FUNCTIONAL FOOD JOURNAL

Publication of the Functional Foods and Nutraceuticals Association of Nigeria

# Nigerian Medicinal Plants with Anticancer Properties: An Updated Review

Joan U. Imah-Harry*, Charles C. Chidume, Felix O. Okunlola, Julius K. Oloke

*Department of Natural Sciences, Faculty of Pure and Applied Sciences, Precious Cornerstone University, Ibadan, Nigeria.*

**Abstract**

Cancer is a critical global health issue and a significant contributor to mortality rates worldwide, with the number of mortality rates and the development of new and effective anticancer agents rising daily. Nigerian medicinal plants (NMPs) have been widely investigated in the management of diseases, including cancer. NMPs engage in pharmacological actions of inherent bioactive compounds and systematic investigations are done to confirm their therapeutic resolutions. Multidrug-resistant malignancy cases are increasing, but natural plant-derived products are still of high significance, despite improvements in drug design. Nigeria is a country blessed with an array of plants used in folklore medicine for cancer and other disease therapies. This review focused on 13 NMPs that have been investigated for their anticancer potentials, both *in vitro* and *in vivo*. These plants though phytochemical-rich exhibited cytotoxic, antiproliferative, and apoptotic properties, indicative of their potential as novel anticancer drugs, while stressing the need for safety assessment.

**Keywords:** Nigerian medicinal plants (NMPs); Cancer; Mortality; Multidrug resistant malignancy; Bioactive compounds

***Corresponding author:**

joanharry74@gmail.com, imah-harryjoan@pcu.edu.ng,

ORCID ID: 0000-0001-7361-0385

Received: 07/06/2024

Received in revised form: 24/08/2024

Accepted: 06/09/2024

## 1.0 INTRODUCTION

Today, one in five individuals globally will develop cancer at some stage in their lives. Cancer ranks as the second largest cause of mortality following cardiovascular diseases. In economically advanced countries, it is the primary cause of mortality, while in developing nations; it is the second most significant cause of death (WHO, 2024; Soerjomataram & Bray, 2021). Given this, cancer prevention has become a critical public health priority in the twenty-first century. Cancer poses a significant public health challenge on a global scale, currently ranking among the top causes of death worldwide. The number of deaths due to various forms of cancer mounts steadily. The number of deaths recorded worldwide as a result of cancer increased by 17% between 2005 and 2015 with about 90.5 million people diagnosed with cancer in 2015 (Adewole, 2020). Across the globe in 2018, about 18.1 million people suffered from cancer, and 9.6 million people died of cancer (Bray *et al*., 2018). An estimated value of new cancer cases of about 1.9 million leading to 609,360 cancer-related deaths were reported in the USA, in 2022 (Siegel *et al*., 2022). Each year, 100,000 new instances of cancer are found in Nigeria, with a high case fatality rate (Fapohunda *et al*., 2020). In 2030, deaths due to cancer worldwide are estimated to be more than 13.1 million (Kooti *et al*., 2017). Hence, ending safe, novel, and effective interventions to curtail cancer and its intricacies is extremely vital. Traditional medicines, which have been consumed for extended periods with limited reports on toxicity, may provide protective benefits against cancer by destroying tumor cells or preventing them from acquiring new characteristics (AlQathama *et al*., 2020). Prior to the establishment of the Nigerian National System of Cancer Registries in 2009 accurate data on cancer in Nigeria was limited due to underreporting. However, recent data shows that over 100,000 cases of cancer are diagnosed and 70,000 deaths occur annually in Nigeria, meaning that roughly 1 in 10, Nigerians are at a risk of developing cancer before reaching age 75, according to the International Agency for Research on Cancer (AlQathama *et al*., 2020). The chemical makeup of plants forms the foundation for utilizing herbs as medicine. Having a thorough understanding of a plant's chemical composition improves our ability to identify its potential medicinal benefits. Advances in chemistry have revealed the crucial role primary plant metabolites play in fundamental processes like cell growth, respiration, storage, and reproduction. These primary metabolites give rise to secondary plant metabolites, which are diverse chemical compounds produced by plants through metabolic pathways that branch off from the core metabolic pathways.

These compounds exhibit various biological effects, forming the scientific rationale for the traditional application of herbs in many ancient communities (Hussein & El-Anssary, 2019). Medicinal plants have been known to have properties like antibiotic, antifungal, antiviral, antitumor, or anticancer effects. Natural products, which include traditional medicines, are both a foundation for traditional medicine and a crucial source of potential drugs in the drug discovery process. A major challenge in modern cancer therapy is the rise of multidrug resistance, which

occurs when cancer cells become resistant to multiple types of chemotherapy drugs. Research has shown that various herbal extracts, or traditional remedies, can function as chemo sensitizers or resistance modifiers and may help combat multidrug resistance (AlQathama *et al*., 2020). Their effectiveness lies in their ability to affect several survival pathways with minimal harm to normal cells (AlQathama *et al*., 2020). Cancer is a disease described by the deformation and propagation of human traditional cells, resulting from cellular modulations and impediments in the normal cell cycle development, leading to abnormal growth and spread of cells caused by genetic mutations in the body (Tyagi *et al*., 2017). It is therefore defined as a collection of ailments branded by loose separation and multiplication of cells. The abnormal growth of cells is a result of uncontrolled reproduction and regulation of cell division through asexual reproduction, which results in the formation of malignant tumor cells capable of becoming metastatic. Cancer cells are characterized by their ability to invade and destroy normal cells and therefore cause changes within surrounding tissues. For cancer cells to grow and sustain growth, deregulation of the cell cycle and checkpoint disruption is crucial. While a greater number of the malignant cells occur as compact growths that must have initially appeared in several body parts and tissues, the malignant cells may arise as hematological malignancies (leukemia), (Titoy *et al*., 2017). Cancers are traditionally classified according to the organ or tissue of origin, but there is a growing emphasis on categorizing them by the molecular characteristics of the specific cancer cells (Krieghoff-Henning *et al*., 2017).

Cancer is not caused by external factors like diseases or parasites, but by human cells that have become abnormal and form tumors. Cancer is a multifaceted genetic disorder that is mostly brought on by environmental causes, including UV exposure and exposure to food, water, air, and chemicals (Sushma, 2012). The activity of free radicals and pathogenic microorganisms has been linked to cancer development. Research has shown that when reactive free radicals interact with cellular macromolecules, such as DNA, they cause damage to the cell's structure and functions (Vineis & Wild, 2014). ROS-mediated DNA alterations can cause mutations in genes involved in the control of the cell cycle, apoptosis, and/or growth factor signaling pathways, which are frequently required for the start of cancer cells (Carvalho *et al*, 2018). Additionally, it has been discovered that pathogenic bacteria are connected to certain types of cancer. Pathogenic bacteria such as Helicobacter organisms are associated with the progress of colon and gastric cancer in humans (Varon *et al*., 2022). *H.pylori* is a major cause of peptic ulcer disease and a significant risk factor for gastric cancer. Anybody can develop cancer, and as people get older, their chances of getting it also rise. Numerous issues, including nausea, cachexia, vomiting, discomfort, diarrhea, constipation, hypercalcemia, appetite loss, anemia, lethargy, leucopenia, neutropenia, and thrombocytopenia, are connected to cancer disorders (Hassan, 2020). Owing to the unimpeded and irregular propagation of malignance, tumors, or malignant disease is a

disturbing situation currently. Furthermore, death tragically arises due to the most unfavorable side effect of tumor management, metastasis. Additionally, the mortality rate of cancer patients is increasing globally with statistical records that are not predominantly promising (Ediriweera *et al*., 2016). This current review potted the anticancer activity of Nigerian plants with medicinal potential that have been examined empirically, providing highlights on the different parts of the plants with the bioactive agents accountable for both the pharmacological and antitumor activities.

In this review, the information used was retrieved from, using two internet based search engines; Google scholar and Pubmed Central. Systematic records encompassing Science Direct SpringerLink, Medline, and Mendeley were combed, and articles between the years 2009 and 2023 were retrieved giving rise to 115 papers that were referenced and fully cited in this paper.

## 2.0 Hallmark of Cancer

Cancer does not represent only one disease. The hallmark of cancer consists of different parameters that apply to most, if not all spectrum of human cancer. They portray the necessary properties needed for sustaining proliferative signaling, avoiding growth inhibitors, resisting apoptosis, promoting blood vessel formation, facilitating invasion and metastasis, altering cellular metabolism, and escaping immune system destruction (Hanahan, 2022).

**2.1 Sustaining Proliferative Signaling** – one fundamental characteristic of cancer cells is their ability to undergo unregulated cell proliferation. Cancer cells undergo inappropriate cell growth and division without the necessary signals required for this process. This is because cancer cells undergo genetic mutations that transform certain genes into active drivers of cell proliferation (Zhong *et al*., 2020; Hanahan, 2022).

**2.2 Insensitive To Growth Suppressor Signals** – cancer cells are insensitive to secreted, cellular, or extracellular growth suppressors that inhibit the division of normal cells. Hence, cancer cells can regain the ability to stimulate cell division, allowing them to re-enter the cell cycle (Zhong *et al*., 2020; Hanahan, 2022).

**2.3 Evading cell death**-, this is a characteristic of most, if not all, kinds of cancer. Cancer cells are immune to both cell-intrinsic and external signals that detect different forms cellular anomalies such as cell damage, irregular migration or proliferation of cells, and DNA damage required for apoptosis to occur (a prominent type of programmed cell death) (Zhong *et al*., 2020; Hanahan, 2022).

**2.4 Genome instability and mutation**- Cancer cells can undergo mutations that confer on them the ability to replicate continuously, a characteristic necessary for their continuous expansion and dominance (Zhong *et al*., 2020; Hanahan, 2022).

**2.5 Sustained Angiogenesis**- To sustain viability and proliferation, cancer cells require a constant supply of glucose, oxygen, and other nutrients. Angiogenesis, the

process of forming new blood vessels, is crucial for this supply, as it enables the creation of a vascular network that delivers essential nutrients and oxygen to the tumor. This process is carefully regulated by various inhibitory and stimulatory factors, although cancer cells bypass the need for some of these controls to ensure continuous blood vessel formation (Zhong *et al*., 2020; Hanahan, 2022).

**2.6 Tissue invasion and metastasis** – cancer cells are capable of invading nearby tissues as well as entering blood and lymphatic vessels and colonize other parts of the body both nearby and distant parts (Zhong *et al*., 2020; Hanahan, 2022).

**2.7 Alternating Cellular Metabolism** – In other to sustain their proliferation, cancer cells can alter metabolic pathways to satisfy their need for nutrients and energy (Zhong *et al*., 2020; Hanahan, 2022).

**2.8 Avoiding immune destruction** – cancer cells are capable of evading the action of the immune system. This is evident in the fact that most antigens expressed by spontaneously developing cancer cells are likely identical to those found in the normal tissue from which they originated, causing them to be ignored by the immune system (Zhong *et al*., 2020; Hanahan, 2022).

**2.9 Promotion of inflammation by tumor** - Tumor-promoting immune cell infiltration (inflammation) is associated with many types of cancer (Zhong *et al*., 2020; Hanahan, 2022).

## 3.0 Stages of Cancer

There are various forms of cancer such as carcinoma, sarcoma, leukemia, lymphoma and myeloma, and central nervous system cancer with the most common types including that of the lungs, liver, cervix, colon, prostate, and breast. Cancer of the lungs, prostate, colon, and stomach is more common in males, while cancer of the breast, cervix, lung, and colon is more common in females. Cancer has various levels, from I to IV, and the highest level, which is IV, is the most severe. Cancer staging and grading are used to develop appropriate medicines, predict the clinical progression of malignancies, and ensure accurate communication among physicians. Surgery, radiation, chemotherapy, and hormonal/biological therapies are considered effective treatment for illnesses in stages I through III. The disease is regarded as incurable at stage IV. Most Cancers with tumors are staged into five major categories using Roman numerals, although other kinds of cancer, such as lymphoma, brain, and blood malignancies, have their staging methods, each one indicates the stage of the malignancy (Adetuyi *et al*., 2022).

Stage 0 is identified by the presence of abnormal cells that have the potential to transform into cancer cells, rather than the actual presence of cancer. This is also known as carcinoma in situ.

Stage I means the tumor is present but it is confined to its organ of origin without any nodular involvement or vascular spread, often termed early-stage cancer. Stage II means the local tumor spreads to nearby tissue and local lymph nodes. Stage III indicates that the large primary tumor has

occupied deeper tissues and lymph nodes. Stage IV indicates proof of distant metastasis outside of the tumor's primary organ, meaning the cancer has spread beyond the primary organ to other parts of the body (Telloni, 2017).

**4.0 Tumor-Node-Metastasis (TNM) System**

The TNM classification system, which evaluates the size and local extent of the tumor (T), the extent of lymph node involvement (N), and the presence of distant metastases(M), is the most widely used and standard method for determining stages in cancer (Rosen *et al*., 2020).

