3-O-β-D-

glucoside, Ethyl gallate and Gallic corrosive form. Specific mixes of sugar (16.8%) and β-sitosterol are included in the fundamental roots of this waste (Mthembu, 2007).

Signified levels of precipitating liquor (0.7-7.0%), which include polysaccharide and glycoprotein, amino acids (α-aminobutyric corrosive, valine, serine, aspartic corrosive, asparagine, and alanine which is usually copious) as well as certain undetected terpenes from medium and low amounts are also included in the foundations of *P. prunelloides*. In fact, palmitic corrosive has been reported in *P. prunelloides* as a large non-polar compound (Yff et al., 2002).

The underground rhizomes (root) are used as remedies to diabetes in modern medicine. Besides, it is also used for the bowel loosening and diarrhea, heart disease, high blood pressure, gastrointestinal cancer, syphilis, female barrenness, midriff torments in babies, fever and hemorrhoids, as well as sexual enhancer and meaconing agent to ease precursors' indignation (Balogun et al., 2016). The root concentrates of *E. elephantine* have been shown in experiments, for example, anthelmintic, antibacterial, antifungal, calming, hostile to plasmodia, cancer prevention agent, anti-bestial and anti-rickettsia. It produces a wide variety of organic ingredients, including triterpenes, sterols, polyphenols, coumarins, alkaloids and various metabolites (Maroyi, 2017). Plants have considerable employment in the decrease of many illnesses, including diabetes mellitus, incessant disease indicated by hyper-glycemia (Olaokun et al., 2013).

Although that *E. elephantina* has been used since the treatment of various diseases, including diabetes in people's medication, and there is no clear evidence on this plant's counter-diabetic operation (Balogun et al., 2016).

3.8.1 Anticancer activity

E.elephantina concentrate was tested for the use of an MTT, using the cytotoxic movement of liver hepatoma, undifferentiated muscle cells (myocytes) and muscle cells segregated (myotubule) (Olaokun et al., 2017). Separated myotubules and C2C12 hatched C2C12 (25.000 cells/mL) and Hepatitis (30.000 cells/mL) of H4IIE were used for harmful steps in RPMI supplemented 10 percent FBS (200 ml) in 96-well plate. In five-sequential weakening (500 31.25 mg/mL), the mediums of cells were ejected after a medium-term hatch at 37° C in a 5 percent hatch and supplanted with 200 ml of crisp media that contains either extricate, DMSO (dissolved control) or doxorubicin.

The media has been flushed off after 48 h, with crisp media of 30 ml of MTT (5 mg/mL of PBS) included. With another time of brooding (4h), 50 mL of undiluted DMSO has been applied to the medium to disintegrate the MTT precious stones in the good foundation. Upon careful shaking in a microplate peruse, absorption is measured at 570 nm. The analyses of LC_{50}, which contributed to around half the absorption decrease incomparable to the untreated cells, were focused on a plot of log fixation compared to normal concentrate absorption. Reduced thyroid peroxidase activity has been reported in rodents that promote a genistein-enhanced food regimen, which is slowly expressed in cases of deficient iodine (Scalbert et al., 2005).

Studies have been studied on the cytotoxic activity of *E.elephantina*, which divides against H4IIE liver, undifferentiated muscle C2C-12 (myocytes) and divided muscle C2C12 (myotubules). By comparison to doxorubicin, the concentrates were less cytolethal against the cell lines. The H4IIe liver cells displayed moderate cytotoxicity with a death focus (LC_{50}) more pronounced than 1000 mg/ml. Both concentrates are normally not cytotoxic and have an ethanol leaf isolate. Both concentrates were not cytotoxic against the isolated C2C12 myotubules with LC_{50} that were in both instances prominent than 1000 mg/mL and concentrate was all relative cytotoxic to this cell line for the undifferentiated C2C12 myocytes, whereas the least cytotoxic is the elimination of the ethanol leaf (LC_{50}= 256, 05 and 0.05 mg/ml). No matter if *E.elephantina* is used for a long time as a remedy developed at home to treat human infirmity and animal disease, it is understood that the roots and seeds are resistant when they are used in high concentrations.

