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**Research Paper**

# Natural Products as Anticancer Agents: Current Status and Future Perspectives

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***Abstract***
*Cancer is one of the leading causes of global death. For ages, research has been carried out to find a lasting cure to this global burden. Conventional cancer treatment such as Chemotherapy, Radiotherapy had been helpful over the years. But this treatment has its adverse side effect which makes it not an effective tool in cancer treatment. Of recent, Scientists have shifted their focus to Natural Products from Medicinal Plants. Natural products are integral to the development of innovative anticancer drugs in cancer research, offering the scientific community the possibility of exploring novel natural compounds against cancers. This study focuses on the diversity of Nigeria plants; its traditional uses and also its anticancer activities. This study also focuses on scientific studies and research trends on Nigeria Medicinal plants, In Vivo and In vitro studies conducted on the plants to assess their antitumor activities. The study also shows the mechanism of action and potential benefits of natural products over conventional cancer treatment. And also highlights investigative methods for further and effective research on cancer treatment.*

***Key Word:*** *cancer, Nigeria, natural product, health, medicinal plants, treatment, alternative*.

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## I. INTRODUCTION

### 1.1 Global Burden of Cancer

Cancer is one of the leading causes of death worldwide and a significant obstacle to increasing life expectancy in all countries (Hyuna et al., 2020). According to the World Health Organization (WHO) estimates from 2019, cancer ranks as the first or second leading cause of death before the age of 70 in 112 out of 183 countries, while in an additional 23 countries, it holds the third or fourth position (Fig. 1). The growing impact of cancer as a major cause of death is partly due to a substantial decline in mortality rates from stroke and coronary heart disease compared to cancer in many regions (Hyuna et al., 2020).

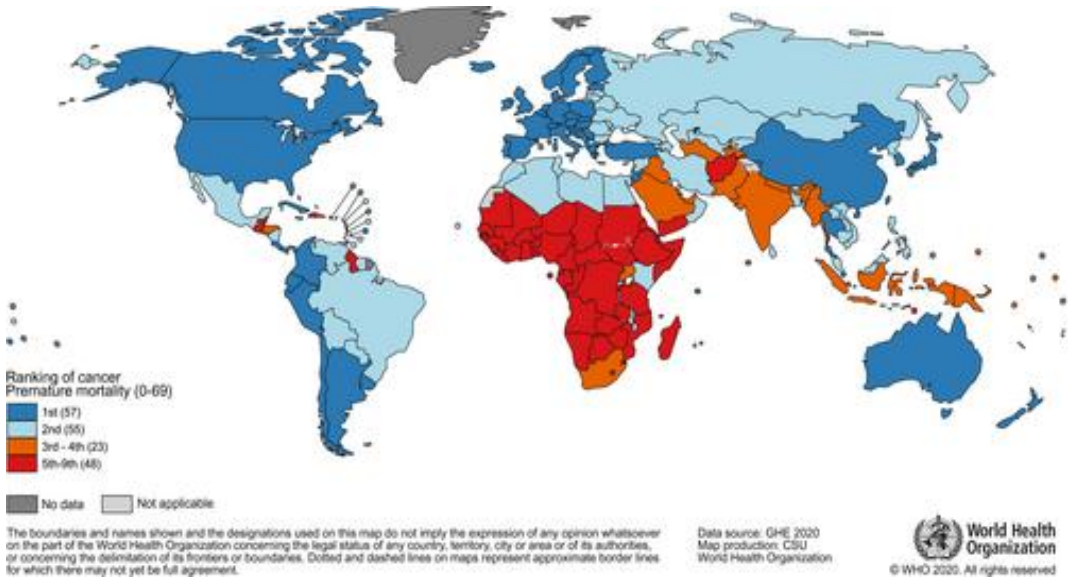


**Figure 1 National Ranking of Cancer as a Cause of Death at Ages <70 Years in 2019. (Hyuna *et al.*, 2020)**

Cancer results from a pathological breakdown in the mechanisms that regulate cell proliferation, differentiation, and programmed cell death (IARC Publications, 2000). In most cases, malignant cells that form tumors originate from epithelial tissue and are classified as "carcinomas." Carcinomas account for the majority of cancers in organs such as the breast, lungs, and bowel. Although different types of cancer share some common traits, they vary significantly in their causes and responses to treatment (IARC Publications, 2000).

In 2020, the global cancer burden was estimated at 19.3 million new cases and 10.0 million deaths. Around one in five people worldwide will develop cancer in their lifetime, while one in eight men and one in eleven women will die from the disease (Lyon, 2020). The number of individuals living within five years of a cancer diagnosis, known as the 5-year prevalence, is estimated to be 50.6 million globally (Lyon, 2020). The rising incidence and mortality of cancer worldwide are driven by population growth, aging, and shifts in the prevalence and distribution of key risk factors, many of which are linked to socioeconomic development (Hyuna *et al.*, 2020).

According to Ibrahim et al., (2020), traditional medicine practitioners in Kebbi State use 48 medicinal plants for cancer treatment, as reported by the Hausa-Fulani tribes. Pharmacological studies have shown that many of these plants exhibit active properties in cancer treatment.

### 1.1.1Major Cancer Types in 2020

The ten most prevalent types of cancer account for over 60% of newly diagnosed cases and more than 70% of cancer-related deaths. Female breast cancer is the most frequently diagnosed cancer worldwide, representing 11.7% of all new cases, followed closely by lung cancer (11.4%), colorectal cancer (10.0%), prostate cancer (7.3%), and stomach cancer (5.6%). Lung cancer remains the leading cause of cancer-related deaths, contributing to 18.0% of total cancer deaths, followed by colorectal cancer (9.4%), liver cancer (8.3%), stomach cancer (7.7%), and female breast cancer (6.9%) (Lyon, 2020).

Among men, lung cancer is the most commonly diagnosed cancer and the primary cause of cancer-related death, with prostate cancer and colorectal cancer ranking next in incidence, while liver cancer and colorectal cancer follow in mortality rates. In women, breast cancer is both the most frequently diagnosed cancer and the leading cause of cancer-related death. Colorectal cancer and lung cancer are the next most common in terms of incidence, whereas lung cancer and colorectal cancer rank second and third in cancer mortality among women (Lyon, 2020).

### 1.1.2Epidemiology of Cancer

The global cancer burden continues to rise due to an aging and growing population, along with the increasing prevalence of cancer-related risk factors such as smoking, consumption of processed foods, and sedentary lifestyles (Zhang *et al.*, 2020). In developed countries, cancer ranks as the second leading cause of death. According to GLOBOCAN 2018 data, the number of cancer cases worldwide had reached 18.1 million, with 9.6 million cancer-related deaths. Developing countries accounted for 56% of all cases and 64% of cancer deaths (Ferlay *et al.*, 2018).

Although cancer incidence in developed nations is half that of developing countries, overall cancer-related mortality remains nearly the same in both regions (Magalhaes *et al.,* 2018). Despite the rising incidence and prevalence, cancer remains a low public health priority in Africa due to limited economic resources and the burden of other communicable and non-communicable diseases (Morales-Cruz *et al.,* 2019). In Ethiopia, cancer accounts for approximately 6.2% of all deaths, with an estimated annual incidence of 68,960 new cases and over 54,000 deaths. The most common cancers among Ethiopian adults are breast cancer, cervical cancer, and colorectal cancer (Kumar *et al.,* 2015).

**1.1.3 Pathophysiology of Cancer**

The exact mechanism behind cancer development remains unclear and is not yet fully understood. It is believed that normal regulatory systems controlling cell growth and proliferation become disrupted (O'Higgins *et al.,* 2018). Cancer develops in a stepwise process, beginning with initiation, where exposure to a carcinogenic substance causes genetic damage in normal cells, leading to mutations. In the promotion stage, carcinogens or mutated cells alter the cellular environment, disrupting normal cell growth (Klaunig *et al.*, 2011).

Next, transformation (or conversion) occurs when the mutated cell becomes malignant. The time between exposure to carcinogens and the clinical appearance of a tumor can take up to 20 years, depending on the type of cancer. Finally, in the progression stage, uncontrolled cell proliferation leads to tumor expansion and eventual spread to other parts of the body, a process known as metastasis (Zemene *et al.*, 2021).

**1.1.4Projected Burden of Cancer in 2040**

By 2040, the global number of new cancer cases is projected to reach approximately 28.4 million, reflecting a 47% increase from the 19.3 million cases estimated in 2020. Based on the four-tier Human Development Index (HDI) used to assess a country's social and economic transition, nations with low or medium HDI are expected to experience the highest relative increases in cancer incidence, with rises of 95% and 64% from 2020, respectively. Additionally, many of these countries are seeing a significant surge in the prevalence of established cancer risk factors such as smoking, poor diet, obesity, and physical inactivity that are currently more common in nations with high and very high HDI (Lyon, 2020).

**1.2 Need for Novel Therapeutic Agents**

Despite significant progress in cancer diagnosis, prevention, detection, and treatment, the disease is still expected to become the leading cause of death worldwide. While chemotherapy has advanced in its design, no single medication is fully effective against all cancer types and stages (Zemene *et al.,* 2021).

Cancer management involves both pharmacologic and non-pharmacologic treatment approaches, including surgery, radiation therapy, and chemotherapy. The choice of treatment depends on factors such as the cancer stage, cell type, and the patient's overall clinical condition (Chan *et al.,* 2015). Since most cancers are not curable in advanced stages, prevention remains a critical focus of research. Lifestyle modifications and the use of chemopreventive agents have been shown to significantly reduce the risk of developing cancer (Zemene *et al.,* 2021).