A tumor (T): The extent of tissue infiltration and the prime tumor's size is characterized by T0 – T4 while T1-T4 is used to define the scope and extent of the tumor, with advanced development and intrusiveness from T1 to T4 reflecting larger size and/or local spread of the tumor, whereas T0 designates the nonappearance of tumor signal. Nodes (N): When the tumor spreads to the lymph nodes, which act as biological filters, bodily fluids from tissues, are taken up by lymphatic capillaries, and lymph nodes, they are described using N0 -N3, while N1-N3 designates malignancy has spread to some degree in the lymph nodes, with an increasing distance in spread from N1 to N3.

Metastasis (M): M0-M1 indicates if cancer has spread to different areas of the body. If the cancerous tumor has spread beyond the nearby lymph nodes, then it is considered to have metastasized. A tumor is classified as M0 indicates no distant metastasis has occurred and M1 indicates distant metastasis (Rosen *et al*., 2020). Metastasis is a frequent occurrence in the latter stages of cancer and can occur via the bloodstream, lymphatic system, or both. The typical stages of metastasis include Local invasion, entry into the blood or lymph vessels, circulation throughout the body, and exit from the vessels into new tissues, proliferation, and formation of new blood vessels. Although cancer often spread to specific organs, common sites for metastases in solid tumors include bone, liver, lymph nodes, lungs, and bone marrow (Adetuyi *et al*., 2022).

"Metastasis" describes the formation of secondary tumors in parts of the body that are far from the original cancer location. Although it is the primary cause of cancer treatment failure and mortality, the process of metastasis remains not fully understood. While cancer patients release large numbers of cancer cells into their bloodstream daily research on melanoma in animal models indicates that only about 0.1% of these cells manage to spread. For metastases to occur, cancer cells must leave the primary tumor, travel through the bloodstream, withstand the pressure within the blood vessels, adapt to the new environment at a secondary site, and evade destruction by immune cells. Ultimately, metastasis is responsible for over 90% of cancer related deaths. Gaining a deeper understanding of this process could help identify potential molecular targets for therapies aimed at slowing or stopping the spread of cancer (Fares *et al*., 2020).

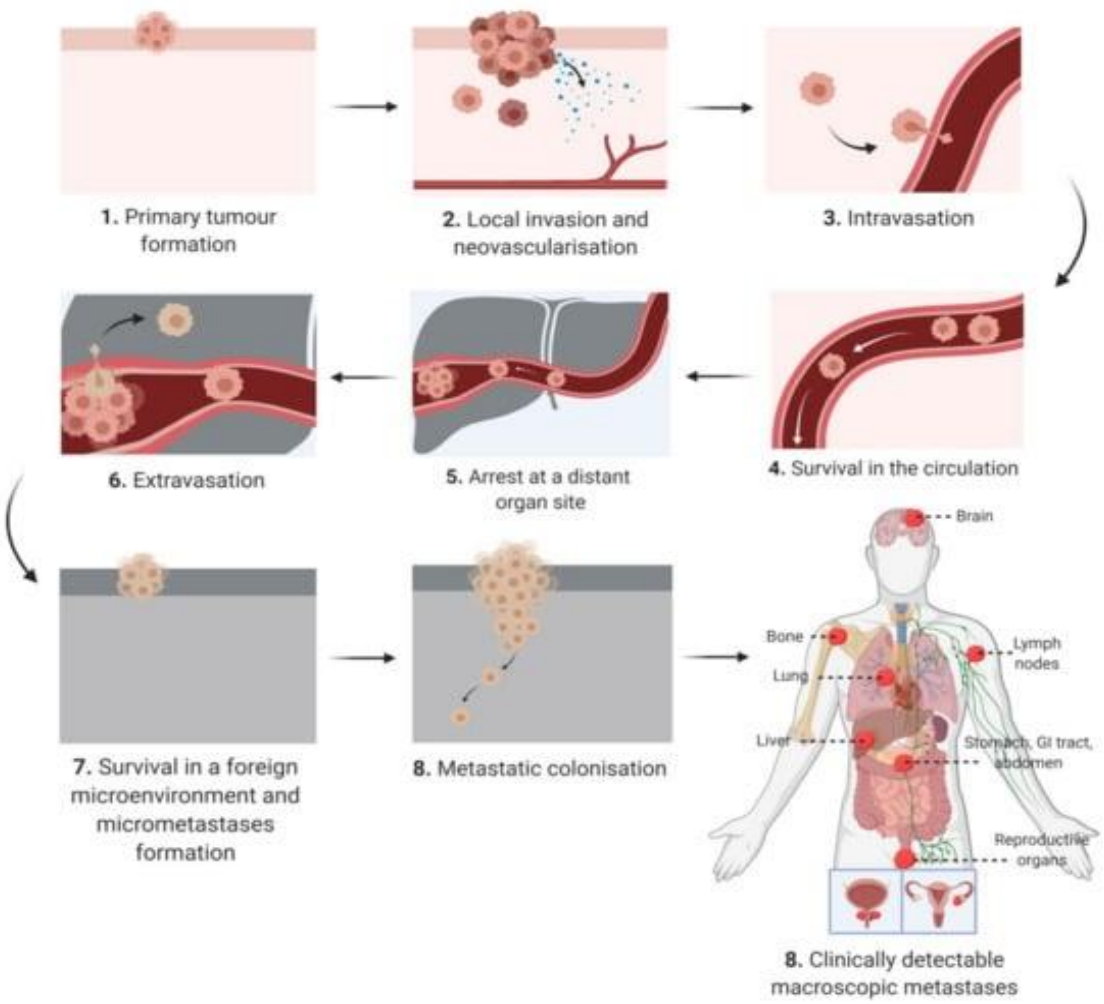


**Figure 1:** Cancer Metastasis (Annet *et al*., 2020)

## 5.0 Plant-Based Anti-Cancer Therapy

Cancer is a highly growing disease that is limited to neither age nor time (Joshi & Joshi, 2017) and the need for more research and development of new anti-cancer therapies is highly essential. Currently, cancer is treated via various methods such as surgical operation, radiotherapy, and chemotherapy, which is often complemented by noxious effects. Unfortunately, the treatment of cancer is highly expensive, and yet the chemotherapeutic agents used have not been clinically successful in controlling cancer. Chemotherapy often leads to an increase in reactive oxygen species (ROS) production, causing oxidative stress in both tissues and cancer cells. The overproduction of ROS may interfere with cellular equilibrium and cause toxicity (Thyagaragan & Sahu, 2018). Chemotherapy destroys cancer cells either directly by disrupting DNA synthesis, or indirectly by interfering with mitotic components.

Unfortunately, this toxicity affects both cancerous and normal cells, raising risks and making it difficult to treat the various side effects (Hassan, 2020). A major setback in the treatment of cancer via this method is the

ability of these chemical agents to cause harm/damage to normal cells while destroying tumor cells because of their non-selective nature thereby resulting in the reduction of functional capacity and quality of life in cancer patients and survivors (Nurgali *et al*., 2018). Other than the toxicity of these chemical agents in the treatment of cancer, cancer treatment is also accompanied by challenges such as resistance and ineffectiveness of some anti-cancer agents. Researchers are working to create natural alternatives to chemotherapy to lessen the frequency of important issues like resistance (Ahmed *et al*., 2017).

Given the persistent emergence of medication resistance, tumor recurrence, and metastasis, the demand for novel treatment approaches continues to be of the utmost importance. For patients to experience successful therapeutic outcomes and improve their quality of life, new tactics must be developed to increase chemotherapy sensitivity and reduce harmful side effects. New research indicates that many cancer patients around the world utilize either dietary substances that affect cellular signaling or herbs used in complementary therapies (Kikuchi *et al*., 2019).Despite significant progress in cancer treatment, the global burden of the disease continues to rise, therefore it is crucial to develop highly effective anti-cancer agents with minimal side effects that are also accessible at an affordable price (Ohiagu *et al*., 2021). Additionally, the prevalence of cancer and cancer-related fatalities are rising steadily in several parts of Africa, particularly Nigeria. This may be due to the absence of accessible, reasonably priced healthcare for early detection and treatment (Abubakar *et al*., 2020). Research for natural anti-cancer agents with higher effectiveness and safety is a fast-growing field. As a marker towards establishing their anti-cancer potentials, many NMPs have been investigated, analyzed and clinically screened for their antioxidant capacity. In addition, these plants are evaluated to determine their safety and mechanism of action in cancer cell Inhibition (Thomford *et al*., 2018). A major class of novel immunomodulators, particularly effective anti-inflammatory and anticancer medicines, has been identified in natural products, particularly those derived from plants. Researchers have become interested in plant-based therapies because they offer alternate methods for treating a variety of contagious and crippling diseases. These treatments also have anti-inflammatory and anticancer characteristics (Wahab *et al*., 2018). Various studies and research have demonstrated the effectiveness of plants in treating several diseases including, fertility, sterility, diabetes, thyroid disorders, anemia, and psychological disorders and the use of these plants will help reduce exposure of patients to the effect/toxicity of chemical therapeutic agents. Natural substances are discovered to be more readily available, less expensive, have fewer or less severe side effects compared to synthetic drugs. They are also rich in a wide range of biologically active chemotypes than synthesized medications. In addition to acting as anticancer drugs, natural substances derived from plants can also improve chemotherapy sensitivity (Ahmad *et al*., 2017, Hassan, 2020). Most research efforts on anticancer drugs have focused more on natural products

with high therapeutic efficacy for cancer treatment with little toxicity and side effects. Recently, more than 60% of anticancer compounds valuable in the management of tumors are sourced and originating from plants, maritime, and microorganisms.

## 6.0 Application of Medicinal Plants in Cancer Treatment

Throughout history, plants have served both therapeutic and preventive purposes. Plants are a novel source of bioactive natural compounds, and drug discovery has primarily relied on their ethno pharmacological effects. Ethno pharmacology is a vital field for creating new drugs that are crucial for preserving and advancing the use of natural goods in traditional ways. It is also unquestionably one of the key sources for the rational development of new drugs (Siegel *et al*., 2022). Research indicates that the plant kingdom comprises approximately 250,000 species, yet only about 10% have been explored for their potential in treating various diseases. Traditional medical practitioners in the treatment of cancer have used plants and their compounds, which are crucial in the development of chemotherapeutic agents (Abbas & Rehman, 2018). Medicinal plants are plants that contain one or more bioactive compounds, which are utilized for therapeutic purposes, and function as forerunners for the semi production of chemo-pharmaceuticals or the production of medications (Hamuel, 2012, Musa, 2018).

The World Health Organization (WHO) estimates that more than 80% of people globally depend on medicinal plants for traditional healthcare. In developing countries, 80% of the population relies on traditional herbal medicine to treat infectious diseases caused by their environment (Bhatwalkar *et al*., 2021). Modern medicine also makes use of medicinal plants for both the treatment and prevention of cancer, making it crucial to identify and extract antitumor-enhancing compounds found in commonly used medical plants.

Medicinal plants play a vital role in meeting healthcare needs in developing nations, particularly in Africa where a significant portion of the populace depends on them for this. Despite the use of synthetic chemotherapeutic agents, plant extracts represent a significant source of chemotherapeutic agents in Nigeria. Over the years, medicinal plants have been used worldwide, particularly in Nigeria and other underdeveloped nations, for the treatment of cancer. Traditional medicine is an essential part of healthcare in sub-Saharan Africa, where it is frequently the most readily available and least expensive kind of therapy. Herbal medicine has gained widespread popularity throughout time, as seen by the high attendance and growing media attention tied to the several yearly herbal medicine trade fairs (Segun *et al*., 2018). According to researchers, herbal-based medications are among the greatest options for treating and/or preventing the development of cancer. This is mostly because plants contain a variety of active chemicals that fight cancer in several different ways (Ahmad *et al*., 2017, Hassan, 2020). The anticancer properties of medicinal herbs are promising. The development of drugs from herbal sources has been essential in the fight against cancer. Most of the chemotherapeutic drugs used in the

management of tumors/cancer are sourced from artificial products or chemicals extracted from plants (Ukwubile *et al*., 2020). The bioactive chemicals found in medicinal plants are what give them their anticancer properties. Plants contain non–nutritive biologically occurring active chemical compounds called phytochemicals, which serve as a natural defense mechanism for the host plants while also contributing to their flavor, color, and aroma. These phytochemicals are sub-classified into two categories known as primary metabolite and secondary metabolites (Okezie & Ugbogu, 2017). With the identification of the secondary constituents of natural goods and medicinal plants, numerous improvements in conservative cancer therapy have been recorded. The bioactive substances that make up these therapeutic plants do not seem to directly affect how they grow. These substances, known as secondary metabolites, are in charge of the pharmacological effects that the drug has on the body. These secondary metabolites are synthesized, accumulated, and distributed in diverse portions of medicinal plants such as the roots, stems, leaves, flowers, fruits, and seeds (Li *et al*., 2020). Secondary metabolites have been found to exhibit anti-inflammatory, anti-mutagenic, and anti-cancer in addition to biological effects on hematopoietic cells, lipids, and cardiovascular systems. These include alkaloids, polyphenols, saponins, triterpenes, flavonoids, etc., which are the core types of bioactive agents accountable for the pharmacological and antitumor activities, cell cycle arrest, inhibiting angiogenesis, reducing tumor cell viability, and demonstrating anti proliferative, cytotoxic, cytostatic, anti-metastatic, apoptotic, and antioxidative properties.