The use of root separates has been responsible for causing a blockage in humans, while seeds are a big aggravation and are linked to causing disappearing (Maroyi, 2017). Concentrate reveals adverse impacts in species models including lack of craves, bodyweight increases, changes in hematological and serum biochemical parameters, as well as histopathological shifts in the heart, pulmonary tract and spleen. A reason for the poisonous content of the root concentrates *E.elephantina* could be required in a limited way, especially for plants collected in nature, for significant soil metals recovery. The level of the overwhelming metal introduction which promotes viability was recognized as a high polyphenolic substance of plants (Ernst, 2002; Mtunzi et al., 2012).

Besides, Epicatecin can be derived from *Elephantorrhiza elephantine* which can be used for human breast cancer cells (Mpofu et al., 2015; Nagarajan et al., 2008).

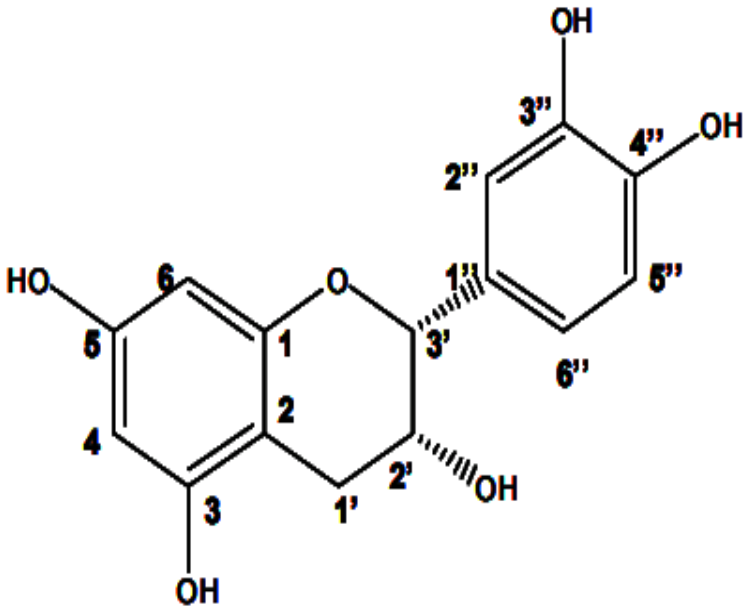


Figure 15: Structure of Epicatecin (Mpofu et al., 2015)

The leaf concentrates on *E. elephantina* had a few potential restorative advantages with insignificant cytotoxicity and might be used as an option in contrast to the roots. Be that as it may, because of the historical backdrop of this plant species' danger, more investigations should be led on the poisonous quality of the leaf concentrates to viably expand the medical advantages. Besides, other parts of the *E. elephantine* should be tested for anticancer activity.

3.9 *Tithonia diversifolia*

Tithonia diversifolia (Asteraceae: Heliantheae) is also classified as Mexico's sunflower, but is natured in Europe, Australia and Asia, which is an invasive and strong aggressive bush-like perennial or annual, north-and central-America (Varnham & others, 2006). The introduction of the plant in Nigeria has made it difficult for ranchers to test Mexican sunflowers from protected land (Chukwuka et al., 2007). The seed dispersal is by vectors, for instance, humans, domesticated animals and water flows; this form of plant produce about 80,000 to 160,000 seeds each year (Wang et al., 2004).

Usually, 1, 2–3 m high are *Tithonia diversifolia*. On the other side, the leaves are lobed, with low or decreasing roots, extreme, or tapered tops, and the edges of a crenate (sporadically upper leaves are not lobed), densely pubescent beneath with palmate venation. The leaf has normocytic stomachs on both hands, mesophyll dorsoventrally and a variety of expected

vesicle groups grouped as a midrib chain. The stem is identified with correct digressive collenchyma, prominent endoderm with the phloem sclerenchymatous tops. Place features for *T.diversifolia's* fundamental recognition are glandular and non-glandular trichomes (capita and non-capital) on the leaves and midrib pipes which are unusually close to the vascular structure (Falcone Ferreyra et al., 2012).

The plant is used as natural manure to produce vegetable crops and maize in Nigeria and Kenya (Jama et al., 2000; Nziguheba et al., 2002). Throughout various racial events, *T.diversifolia* is used all around the tradition. Stem and leaf extirpate are taken orally for the diagnosis of abscesses, hematomas and serious complications in America and Venezuela (Játem-Lásser et al., 1998) and orally for the prevention of intestinal illness in Mexico and Nigeria (Ajaiyeoba et al., 2006). Including dried leaves, which are used centrally for wounds in Costa Rica, *T.diversifolia* is also popular for the treatment of dermatological disorders, including lesions and skin inflammation, through several ethnic groups in India where the powder from toasted leaves is used (Frei et al., 1998; Heinrich, 2000).