**1.2.1. Managements of Cancer**

The goals of cancer treatment are based on the stage of the disease and other factors affecting the patient's health. Chemotherapy may be used to slow disease progression, relieve symptoms, and, when possible, achieve a cure (Zemene *et al.,* 2021). Cancer management is generally categorized into two approaches: pharmacological and non-pharmacological treatments.

**1.2.1.1 Pharmacologic Management of Cancer**

At present, surgery, radiation therapy (RT), and chemotherapy are the primary treatment methods for cancer. Chemotherapeutic drugs generally have a very limited therapeutic window (Zemene *et al.,* 2021).

**1.2.1.2 Non-pharmacological Management of Cancer**

Pain is a frequent symptom in patients with advanced cancer, yet its treatment is often inadequate. Non-pharmacological approaches, including hot/cold therapy, physical therapy, and dietary adjustments, are recommended for pain management. Additionally, surgery and radiation therapy serve as key non-pharmacological treatment modalities (Zemene *et al.,* 2021).

**1.2.2 New Therapeutic Agents and Novel Drug Target**

With the sequencing of the human genome and advancements in genetic technology, there is an expanding body of knowledge regarding cancer's genetic alterations, initiation, proliferation, therapeutic mechanisms, and emerging treatment targets (Zemene *et al.,* 2021).

A deep understanding of the disease's pathophysiology, human gene sequencing, and the identification of novel molecular targets form the foundation of modern medicine in the fight against cancer. Significant progress has

been made in developing targeted therapies, which are designed to selectively attack cancer cells while causing minimal harm to normal, healthy cells (Ke and Shen, 2017).

Targeted therapies involve drugs or other substances that inhibit cancer growth and spread by interfering with specific molecules or targets responsible for tumor development and progression. These therapies are currently at the forefront of anticancer drug development and serve as the foundation of precision medicine (Zemene *et al.,* 2021).

**1.3 Historical and Cultural Use of Medicinal Plants in Nigerian Traditional Medicine**

Medicinal plants play a crucial role in both traditional and modern medicine. They have demonstrated significant therapeutic value, with approximately 80% of rural populations relying on them as their primary healthcare source (Akinyemi, 2000). The use of plants for treating various diseases dates back to ancient times and remains a deeply rooted tradition across all continents, particularly in Africa. Despite major advancements in synthetic medicinal compounds during the twentieth century, over 25% of prescribed drugs in industrialized nations are still derived, either directly or indirectly, from plants (Newman *et al.,* 2000). However, many plants utilized in traditional medicine remain under-researched (Kirby, 1996).

In developing regions, especially in West Africa, the high cost of modern pharmaceuticals makes them less accessible. As a result, up to 80% of the population relies on medicinal plants for treatment (Kirby, 1996; Hostellmann and Marston, 2002). The World Health Organization (WHO) defines traditional medicine as the collective body of knowledge and practices whether scientifically explained or not—used in diagnosing, preventing, and treating physical, mental, and social imbalances. This knowledge is based entirely on practical experience and observation, passed down orally or in written form through generations (Monier, 2016).

Nigeria's ecosystem is highly diverse, housing a rich array of biological resources and biodiversity. It serves as a source of medicine, food, and various natural products that support traditional medicine in the country. The use of herbal remedies has been practiced for centuries, with methods and applications varying among ethnic groups (Adams *et al.,* 2023).

However, the practice of herbal medicine faces significant challenges, particularly in terms of documentation and a lack of clinical validation, which hinders its integration into standardized medical practice. This lack of scientific evidence presents difficulties in establishing herbal medicine as a reliable and adoptable treatment in clinical settings. Despite these challenges, Nigeria is home to a vast collection of medicinal plants, many of which have shown therapeutic potential in research studies (Adams *et al.,* 2023).

**1.3.1 Traditional Uses of Medicinal Plants for Treatment of Some Ailments**

Medicinal plants are utilized in various ways, with different plant parts—including leaves, roots, stems, bark, and fruits—being used either individually or in combination with other species (Monier, 2016).

i. For common ailments such as cuts and wounds, plants like *Milicia excelsa, Chromolaena odorata, Aspilia Africana,* and *Manihot esculenta* are used to accelerate wound healing. This suggests that these plants contain therapeutic compounds, such as vitamin C and essential amino acids, which aid in the rapid recovery of wounds (Monier, 2016).

ii. More severe conditions, such as epilepsy, are treated using a concoction made from the leaves of *Bryophyllum pinnatum* and *Emilia sonchifolia*, which is administered orally. Additionally, *Newbouldia laevis* leaves are used to treat scrotal elephantiasis, while *Acanthospermum hispidus* leaves are utilized for tuberculosis treatment (Monier, 2016).

iii. Respiratory conditions like coughs are managed using various plant species, including *Abrus precatorius, Ocimum gratissimum, Garcinia kola*, and *Terminalia macroptera* (Monier, 2016).

iv. For sexually transmitted infections, *Vernonia amygdalina* is used to alleviate vaginal itching, while *Azadirachta indica* is applied in the treatment of syphilis. Additionally, *Alchornea cordifolia* and *Carica papaya* are employed for managing gonorrhea (Monier, 2016).

**1.4 Nigeria's Rich Flora as a Source of Undiscovered Anticancer Compounds**

In Nigeria, plant extracts are extensively utilized as key sources of chemotherapeutic agents, despite the widespread use of synthetic drugs among the population. Medicinal plants have long been employed in cancer management, particularly in developing countries like Nigeria (Lasswell, 1977).

The use of synthetic drugs for cancer treatment is often associated with harmful side effects. Therefore, the readily available and cost-effective nature of medicinal plants presents a viable alternative to mitigate the toxic effects linked to synthetic drugs (Rashid, 2002). These plants contain bioactive compounds that contribute to their pharmacological effects in the human body (Franklyn *et al.,* 2021).

A study by Godwin et al., (2023), demonstrated the anticancer potential of leaf extracts from*U. chamae* and *D. paniculata*, revealing that their cytotoxic effects operate through the induction of apoptosis. Utilizing *U. chamae*

leaves instead of the roots and stem bark often overharvested in traditional anticancer treatments provides a more sustainable approach to preserving the plant (Godwin *et al.,* 2023).

**Diversity of Nigeria Flora and its Significance**

**2.1 Plant Diversity in Nigeria**

There are about 7,895 plant species identified in 338 families and 2,215 genera(Ajao, 2012).Table 1.

| S/N | Groups of plants | Families | Genera | Species |
|---|---|---|---|---|
| 1 | Algae | 67 | 281 | 1335 |
| 2 | Lichens | - | 14 | 17 |
| 3 | Fungi (mushrooms) | 26 | 60 | 134 |
| 4 | Mosses | - | 13 | 16 |
| 5 | Liverworts | - | 16 | 6 |
| 6 | Pteridophytes | 27 | 64 | 165 |
| 7 | Gymnosperms | 2 | 3 | 5 |
| 8 | Chlamydosperms | 2 | 2 | 6 |
| 9 | Monocotyledons | 42 | 376 | 1575 |
| 10 | Dicotylrdons | 172 | 1396 | 4636 |
| | Total | 338 | 2215 | 7895 |

The northern region of Nigeria, which has Sudanian ecological influences, is home to 39 endemic plant species, while the western and central regions contain 38, and the eastern region has 128 endemic species (Borokini *et al.,* 2010). Approximately 0.4% of plant species in the country are classified as threatened, while 8.5% are considered endangered. According to the IUCN list of threatened species, 146 species are found in Nigeria, with 18 categorized as 'endangered' and 15 as 'critically endangered' (NACGRAB, 2008).

These plant species are distributed across Nigeria's diverse vegetation zones. The Niger Delta region of Nigeria contains the most extensive mangrove forest in Africa (FGN, 2010). Land use analysis of Nigeria's 923,768 square kilometers indicates that 34% is used for crops, 23% is covered by grassland, and 16% consists of forests. Additionally, about 13% of the land is occupied by rivers, lakes, and reservoirs, while the remaining 14% falls under other uses (NACGRAB, 2008).

Nigeria ranks 11th in Africa in terms of biodiversity due to its significant variety of plant species. Furthermore, the West African forests are recognized as one of the 25 global biodiversity hotspots essential for conservation efforts (Myers *et al.,* 2000), with Nigeria's tropical rainforests playing a crucial role within this ecosystem.

**2.1.1 Protected Areas in Nigeria**

The conservation and sustainable utilization of plant biodiversity in any country depend on establishing and maintaining protected areas such as national parks and game reserves that support high biodiversity. As previously mentioned, Nigeria is considered a biodiversity hotspot and has several protected areas. Currently, approximately 2.4 million hectares of land are designated as national parks.

Nigeria's network of protected areas consists of a biosphere reserve, seven national parks, 445 forest reserves, 12 strict nature reserves, and 28 game reserves (Moses *et al.,* 2013). Additionally, proposals have been made for the conservation of other sanctuaries and game reserves (FGN, 2010). The country's forest ecosystems include open tree savanna, lowland wet and deciduous forests, freshwater swamp forests, mangrove and coastal forests, as well as riparian or fringing forests (Blaser *et al.,* 2011).

**2.1.2 Threats to Plant Diversity in Nigeria**

The majority of threats to biodiversity are primarily driven by human activities, stemming from interactions with the environment for development, enhanced living standards due to industrialization, technological progress, and the rapid expansion of urbanization (Moses *et al.,* 2013).Some threats to biodiversity in Nigeria include:

1. Overpopulation
2. Over exploitation
3. Agriculture
4. Deforestation
5. Global Climate Change
6. Drought and Desertification

**2.2 Established Role of Plant Secondary Metabolites**

Natural products, particularly plant-based medicines and remedies, have been studied for centuries due to their therapeutic efficacy in treating various diseases and ailments (Choudhari *et al.,* 2020). This has led to the exploration and isolation of numerous phyto-compounds with clinical benefits, significantly impacting medical science. In cancer therapy, nearly 60% of anticancer drugs currently in clinical use with proven effectiveness are

derived from natural products (Rayan *et al.,* 2017). These compounds serve as valuable lead molecules and provide cost-effective resources for modern drug discovery.