## 7.0 Classification of Bioactive Compounds with Anticancer Activity

Bioactive molecules are compounds that are essential for human growth and development offering various health benefits such as inhibiting low density lipoproteins and cholesterol, providing antioxidant effects, strengthening immunity, digestive health, and anticancer among others. The phytochemical classes mentioned earlier in the review are the main types of bioactive substances from medicinal plants with potential anticancer effects.

### 7.1 Polyphenols

Higher plants produce polyphenols as secondary metabolites, which offer potential health benefits for people as well as several vital roles in plant physiology, including anti-hypertensive, antioxidant, and anti-allergic, anti-cancer, anti-inflammatory, and antimicrobial agents. The ability of these compounds to inhibit or reduce the activity of enzymes like telomerase, cyclooxygenase, or lipoxygenase, as well as their engagement with signal transduction pathways and cell receptors, have all been implicated in the protective effect of these compounds (Daglia 2012). According to reports, polyphenols have cytotoxic and antioxidant effects on cancer cells. The ability of the polyphenols to start apoptosis is crucial to their anti-carcinogenicity. On chromatin, polyphenols control how copper ions are arranged. Polyphenols, such as resveratrol, facilitate the arrangement of copper ions of chromatin, leading to DNA fragmentation (Ohiagu *et al*.,

2021). Polyphenols which are abundant in plants possess numerous anti-carcinogenic properties, including the suppression of tumor formation, metastasis, angiogenesis, and inflammation as well as to trigger apoptosis. Additionally, they can modulate immunological response and protect healthy cells from free radical damage (Niedzwiecki *et al*., 2016). Through processes such as acetylation, phosphorylation, and methylation, plant polyphenols interfered with the proteins of cancer cells, preventing their proliferation. Polyphenols directly associated with carcinogens interfered with their tumor-enhancing actions. For example, curcumin a polyphenol, has been found to inhibit the effects of tumor necrosis factor (TNF) in cell lines (Gupta *et al*., 2014).

**7.2 Flavonoids**

Flavonoids are secondary metabolites belonging to the class of polyphenolic phytochemicals found in plants. They consist of two benzene rings (A and B) bounded by three carbons and one oxygen atom, forming a central pyrone ring, C (C6-C3-C6). Flavonoids, which possess both antioxidative and anti-inflammatory characteristics, can be located in various sources such as fruits, vegetables, legumes, green tea, and red wine (Niedzwiecki *et al*., 2016). Flavonoids are classified into, flavones, flavanones, anthocyanins, flavanols, flavanonols, flavanols or catechins, chalcones all of which can act as antioxidants (Panche *et al*., 2016). Numerous studies have also noted flavonoids' exceptional and important capabilities as chemopreventive and/or anticancer agents, pointing to a link between a diet high in flavonoids and a decreased chance of developing cancer. Additionally, it has recently been demonstrated that flavonoids can influence immune system response and may have immune-modulating effects (Kikuchi *et al*., 2019). By activating both extrinsic and intrinsic signaling pathways, the flavonoid salpinumisoavone and 4'-methoxy licoavanone caused human leukemia cells to undergo apoptosis, which ultimately resulted in cell death (Kumar *et al*., 2013). The flavonoids prevented the expression of NF-kB, which is necessary for angiogenesis, cell growth, and malignant cell persistence (Greenwell & Rahman, 2015, Ohiagu *et al*., 2021). The three following mechanisms must be met by flavonoids to function as chemo-preventive agents: inhibition of carcinogen metabolic activation, inhibition of cancer cell propagation by sedentary or down-regulated pro-oxidant or signal transduction enzymes, and induction of cancer cell death, CCD (apoptosis) (Vo *et al*., 2022).

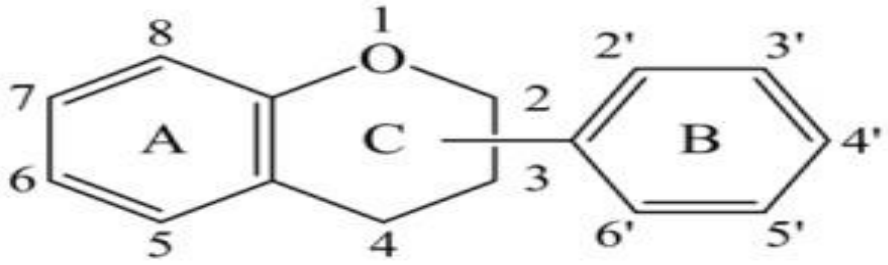


**Figure 2:** Structure of flavonoids (Sak, 2017)

### 7.3 Alkaloids

Alkaloids are bioactive substances that are present in plants and are a major source of concern in the creation of plant-based anticancer agents. Alkaloids represent a broad category of chemicals with cyclic structures that include at least one basic nitrogen atom (Lu *et al*., 2017). Due to their structural diversity, alkaloids, which are nitrogenated chemicals metabolized mostly by plants, are of special interest in the development of novel medications (Tallini *et al*., 2022). Alkaloids are nitrogen-containing heterocyclic secondary metabolites derived from amino acids or by the transamination process, which gives them their basic characteristics (Diaz *et al*., 2015). Alkaloids majorly exist in Leguminosae, Menispermaceae, ranunculacae, loganiacea, and papaveracae family species (Musa, 2018). Various alkaloids including camptothecin, vincristine, vinblastine, barberine, sanguinarine, evodiamine, piperine, matrine, and tetrandrine are recognized for their effectiveness as chemotherapeutic agents. Numerous alkaloids from medicinal plants demonstrated antiproliferative and anticancer activities on a variety of malignancies both in vitro and in vivo. Breast, ovarian, non-small cell lung cancers, and soft tissue sarcoma are among the cancers treated with chemotherapy using *Catharanthus roseus*, which has been shown to contain a variety of alkaloids (Lichota & Gwazdzinski, 2018).

### 7.4 Saponins

Amphiphilic molecules like Saponins are made up of polar (water-liking) saccharide chains joined to a non-polar (fat-soluble) aglycone. The aglycone of saponins has a polycyclic ring structure (either 27-carbon sterol or 30-carbon triterpene). Seeds of pulses and edible legumes are the major possessors of saponins. These high molecular weight compounds are created when a sugar molecule binds to a triterpene or steroid aglycone. Saponins are categorized into steroidal and triterpene types. They are insoluble in polar solvents like ether but soluble in water. They hydrolyze to produce aglycones, just like glycosides. They play a crucial role in treatment since they have anticancer and hypolipidemic properties (Hamuel, 2012). Saponins are considered important for lowering cancer risk as they may operate against pathways related to the potential for carcinogenesis, they have been proposed as anti-carcinogens. Saponins have the power to eliminate cancer cells from the body (Singh *et al*., 2017).

Natural glycosidic substances known as saponins are present in a wide variety of plants and have several biological effects. The aglycone moiety, which might be triterpene or steroidal, differs between the two main classes of saponins. The anticancer action of triterpene saponins is one of their most promising biological characteristics (Koczurkiewicz *et al*., 2019). Through cytokine interaction, saponins showed immunomodulatory effects (Sun *et al*., 2009, Ohiagu*et al*., 2021). It was discovered in a published study that the saponins from Astragalus (Fabaceae) have anticancer effects on HT-29 human colon cancer cells and tumor xenografts. These saponins inhibit cell growth by causing accumulation in the S phase and G2/M arrest, along with concurrent suppression of p21 expression and inhibition of cyclin-dependent kinase activity, they prevent cell growth. Additionally, AST induces apoptosis in HT-29 cells by activating caspase 3 and cleaving poly (ADP-ribose) polymerase, as evidenced by DNA fragmentation and nuclear chromatin condensation. In addition, saponins from B. aegyptiaca (Zygophyllaceae) have shown strong anti-proliferative properties against the HT-29 human colon cancer cell and MCF-7 human breast cancer cell (Beit-Yannai *et al*., 2011, Yildirim & Kutlu, 2015).

### 7.5 Triterpenes

Triterpenes, consisting of six-isoprene compounds, are a group of chemical substances with chemical formula $C_{30}H_{48}$, made up of three terpene units. All living things, fungi and squalene, the precursor of all steroids generate Triterpenes. Triterpenes are a common group that is created when squalene epoxide is arranged in a chair-chair-chair-boat pattern under the direction of condensation. They are an essential component of plant membrane structures that stabilize the phospholipid bilayers in cell membranes. Triterpenes target anti-cancer, anti-inflammation, antioxidative, antiviral, antibacterial, and antifungal actions because of their diverse medical significance. Terpenoids target various cancer-specific targets such as the proteasome, B cell lymphoma 2 (Bcl-2), NF-kB, STAT3, TNF, angiogenesis, PI3K/Akt/mTOR, and (TLR) to suppress cell proliferation and promote the progression of tumor cell death(Gill *et al*., 2016). 3-O-acetyl-11-keto-boswellic acid a known triterpene stimulated the death receptor DR-5 signaling pathway, which in turn triggered the apoptosis of tumor cells. Triterpenes have also triggered apoptosis by increasing intracellular $Ca^{2+}$ levels and promoting p53 release (Ohiagu *et al*., 2021).

### 7.6 Tannins

Numerous plants, including fruits, green and black teas, nuts, and grains, contain tannins. Tannins are soluble in water and alcohol. These compounds are present in many plant parts, including bark, wood, leaves, fruit, roots, plant galls, and seed. Tannins are recognized for their ability to prevent lipid peroxidation and scavenge free radicals, which play a key role in controlling oxidative stress within cells. The structure and degree of polymerization of tannins dictate the majority of their actions, including their capacity to neutralize free radicals (Sjeniawska & Bai, 2017). Tannins can form complexes with alkaloids, proteins, carbohydrates, and gelatin. There are two

different kinds of tannins: (1) those that can be hydrolyzed to produce gallic acid (gallotannins) and ellagic acid (egallitannins), and (2) condensed tannins. Tannin-rich medicinal herbs are utilized as remedies for a variety of illnesses (Hamuel, 2012). Corilagin, a type of tannin, reduces the proliferation of malignancy in cells by interfering with the TGF-/AKT/ERK/ smad signaling pathways and induces cell cycle arrest at the G2/M phase. It also had anti-inflammatory effects (Jia *et al*., 2013). Tannic acid a specific form of tannin containing 2-12 galloyl moieties exhibits anticancer effect on various cancer cell lines via mechanisms such as cell cycle arrest, apoptotic induction, reduced proliferation, and diminished cell migration and adhesion (Baer-Dubowska *et al*., 2020).

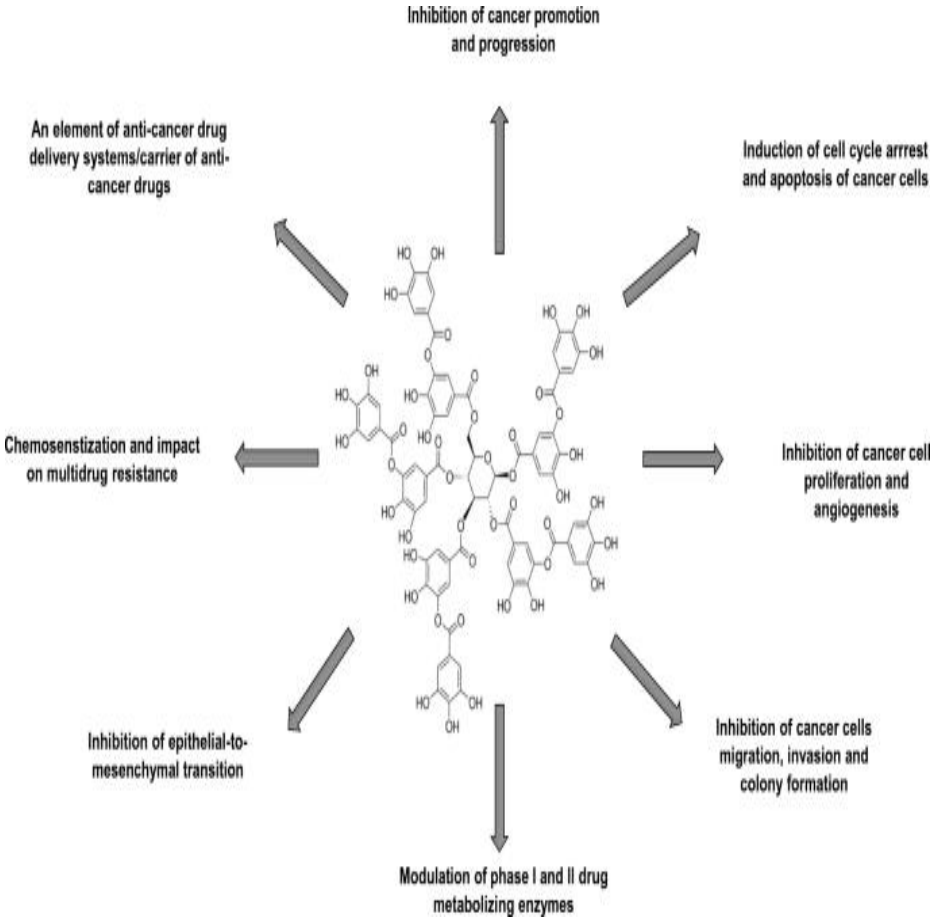


**Figure 3:** Overview of the mechanism of action of Tannic acid on cancer (Baer-Dubowska*et al.,* 2020)

### 7.7 Quinones

Quinones are chemical compounds that are produced by plants. They are divided into four main categories according to their structure, including benzoquinone, naphthoquinone, phenanthrenequinone, and anthraquinone. These compounds can be found in many different types of plants, but they are particularly common in certain plant families such as *Polygonaceae*, *Rubiaceae*,

*Leguminosae, Rhamnaceae, Labiatae, and Boraginaceae* (Lu *et al*., 2013). Quinones are highly reactive substances that can accept electrons from enzymes and proteins to form semiquinone or hydroquinone. This modification of the redox cycle generates ROS, which can harm proteins or DNA and lead to cell death, DNA oxidation, and inflammation. They are toxic to cells (Tsao *et al*., 2020). Quinones can fight cancer and are biologically active against several disorders. There have been reports of numerous quinones, including aloe emodin, thymoquinone, shikonin, lapachone, plumbagin, and juglone, having anticancer effects (Lu *et al*., 2013). Quinone exert their anti-cancer properties via the alteration of several molecular targets, such as tubulin, p73, STAT3, NF-B, AKT, phosphatase and tensin homolog (PTEN), peroxisome proliferator-activated receptor (PPAR), polo-like kinase 1 (PLK1), androgen receptor (AR), E2F-1, Bcl-2, FAK, MMPs, and so on (Lu *et al*., 2013). The capacity of bioactive chemicals to reduce the manifestation of some enzymes like urokinase, MMP-2, MMP-9 proteins and inhibition of nuclear translocation has also been linked to the quinones' anticancer potential (Ohiagu*et al*., 2021).