T.diversifolia in Uganda is used either orally or for managing infectious diseases in reproductive bodies in the affected region (Kamatenesi-Mugisha et al., 2008). The blade is being treated in the traditional echo-parasite medication and custodial snake-parasite veterinary in Kenya (Njoroge & Bussmann, 2006). The Taiwanese take advantage of the leaves implantation to cure diabetes (Miura et al., 2005), while they use the herb to manage malnutrition, free the bowels, hepatic diseases, abdominal strokes, and accidents (Wahyuningsih et al., 2015).

3.9.1 Anticancer activity

The researchers discovered that, in fluid and ethanol concentrate from the three parts of the plant, phytochemicals such as alkaloids, flavonoids, phenols, saponins, tannins and terpenoids can be made. Nevertheless, in the root and stem educated plants, apart from phenol which is predominantly circulatory in the stems, phytochemicals are seen as progressively noticeable (Gabriel et al., 2015). Manganese zinc, copper, nickel, magnesium is similar to each leaf of *T.diversifolia* (John-Dewole, 2013).

The chemical composition of *T.diversifolia* are sesquiterpenes, Tagitinin C, 2alpha-hydroxytirotundin, Tagitinin A, 1beta, 2alpha-epoxytagitinin C, Tithofolinolide, 3alpha-acetoxydiversifolol and tirotundin. The study ended with an estimation of the counter-

proliferative movement of mixes in human colon malignancy (Col2) cells, their capacity to mitigate preneoplastic sores in a mouse mammary organ with 7, 12-dimethylbenz and their capability to induce cell breakdown in human promyelocytic leukemia (HL-60) cells. Tagitinin C and 1beta, 2alpha-epoxytagitinin C showed significant hostile to proliferative movement, 3beta-acetoxy-8beta-isobutyryloxyreynosin, and 4alpha, 3alpha-acetoxydiversifolol, 10 alpha-dihydroxy-3-oxo-8beta-isobutyryloxyguaia-11(13)-en-12 incited HL-60 cell separation. 3beta-acetoxy-8beta-isobutyryloxyreynosin has significantly reduced the sore growth in the mouse mammalian brain (Gu et al., 2002).

Additionally, it likewise shows that B2 disconnect is a significant cytotoxic compound from the leaves of *T. diversifolia* and is recognized as Tagitinin C based on spectroscopic information and examination with writing information. Tagitinin C is the most delicate on colon malignancy (WiDR, IC_{50}= 0,585±0.08 ug/ml).

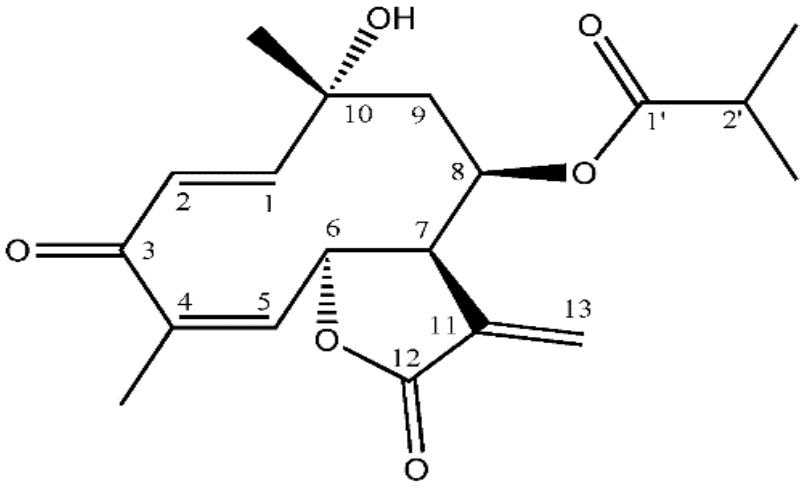


Figure 16: Structure of Tagitinin C (Sánchez-Mendoza et al., 2011).

In conclusion, *T. diversifolia* has a cytotoxic activity against cancer. The bioactive part of *T. diversifolia* and the mechanism of action should also be researched as this is necessary for this plant and also for modern medicine. Tagitinin C can be derived from these anticancer species and it has anticancer activity.