Plant-based natural products tend to produce fewer adverse side effects, likely due to their structural similarity to chemical compounds found in the human diet, which enhances their tolerance (Yasir *et al.,* 2022). Secondary metabolites in plants, such as flavonoids, tannins, alkaloids, and terpenoids, are widely recognized for their potent anticancer properties (Mamta *et al.,* 2013). These compounds influence metabolic pathways that regulate cell proliferation, migration, and apoptosis through various biological mechanisms. As a result, phyto-compounds remain a major focus in preclinical and clinical investigations for chemotherapeutic drug development (Bertha *et al.,* 2023). For example, paclitaxel, a plant-derived alkaloid, was discovered in 1962 during the screening of natural products for cancer treatment. Marketed under the brand name Taxol®, it remains one of the most effective drugs for treating breast and ovarian cancer (Saklani *et al.,* 2008).

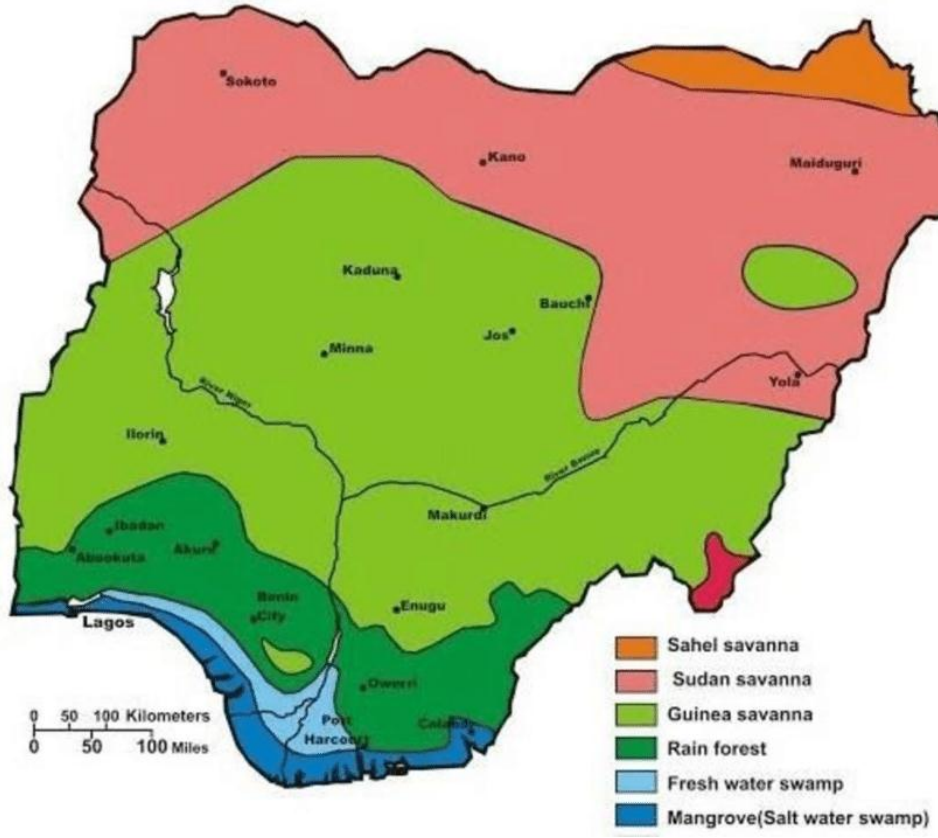


**Figure 2Map of Nigeria showing the various vegetation zone (FGN, 2002)**

**Scientific Evidence and Research Trends**

3.1 Plants identified with promising anticancer properties:

**3.1.1 *Alliumsativum* (Garlic)**

**Figure 3 Allium sativum (Garlic)**

This plant belongs to the Lilaceae family and is known by different names across various regions in Nigeria, including 'Aayu' in Yorubaland, 'Ayo-ishi' in Igboland, and 'Tafarunua' in Hausaland. Its bulb is widely utilized in traditional medicine for the treatment of fever, coughs, asthma, bronchial dilation, and flatulence. Additionally, it serves as an anthelmintic, antibiotic, diuretic, antimicrobial agent, blood tonic, and emmenagogue.

Studies have shown that the topical application of garlic oil during the initiation stage of benzo(a)pyrene (BP)-induced carcinogenesis in mice resulted in a decreased incidence and number of tumors. Furthermore, oral administration of fresh aqueous garlic extract has been found to reduce chemically induced cervical carcinomas in mice (Taye, 2013).

### 3.1.2 *Chenopodiumambrosioides* (Wormwood)

**Figure 4*Chenopodiumambrosioides* (Wormwood)**

This plant belongs to the *Chenopodiaceae* family and is commonly known as 'Ewe-imi,' 'Asin,' and 'Arunpale' in various parts of Nigeria. Both the whole plant and its leaves are traditionally used as anthelmintics, emollients, and for the treatment of rheumatism and tumors in different regions of the country.

Research has shown that the hydroalcoholic extract of wormseed leaves possesses anti-tumor properties in mice (Nascimento *et al.*, 2006). Additionally, ascaridol, a compound derived from *Chenopodium ambrosioides*, has demonstrated in vitro antineoplastic effects against various tumor cell lines (Efferth et al., 2002). Sowemimo et al., (2007), reported that *Chenopodium ambrosioides* was non-toxic to brine shrimp and rat lymphocyte chromosomes, yet it exhibited inhibition in a conventional telomerase assay, suggesting potential selectivity for human chromosomes. These findings support its traditional use in cancer management in southwestern Nigeria. Furthermore, *Chenopodium ambrosioides* has been found to be neither mutagenic nor cytotoxic.

### 3.1.3 *Kigelia* Africana (Sausage tree)

**Figure 5*Kigelia* Africana (Sausage tree)**

This plant belongs to the *Bignoniaceae* family and is commonly referred to as 'Pandoro' in Yorubaland, 'Rawuya' in Hausaland, and 'Uturubein' in Igboland. Various parts of the plant, including the root, stem bark, fruits, and leaves, are traditionally used for treating kidney disorders, malaria, dysentery, rheumatism, gonorrhea, hemorrhage, spleen infections, cough, leucorrhea, and as an astringent (Taye, 2013; Yusuf *et al.*, 2025).

The root bark is specifically recommended for the treatment of uterine cancer. Studies have tested the plant extract against melanoma cells, a tumor of pigmented skin cells that can develop into malignant melanoma, a potentially fatal form of skin cancer. Findings revealed that the extract significantly inhibited the growth of cultured melanoma cells. Additionally, extracts from the stem bark and fruit have demonstrated cytotoxic properties and have shown promising potential in the treatment of melanoma and renal carcinoma (Taye, 2013).

Table 2.Nigerian medicinal plants and their anticancer activity (Franklyn *et al.*, 2021; Godwin *et al.*, 2023).

| **Anticancer plant (family)** | **Part used for study** | **Extractant used for study** | **Bioactive compound** | **Cancer cell type** | **Pharmacological actions** |
|---|---|---|---|---|---|
| *Acronychia baueri* (Rutaceae) | Bark | Aqueous | Normelicopidine, melicopine, acronycine, and triterpenelupeol | Not specified | Antiproliferative effect |
| *Ageratum conyzoides* (Compositae) | Leaf | Ethylacetate | Kaempferol, oxygenated terpenes, sesquiterpene hydrocarbons, and monoterpene hydrocarbons | Lung, blood, central nervous system and prostate | Cytotoxic and antiproliferative effects |
| *Alchornea cordifolia* (Euphorbiaceae) | Leaf and bark | Methanol | Flavonoids, saponins, cardiac glycosides, steroids, anthraquinone, terpenes, xanthones, alkaloids, and tannins | Blood | Apoptotic effect |
| *Allium sativum* (Amaryllidaceae) | Bulb | Ethanol | S-allylcysteine, S-allylmercapto-L-cysteine, diallyl disulfide, diallyltrisulfide, and allicin | Skin, colon, lung, prostate, blood, and breast | Cytotoxic and antiproliferative effects |
| *Aloe barbadensis* (Asphodelaceae) | Leaf | Ethanol | Aloe-emodin | Liver and lung | Modulation of lipid peroxidation, cytotoxic and antioxidant effects |
| *Alstonia boonei* (Apocynaceae) | Stem-bark, leaf and root | Methanol and *n*-hexane | Echitamine, eugenol, 1, 2-benzenedicarboxylic acid, and alstiboonine | Pancreas, lung, prostate, colon | Antiproliferative and cytotoxic effects |
| *Anacardium occidentale* (Anacardiaceae) | Leaf and stem-bark | Hydroethanol | Agathisflavone, methyl gallate, anacardicin, zoapatanolide A, tannins, alkaloids, saponins, and polyphenols | Laryngeal, blood, and cervical | Cytotoxic and antiproliferative effects |
| *Anogeissus leiocarpus* (Combretaceae) | Leaf and root | Ethanol | Ellagic acid, castalagin, and flavogallonic acid | Liver | Antiproliferative effect |
| *Astragalus membranaceus* (Fabaceae) | Root | Not specified | Isoflavones, calycosin, ononin, formononetin, and campanulin | Breast | Antiproliferative, apoptotic and cytostatic effects, restoration of deformed T cells |
| *Atractylis lancea* (Compositae) | Root | Ethanol and petroleum ether | Polyacetylenes, sesdquiterpenes, and sesquiterpene lactones | Liver and stomach | Cell cycle arrest, antiproliferative and apoptotic effects |
| *Azadirachta indica* (Meliaceae) | Leaves, seeds | Ethanol | flavonoids, phenolics, limonoids, triterpenoids | Skin, prostate, breast, cervical, blood, liver, colon, lung, and stomach | Antiproliferative effects through the induction of autophagy, apoptosis and cell cycle arrest |
| *Boerhaavia diffusa* (Nyctaginace | Leaf | Ethanol and methanol | Alkaloids, flavonoids, tannins, saponins, terpenes, | Cervical and breast | Cell cycle arrest, antiproliferative |