## 8.0 Common Medicinal Plants with Anticancer Properties in Nigeria

Nigeria is known for its diverse ora and array of native plants that are frequently used as medicine to cure and manage several illnesses including cancer. These plants were used for medicinal purposes for centuries. Several kinds of research have been conducted to investigate the possible anticancer effects of some of these plants. Research is ongoing to understand how natural plant compounds might prevent cancer by inducing apoptosis and inhibiting development is being thoroughly researched. This review highlighted 14medicinal plants with anticancer potentials, which are readily available and accessible in Nigeria. Additionally, the proposed anticancer actions, the bioactive constituents responsible, and the kind of tumor cell repressed were highlighted together with the parts of the plants used for the preparation of the extracts or solvent fractions responsible for the anticancer activity in most of the studies.

### 8.1 Garlic (*Allium sativum*)

*Allium sativum* widely known as garlic is a member of the Allium genus. Garlic is a rich source of several phytochemicals, which are responsible for its anticancer, anti-inflammatory, antifungal, antiviral, and antibacterial properties. These phytochemicals include a group of non-volatile compounds known as γ-glutamyl-S-alk(en)yl-L-cysteines, a class of compounds called S-alk(en)yl-L-cysteine sulfoxides and also a small amount of another compound called S-allyl cysteine (SAC), (Bhatwalkar *et al*., 2021). The bioactive compounds Sallylcysteine and S-allylmercapto-L-cysteine in garlic exhibit significant free radical scavenging activity necessary for the prevention of the cancer growth. In addition, S-allylcysteine lessens tumor maturation. Additionally, *A. sativum* inhibits *in vitro proliferation in* certain parts of the human body, the skin, colon, prostate, lungs etc. inclusive (Ohiagu *et al*., 2021, Petrovic *et al*.,

2018). Allicin a thiosulfate compound from *A. sativum* also possess antioxidant and anticancer properties (Bolinghaus *et al*., 2014) Its potential mechanism of action include activating metabolizing enzymes, inhibiting ROS, scavenging radicals, preventing DNA damage, and inhibiting tumor growth (Bhatwalkar *et al*., 2021).

### 8.2 Aloe Vera (*Aloe barbadensis*)

*Aloe barbadensis* also known as aloe vera is a cactus-like plant `which belongs to the family of *Asphodelaceae*. *A. barbadensis* contains alonin and aloe-emodin, the bioactive compounds responsible for the anti-cancer effects of the plant. The Aloe-emodin exhibits dynamic anticancer and cytotoxic effects against neuroectodermal tumors, lung squamous cell carcinoma, and hepatoma cell. Studies have revealed that it reduces tumor growth and formation by blocking signal transducers and transcription activators. It induces cellular apoptosis in hepatocellular carcinoma by heightening the levels of p53 and p21, which disrupts the cell cycle (Guo *et al*., 2019). Ethanol extract of *A. barbadensis* presented anti-tumor effects by regulating lipid peroxidation and enhancing its antioxidant defense system in mice, and exhibited cytotoxic effects in HepG2 and HCC cell lines ((Ohiagu *et al*., 2021, Prasad *et al*., 2019). An in *vitro* study on aloe vera extracts revealed anticancer effects on hepatocellular carcinoma (HepG2) cells, thus, the plant can be a promising source for future anticancer treatment (Shalabi *et al*., 2015).

### 8.3 Cashew (*Anacardium occidentale*)

*Anacardium occidentale* generally identified as cashew tree belongs to the family *Anacardiacea.A. occidentale* leaves possess bioactive compounds such as Zoapatanolide A, agathisflavone, anacardicin, and methyl gallate which has cytotoxic features on HeLa cell lines. Cytotoxicity was exhibited against leukemia cells by the hydroethanolic leaf extract of *A. occidentale*due to the presence of the bioactive compound agathisflavone (Konan *et al*., 2012).Anacardic acid, a compound isolated from *A. occidentale.* exert cytotoxic effects on numerous human cancer cell lines; It significantly blocks estrogen receptor alpha (ERα)-expressing breast cancer cell proliferation (Salehi *et al*., 2020).

### 8.4 Neem plant (*Azadirachta indica*)

*A. indica*, also known as Neem plant, is an evergreen tree, which belongs to *meliaceae* family widely distributed in the northern part of Nigeria. The extracts of the seed and leaf of *A. indica* have been successfully demonstrated to induce apoptosis and encourage autophagyin a range of human malignancies, including leukemia, prostate, cervical, and breast cancer cells, resulting in their death (Agrawal *et al*., 2020). Neem is known for its ability to prevent the activation of pro-carcinogens and oxidative DNA damage, as well as for upregulating antioxidant and carcinogen detoxification systems, inhibiting tumor cell growth, invasion, and angiogenesis, and inducing apoptosis (Nagini *et al*., 2021). The neem tree's leaves and flowers are a rich source of Nimbolide, a tetranortriterpenoid limonoid, that exerts its anticancer effect on a variety of cancer cell lines by interrupting the cell cycle

and growth of cancer cells indicating its chemopreventive, and cancer-preventive potential (Babykutty *et al*., 2012, Wang *et al*., 2016). It exerts its chemo preventive potential by preventing procarcinogen activation and oxidative DNA damage through the inhibition of enzymes necessary for phase I carcinogen triggering and concurrently activating enzymes in phase II essential for detoxification (Wang *et al*., 2016). Nimbolide primarily functions by constraining metastasis and angiogenesis, activating apoptosis, inhibiting proliferation and regulating enzymes that breakdown carcinogen, regulating epigenome, modulating PI3K/Akt/MAPK Signaling Network, and suppressing cancer-Related Inflammation (Nagini *et al*., 2021, Wang *et al*., 2016).

**8.5 Tea plant (*Camellia sinesis*)**

*Camellia sinensis* commonly known as the tea plant or green tea is of the family *Theaceae* (the tea family). The leaf extract of *C. sinensis* have demonstrated significant anti-cancer and antioxidant potentials, attributed to the presence of several secondary metabolites such as flavonoids, alkaloids, and terpenoids which provides it with its therapeutic efficacy. It has been revealed to possess potent antioxidant efficacy through ferric-reducing antioxidant power, DPPH radical scavenging , ferrous-ion chelating ability, as well as its anticancer activities against MCF-7 breast cancer cell line (Ukwubile *et al*., 2020).Key flavonoids in *C. sinensis* , including (−)-epigallocatechin-3-gallate (EGCG), (−)-epicatechin-3-gallate (ECG), (−)-epigallocatechin (EGC) and (−)-epicatechin (EC); are noted for their ability to scavenge reactive oxygen species, prevent free radical formation, and peroxidate lipids (Musial *et al*., 2020). EGCG increases apoptosis and suppress tumor growth in H1299 human lung cancer xenograft in mice models , while also increasing ROS in the mitochondria of malignant lung cells (Musial *et al*., 2020). Additionally (-)- epigallocatechin-3-gallate from *C. sinensis* can inducecell cycle arrest and prevent the development of carcinomas (especially in the liver) (Ohiagu *et al*., 2021).Critical cell signaling pathways such as the mitogen-activated protein kinase (MAP-kinase), nuclear factor-kappaB (NF-kB), and insulin-like growth factor (IGF)/IGF-1 receptor pathway necessary for cancer cell transformation and survival can be modulated by catechins from *C. sinensis*, especially EGCG (Padmaharish & Lakshimi, 2017).

**8.6 Pawpaw fruit (*Carica papaya*)**

*Carica papaya* also called pawpaw is a popular fruit that belongs to the family *Caricaceae*. *In vitro* cancer cell investigations have shown that papaya leaf extracts have anticancer properties that affect the blood, pancreas, colon, lymphatic system, ovary, liver, stomach, breast, cervix , mesothelioma, and oral squamous cells. Aqueous extract from *Carica papaya* leaves suppresses the growth of several hematopoietic cell lines, such as T-cell lymphoma (Jurkat), plasma cell leukemia (ARH77), Burkitt's lymphoma (Raji), and large-cell anaplastic lymphoma (Karpas-299), (Santana *et al*., 2019). Furthermore, extracts from papaya fruit and seeds significantly inhibit the proliferation of

cancer cells in leukemia (HL-60), liver (HepG2), and breast (MCF-7) cancers (Abdullahi *et al*., 2018). Chlorogenic acid (CGA) another bioactive found in *C. papaya* disrupted the HIF-1α/AKT signaling pathway, thereby inhibiting hypoxia-induced angiogenesis in A549 lung cancer cells (Heung *et al*., 2021).The activation of genes related to tumor angiogenesis is one of the important functions of HIF-1 in cellular responses to hypoxia. Heung *et al.* described bioactive compounds contained in extracts of *C. papaya* to possess anticancer effects against most cancer hallmarks.

### 8.7 Turmeric (*Curcuma longa*)

*Curcuma longa*, commonly referred to as Turmeric, belongs to the ginger family, *Zingiberaceae. Curcuma longa* contain several secondary metabolites, known as curcuminoids, including curcumin and its derivatives such as demethoxycurcumin, bis-demthoxycurcumin, 5′-methoxycurcumin, dihydrocurcumin, cyclocurcumin, Sesquiterpenes, steroids, and essential oils (Omosa *et al*., 2017).Curcumin suppress breast cancer carcinoma via multiple pathways, promoting apoptosis in human breast cancer cells by inducing of p53-dependent Bax activation. *Curcuma longa* has been reported in the treatment of leukemia, lymphoma, gastrointestinal, genitourinary, breast, melanoma, neurological, lung, ovarian head, and neck squamous carcinomas (Sushma, 2012). The crude extract of *C. longa*, inhibits cell proliferation in Chinese hamster ovary (CHO) cells and cytotoxic effect on both lymphocytes and Dalton's lymphoma cells (Omosa *et al*., 2017). Additionally, the ethanolic extract from the rhizome of *C. longa* also possess potential anticancer activity against human breast cancer cell line MDA-MB-231 (Khan *et al*., 2016).

### 8.8 African Yellow wood (*Enantia chlorantha*)

*Enantia chlorantha* ordinarily known as African yellow wood in English belongs to the family *Annonacea*. Phytochemical analysis of the ethanol extract from the stem bark of *E. chlorantha* revealed the presence of alkaloids, flavonoids, saponins, and phenols (Abubakar *et al*., 2020). Human colorectal adenocarcinoma (DLD-1 cell line), mesothelioma (SPC212 cell line), MCF-7, HepG2 liver cell line, and CRL2120 fibroblasts have all been shown *in vitro* to be inhibited by methanol extract of the stem bark of *E. chlorantha* (Kuete *et al*., 2017).

### 8.9 Oil palm tree (*Elaeis guineensis*)

*Elaeis guineensis* commonly known as the oil palm tree belongs to the family *Arecaceae*. Various parts of the *E.guineensis* tree are widely used as traditional medicine in West Africa. Methanol extracts of *E. guineensis*, contains numerous bioactive substances, such as tannins, alkaloids, steroids, saponins, terpenoids, and flavonoids that have a variety of biological actions (Agostin-Costa & Da, 2018). Tocotrienols from palm oil are potent anti-cancer agents, and reduces the occurrence of azoxymethane-induced aberrant crypt foci in rats, suggesting that it may help lower the risk of colon cancer (Owoyele & Owolabi, 2014). More also, methanol extract of *E. guineensis* has strong anticancer effects against MCF-7 breast

cancer cell line (Vijayarathna & Sasid-Haran, 2012).