3.10 *Combretum roxburghii*

Combretum roxburghii has a position with the Combretaceae family that is therapeutically important. Combretum and Terminalia were used to diagnose syphilis, gastrointestinal agonies, intestinal looseness and numerous ailments (Fyhrquist et al., 2002). Antibacterial activity was

described in different types of Combretum (Eloff, 1999; Martini et al., 2004). Pharmacognosy is the indications for the adequacy of herbal content for the treatment of diseases including malignant development, parasitic infection and so on, like cytotoxicity and cell reinforcement movements. Powerful plant environment with many free radical particulate matter includes phenolic mixtures such as phenolic acids, flavored acids, quinines, lignin, tannins, nitrogen compounds, minerals, terpenoids (including carotenoids) and some other natural metabolites abundant in cancer prevention and action agents (Y. Cai et al., 2003; Zheng & Wang, 2001).

Eventually, the mechanisms of cancer prevention agents either eliminate or expel sensitive organisms before they can destroy important parts of the tissue. Our sensitive toxic molecules, such as breath and certain cell-interfered immune properties, allow for the use of oxygen by our organism with the absorption of hydrogen peroxide (H_2O_2), hypo chlorinated corrosive (HOCl) and free radicals, such as hydroxyl radical(-OH) and superoxide anions (O-). The radical hydroxyl is highly unstable and reacts with most natural components easily and loosely.

Additionally, free radicals or free oxygen species are formed by natural contaminations, pollution, waste, pollutants, air contamination, chemicals, etc. At a period, when the age of those free radicals approaches the organic structure cancer prevention limits, it creates upward momentum (Zima et al., 2001). Heart and intestinal disorders, neurodegenerative diseases, malignant development, AIDS and maturity are vulnerable to oxidative pressure (Astley, 2003).

Epidemiological work has shown that a wide range of such mixtures of preventive agents are soothing to atherosclerotic, tumor-hostile, mutagenic, cancer-causing, anti-bacterial, and anti-viral exercise to a greater or lesser extent (Sala et al., 2002). In any case, the hugeness of the plant for the determination of useful mixtures for medicinal use is still not yet to be investigated by the Indian species such as *Combretum roxburghii*, to find cellular reinforcements and cytotoxic capacity.

3.10.1 Anticancer activity

The cytotoxic activity of all five solvent extracts, which is a popular cytotoxic research pattern, has been tested in brine shrimp assay calculation and numerous new malignant blends have been evaluated using a similar test form, such as piperydinyl-DES and pyrollidinyl-$_1$DES (Badisa et al., 2009). To guarantee that the plant material was most stable, it was harvested in

several times, and every single leaf showed great mobility between 56-100% and 86-100%, respectively, for the long period between July and October.

Even hexane isolated showed a large 98 percent increase in the long run of February, and in October it recorded a higher percentage of 50 micrograms per ml. A single unadulterated fluid section was also subjected to the technique of Trypan blue color prevention; division revealed some cytotoxic activity. The same was subjected to an apoptosis check utilizing Jurkat and B_16 (Human tumor cell lines) on the reported cytotoxic potential of the unadulterated section. In apoptosis phosphatidyl serine (PS), usually found within the plasm, the lack of phospholipids equilibrium of the cell layer is identified. This plant can be used for human skin cancer.

Annexin V connects to this PS through apoptosis, if the separation intended to occur there was no suggestion that this could be very well expected to occur because of some other method, but not because of apoptosis, that the cell demise would result. Countless cytotoxic cell reinforcement particles are useful to fight numerous parasite diseases, holding it at sight the unadulterated division may be beneficial because it is an enemy of malaria, leishmania and other parasites (Ademola & Eloff, 2010).

Besides, the cytotoxic effects of combretastatins obtained from *Combretum roxburghii*. The leaf was recorded on the root meristem cells of *Allium cepa*. Crude leaf methanol extracts have been dissolved in DMSO (dimethyl sulfoxide) (0.5 mg/ml) and examined in allium cepa root meristem cells. The cancerous effect of rough extracts was found to be high-dose-based inhibition with induced chromosome aberrations such as chromosomal clumping, sticky bridge, early division, late division, chromosome breakage (fragmentation), and direct erosion (heavy fragmentation) at 24h and 48h (A. Das et al., 2018).