| **Anticancer plant (family)** | **Part used for study** | **Extractant used for study** | **Bioactive compound** | **Cancer cell type** | **Pharmacological actions** |
|---|---|---|---|---|---|
| ae) | | | anthraquinones, and steroids | | effects |
| *Cajanus cajan* (Fabaceae) | Leaf | Ethanol | Longistylin C, longistylin A, stilbenoids, and flavonoids | Colorectal, breast, cervical, lung, blood and liver | Antiproliferative effect |
| *Camellia sinensis* (Theaceae) | Leaf | Not specified | (+)-gallocatechin, (-)-epigallocatechingallate, and (-)-epigallocatechin | Colon, lung, breast, and liver | Antiproliferative and cytotoxic effects, cell cycle arrest |
| *Carica papaya* (Caricaceae) | Leaf | Aqueous | Ascorbic acid, quercetin, kaempferol, tetrahydroxyflavone, kaempferol-*β*-D-glucopyranoside, papain, lycopene, morin, cystatin, fisetin, benzylisothiocyanate, luteolin-*β*-D-glucopyranoside, luteolin, and myricetin-3-O-rhamnoside | Prostate, lung, blood, pancreas, and liver | Antiproliferative effect |
| *Cassia occidentalis* (Fabaceae) | Whole plant | Aqueous | Flavonoids, tannins, alkaloids, anthraquinones, and saponins | Colon, ovary, cervical, breast, and prostate | Antiproliferative effect |
| *Chromolaena odorata* (Compositae) | Leaf | *n*-Hexane and ethanol | 2-hydroxy-4, 4, 5, 6-tetramethoxychalcone, acacetin, kaempferol-3-O-rutinoside, quercetin-3-O-rutinoside, kaempferide, and rhamnazin | Breast, lung, and blood | Cytotoxic effect |
| *Citrus aurantifolia* (Rutaceae) | Not specified | Aqueous | Polymethoxyflavones | Colon, pancreas, and breast | Induction of apoptosis, cell cycle arrest, cell lysis, inhibition of metastasis, strengthening immunity |
| *Croton zambesicus* (Euphorbiaceae) | Leaf | Dichloromethane | Ent-trachyloban-3-*β*-ol, ent-trachyloban-3-one, ent-18-hydroxy-trachyloban-3-one, trans-phytol, isopimara-7, and 15-dien-3-*β*-ol | Cervical | Cytotoxic effect |
| *Cryptolepis sanguinolenta* (Asclepiadaceae) | Root | Aqueous | Cryptolepine, ascryptolepinoic acid, quindoline, and methyl cryptolepinoate | Lung | Antiproliferative effect, reduction of cancer cell viability |
| *Curcuma longa* (Zingiberacea) | Rhizome | Ethanol | Curcumin | Breast, stomach, colon, lung, and liver | Apoptotic, antiproliferative, antioxidant and anti-inflammatory effects, Cell cycle arrest |
| *Derris scandens* (Fabaceae) | Not specified | Ethanol | Glyurallin, derriscandenon B and C, isochandaisone, and derrubone | Colon | Apoptotic effects, inhibition of mitosis |
| *Enantia* | Stem- | Methanol | Columbamine, saponins, | Colorectal, | Antiproliferative and |

| **Anticancer plant (family)** | **Part used for study** | **Extractant used for study** | **Bioactive compound** | **Cancer cell type** | **Pharmacological actions** |
|---|---|---|---|---|---|
| *chlorantha* (Annonaceae) | bark | | pseudocolumbamine, and palmatine | liver, and lung | cytotoxic effects |
| *Fagara zanthoxyloides* (Rutaceae) | Root | Aqueous | Fagaronine | Blood and prostate | Antiproliferative and cytotoxic effects, inhibits cancer cell viability |
| *Glochidion zeylanicum* (Euphorbiaceae) | Stem-bark, leaf and root | Methanol and aqueous | Triterpinoids and megastigmane glycosides | Prostate, colon, and liver | Cytotoxic and antiproliferative effects |
| *Glycyrrhiza glabra* (Fabaceae) | Whole plant | Aqueous | Licochalcone and isoliquiritigenin | Prostate, breast, and colon | Apoptotic and antiproliferative effects, cell cycle arrest |
| *Goniothalamus macrophyllus* (Annonaceae) | Root and stem | Methanol | Goniothalamin | Cervical, breast, and colon | Cytotoxic and apoptotic effects |
| *Harungana madagascariensis* ( Guttiferae) | Stem-bark | Methanol and dichloromethane | Coumarins, anthraquinones, bioflavonoids, anthrone derivatives, and xanthones | Blood | Cytotoxic effect, activates nitric oxide secretion |
| *Khaya senegalensis* (Meliaceae) | Stem-bark | Methanol and hydroethanol | 3α, 7α-dideacetylkhivorin, 1-O-deacetylkhayanolide E4, khayanolide B2, 6-dehydroxylkhayanolide E5, 1-O-acetylkhayanolide B1, and khayanolide E3 | Colon, cervical, liver, and breast | Antiproliferative and apoptotic effects |
| *Lophira alata* (Ochnaceae) | Stem-bark | Methanol | Azobechalcone A, flavonoids, isolophirachalcone, lophirone F, lophirone A, triterpenes, sterols, polyphenols, lophirones C, and lophirones B | Liver, lung, breast, skin, and colon | Antiproliferative, antitumor and cytotoxic effects |
| *Mangifera indica* (Anacardiaceae) | Stem-bark | Methanol | Galloyl glycosides , lupeol, mangiferin, gallotannins, and gallic acid | Breast, kidney, ovary, and colon | Antiproliferative effect |
| *Milicia excelsa* (Moraceae) | Root | Methanol | Neocyclomorusin, cudraxanthone I, betulinic acid, 6-geranylnorartocarpetin, and atalantoflavone | Cervical, liver, colon, and brain | Antiproliferative and cytotoxic effects |
| *Morinda lucida* (Rubiaceae) | Leaf and stem-bark | Aqueous and methanol | Molucidin, β-sitosterol, stigmasterol, oruwacin, digitolutein, , ursolic acid, rubiadin-1-methyl ether, phytol, cycloartenol, oleanolic acid, damnacantha and campesterol | Prostate, stomach, colon and blood | Antiproliferative effect |
| *Newbouldia laevis* (Bignoniaceae) | Root-bark | Methanol | 2-acetylfuro-1, 4-naphthoquinone, triterpenoid, tannins, steroids, and quinone derivatives | Pancreas and blood | Antiproliferative and cytotoxic effects |
| *Ocimum gratissimum* (Labiat | Leaf | Ethanol and aqueous | 3, 4-dihydroxycinnamic acid, oleanolic acid, | Cervical, breast, | Antiproliferative effect |

| **Anticancer plant (family)** | **Part used for study** | **Extractant used for study** | **Bioactive compound** | **Cancer cell type** | **Pharmacological actions** |
|---|---|---|---|---|---|
| ae) | | | saponins, linalool, eugenol, gerianol, alkaloids, thymol, and citral | prostate, lung, colon, pancreas, kidney, and bone | |
| *Panax ginseng* (Araliaceae) | Root and rhizomes | Not specified | Ginsenoside Rp1 | Breast | Antiproliferative and apoptotic effects, cell cycle arrest |
| *Picrorhiza kurroa* (Plantaginaceae) | Root | Hydroalcohol | Apiocynin, cucurbitacinesaglycone, caffeic esters, and picrosides | Cervical and breast | Cytotoxic, anti-inflammatory and antioxidant effects |
| *Phyllanthus amarus* (Euphorbiaceae) | Whole plant | Methanol | Flavonoids, ellagitannins, polyphenols, triterpenes, sterols, phyllanthin, saponins, and alkaloids | Lung, breast, pancreas, neuron, skin, ovarian, and prostate | Apoptotic, antiproliferative and cytotoxic effects, cell cycle arrest |
| *Phyllanthus emblica* (Phyllantha cae) | Fruit and leaf | Aqueous and ethanolic | Ellagic acid, chebulagic acid, and gallic acid | Cervical and colon | Reduction of cancer cell viability, cytotoxic and antiproliferative effects |
| *Psidium guajava* (Myrtaceae) | Leaf | Hexane | Cryptonine, tannins, apigenin, dihydrobenzophenanthridine, lycopene, and saponins | Breast, blood cervical, and prostate | Antiproliferative and apoptotic effects |
| *Punica granatum* (Lythraceae) | Fruit | Aqueous | Ellagic acid, ellagitannins, punicalagin, and tannins | Colorectal and colon | Cell cycle arrest, antiproliferative and apoptotic effects |
| *Rauvolfia vomitoria* (Apocynaceae) | Root | Ethanol | β-carboline, terpenes, tannins, alkaloids, steroids, saponins, and flavonoids | Pancreas, ovarian, and prostate | Cytotoxic, apoptotic and antiproliferative effects, cell cycle arrest |
| *Scoparia dulcis* (Scrophulariaceae) | Leaf | Petroleum ether, ethanol and methanol | Dulcidiol, iso-dulcinol, scopadiol, 4-epi-scopadulcic acid B, and scopanolal | Stomach and prostate | Cytotoxic effect |
| *Tabebuia avellanedae* (Bignoniaceae) | Bark | Not specified | β-lapachone | Liver | Antiproliferative and apoptotic effects |
| *Thymus vulgaris* (Lamiaceae) | Leaf bulb | Butanol ethanol | Tannins, triterpenes, sterols, flavonoids, and glycosides | Cervical | Cytotoxic effects |
| *Tinospora cordifolia* (Menispermaceae) | Stem | Dichloromethane and methanol | Epoxycleodanediterpene, arabinogalactan, berberine, and phenolics | Breast and cervical | Cytotoxic and antiproliferative effects |
| *Tithonia diversifolia* (Compositae) | Leaf | Ethanol and methanol | Tagitinin C, 1β - methoxydiversifolin 3-O-methyl ether, and 1β and 2α-epoxytagitinin C | Colon and blood | Antiproliferative effect, cell cycle arrest, inhibition of cancer cell viability, stimulation of cancer cell autophagy |
| *Uvaria chamae* (Annonaceae) | Stem-bark and root | Ethanol | Dichamanetin, diuvaretin, uvaretin, chamanetin, pinocembrin, isouvaretin, | Blood | Antiproliferative effect |