### 8.10 Bitter kola (*Garcinia kola*)

*Garcinia Kola*, commonly referred to as bitter kola, is a plant species from the *Clusiaceae* family. Studies reveal the antioxidant and anti-lipid peroxidation properties of its stem bark extract, which may be pertinent to cancer chemoprevention and chemotherapy. In addition, the extract has mito-depressant and DNA-damaging effects, indicating its chemotherapeutic potentials. *Garcinia Kola* has been shown to effect cell propagation and cancer cell death CCD through chemical reactions with DNA (Popoola *et al*., 2019). Oluremi *et al*. 2021 investigated the effects of the n-hexane, dichloromethane, ethyl acetate, and methanol extracts from *Garcinia kola* on breast cancer, cervical cancer, and epidermoid carcinoma of the larynx, revealing that all the extracts had 100% anticancer activity on HeLa, Hep-2, and MCF-7 cell lines, completely inhibiting the survival of the cells.

### 8.12 Drumstick tree (*Moringa oleifera*)

*Moringa Oleifera*, commonly known as the Drumstick tree, is a member of the *Moringaceae* family. *M. oleifera* leaf extracts interrupts the growth of several cancer cell lines, including those from human lung, melanoma, cervical, and hepatocellular carcinoma cells, through the initiation of apoptosis and modulation of cell cycle proteins (Wisitpongpun *et al*., 2020). As well, the phytochemicals presents in the methanolic extracts of the seeds of *Moringa Oleifera* possesses cytotoxic effects, restraining the growth of MCF7 breast cancer cells, while having minimal impact on the normal MCF10A breast cells (Adebayo *et al*., 2017).

### 8.11 African peach (*Sacrocephalus latifolus*)

*Sacrocephalus latifolius* is a plant belonging to the Rubiaceae family. It is commonly known by several names, including pincushion tree, African, Guinea, and Sierra Leone peach.

Phytochemical analysis of its extracts and fractions has identified several secondary metabolites, including flavonoids, alkaloids, saponins, anthraquinones, terpenes, tannins, and cardiac glycosides. Notably, the chloroform fraction of *S. latifolius* significantly declines cell growth in the MCF-7 and NCI-H460 cancer cell lines as well as the DPPH-antioxidant activity. The extract possesses antiproliferative activity, probably due to the existence of high levels of phenolic and flavonoid compounds in the chloroform fraction (Emmanuel *et al*., 2021). In addition, alkaloid extracts from *S. latifolius* bark and roots has activity on MCF-7 breast cancer cells (Mendiebiba *et al*., 2022).

### 8.13 Bitter leaf (*Vernonia amygdalina*)

*Vernonia amygdalina*, commonly known as bitter leaf, belongs to the *Asteraceae* family. *V. amygdalina* possesses active compounds including saponins, anthraquinones, flavonoids, alkaloids, terpenes, phenolic acids, steroids, coumarins, lignans, xanthones, and sesquiterpenes. It has a 100% and 75% cytotoxic effect on both HepG2 hepatocellular carcinoma cells and blood cancer cells K562, respectively (Thanh

&Tran, 2021). In addition, the ethanol extract and nanoparticles of *V. amygdalina* damages the DNA in MCF-7 cells, with resulting cellular apoptosis; this damage is indicated by the increased presence of single-stranded DNA, which is a key signal of DNA damage in the samples that were treated with the extract and nanoparticles (Joseph *et al*., 2021). Furthermore, *V. amygdalina* extracts contains steroid glycosides, which diminishes the maturation of breast cancer cell lines, specifically BT-549 and MCF-7 (Ohiagu *et al*., 2021). Studies have revealed the presence of two new anticancer compounds, a sesquiterpene lactone and vernodalin, in *Vernonia amagdalina* (Abdullahi *et al*., 2018).

### 8.14 Ginger (*Zingiber officinale*)

Zingiber officinale , commonly known as ginger, is a member of the Zingiberaceae family and contains a variety of phytochemicals including phenolic compounds, terpenes, polysaccharides, lipids, organic acids, and fibers. The compounds [6]-gingerol and [6]-shogaol found in Ginger extract prevents the growth of cancer cells. [6]-gingerol modulates the activity of genes that cause cells to die through the alteration of the involving biochemical pathways, thereby suppressing tumor growth and increases the synthesis of tumor necrosis factor (TNF-α) in cancer patients undergoing chemotherapy with the consequent promotion of Tumor cell apoptosis (Tonin *et al*., 2019, Liu et al., 2019). Also, *Zingiber officinale*, contains bioactive compounds10-gingerol and 10-shogaol which are effective in inhibiting the growth of PC-3 prostate cancer cells (Liu *et al.,* 2017). Ginger extract and its elements have been found to retard and ultimately terminate an extensive sort of cancer cells comprising those associated to colon, gastric, lung, breast, leukemia, osteosarcoma, hepatoma, cervical, and fibrosarcoma with similar effects on these types of cancer cells (Akimoto *et al*., 2015).

## 9.0 Some Mechanisms by which Nigerian Medicinal Plants Exert their Anticancer Potentials

Herbal medicine has a long history of being used to treat and cure various illnesses. Today, research into herbal remedies is focused on finding new cancer treatments. These remedies typically involve using natural compounds found in plants that can combat disease. Medicinal plants are a valuable resource for human health, offering natural remedies that have been utilized for centuries. These plants contain bioactive compounds capable of inhibiting cancer growth and development. These phytochemicals are present in various parts of the plant including the flower, stem, roots, and leaves. Many different types of compounds, such as alkaloids, flavonoids, and minerals, are found in medicinal plants and play a role in blocking cancer-causing proteins, enzymes, and signaling pathways (Igbal *et al*., 2017). The primary ways that medicinal plant remedies work to treat cancer include causing CCD through apoptosis and autophagy, preventing the cancer growth and reproduction, increasing the production of ROS, hindering the formation of new blood vessels in cancer cells, antioxidant activity and immune system modulation and metabolism inhibition (Adewole, 2020).

Table 1 shows some Nigerian plants, which can be used in the production of anticancer drugs, as well as the bioactive compounds responsible for their anticancer and pharmacological effects.

### 9.1 Induction of Apoptosis and Autophagy

Apoptosis is a critical process in the elimination of cancer cells, which are controlled by various gene-regulated cell deaths. Characteristics of apoptotic cells include changes in morphology, such as condensed chromosomes, broken DNA, reduced cell size, and the formation of apoptotic bodies (Christiana *et al*., 2022). The study highlights that various medicinal plants can trigger apoptosis in cancer cells through both mitochondrial-dependent and cell-mediated pathways.

Some examples of such plants include *A. indica, A. cordifolia, A. occidentale, C. cajan, M. oleifera, V. amygdalina, and Z. officinale*. Literature documentation on investigation of *A. indica*, reveals that extracts and compounds from *A. indica* can trigger apoptosis in cancer cells by promoting the release of cytochrome c from the mitochondria. This is a process regulated by both pro-apoptotic and anti-apoptotic proteins .For example, 6-shogaol from *Z. ofcinale* has been found to increase pro-apoptotic proteins, such as Bad and Bax, while decreasing the activity of anti-apoptotic proteins from the Bcl-2 family like Bcl-2 and Bcl-Xl (HaO *et al*., 2014). Additionally, medicinal plants can induce apoptosis by inhibiting the activity of nuclear factor kappa B (NF-κB), a protein that prevents cell death (Li *et al*., 2020). Another process these plants induce apoptosis is by affecting the apoptosis-inducing factor (AIF). Thus, DNA fragmentation and chromatin condensation, leading to caspase-independent apoptosis are inevitable at the release of AIF from the mitochondria, (Prasad *et al*., 2020). Limonoids from *A. indica* have been found to trigger this action (HaO *et al*., 2014).

### 9.2 Inhibition of Cell Proliferation

Mitosis, or cell division, is an essential part of the cell cycle, resulting in the formation of two identical daughter cells, each receiving an equal share of genetic material. The mitotic spindle, formed by the cytoskeleton, is crucial for the various steps of cell division. Uncontrolled cell division can cause excessive growth of cells, as seen in cancer. Inhibiting any stage of mitosis can prevent cells from completing the process, leading to cell cycle arrest and eventually leading to cell death. Research into using of drugs derived from medicinal plants, as a potential treatment for cancer, specifically targeting cell division, is a rapidly expanding field (Zulkipliet *et al*., 2015). *A. sativum*, also known as garlic, has been shown to inhibit cell cycle progression by reducing Cdk1/cyclin B kinase activity or activating ERK1/2 through the compound diallyl disulfide. Other medicinal plants have been found to have similar effects on the cell cycle, at various phases. These include *A. occidentale* (Santos *et al*., 2019) and *A. indica,* (at the G0/G1 phase),(Patel *et al*., 2016).*C. cajan*, (at the G2/M phase), (Fu *et al*., 2015), *V. amygdalina*, (at the G1/S phase), 6-shogaol from *Z. officinale*, (at the G2/M phase), (Li & Chiang, 2017), *M.*

*oleifera*, K. senegalensis, *A. cordifolia*, *T. diversifolia* leaf extract and its compound tagitinin C at the G2/M phase (Adewole, 2020).

**Table 1:** Anticancer drugs from Nigerian Medicinal plants after undergoing research and clinical trials (Ohiagu *et al.,* 2021)

| Anticancer drug | Plant source | Plant family | Common name | Bioactive compound present | Pharmacological actions |
|---|---|---|---|---|---|
| **Combretastatin-A-4 phosphate** | *Combretum caffrum* | *Combretaceae* | Bushwillow tree | Water-soluble analogue of combrestastatin | Suppresses the formation of blood vessels, cuts off blood supply, and causes death of cancer cells. |
| **Epigallacotechin -3-gallate** | *Camellia sinensis* | *Theaceae* | Green tea | Catechin | Prevents the activity of specific kinases, impedes the growth of tumor cells, displays antioxidant properties, and reduces carcinogenesis resulting from chemical and UV exposure |
| **Epipodophyllotoxin** | *Podophyllum peltatum* | *Berberidaceae* | Mayapple | Podophyllotoxin isomer | Interferes with the cell cycle and triggers pro-apoptotic effects in cancer cells |
| **Flavopiridol** | Dysoxylum binectariferum | *Meliaceae* | Red Mahogany | Synthetic flavonoid derivative, rohitukine | The capability to impede cell growth, control the immune system, exhibit tyrosine kinase activity, and improve inflammation |
| **Noscapine** | *Papaver somniferum* | *Papaveraceae* | Opium poppy | Noscapine alkaloid | The suppression of cancer cell proliferation obstructs tumor growth and disrupts microtubules |
| **Paclitaxel ( Taxol)** | *Taxus brevifolia* | *Taxaceae* | Pacific Yew | Taxane | The disruption, polymerization, and stabilization of microtubules result in the stimulation of cancer cell apoptosis, interference with the translational machinery, disruption of spindle synthesis, and inhibition of mitosis. |
| **Pomiferin** | *Maclurapomifera* | *Moraceae*<br><br>*Leguminosae* | Osage Orange | Isolflavonoid | The inhibition of histone deacetylases has been linked to DNA fragmentation, toxicity to |

| | | | | | |
|---|---|---|---|---|---|
| | *Derris malaccensis* | | Iroko | | cancerous cells, and the promotion of pro-apoptosis |
| **Roscovitine** | *Raphanus sativus* | *Brassicaceae* | Radish | Olumucine | Inhibits cell cycle progression and cyclin-dependent kinases |
| **Sulphoraphane** | *Brassica rapa* | *Brassicaceae* | Turnip | Isotiocynanate | Breast tumor development is slowed, cancer cell proliferation is inhibited, and phase 2 enzymes for detoxification are stimulated |

### 9.3 Generation of Reactive Oxygen Species

This can lead to reduced matrix metalloproteinase (MMP) and the activation of pro-apoptotic processes, comprising effects on caspases, ultimately leading to cancer cell death (Arumugam *et al*., 2014, Zou *et al*., 2017). Cajanin stilbene and cajanol, compounds found in *Cajanus cajan*, have been shown to induce the breakdown of matrix metalloproteinase (MMP), resulting in the discharge of cytochrome c and the stimulation of caspase-9 and caspase-3. This ultimately leads to cancer cell death. Similarly, ethanol extract from *Abrus leiocarpus* leaf was found to induce cell death through the activation of caspase-3 and caspase-7, as well as the depletion of cellular adenosine triphosphate levels (Olugbami *et al*., 2017). Additionally, *Abrus cordifolia* was found to exhibit antitumor activity through augmented production of reactive oxygen species (ROS), stimulation of caspases, and interruption of mPT (Kuete *et al*., 2016). These studies suggest that both of these plants have the potential as a source of anticancer compounds.

### 9.4 Inhibition of Angiogenesis

Angiogenesis, the formation of new blood vessels from pre-existing ones, is a key in certain disease states, including the expansion of tumors and the spread of cancer cells. Many medicinal plants possess anti-angiogenic properties, which enable them to inhibit the development of new blood vessels. Various medicinal plants have been found to have anti-angiogenic effects such as Curcumin, a component of *C. longa*, which has been found to inhibit the growth of new blood vessels in certain types of cancer (Giordano & Tomminaro, 2019). Nimbolide, an isolated compound from the plant *A. indica*, has been found to decrease the manifestation of VEGF, responsible for its anti angiogenic effect on cancer cells (Gupta *et al*., 2017), as well as *C. roseus*, *C. sinesis* (Hoseinkhani *et al*., 2020) among others.