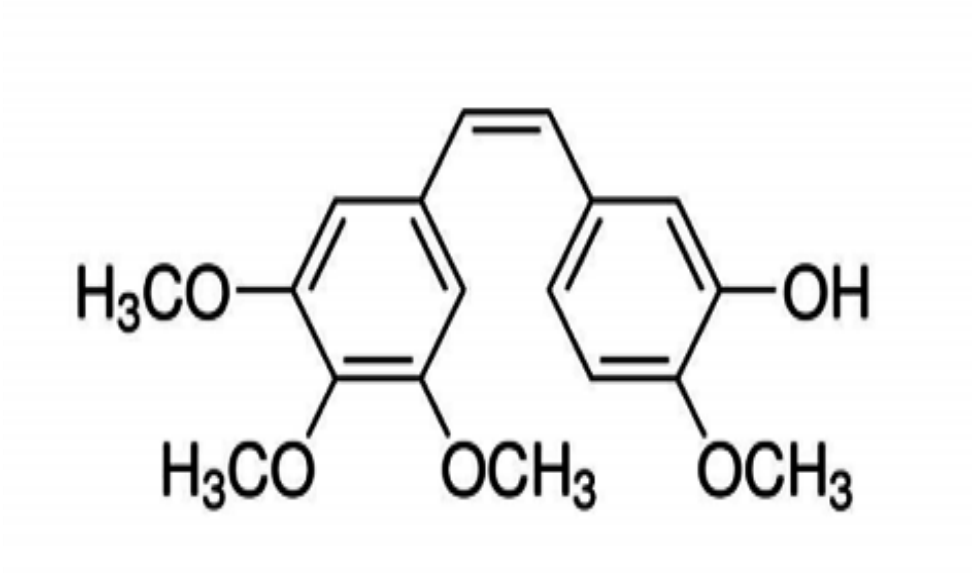


Figure 17: Structure of Combretastatins A4, Molecular Weight 316.35 (A. Das et al., 2018).

As per the previously mentioned outcomes, it may be inferred that the methanol leaf and bark concentrate of *Combretum roxburghii* indicated huge cytotoxic exercises that bolster these plants for the treatment of conventional medication. This examination additionally proposes further examination to confine most bioactive mixes answerable for the employments of this plant as customary medication. But there is so many studies needed especially in the stem of *Combretum roxburghii* about the anticancer activity.

Chapter 4

Conclusion

There are arguments that we are endowed with a vast amount of herbal medicine from our nation with ten thousand plant species on earth and that therefore we can take the medicine under the umbrella of green therapy and without side effects on the long run. Plants have an immense diversity, many of which are important to humanity as pharmaceutical products, flavors, fragrances, etc. But only a small fragment of the huge plant metabolism diversity was investigated. The root of *Phoenix pusilla* showed good cytotoxic activities but cancer cell lines such as MKN74 and HT1080 are not yet tested. *Combretum albidum* and *Aporosa wallichi* showed their leaves and bark to be cytotoxic to the cancer cell, but research on HELA or HT-29 cells is still needed. *Schleichera oleosa, Combretum roxburghii,* and *Elephantorrhiza elephantina* have been studied and showed good anticancer behavior in several cell lines such as HELA and MCF-7. However, testing of these plants is still necessary. Several parts of *Lasiosiphon eriocephalus Decne* such as stem, bark, and blossoms are tested for cancer. *Atuna travancorica* had strong cytotoxic activity against cancer cells between *Atuna indica* and *Atuna travelancorica*. *Rutidea Parviflora* and *Tithonia diversifolia's* root and bark were recently studied, but these plants need so many cancer cell line checks. These plants are less explored because a few research has been taken for them and in the future, they need more study and experiment. This research will be able to identify new secondary biologically active metabolites, utilizing large facets of plant biology to discover new medicines.

Chapter 5

Future Direction

In this study, certain plants are used for anticancer operation utilizing stem or bark or root or leaves. In the near future, the characterization of the different bioactive components of these less explored plants should be tested. Interdisciplinary work into plant genomics along with large-scale methods for metabolisms is essential for rapidly finding new pathways. Researchers are to examine the behavior of anticancer plants and their mechanism of action through *in-vivo* research. The potential prospects for this study will involve a thorough study of the effective combination by *in-vivo* and *in-vitro* testing, and providing more evidence of the efficacy of these plants so that the therapy can reach to clinical trial and thereby to provide an effective result to prevent the side effects of these plants.

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