| Anticancer plant (family) | Part used for study | Extractant used for study | Bioactive compound | Cancer cell type | Pharmacological actions |
|---|---|---|---|---|---|
| | | | pinostrobin, and isochamanetin | | |
| *Vernonia amygdalina* (Compositae) | Leaf | Chloroform | Steroid glycosides and edotide | Breast and cervical | Antiproliferative effect |
| *Zanthoxylum nitidum* (Rutaceae) | Root | Not specified | Nitidine and benzophenanthridine | Lung, cervical, and liver | Cytotoxic and antiproliferative effect |
| *Zingiber officinale* (Zingiberaceae) | Whole plant | Ethyl acetate | 10-gingerol, 10-shogaol, 6-gingerol, and 6-shogaol | Prostate, liver, breast, and esophageal | Antiproliferative and antimetastatic effects |

### 3.2 In vitro and In vivo Studies

The ability of in vitro tests to rapidly and cost effectively screen a large number of compounds makes them highly valuable in drug development. These tests provide critical insights into the potential therapeutic effects of new drugs, serving as a foundation for further research and development (Pritee *et al.*, 2024).

On the other hand, in vivo studies involve assessing potential anticancer agents within living organisms, primarily using animal models. These studies evaluate the overall biological and pharmacological impacts of compounds, including toxicity, metabolism, and therapeutic efficacy. In vivo research plays a crucial role in confirming the anticancer properties observed in vitro and in determining the applicability of a molecule as a viable therapeutic agent (Pritee *et al.*, 2024).

#### 3.2.1 Examples of In vitro and In vivo Studies Conducted on Some Nigerian Plants

##### 3.2.1.1 *Securidacalongepedunculata*

**Figure 6 Securidaca longepedunculata**

Securidaca longepedunculata, belonging to the Polygalaceae family, is commonly referred to as ‘Uwar Magunguna’ in Hausaland, meaning "the mother of all drugs," a testament to its extensive medicinal applications (Taye, 2013).

A study by Lawal (2012), investigated the in vitro and in vivo cytotoxic properties and potential pro-apoptotic effects of the aqueous extract of *Securidaca longepedunculata* (SLE) on Ehrlich ascites carcinoma cells. The in vitro cytotoxicity was assessed using the Trypan blue assay, where Ehrlich ascites carcinoma cells were incubated with SLE at concentrations of 0.1, 1, 10, 100, and 1000 µg/ml. The in vivo study involved administering intraperitoneal doses of 10, 25, 50, and 75 mg/kg body weight of SLE to tumor-bearing mice. DNA extracted from Ehrlich ascites carcinoma cells of both treated and untreated animals was analyzed using a DNA fragmentation assay on agarose gel.

Results indicated that *Securidaca longepedunculata* aqueous extract exhibited cytotoxic effects on Ehrlich ascites carcinoma cells both in vitro and in vivo, with an IC50 value of 67 µg/ml. The extract reduced angiogenesis, as evidenced by a decrease in the weight of treated animals and a reduction in ascitic fluid volume in treated mice. DNA fragmentation analysis of carcinoma cells from treated subjects, along with apoptotic blebbing observed under Giemsa staining, suggested a potential pro-apoptotic effect of SLE. The characteristic

DNA laddering pattern was similar to that observed with fluorouracil, a standard anticancer drug, reinforcing its apoptotic influence (Taye, 2013).

#### 3.2.1.2 *Elaeisguineensis* (Red oil palm)

**Figure 7 Elaeis guineensis (Red oil palm)**

*Elaeis guineensis*, a member of the Arecaceae family, is known as 'Ope' in Yoruba, 'Nkwe' in Igbo, and 'Kwakwar' in Hausa. Various parts of the plant, including the root, palm oil, bark, and kernels, are traditionally used to treat malaria, mental disorders, diarrhea, asthma, and measles.

A study by Vijayarathna and Sasidharan (2012) explored the cytotoxic effects of *Elaeis guineensis* on MCF-7 and Vero cells. The in vitro cytotoxicity was assessed using the MTT assay, while morphological changes in the cells were observed under a light microscope. The results demonstrated that the methanol extract of *Elaeis guineensis* exhibited significant cytotoxic effects on MCF-7 breast cancer cells. Additionally, phase contrast microscopy revealed dose-dependent morphological alterations in the treated cell lines. These findings suggest the potential application of *Elaeis guineensis* methanol extract in formulations for cancer treatment.
Further evidence of the anticancer properties of vitamin E (tocopherols and tocotrienols) present in palm oil has been documented in a comparative study examining their effects on breast cancer. The study revealed that tocotrienol fractions successfully inhibited the growth of human breast cancer cells, whereas alpha-tocopherols did not exhibit similar inhibitory properties (Taye, 2013).

#### 3.2.1.3 *PsorospermumFebrifugum*

**Figure 8*PsorospermumFebrifugum***

Known as 'Legun-oko' in southwestern Nigeria, *Psorospermum febrifugum* has been studied for its potent antileukemic and anticancer properties. Kupchan et al., (1980), reported the isolation of psorospermin, a novel antileukemic xanthone, from an ethanolic extract of *Psorospermum febrifugum*. The fractionation process, guided by antileukemic activity, demonstrated its effectiveness in vivo against P388 lymphocytic leukemia in mice and in vitro against KB cell cultures. Psorospermin exhibited significant antitumor activity in the P388 in vivo model and displayed cytotoxicity against KB cells in vitro.

Additionally, Marston et al., (1986), identified five anthranoid pigments from the root bark of *Psorospermum febrifugum*, including a newly discovered anthraquinone and a tetrahydroanthracene. The cytotoxic properties of these pigments were tested against the human colon carcinoma cell line Co-115. Among them, the tetrahydroanthracenes vismione D and acetylvismione D demonstrated consistent cytotoxic effects in

this in vitro system, further supporting the potential anticancer properties of *Psorospermum febrifugum* (Taye, 2013).

#### 3.2.1.4 *VernoniaAmygdalina*

**Figure 9 Vernonia Amygdalina**

Yedjou et al., (2008), evaluated the anti-cancer potential of *Vernonia amygdalina* (VA) leaf extracts against human breast cancer cells in vitro. The study employed the MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay and the alkaline single-cell gel electrophoresis (Comet) assay to assess its cytotoxic and genotoxic effects.

In this experiment, human breast adenocarcinoma (MCF-7) cells were exposed to varying concentrations of VA leaf extracts for 48 hours. Results from the MTT assay demonstrated a significant ($P< 0.05$) dose-dependent reduction in MCF-7 cell viability following 48 hours of treatment. The comet assay data further revealed a mild, dose-dependent increase in DNA damage in MCF-7 cells upon VA exposure. This was evidenced by a slight increase in comet tail length, tail arm, tail moment, and percentage of DNA cleavage at all tested concentrations, indicating minimal genotoxic effects.

Overall, the findings suggest that VA extracts exert moderate cytotoxicity and induce minimal DNA damage in MCF-7 cells. This highlights the potential of *Vernonia amygdalina* as a DNA-damaging anti-cancer agent, with its mechanism of action partially linked to its ability to cause moderate toxicity in tumor cells (Taye, 2013).

#### 3.2.1.5 *WithaniaSomnifera*

**Figure 10*WithaniaSomnifera***

The anticancer properties of Withaferin A, a compound derived from *Withania somnifera*, were assessed in mouse models of breast cancer. In vivo studies serve as a critical step in validating potential anticancer drugs, following essential in vitro experiments. These studies are vital for evaluating the safety and therapeutic efficacy of drug candidates within a living organism, providing comprehensive insights into their pharmacokinetics and pharmacodynamics (Atteeq, 2022).

Computational studies have identified the anticancer potential of Withaferin A (WFA), a bioactive compound from *Withania somnifera* (commonly known as Ashwagandha). Prior research involving molecular docking and simulations suggested that WFA could effectively target key pathways involved in breast cancer progression. Investigations focused on its antitumor effects against molecular targets that maintain the stemness of breast cancer stem cells (Lee *et al.,* 2016; Hassannia *et al.,* 2020).

In vivo studies demonstrated a significant suppression of tumor growth in mouse models treated with Withaferin A. Tumor size was notably reduced, and tumor progression was delayed compared to the control group. Additionally, WFA exhibited a favorable safety profile at therapeutic doses, with minimal reported adverse effects (Xing *et al.,* 2023).