## 10.0 CONCLUSION

Cancer is a major contributor to mortality worldwide. The medications used in cancer therapy and management often come with significant adverse effects. Additionally, the expenses linked with tumor management are steep, making it demanding for many individuals to access the medical care they need to live on. There is a wealth of medicinal

plants in Nigeria that have been proven to possess anti-cancer properties.

These plants, many of which have been in use for centuries in folklore medicine, inhibit the maturation and proliferation of cancer cells, owing to their richness in bioactive compounds known to possess cancer-inhibiting properties. NMPs have been discovered to have significant anticancer potentials. The detection of anticancer agents from natural products has a long history, and novel ones are being developed continuously. The present review has advanced our understanding of the potential of medicinal plants in inhibiting mechanisms that promote cancer development. It marked the progress in exploring the rich diversity of the Nigerian Medicinal Plants (NMPs). In furtherance, Nigerian plants that have demonstrated cytotoxic potency in laboratory tests are also frequently used in traditional cancer treatments, with different research revealing the presence of anticancer bioactive substances in the extract of these plants. These findings hold great promise for the development of cost-effective cancer treatments made from natural products, especially in local communities that have limited access to modern medical facilities and treatments. The potential of natural products as a source of new anticancer drugs is a significant area of research.

**ACKNOWLEDGEMENT**

Not applicable

**AUTHOR'S CONTRIBUTION**

JUI deliberated and planned the scope of the report, conceptualization, methodology, supervision, writing (review and editing), and visualization. CCC writing (original draft), data acquisition, data analysis, resources. FOO resources and editing, JKO supervision and visualization. JUI/CCC authors were the resource persons who provided all the necessary materials for writing the manuscript. All authors have read and approved the manuscript in the present form and gave the permission to submit the manuscript for publication.

**FUNDING**

The authors did not receive financial support and sponsorship from individuals or organizations/institutions. Availability of data and materials are available upon request.

**DECLARATIONS**

**ETHICS APPROVAL AND CONSENT TO PARTICIPATE**

Not applicable.

**CONFLICTING INTERESTS**

The authors declare no conflicting interests.

**REFERENCES**

Abbas, Z., & Rehman, S. (2018). An Overview of Cancer Treatment Modalities. In *Neoplasm*. InTech. https://doi.org/10.5772/intechopen.76558

Abdullahi, A. D., Mustapha, R. K., Yau, S., & Adam, M. S. (2018). Exploring the Nigerian medicinal plants with anticancer activities: A pharmacological review. *Modern Chemistry*, *6*(2), 35-38.

Abubakar, A., Ahmad, N. S., Akanya, H. O., Abdulkadir, A., & Abubakar, A. N. (2020). Antiplasmodial activity of total

alkaloids and flavonoids of stem bark extracts of Enantiachlorantha in mice, *Comparative Clinical Pathology*, 29(4): 873–881. https://doi.org/10.1007/s00580-020-03138-4

Abubakar, I. B., Ukwuani-Kwaja, A. N., Olayiwola, F. S., Malami, I., Muhammad, A., Ahmed, S. J., Nurudeen, Q. O., & Falana, M. B. (2020). An inventory of medicinal plants used for treatment of cancer in Kwara and Lagos state, Nigeria. *European Journal of Integrative Medicine*, *34*. https://doi.org/10.1016/j.eujim.2020.101062

Adebayo, I. A., Arsad, H., & Samian, M. R. (2017). Antiproliferative effect on breast cancer (MCF7) of *Moringa Oleifera* seed extracts. *African Journal of Traditional, Complementary and Alternative Medicines*, *14*(2): 282–287. https://doi.org/10.21010/ajtcam.v14i2.30

Adetuyi, B. O., Olajide, P. A., Oluwatosin, A., &Oloke, J. K. (2022). Preventive Phytochemicals of Cancer as Speed Breakers in Inflammatory Signaling. *Research Journal of Life Sciences, Bioinformatics, Pharmaceutical and Chemical Sciences*, *8*(1), 30-61.

Adewole, K. E. (2020). Nigerian antimalarial plants and their anticancer potential: A review, *Journal of Integrative Medicine*, 18(2): 92–113. https://doi.org/10.1016/j.joim.2020.01.001

Agostini-Costa, T. da S. (2018). Bioactive compounds and health benefits of some palm species traditionally used in Africa and the Americas – A review, *Journal of Ethnopharmacology*, 224: 202–229. https://doi.org/10.1016/j.jep.2018.05.035

Agrawal, S., BablaniPopli, D., Sircar, K., &Chowdhry, A. (2020). A review of the anticancer activity of Azadirachta indica (Neem) in oral cancer, *Journal of Oral Biology and Craniofacial Research*, 10(2): 206–209. https://doi.org/10.1016/j.jobcr.2020.04.007

Ahmad, R., Ahmad, N., Naqvi, A. A., Shehzad, A., & Al-Ghamdi, M. S. (2017). Role of traditional Islamic and Arabic plants in cancer therapy. *Journal of Traditional and Complementary Medicine*, 7(2): 195–204. https://doi.org/10.1016/j.jtcme.2016.05.002

Akimoto, M., Iizuka, M., Kanematsu, R., Yoshida, M., & Takenaga, K. (2015). Anticancer Effect of Ginger Extract against Pancreatic Cancer Cells Mainly through Reactive Oxygen Species-Mediated Autotic Cell Death. *PLOS ONE*, 10(5): e0126605. https://doi.org/10.1371/journal.pone.0126605

AlQathama, A., Ezuruike, U. F., Mazzari, A. L. D. A., Yonbawi, A., Chieli, E., & Prieto, J. M. (2020). Effects of Selected Nigerian Medicinal Plants on the Viability, Mobility, and Multidrug-Resistant Mechanisms in Liver, Colon,

and Skin Cancer Cell Lines. *Frontiers in Pharmacology*, *11*. https://doi.org/10.3389/fphar.2020.546439

Annett, S., Moore, G., & Robson, T. (2020). Obesity and Cancer Metastasis: Molecular and Translational Perspectives,*Cancers*, 12(12): 3798. https://doi.org/10.3390/cancers12123798

Arumugam, A., Agullo, P., Boopalan, T., Nandy, S., Lopez, R., Gutierrez, C., Narayan, M., & Rajkumar, L. (2014). Neem leaf extract inhibits mammary carcinogenesis by altering cell proliferation, apoptosis, and angiogenesis, *Cancer Biology & Therapy*, *15*(1): 26–34. https://doi.org/10.4161/cbt.26604

Babykutty, S., S, P. P., J, N. R., Kumar, M. A. S., Nair, M. S., Srinivas, P., & Gopala, S. (2012). Nimbolide retards tumor cell migration, invasion, and angiogenesis by downregulating MMP-2/9 expression via inhibiting ERK1/2 and reducing DNA-binding activity of NF-κB in colon cancer cells. *Molecular Carcinogenesis*, 51(6): 475–490. https://doi.org/10.1002/mc.20812

Baer-Dubowska, W., Szaefer, H., Majchrzak-Celińska, A., &Krajka-Kuźniak, V. (2020a). Tannic Acid: Specific Form of Tannins in Cancer Chemoprevention and Therapy-Old and New Applications. *Current Pharmacology Reports*, 6(2): 28–37. https://doi.org/10.1007/s40495-020-00211-y

Beit-Yannai, E., Ben-Shabat, S., Goldschmidt, N., Chapagain, B. P., Liu, R. H., &Wiesman, Z. (2011). Antiproliferative activity of steroidal saponins from Balanites aegyptiaca—An *in vitro* study. *Phytochemistry Letters*, *4*(1), 43–47. https://doi.org/10.1016/j.phytol.2010.11.004

Bhatwalkar, S. B., Mondal, R., Krishna, S. B. N., Adam, J. K., Govender, P., & Anupam, R. (2021). Antibacterial properties of organosulfur compounds of garlic (Allium sativum). *Frontiers in Microbiology*, *12*, 1869

Bhatwalkar, S. B., Mondal, R., Krishna, S. B. N., Adam, J. K., Govender, P., & Anupam, R. (2021). Antibacterial Properties of Organosulfur Compounds of Garlic (Allium sativum). In *Frontiers in Microbiology*,12. https://doi.org/10.3389/fmicb.2021.613077

Borlinghaus, J., Albrecht, F., Gruhlke, M., Nwachukwu, I., &Slusarenko, A. (2014). Allicin: Chemistry and Biological Properties,*Molecules*, 19(8): 12591–12618. https://doi.org/10.3390/molecules190812591

Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R. L., Torre, L. A., & Jemal, A. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries,*CA: A Cancer Journal for Clinicians*, 68(6): 394–424. https://doi.org/10.3322/caac.21492

Carvalho, J. C. T., Fernandes, C. P., Amado, J. R. R., Navarrete, A., & Quintans-Júnior, L. J. (2018). Ethnopharmacological Studies for the

Development of New Drugs. *Evidence-Based Complementary and Alternative Medicine*, 2018: 1–2. https://doi.org/10.1155/2018/7593296

Christina, Y. I., Rifa'i, M., Widodo, N., &Djati, M. S. (2022). Comparative Study of Antiproliferative Activity in Different Plant Parts of Phaleria macrocarpa and the Underlying Mechanism of Action, *The Scientific World Journal*, 2022: 1–13. https://doi.org/10.1155/2022/3992660

Daglia, M. (2012). Polyphenols as antimicrobial agents. *Current Opinion in Biotechnology*, *23*(2), 174–181. https://doi.org/10.1016/j.copbio.2011.08.007

Diaz, G., Miranda, I. L., & Diaz, M. A. N. (2015). Quinolines, Isoquinolines, Angustureine, and Congeneric Alkaloids — Occurrence, Chemistry, and Biological Activity. *Phytochemicals - Isolation, Characterisation and Role in Human Health*. InTech. https://doi.org/10.5772/59819

Ediriweera, M. K., Tennekoon, K. H., Samarakoon, S. R., Thabrew, I., &Dilip De Silva, E. (2016). A study of the potential anticancer activity of Mangifera zeylanica bark: Evaluation of cytotoxic and apoptotic effects of the hexane extract and bioassay-guided fractionation to identify phytochemical constituents. *Oncology Letters*, *11*(2): 1335–1344. https://doi.org/10.3892/ol.2016.4087

Emmanuel, I. O., Adesina, A. B., Ohonmoimen, I. J., Azah, M., & Dar, F. A. (2021). *In vitro,* Anticancer Potential of *Sacrocephaluslatifolius* Leaves Extract and Its Fractions on Human MCF-7 and NCI-H460 Cancer Cell Lines.*Asian Journal of Agriculture and Biology*, 2021(3): 1–7. https://doi.org/10.35495/ajab.2020.10.520

Fapohunda, A., Fakolade, A., Omiye, J., Afolaranmi, O., Arowojolu, O., Oyebamiji, T., Nwogu, C., Olawaiye, A., &Mutiu, J. (2020). Cancer presentation patterns in Lagos, Nigeria: Experience from a private cancer center,*Journal of Public Health in Africa*, 11(2): 1138. https://doi.org/10.4081/jphia.2020.1138

Fares, J., Fares, M. Y., Khachfe, H. H., Salhab, H. A., & Fares, Y. (2020). Molecular principles of metastasis: a hallmark of cancer revisited, *Signal Transduction and Targeted Therapy*, 5(1): 28. https://doi.org/10.1038/s41392-020-0134-x

Fu, Y., Kadioglu, O., Wiench, B., Wei, Z., Gao, C., Luo, M., Gu, C., Zu, Y., &Efferth, T. (2015). Cell cycle arrest and induction of apoptosis by cajanin stilbene acid from *Cajanus cajan* in breast cancer cells.*Phytomedicine*, *22*(4): 462–468. https://doi.org/10.1016/j.phymed.2015.02.005

Gao, Y., Kuok, K. I., Jin, Y., & Wang, R. (2019). Biomedical applications of *Aloe vera*.*Critical Reviews in Food Science and Nutrition*, 59(1), 244–256. https://doi.org/10.1080/10408398.2018.1496320

Giordano, &Tommonaro. (2019). Curcumin and Cancer, *Nutrients*, 11(10): 2376. https://doi.org/10.3390/nu11102376

Greenwell, M., & Rahman, P. K. S. M. (2015). Medicinal Plants: Their Use in Anticancer Treatment. *International Journal of Pharmaceutical Sciences and Research*, 6(10): 4103–4112. https://doi.org/10.13040/IJPSR.0975-8232.6(10).4103-12

Gupta, S. C., Prasad, S., Tyagi, A. K., Kunnumakkara, A. B., & Aggarwal, B. B. (2017). Neem (Azadirachta indica): An indian traditional panacea with modern molecular basis, *Phytomedicine*, 34: 14–20. https://doi.org/10.1016/j.phymed.2017.07.001