**Mechanism of Action of Bioactive Compounds from Nigeria Plants**

**4. 1 Anticancer Effect of Some Active Compounds from Nigeria Plants**

The primary categories of bioactive compounds found in medicinal plants with anticancer properties include polyphenols, flavonoids, alkaloids, saponins, triterpenes, tannins, and quinones. These compounds exhibit various anticancer effects, including antiproliferative, cytotoxic, and cytostatic activities. They also demonstrate anti-metastatic and apoptotic properties, possess antioxidative potential, induce cell cycle arrest, inhibit angiogenesis, and decrease cancer cell viability (Franklyn *et al.,* 2021).

**4.1.1 Polyphenols**

Polyphenols have been identified as possessing both antioxidant and cytotoxic properties against cancer cells (Franklyn *et al.,* 2021). Their anticancer effects are largely attributed to their ability to induce apoptosis. One key mechanism involves polyphenols facilitating the aggregation of copper ions on chromatin, which, in turn, triggers DNA fragmentation, as observed with compounds like resveratrol (Azmi *et al.,* 2006).

Additionally, plant-derived polyphenols interact with and disrupt cancer cell proteins, thereby inhibiting their proliferation. These compounds can bind directly to carcinogens and mitigate their cancer-promoting effects through mechanisms such as acetylation, phosphorylation, and methylation. For example, the polyphenol curcumin has been found to suppress tumor necrosis factor (TNF) activity in cell lines (Gupta *et al.,* 2014). Curcumin also promotes apoptosis, induces cell cycle arrest, inhibits protein tyrosine kinase activity, and suppresses the expression of c-myc mRNA and bcl-2 mRNA (Lee *et al.,* 2001).

**4.1.2 Quinones**

Quinones, such as aloe-emodin, have been shown to inhibit cancer cell proliferation by disrupting specific cell cycle phases, including G1, G2/M, and S-phases (Franklyn *et al.,* 2021). These compounds induce DNA damage by generating reactive oxygen species (ROS) (Lee *et al.,* 2006). Additionally, quinones promote apoptosis in cancer cells by activating pathways such as c-Jun N-terminal kinase, caspases, the Fas signaling pathway, and the p53 pathway (Franklyn *et al.,* 2021).

The anticancer potential of quinones is also linked to their ability to downregulate the expression of urokinase, MMP-2, and MMP-9 proteins while preventing nuclear translocation (Franklyn *et al.,* 2021). Furthermore, the quinone β-lapachone has been reported to induce DNA fragmentation and apoptotic body formation, suppress Bcl-2 and Bcl-XL protein expression, and enhance Bax activity. This process promotes cancer cell apoptosis by activating poly (ADP-ribose) polymerase protein as well as caspase-3 and caspase-9 (Hyun *et al.,* 2006).

**4.1.3 Flavonoids**

Flavonoids have been found to be toxic to cancer cells and possess strong free radical scavenging properties (Cao *et al.,* 2013). Specific flavonoids, such as alpinumisoflavone and 4-methoxy lico flavanone, induce apoptosis in human leukemia cells through both intrinsic and extrinsic signaling pathways. This process results in mitochondrial disruption, ultimately leading to cell death (Kumar *et al.,* 2013). Additionally, flavonoids suppress the expression of NF-κB, a protein complex essential for cancer cell survival, proliferation, and angiogenesis (Greenwell *et al.,* 2015).

**4.1.4 Alkaloids**

These bioactive compounds interfered with tumor formation and hindered the progression of tumor cell growth (Franklyn *et al.,* 2021). Alkaloids suppressed cancer cell proliferation by triggering apoptosis and halting the cancer cell cycle at either the G1 or G2/M phase. Additionally, alkaloids induced autophagy in cancer cells and caused damage to the endoplasmic reticulum. Their anticancer effects were primarily achieved through the inhibition of tumor invasion and metastasis (Franklyn *et al.,* 2021).

**4.1.5 Saponins**

Saponins demonstrated immune-modulating effects through interactions with cytokines (Sun *et al.,* 2009). Their anticancer properties were primarily linked to cytotoxic and cytostatic activities (Franklyn *et al.,* 2021). Triterpene saponins inhibited cancer cell growth and triggered apoptosis (Park *et al.,* 2010), while steroidal saponins facilitated cell cycle arrest, induced apoptosis, and functioned as antitumor agents (Man *et al.,* 2010).

**4.1.6 Tannins**

The anticancer effects of tannins, such as ellagitannin, have been linked to the upregulation of cyclin E and the downregulation of cyclins A and B1. They also cause cell cycle arrest at the S-phase and trigger apoptosis through the intrinsic pathway by downregulating bcl-XL. This process is accompanied by the release of cytochrome C from mitochondria into the cytosol and the activation of caspase-3 and caspase-9 (Larrosa *et al.,* 2006).

**4.1.7 Triterpenes**

Triterpenes, such as 3-O-acetyl-11-keto-β-boswellic acid, triggered apoptosis in tumor cells by activating the death receptor DR-5 signaling pathway (Franklyn *et al.,* 2021). Additionally, triterpenes promoted tumor cell apoptosis by regulating the secretion of Bax, a proapoptotic protein, and Bcl-2, an antiapoptotic protein, through their upregulation and downregulation, respectively (Franklyn *et al.,* 2021). They also induced apoptosis by increasing intracellular Ca2+ levels and promoting the release of P53 (Lee *et al.,* 2002).

**4.2 Importance and Potency of Natural Products over Conventional Cancer Therapy**

Conventional cancer therapy refers to treatments that are widely accepted and commonly utilized by healthcare professionals. It differs from alternative or complementary therapies, which are less frequently adopted. Standard cancer treatments include chemotherapy, radiation therapy, and surgical procedures.

Recent research has explored innovative cancer therapies derived from natural compounds and their structural analogs, which exhibit remarkable chemical diversity. Additionally, the unique molecular attributes of natural products contribute to their enhanced safety and therapeutic efficacy (Shaik *et al.,* 2022). However, conventional cancer treatments have several limitations:

1. Chemotherapy agents such as doxorubicin and cisplatin, along with radiation therapy, are frequently used in cancer management but are associated with severe side effects and toxicity.
2. Radiation therapy, in particular, can impair cognitive function and lead to neurological decline (Ongnok *et al.,* 2020).
3. Chemotherapy may contribute to the formation of secondary tumors and cause damage to healthy tissues, posing challenges for long-term cancer survivors.
4. Common complications of chemotherapy include bone marrow suppression, which weakens the immune system, as well as organ toxicities affecting the liver, kidneys, and heart (Nan *et al.,* 2022). For instance, cisplatin has been linked to adverse effects such as nausea, vomiting, acute kidney injury, neurotoxicity, and hearing impairment.
5. Certain chemotherapy drugs may be ineffective against dormant or less-active cancer cells, thereby negatively impacting patient survival and prognosis (Desilets *et al.,* 2020).

In recent years, natural compounds have gained prominence in cancer prevention and treatment. These bioactive substances, including phenols (e.g., curcumin, quercetin, resveratrol, and capsaicin), flavonoids, terpenoids (such as andrographolide, artesunate, and atractylodes), and alkaloids (e.g., matrine, berberine, and piperine), play essential roles in cancer therapy. They exhibit anti-inflammatory properties, induce apoptosis, inhibit tumor invasion and metastasis, and enhance immune responses. Natural compounds have shown efficacy against various cancers, including lung, breast, and ovarian cancers (Cao *et al.,* 2017).

Natural products, derived from bacteria, plants, and marine organisms, have historically played a crucial role in cancer treatment advancements. Due to their vast chemical diversity, unique structural features, and biological activity, they offer potential therapeutic benefits with lower toxicity. Many of these compounds have evolved as protective mechanisms against diseases, including cancer, making them promising candidates for anticancer drug development (Pritee *et al.,* 2024).

**Table 3**.Natural Compounds Used As Anti-Cancer Treatments In Treating Various Cancers (Pritee *et al.,* 2024; Godwin *et al.,* 2023).

| **Natural Compound** | **Source** | **Mechanism of Action** | **Target Genes** | **Cancer** |
|---|---|---|---|---|
| Curcumin | Turmeric (*Curcuma longa*) | Inhibits cell proliferation, induces apoptosis. | TNF, IL-1, VEGF, EGF, FGF, EGFR, HER-2, AR, NF-κB, AP-1, STAT | Breast, lung, skin, gastrointestinal, colorectal, prostate, head and neck. |
| Resveratrol | Grapes, berries, peanuts | Antioxidant, affects cell cycle regulation. | APE1/Ref-1, NF-κB, LSD1, MCP-1 | Breast, cervical, uterine, blood, kidney, liver, eye, bladder, thyroid, esophageal, prostate, brain, lung, skin, gastric, colon, head and neck, bone, ovarian, and cervical. |
| Paclitaxel (Taxol) | Pacific yew tree (*Taxus brevifolia*) | Disrupts microtubule function. | AP-1, JNK1, p38, ERK1, IL-1α, IL-1β, TNF-α | Breast, ovarian, lung cancers. |
| Epigallocatech | *Green tea* | Antioxidant, | retinoic acid receptor β | Breast, lung, bladder, head and neck, prostate, |