Gupta, S. C., Tyagi, A. K., Deshmukh-Taskar, P., Hinojosa, M., Prasad, S., & Aggarwal, B. B. (2014). Downregulation of tumor necrosis factor and other proinflammatory biomarkers by polyphenols. *Archives of Biochemistry and Biophysics*, 559: 91–99. https://doi.org/10.1016/j.abb.2014.06.006

Hamuel, J. (2012). Phytochemicals: Extraction Methods, Basic Structures and Mode of Action as Potential Chemotherapeutic Agents. *In Phytochemicals - A Global Perspective of Their Role in Nutrition and Health*. InTech. https://doi.org/10.5772/26052

Hanahan, D. (2022). Hallmarks of cancer: new dimensions. *Cancer discovery*, *12*(1), 31-46

Hao, F., Kumar, S., Yadav, N., & Chandra, D. (2014). Neem components as potential agents for cancer prevention and treatment, *Biochimica et Biophysica Acta (BBA) - Reviews on Cancer*, 1846(1): 247–257. https://doi.org/10.1016/j.bbcan.2014.07.002

Hassan, B. (2020). Plants and Cancer Treatment, In *Medicinal Plants - Use in Prevention and Treatment of Diseases*. IntechOpen. https://doi.org/10.5772/intechopen.90568

Heung, T. Y., Huong, J. Y. S., Chen, W. Y., Loh, Y. W., Khaw, K. Y., Goh, B.-H., & Ong, Y. S. (2021). Anticancer Potential of *Carica papaya* through Modulation of Cancer Hallmarks.*Food Reviews International*, 1–19. https://doi.org/10.1080/87559129.2021.1928181

Hoseinkhani, Z., Norooznezhad, F., Rastegari-Pouyani, M., & Mansouri, K. (2020). Medicinal Plants Extracts with Antiangiogenic Activity: Where Is the Link? *Advanced Pharmaceutical Bulletin*, 10(3): 370–378. https://doi.org/10.34172/apb.2020.045

Hussein, A. R., & El-Anssary, A. (2019). Plants Secondary Metabolites: The Key Drivers of the Pharmacological Actions of Medicinal Plants. In *Herbal Medicine*. IntechOpen. https://doi.org/10.5772/intechopen.76139

Iqbal, J., Abbasi, B. A., Mahmood, T., Kanwal, S., Ali, B., Shah, S. A., & Khalil, A. T. (2017). Plant-derived anticancer agents: A green anticancer approach, *Asian Pacific Journal of Tropical Biomedicine*, 7(12): 1129–

1150. https://doi.org/10.1016/j.apjtb.2017.10.016

Jia, L., Jin, H., Zhou, J., Chen, L., Lu, Y., Ming, Y., & Yu, Y. (2013). A potential anti-tumor herbal medicine, Corilagin, inhibits ovarian cancer cell growth through blocking the TGF-β signaling pathways.*BMC Complementary and Alternative Medicine*, *13*. https://doi.org/10.1186/1472-6882-13-33

Joseph, J., Khor, K. Z., Moses, E. J., Lim, V., Aziz, M. Y., & Abdul Samad, N. (2021). In vitro Anticancer Effects of Vernonia amygdalina Leaf Extract and Green-Synthesised Silver Nanoparticles.*International Journal of Nanomedicine*, 16: 3599–3612. https://doi.org/10.2147/IJN.S303921

Joshi, R. A., & Rashmi Joshi, C. A. (2017). Antrodiacamphorata with potential anti-cancerous activities: A review, In ~ *284 ~ Journal of Medicinal Plants Studies*, 5(1).

Khan, M. A., Ahmad, R., & Srivastava, A. N. (2016). Therapeutic effect of short-term *Beta vulgaris* supplementation in patients of Non Alcoholic Fatty Liver disease. View project Role of *Anulomanadravya*, View project *Rumana Ahmad*. Evaluation of *in vitro* anticancer activity of rhizome of *Curcuma longa* against human breast cancer and Vero cell lines.www.botanyjournals.com

Kikuchi, H., Yuan, B., Hu, X., & Okazaki, M. (2019). Chemopreventive and anticancer activity of flavonoids and its possibility for clinical use by combining with conventional chemotherapeutic agents,*American Journal of Cancer Research*, 9(8): 1517–1535.

Koczurkiewicz, P., Klaś, K., Grabowska, K., Piska, K., Rogowska, K., Wójcik-Pszczoła, K., Podolak, I., Galanty, A., Michalik, M., &Pękala, E. (2019). Saponins as chemosensitizing substances that improve effectiveness and selectivity of anticancer drug—Minireview of in vitro studies.*Phytotherapy Research*, 33(9): 2141–2151. https://doi.org/10.1002/ptr.6371

Konan, N. A., Lincopan, N., Collantes Díaz, I. E., de Fátima Jacysyn, J., TanaeTiba, M. M., PessiniAmarante Mendes, J. G., Bacchi, E. M., &Spira, B. (2012). Cytotoxicity of cashew flavonoids towards malignant cell lines.*Experimental and Toxicologic Pathology*, 64(5): 435–440. https://doi.org/10.1016/j.etp.2010.10.010

Kooti, W., Servatyari, K., Behzadifar, M., Asadi-Samani, M., Sadeghi, F., Nouri, B., &ZareMarzouni, H. (2017). Effective Medicinal Plant in Cancer Treatment, Part 2: Review Study,*Journal of Evidence-Based Complementary & Alternative Medicine*, 22(4): 982–995. https://doi.org/10.1177/2156587217696927

Krieghoff-Henning, E., Folkerts, J., Penzkofer, A., &Weg-Remers, S. (2017). Cancer – an overview. *MedizinischeMonatsschrift Fur Pharmazeuten*, 40(2): 48–54.

Kuete, V., Fokou, F. W., Karaosmanoğlu, O., Beng, V. P., & Sivas, H. (2017). Cytotoxicity of the methanol extracts of Elephant opus mollis, Kalanchoe crenata and 4 other Cameroonian medicinal plants towards human carcinoma cells, *BMC Complementary and Alternative Medicine*, 17(1): 280. https://doi.org/10.1186/s12906-017-1793-1

Kuete, V., Tchinda, C. F., Mambe, F. T., Beng, V. P., &Efferth, T. (2016). Cytotoxicity of methanol extracts of 10 Cameroonian medicinal plants towards multi-factorial drug-resistant cancer cell lines, *BMC Complementary and Alternative Medicine*, 16(1): 267. https://doi.org/10.1186/s12906-016-1253-3

Kumar, S., Pathania, A. S., Saxena, A. K., Vishwakarma, R. A., Ali, A., & Bhushan, S. (2013). The anticancer potential of flavonoids isolated from the stem bark of Erythrina suberosa through induction of apoptosis and inhibition of STAT signaling pathway in human leukemia HL-60 cells. *Chemico-Biological Interactions*, 205(2): 128–137. https://doi.org/10.1016/j.cbi.2013.06.020

Li, T.-Y., & Chiang, B.-H. (2017). 6-shogaol induces autophagic cell death then triggered apoptosis in colorectal adenocarcinoma HT-29 cells, *Biomedicine & Pharmacotherapy*, 93: 208–217. https://doi.org/10.1016/j.biopha.2017.06.038

Li, Y., Kong, D., Fu, Y., Sussman, M. R., & Wu, H. (2020). The effect of developmental and environmental factors on secondary metabolites in medicinal plants,*Plant Physiology and Biochemistry*, 148: 80–89. https://doi.org/10.1016/j.plaphy.2020.01.006

Li, Z., Wang, Y., Gao, M., Cui, W., Zeng, M., Cheng, Y., & Li, J. (2018). Nine New Gingerols from the Rhizoma of Zingiber officinale and Their Cytotoxic Activities, *Molecules*, 23(2): 315. https://doi.org/10.3390/molecules23020315

Lichota, A., &Gwozdzinski, K. (2018). Anticancer Activity of Natural Compounds from Plant and Marine Environment.*International Journal of Molecular Sciences*, 19(11): 3533. https://doi.org/10.3390/ijms19113533

Liu, C.-M., Kao, C.-L., Tseng, Y.-T., Lo, Y.-C., & Chen, C.-Y. (2017). Ginger Phytochemicals Inhibit Cell Growth and Modulate Drug Resistance Factors in Docetaxel Resistant Prostate Cancer Cell, *Molecules*, 22(9): 1477. https://doi.org/10.3390/molecules22091477

Liu, Y., Liu, J., & Zhang, Y. (2019). Research Progress on Chemical Constituents of *Zingiber officinale* Roscoe, *BioMed Research International*, 2019: 1–21. https://doi.org/10.1155/2019/5370823

Lu, J. J., Bao, J. L., Wu, G. S., Xu, W. S., Huang, M. Q., Chen, X. P., & Wang, Y. T. (2013). Quinones derived from plant secondary metabolites as anti-cancer agents. *Anti-Cancer Agents in Medicinal Chemistry (Formerly*

*Current Medicinal Chemistry-Anti-Cancer Agents), 13*(3), 456-463.

Lu, J.-J., Bao, J.-L., Chen, X.-P., Huang, M., & Wang, Y.-T. (2012). Alkaloids Isolated from Natural Herbs as the Anticancer Agents.*Evidence-Based Complementary and Alternative Medicine*, 2012: 1–12. https://doi.org/10.1155/2012/485042

Lu, J.-J., Bao, J.-L., Wu, G.-S., Xu, W.-S., Huang, M.-Q., Chen, X.-P., & Wang, Y.-T. (2013a). *Anti-Cancer Agents in Medicinal Chemistry*, 13.

Mindiédiba, J. B., Emmanuel, A. M., Thiombiano, M. H., Sibdou, O., & Georges, A. O. (2022). Inhibition of prostate cancer by plant extracts used in the treatment of malaria in Burkina Faso.*GSC Biological and Pharmaceutical Sciences*, 19(3): 100–108. https://doi.org/10.30574/gscbps.2022.19.3.0209

Musa Kutama, R. (2018). Phytochemical Compositions in Some Nigerian Medicinal Plants and Their Pharmacological Properties: A Review. *Journal of Anesthesiology*, 6(1): 15. https://doi.org/10.11648/j.ja.20180601.14

Musa Kutama, R. (2018). Phytochemical Compositions in Some Nigerian Medicinal Plants and Their Pharmacological Properties: A Review, *Journal of Anesthesiology*, 6(1): 15. https://doi.org/10.11648/j.ja.20180601.14

Musial, C., Kuban-Jankowska, A., &Gorska-Ponikowska, M. (2020). Beneficial Properties of Green Tea Catechins, *International Journal of Molecular Sciences*, 21(5): 1744. https://doi.org/10.3390/ijms21051744

Nagini, S., Nivetha, R., Palrasu, M., & Mishra, R. (2021). Nimbolide, a Neem Limonoid, Is a Promising Candidate for the Anticancer Drug Arsenal, *Journal of Medicinal Chemistry*, 64(7): 3560–3577. https://doi.org/10.1021/acs.jmedchem.0c02239

Niedzwiecki, A., Roomi, M., Kalinovsky, T., & Rath, M. (2016). Anticancer Efficacy of Polyphenols and Their Combinations. *Nutrients*, 8(9): 552. https://doi.org/10.3390/nu8090552

Nurgali, K., Jagoe, R. T., &Abalo, R. (2018). Editorial: Adverse effects of cancer chemotherapy: Anything new to improve tolerance and reduce sequelae? In *Frontiers in Pharmacology*, 9( MAR). Frontiers Media S.A. https://doi.org/10.3389/fphar.2018.00245

Ohiagu, F. O., Chikezie, P. C., Chikezie, C. M., &Enyoh, C. E. (2021). Anticancer activity of Nigerian medicinal plants: a review,*Future Journal of Pharmaceutical Sciences*, 7(1). https://doi.org/10.1186/s43094-021-00222-6

Okezie, E., &Ugbogu, E. A. (2017). A Review of Selected Medicinal Plants with Potential Health Benefits in South-Eastern Nigeria Red palm oil extracted from palm fruit protects against toxicities in rats exposed to carbon tetrachloride.View project Quarry mining activities on nutritional and

medicinal constituents of plants. *View project*. www.ijpcsonline.com

Olugbami, J. O., Damoiseaux, R., France, B., Onibiyo, E. M., Gbadegesin, M. A., Sharma, S., Gimzewski, J. K., &Odunola, O. A. (2017). A comparative assessment of antiproliferative properties of resveratrol and ethanol leaf extract of *Anogeissusleiocarpus* (DC) Guill and Perr against HepG2 hepatocarcinoma cells, *BMC Complementary and Alternative Medicine*, 17(1): 381. https://doi.org/10.1186/s12906-017-1873-2

Oluremi, B. B., Oloche, J. J., &Adeniji, A. J. (2021). Anticancer and antibacterial activities of solanum aethiopicum L., solanum macrocarpon L. and garcinia kola heckle, *Tropical Journal of Natural Product Research*, 5(5): 938–942. https://doi.org/10.26538/tjnpr/v5i5.23

Omosa, L. K., Midiwo, J. O., &Kuete, V. (2017). Curcuma longa, *Medicinal Spices and Vegetables from Africa: Therapeutic Potential Against Metabolic, Inflammatory, Infectious and Systemic Diseases*, 425–435. Elsevier Inc. https://doi.org/10.1016/B978-0-12-809286-6.00019-4

Owoyele, B. V., & Owolabi, G. O. (2014). Traditional oil palm (Elaeisguineensisjacq.) and its medicinal uses: A review, *Tang [Humanitas Medicine]*, 4(3): 16.1-16.8. https://doi.org/10.5667/tang.2014.0004

Padmaharish, V., & Lakshmi, T. (2017). Anticancer Activities of Medicinal Plants-An Update.