| | | | | |
|---|---|---|---|---|
| in gallate (EGCG) | | induces apoptosis, inhibits proliferation. | (RARβ), CDH1 (e-cadherine gene), DAPK1, DNMT1, DNMT3B, HDAC1 | colorectal. |
| Sulforaphane | Cruciferous vegetables | Induces detoxification enzymes, pro-apoptotic. | TIMP1, AURKA, CEP55, CRYAB, PLCE1, and MMP28, CRC | Colorectal. |
| Genistein | Soybeans | Inhibits angiogenesis, modulates hormone activity. | p21-WAF1, p16-INK4a, p21-WAF1 and p16-INK4a | Breast, colorectal, lung, pancreatic. |
| Quercetin | Apples, onions, tea, red wine | Antioxidant, anti-inflammatory, inhibits proliferation. | bcl-2-associated X protein (BAX), Cytochrome c release, Cysteine-aspartic proteases (caspase)-3, Caspase-9, Transforming growth factor β (TGF-β), Anti-apoptotic Bcl-2 | Breast, prostate, colorectal, lung. |
| Capsaicin | Chili peppers | Induces apoptosis, inhibits cell growth. | c-myc, c-Ha-ras, p53 | Breast, lung, bladder, colon and pancreatic, colorectal. |
| Silymarin (Silibinin) | *Milk thistle* | Antioxidant, anti-inflammatory, cell regeneration. | NF-κB, TGF-β, TNF-α, interferon-gamma, IL-2, IL-4, and COX-2 | Breast, lung, colorectal, skin, pancreatic, prostate, gastrointestinal. |
| Berberine | *Berberis plants* | Inhibits cell progression, promotes apoptosis. | IL-1, TNF, IL-6, cyclooxygenase 2 and prostaglandin E2 | Colon. |
| Ellagic acid | *Pomegranates, b erries, nuts* | Antioxidant, anti-proliferative. | p53-dependent genes, NF-kB p50, p65, and the PPAR family | Colorectal, prostate, lung, bladder, ovarian, breast. |
| Lycopene | *Tomatoes, water melon, pink grapefruit* | Antioxidant, anti-proliferative. | *IGFBP-3, c-fos,* and *uPAR* | Breast, colorectal, lung, pancreatic, ovarian, cervical. |
| Indole-3-carbinol | Cruciferous vegetables | Modulates estrogen metabolism, apoptosis. | CYP1A1, CYP1B1 and AhR | Lung, head and neck, bladder, breast. |
| Beta-glucans | Oats, barley, mushrooms | Stimulates immune response. | TLR-2/6, CR3 | Breast, colorectal, prostate, ovarian. |
| Allicin | Garlic | Antioxidant, anti-proliferative, pro-apoptotic. | E2F1, E2F2, and E2F3 | Breast, bladder, lung, colorectal, prostate. |
| Catechins | Tea, cocoa, fruits | Antioxidant, anti-inflammatory, anti-proliferative. | JNK, MAP kinase, JAKs, BCL-2, and Nrf2 | Colorectal, pancreatic, lung, breast. |
| Ursolic acid | Apples, basil, cranberries | Inhibits metastasis, induces apoptosis. | MMP-9, CT45A2, Bcl-2, Bcl-xL, and BAX | Breast. |
| Limonene | Citrus peels | Induces detoxification enzymes, anti-proliferative. | Bcl-2-associated X protein (BAX), Cytochrome c release, Cysteine-aspartic proteases (caspase)-3, Caspase-9, Transforming growth factor β (TGF-β), Anti-apoptotic Bcl-2 | These are not directly associated with causing specific cancers, but rather are involved in cellular pathways related to apoptosis (programmed cell death) and regulation of cell survival. |
| Vinblastine | Periwinkle plant (*Catharanthus roseus*) | Inhibits microtubule assembly. | *CCNB1 and AURKA* | Breast, colorectal, lung, ovarian, prostate. |
| Vincristine | Periwinkle plant (*Catharanthus roseus*) | Binds to tubulin, inhibits microtubule formation. | CYP3A4, CYP3A5 | Liver. |
| Topotecan | Happy tree (*Camptotheca acuminata*) | Inhibits DNA topoisomerase I. | ABCB1, ABCG2, ALDH1A1, IFIH1, SAMD4 and EPHA3 | Breast, ovarian, colon. |
| Irinotecan | Happy tree (*Camptotheca* | Inhibits DNA topoisomerase I. | UGT1A1 | It is not directly responsible for causing cance; variations in this gene can influence |

| | | | | |
|---|---|---|---|---|
| | *acuminata*) | | | how the body processes certain chemotherapy drugs used in cancer treatment. |
| Etoposide | Mayapple plant (*Podophyllum peltatum*) | Inhibits DNA topoisomerase II. | SEMA5A, SLC7A6 and PRMT7 | For these genes, ongoing research might reveal their specific associations with certain cancers or their roles in cancer biology. The understanding of their involvement in cancer development and progression might evolve as more studies uncover their molecular mechanisms and connections to different cancer types. |
| Beta-carotene | *Carrots, sweet potatoes, spinach* | Antioxidant, modulates immune response. | CD38, NCF1B, and ITGAL | These genes are involved in various biological processes, including immune response and cell signalling. Their associations with specific cancers are not as prominent as some other genes, but they have been implicated in certain contexts. |

**5.1 Challenges Associated with Developing Natural Product-Based Anticancer Drugs**

Natural products offer numerous benefits in drug discovery, including structural diversity, potential multi-target effects, and the ability to overcome drug resistance. However, challenges such as difficulties in sourcing and standardization, as well as complications related to patent protection, can hinder their development as anticancer drugs (Pritee *et al.,* 2024).

The discovery of anticancer drugs from natural sources faces several obstacles that slow down the development of effective treatments. The complex molecular structures of these compounds make their isolation, identification, and synthesis both challenging and resource-intensive (Morrison and Hergenrother, 2014). Additionally, their efficacy as anticancer agents is often limited by poor absorption and distribution within the body, raising concerns about their bioavailability (Wang, 2012). Another major concern is toxicity, as some natural substances can pose health risks, requiring comprehensive toxicological evaluations to ensure patient safety. Furthermore, prolonged exposure to natural-product-based treatments may lead to cancer cell resistance, necessitating deeper insights into resistance mechanisms and the development of novel strategies to counteract them (Pritee *et al.,* 2024).

Sourcing these bioactive compounds also presents sustainability challenges, as overharvesting and unsustainable agricultural practices can damage ecosystems and deplete natural resources (Hashmi *et al.,* 2016). A notable example is Combretastatin A4, derived from the African bush willow, which faces clinical development challenges due to its low water solubility and instability.

Moreover, computational approaches for natural-product-based drug discovery encounter difficulties due to the structural complexity and diversity of these molecules (Adelusi *et al.,* 2022). Limited experimental data, incomplete databases, and high structural flexibility hinder precise modeling efforts. Variations in chemical composition and bioactivity, as well as poorly understood mechanisms of action, make it difficult to develop standardized computational models (Hashmi *et al.,* 2016). Additional challenges, such as overfitting, high computational costs, and the need for extensive experimental validation by regulatory agencies, further complicate the process.

Intellectual property and patent issues pose another significant barrier to advancing natural compounds for cancer treatment. Legal complexities surrounding the patenting of biological materials make securing patents on molecules derived from living organisms challenging. Additionally, bio-piracy, where indigenous communities are not fairly compensated for their traditional knowledge, raises ethical concerns. Legal and financial hurdles, combined with the need to balance corporate and researcher rights with the contributions of traditional communities, further complicate drug development (Kartal, 2007; Baxi *et al.,* 2019).

The recruitment of participants and the design of clinical trials add another layer of complexity in developing anticancer drugs from natural products. The diverse nature of these compounds makes designing studies that effectively assess their safety and efficacy more challenging. Enrolling a sufficient number of participants who meet the specific criteria for these trials can be particularly difficult, especially for rare or severe cancers. To overcome these challenges, innovative clinical trial designs, such as adaptive trials, along with improved patient recruitment and retention strategies, are necessary to ensure that research yields reliable and meaningful results (Spreafic *et al.,* 2021; Chen *et al.,* 2023).

**5.2 Strategies to Overcome these Challenges**

1. Indigenous communities and traditional healers, who have relied on natural medicines for centuries, can play a crucial role in the development of innovative medicinal compounds. This collaborative approach not only provides researchers with access to a vast reservoir of untapped therapeutic plants and bioactive compounds but also fosters a more ethical and inclusive drug discovery process (Najmi *et al.,* 2022; Katiyar *et al.,* 2012).

2. The advancement of analytical techniques, such as mass spectrometry and nuclear magnetic resonance, has significantly improved the characterization of complex natural-product structures. These methods have deepened the understanding of their chemical properties and potential medicinal applications (Huang *et al.,* 2021).
3. Nanotechnology has emerged as a key tool in enhancing the bioavailability of natural compounds. The use of nanoparticle-based drug delivery systems can improve the solubility and stability of these substances, leading to better absorption and distribution within the body (Atanasov *et al.,* 2021).
4. Exploring combination therapies that integrate natural products with conventional anticancer treatments may yield synergistic effects. This strategy can help counteract drug resistance and improve therapeutic outcomes by targeting multiple pathways simultaneously (Atanasov *et al.,* 2021).
5. The integration of artificial intelligence (AI) and machine learning is set to revolutionize the discovery and prediction of natural-product-based anticancer drugs. AI-driven systems can analyze vast datasets to identify molecules with strong therapeutic potential, thereby accelerating the drug development process (Pritee *et al.,* 2024).

### 5.3 Emerging Research Directions in the Development of Anti-cancer Drugs

#### 5.3.1 Clinical Trials

The development of anticancer drugs, which involves transitioning natural products from laboratory research to clinical application, is a complex yet essential process. This progression includes preclinical studies followed by clinical trials, each stage playing a crucial role in transforming natural substances into effective cancer treatments (Naeem *et al.,* 2022).

Clinical trials represent the final and arguably most critical phase in anticancer drug development, where previously untested compounds are advanced from laboratory experiments to real-world therapeutic applications. The systematic progression of this process, including preclinical evaluations and subsequent clinical testing, is essential for ensuring that natural compounds are effectively and safely converted into viable cancer treatments.

Preclinical research, which consists of both in vitro and in vivo studies, lays the groundwork by providing essential insights into the safety, efficacy, and pharmacological properties of a potential drug. However, it is only during the clinical trial phase that these compounds are tested in humans to assess their true therapeutic potential and safety profile (Minami *et al.,* 2021; Olivier *et al.,* 2021).

#### 5.3.2 Bioassay Guided Fractionation (BGF)

Bioassay-guided fractionation (BGF) is a method used to isolate biologically active compounds from natural product extracts or synthetic mixtures. This process involves successive chromatographic fractionation and re-fractionation until a pure active constituent is obtained. At each stage of chromatographic separation, the fractions undergo specific bioassays to determine their biological activity, and only the most active fractions are selected for further purification (Muhammed *et al.,* 2018).

**Table 4.**Examples of bioassay-guided fractionation technique based isolated compounds (Neelesh *et al.,* 2017).

| **Plant Name** | **Isolated Compounds** | **Therapeutic Efficacy** |
|---|---|---|
| Hypericum species (Hypericaceae) | Benzopyrans and phloroglucinol | Antimicrobial |
| Kaempferia galanga L. (Zingiberaceae) | Ethyl cinnamate and Ethyl p-methoxycinnamic | Vasorelaxant |
| Melissa officinalis L. (Lamiaceae) | Rosmarinic acid, ursolic acid and oleanolic acid | Potent inhibitor of GABA-T |
| Centaurea arenaria M.B. ex Willd. (Compositae) | Eupatilin, eupatorin, 3'-methyleupatorin, apigenin, isokaempferid, arctigenin, arctiin, matairesinol, moschamine, cismoschamine, β-amyrin, and β-sitosterin-β-Dglycopyranoside | Antiproliferative |
| Anthemis ruthenica M. (Asteraceae) | Eudesmanolide sesquiterpene, sivasinolide 6-O-angelate and centaureidin | Cytotoxic |
| Sorbus decora Sarg. (Rosaceae) | Pentacyclic triterpenes 23,28-dihydroxyursan12-ene-3β-caffeate, 23,28-dihydroxylupan20(29)-ene-3βcaffeate, and 3β,23,28- trihydroxy-12-ursene | Antidiabetic |
| Glycyrrhiza uralensis Fisch. (Fabaceae) | Glycyrrhisoflavone | α-glucosidase inhibitory |
| Vaccinium arctostaphylos L. (Ericaceae) | Malvidin-3-O-betaglucoside | α-amylase inhibitor |
| Tagetes patula L. ( Asteraceae). | Methyl protocatechuate, patuletin and patulitrin | Antioxidant with analgesic properties |
| Tithonia diversifolia Hemsl. (Asteraceae) | Tagitinin C | Anti-ulcer |
| Cassia bakeriana Craib. (Fabaceae) | Cassic acid or rhein | Antimicrobial and cytotoxic activities |

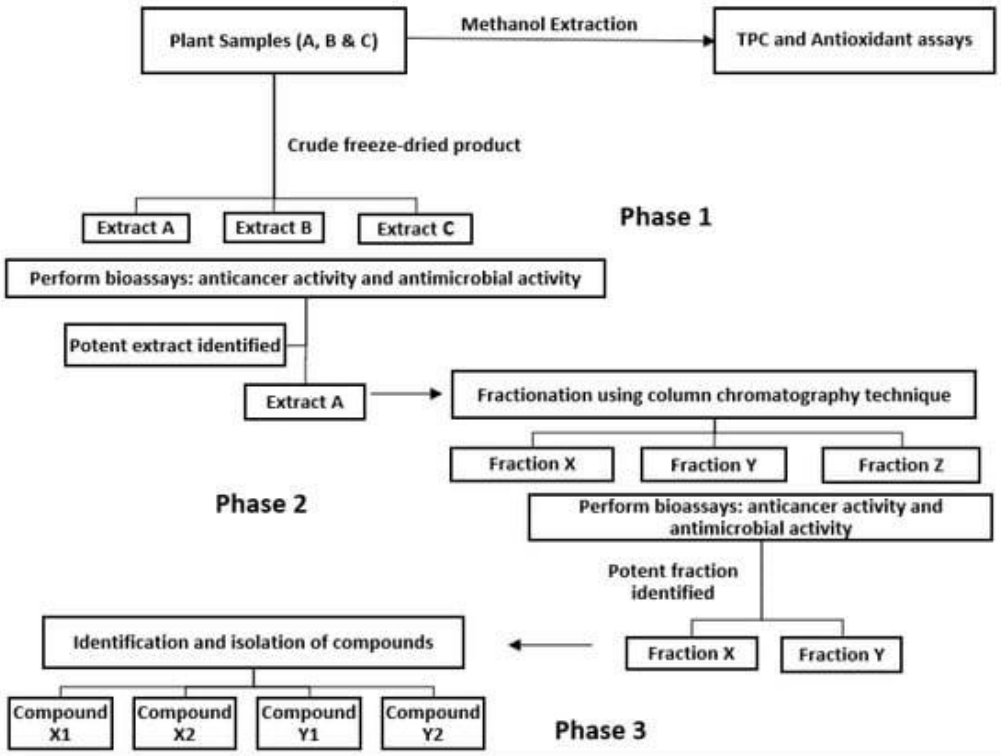


**Figure 11 Schematic diagram of Bioassay-Guided Fractionation of Active compounds (Janice et al., 2022).**

### 5.3.3. Ethnopharmacological Studies

Ethnopharmacology is an interdisciplinary field that explores the anthropological significance and pharmacological foundations of the medicinal use of plants, animals, fungi, microorganisms, and minerals across human cultures (Marco & Laura, 2013).

By documenting the therapeutic properties of plants, ethnopharmacology has laid the groundwork for the medical application of natural compounds. Natural products, whether in their raw state or following the extraction of active ingredients, have historically served as essential resources for drug development. The transition from traditional ethnopharmacology to modern drug discovery has been facilitated by advancements in isolation and characterization techniques, the rise of computational capabilities, and the progress of specialized chemoinformatics methods (Stergios *et al.*, 2022).

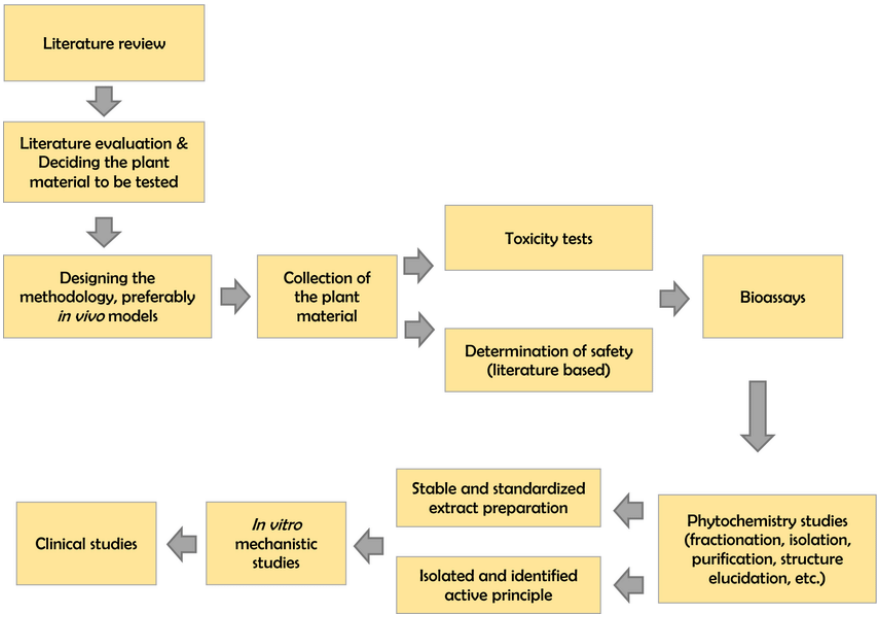


**Figure 12 Schematic Diagram of Ethnopharmacological Studies (www.researchgate.net)**

**5.3.4 Collaboration with Pharmaceutical Companies**

Partnerships between pharmaceutical companies and contract research organizations (CROs) remain a compelling alternative to conducting drug discovery solely within a single company (Victoria, 2018).

The pharmaceutical sector faces increasing pressure not only to sustain a robust drug pipeline but also to ensure value for both investors and healthcare payers. Over the past decade, many companies have sought to lower research and development (R&D) expenses by outsourcing research to CROs. Shifting research that was traditionally performed in-house to external partners enhances capital efficiency by converting fixed costs into variable expenses. It also allows for greater financial flexibility, enabling companies to adjust spending based on portfolio priorities and research outcomes (Contract Pharma, 2016).

Different organizations adopt varied outsourcing strategies (Montana, 2015). Some opt for a diverse network of specialized suppliers, selecting the most proficient experts for different phases of drug discovery. Others prefer working with integrated drug discovery service providers, where a multidisciplinary team within a single CRO leverages its expertise to manage the entire drug discovery process (Levy, 2013).

## Conclusion

Innovative therapeutic strategies are crucial for combating infectious diseases, and bioactive compounds from indigenous medicinal plants offer promising solutions, either independently or in combination with existing antimicrobial agents. Nigeria is rich in medicinal plant species with notable anticancer potential, as evidenced by their effectiveness against various cancers, including those of the prostate, cervix, lungs, skin, colon, blood, and more. This highlights their viability as sources of anticancer drug candidates. The study identified leaves, roots, and stem-bark extracts as key reservoirs of bioactive compounds with anticancer properties, emphasizing the need for further research on these plant parts. However, despite advancements in developing anticancer drugs from natural sources, challenges such as solubility, formulation difficulties, and drug resistance remain significant obstacles to effective treatment development.

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