Panche, A. N., Diwan, A. D., & Chandra, S. R. (2016). Flavonoids: an overview. *Journal of Nutritional Science*, 5:e47. https://doi.org/10.1017/jns.2016.41

Petrovic, V., Nepal, A., Olaisen, C., Bachke, S., Hira, J., Søgaard, C. K., Røst, L. M., Misund, K., Andreassen, T., Melø, T. M., Bartsova, Z., Bruheim, P., &Otterlei, M. (2018). Anti-Cancer Potential of Homemade Fresh Garlic Extract Is Related to Increased Endoplasmic Reticulum Stress. *Nutrients*, 10(4). https://doi.org/10.3390/nu10040450

Popoola, T. D., Awodele, O., Babawale, F., Oguns, O., Onabanjo, O., Ibanga, I., Godwin, H., Oyeniyi, T., Fatokun, A. A., &Akinloye, O. (2019). Antioxidative, antimitotic, and DNA-damaging activities of *Garcinia kola* stem bark, *Uvariachamae* root, and *Olaxsubscorpioidea* root used in the ethnotherapy of cancers.*Journal of Basic and Clinical Physiology and Pharmacology*, 31(3). https://doi.org/10.1515/jbcpp-2019-0073

Prasad, N., Sharma, J. R., & Yadav, U. C. S. (2020). Induction of growth cessation by acacetin via β-catenin pathway and apoptosis by apoptosis inducing factor activation in colorectal carcinoma cells, *Molecular Biology Reports*, 47(2): 987–1001. https://doi.org/10.1007/s11033-019-05191-x

Prasad, S. K., Varsha, V., & Devananda, D. (2019). Anti-cancer properties of Annona muricata (L.): A Review. *Medicinal Plants*, 11(2): 123–134. https://doi.org/10.5958/0975-6892.2019.00016.9

Rosen, R. D., Amit,& Affiliations, S. (2020). *TNM Classification*.

Sak, K. (2017). Anticancer Action of Sulfated Flavonoids as Phase II Metabolites, *Food Bioconversion*, 207–236. Elsevier. https://doi.org/10.1016/B978-0-12-811413-1.00006-1

Salehi, B., Gültekin-Özgüven, M., Kirkin, C., Özçelik, B., Morais-Braga, M. F. B., Carneiro, J. N. P., Bezerra, C. F., Silva, T. G. da, Coutinho, H. D. M., Amina, B., Armstrong, L., Selamoglu, Z., Sevindik, M., Yousaf, Z., Sharifi-Rad, J., Muddathir, A. M., Devkota, H. P., Martorell, M., Jugran, A. K., … Martins, N. (2020). Antioxidant, Antimicrobial, and Anticancer Effects of Anacardium Plants: An Ethnopharmacological Perspective, *Frontiers in Endocrinology*, 11. https://doi.org/10.3389/fendo.2020.00295

Santana, L. F., Inada, A. C., Espirito Santo, B. L. S. do, Filiú, W. F. O., Pott, A., Alves, F. M., Guimarães, R. de C. A., Freitas, K. de C., &Hiane, P. A. (2019). Nutraceutical Potential of Carica papaya in Metabolic Syndrome, *Nutrients*, 11(7): 1608. https://doi.org/10.3390/nu11071608

Santos, J. M., Cury, N. M., Yunes, J. A., López, J. A., & Hernández-Macedo, M. L. (2019). Effect of *Anacardium occidentale* leaf extract on human acute lymphoblastic leukaemia cell lines, *Natural Product Research*, 33(11): 1633–1636. https://doi.org/10.1080/14786419.2018.1425841

Segun, P. A., Ogbole, O. O., &Ajaiyeoba, E. O. (2018). Medicinal plants used in the management of cancer among the ijebus of southwestern Nigeria,*Journal of Herbal Medicine*, 14: 68–75. https://doi.org/10.1016/j.hermed.2018.04.002

Shalabi, M., Khilo, Kh., Zakaria, M. M., Elsebaei, M. G., Abdo, W., &Awadin, W. (2015). Anticancer activity of *Aloe vera* and *Calligonumcomosum* extracts separately on hepatocellular carcinoma cells.*Asian Pacific Journal of Tropical Biomedicine*, 5(5): 375–381. https://doi.org/10.1016/S2221-1691(15)30372-5

Siegel, R. L., Miller, K. D., Fuchs, H. E., & Jemal, A. (2022). Cancer statistics, 2022,*CA: A Cancer Journal for Clinicians*, *72*(1): 7–33. https://doi.org/10.3322/caac.21708

Sieniawska, E., &Baj, T. (2017). Tannins, *Pharmacognosy: Fundamentals, Applications and Strategy*, 199–232. Elsevier Inc. https://doi.org/10.1016/B978-0-12-802104-0.00010-X

Singh, B., Singh, J. P., Singh, N., & Kaur, A. (2017). Saponins in pulses and their health promoting activities: A review. *Food Chemistry*, 233: 540–549. https://doi.org/10.1016/j.foodchem.2017.04.161

Soerjomataram, I., & Bray, F. (2021). Planning for tomorrow: Global cancer

incidence and the role of prevention 2020–2070. Nature Reviews Clinical Oncology, 18(10), 663–672. https://doi.org/10.1038/s41571-021-00514-z

Sun, Y., Xun, K., Wang, Y., & Chen, X. (2009). A systematic review of the anticancer properties of berberine, a natural product from Chinese herbs.*Anti-Cancer Drugs*, 20(9): 757–769. https://doi.org/10.1097/CAD.0b013e328330d95b

Sushma K. (2012). Medicinal Plants of Asian Origin Having Anticancer Potential: Short Review. *Asian Journal of Biomedical and Pharmaceutical Sciences*.

Tallini, L. R., Osorio, E. H., Berkov, S., Torras-Claveria, L., Rodríguez-Escobar, M. L., Viladomat, F., Meerow, A. W., &Bastida, J. (2022). Chemical Survey of Three Species of the Genus Rauhia Traub (Amaryllidaceae), *Plants*, 11(24): 3549. https://doi.org/10.3390/plants11243549

Telloni, S. M. (2017). Tumor Staging and Grading: A Primer, 1–17. https://doi.org/10.1007/978-1-4939-6990-6_1

Thanh, N. P. T., & Tran, T. T. (2021). Investigation of the bioactivities of extracts from *Vernonia amygdalina* Del, *IOP Conference Series: Earth and Environmental Science*, 947(1): 012040. https://doi.org/10.1088/1755-1315/947/1/012040

Thomford, N., Senthebane, D., Rowe, A., Munro, D., Seele, P., Maroyi, A., &Dzobo, K. (2018). Natural Products for Drug Discovery in the 21st Century: Innovations for Novel Drug Discovery. *International Journal of Molecular Sciences*, 19(6): 1578. https://doi.org/10.3390/ijms19061578

Thyagarajan, A., &Sahu, R. P. (2018). Potential Contributions of Antioxidants to Cancer Therapy: Immunomodulation and Radiosensitization, In *Integrative Cancer Therapies*, 17(2): 210–216. https://doi.org/10.1177/1534735416681639

Titov, A., Valiullina, A., Zmievskaya, E., Zaikova, E., Petukhov, A., Miftakhova, R., Bulatov, E., &Rizvanov, A. (2020). Advancing CAR T-Cell Therapy for Solid Tumors: Lessons Learned from Lymphoma Treatment. *Cancers*, 12(1): 125. https://doi.org/10.3390/cancers12010125

Tonin, L. T. D., Camargo, J. N. A., Bertan, A. S., Almeida, I. V. D., Vicentini, V. E. P., &Dusman, E. (2019). Antitumoral activity, antioxidant capacity and bioactive compounds of ginger (Zingiber officinale), *Acta Scientiarum Technology*, 42: e45724. https://doi.org/10.4025/actascitechnol.v42i1.45724

Tsao, Y.-C., Chang, Y.-J., Wang, C.-H., & Chen, L. (2020). Discovery of Isoplumbagin as a Novel NQO1 Substrate and Anti-Cancer Quinone, *International Journal of Molecular Sciences*, 21(12): 4378. https://doi.org/10.3390/ijms21124378

Tyagi, N., Sharma, G. N., Shrivastava, B., Saxena, P., & Kumar, N. (2017). Medicinal plants: used in Anti-cancer treatment. *International Journal of Research and Development in Pharmacy & Life Sciences*, 6(5): 2732–2739. https://doi.org/10.21276/IJRDPL.2278-0238.2017.6(5).2732-2739

Ukwubile, C. A., Malgwi, T. S., Dibal, M. Y., Bababe, A. B., &Bingari, M. S. (2020). Phytochemical composition and toxicity evaluation of Camellia sinensis (L.) O. Kuntze (Theaceae)(Green Tea) leaves collected from mambila beverages Ltd Nigeria. *International Journal of Medicinal Plants and Natural Products*, *6*(2), 7-13.

Varon, C., Azzi-Martin, L., Khalid, S., Seeneevassen, L., Ménard, A., &Spuul, P. (2022). Helicobacters and cancer, not only gastric cancer? *Seminars in Cancer Biology*, 86, 1138–1154. https://doi.org/10.1016/j.semcancer.2021.08.007

Vijayarathna, S., &Sasidharan, S. (2012). Cytotoxicity of methanol extracts of Elaeisguineensis on MCF-7 and Vero cell lines, *Asian Pacific Journal of Tropical Biomedicine*, 2(10): 826–829. https://doi.org/10.1016/S2221-1691(12)60237-8

Vineis, P., & Wild, C. P. (2014). Global cancer patterns: causes and prevention,*Lancet (London, England)*, 383(9916): 549–557. https://doi.org/10.1016/S0140-6736(13)62224-2

Vo, T.-L. T., Yang, S.-E., Huang, L.-G., Li, P.-H., Chen, C.-L., & Song, T.-Y. (2022). Anti-Proliferative and Anti-Metastatic Effects of Ethanol Extract from Cajanus cajan (L.) Millsp. Roots and its Sub-Fractions in Oral Squamous Cell Carcinoma. *Agriculture*, 12(12): 1995. https://doi.org/10.3390/agriculture12121995

Wahab, S. M. A., Jantan, I., Haque, M. A., & Arshad, L. (2018). Exploring the leaves of Annona muricata L. as a source of potential anti-inflammatory and anticancer agents, In *Frontiers in Pharmacology*, 9(JUN). Frontiers Media S.A. https://doi.org/10.3389/fphar.2018.00661

Wang, L., Phan, D. D. K., Zhang, J., Ong, P.-S., Thuya, W. L., Soo, R., Wong, A. L.-A., Yong, W. P., Lee, S. C., Ho, P. C.-L., Sethi, G., & Goh, B. C. (2016). Anticancer properties of nimbolide and pharmacokinetic considerations to accelerate its development.*Oncotarget*, 7(28): 44790–44802. https://doi.org/10.18632/oncotarget.8316

Wisitpongpun, P., Suphrom, N., Potup, P., Nuengchamnong, N., Calder, P. C., &Usuwanthim, K. (2020). In Vitro Bioassay-Guided Identification of Anticancer Properties from Moringa oleifera Lam. Leaf against the MDA-MB-231 Cell Line. *Pharmaceuticals*, 13(12): 464. https://doi.org/10.3390/ph13120464

World Health Organization. (2024). Global cancer burden growing, amidst mounting need for services. https://www.who.int/news/ite

m/01-02-2024-global-cancer-burden-growing--amidst-mounting-need-for-services

Yildirim, I., &Kutlu, T. (2015). Anticancer agents: Saponin and tannin. *International Journal of Biological Chemistry*, 9(6): 332–340. https://doi.org/10.3923/ijbc.2015.332.340

Zhong, Z., Yu, J., Virshup, D. M., & Madan, B. (2020). Wnts and the hallmarks of cancer. *Cancer metastasis reviews*, *39*(3), 625–645. https://doi.org/10.1007/s10555-020-09887-6

Zou, Z., Chang, H., Li, H., & Wang, S. (2017). Induction of reactive oxygen species: an emerging approach for cancer therapy, *Apoptosis*, 22(11): 1321–1335. https://doi.org/10.1007/s10495-017-1424-9

Zulkipli, I. N., David, S. R., Rajabalaya, R., & Idris, A. (2015). Medicinal Plants: A Potential Source of Compounds for Targeting Cell Division. *Drug Target Insights*, 9: DTI.S24946. https://doi.org/10.4137/DTI.S24946

Cite as: Imah-Harry J.U., Chidume C.C., Okunlola F.O., & Oloke J.K. . (2024). Nigerian Medicinal Plants with Anticancer Properties: An Updated Review. Funct Food J 5(1):76-111.