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Traditional African Medicinal Plants as Potential Sources of Anticancer Agents: Bioactive Compounds, Mechanisms, and Future Directions

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ABSTRACT:

Cancer remains a leading cause of mortality worldwide, necessitating the continuous search for novel and effective therapeutic agents. Traditional African medicinal plants, long utilized in indigenous healthcare systems, represent a rich reservoir of bioactive compounds with promising anticancer properties. This review comprehensively explores the anticancer potential of selected African medicinal plants, highlighting their phytochemical constituents, mechanisms of action, and therapeutic relevance. Specific emphasis is placed on compounds such as alkaloids, flavonoids, terpenoids, and phenolics that exhibit cytotoxicity, apoptosis induction, cell cycle arrest, and inhibition of metastasis. The article also examines current limitations in research, including standardization, clinical validation, and bioprospecting challenges. By integrating traditional knowledge with modern pharmacological approaches, these medicinal plants may serve as viable leads for anticancer drug development. Further scientific investigation and clinical validation are imperative to translate these ethnobotanical insights into effective anticancer therapies.

Keywords: *Traditional medicine, African medicinal plants, anticancer agents, phytochemicals, apoptosis, cancer therapy, drug discovery, ethnopharmacology.*

Introduction

Cancer remains one of the most significant global health challenges of the 21st century, accounting for nearly 10 million deaths worldwide in 2020 and disproportionately affecting low- and middle-income countries, including those in Africa [1,2]. In sub-Saharan Africa alone, there were over 800,000 new cases and more than 520,000 deaths in 2020, with breast, cervical, prostate, and liver cancers being the most common types [3]. The increasing burden of cancer in Africa is compounded by limited access to early diagnosis, effective treatment, and chemotherapy, which remains both expensive and often unavailable to the majority of the population [4, 5–7].

Historically, conventional cancer treatments such as surgery, radiotherapy, and chemotherapy have significantly improved patient survival, particularly in high-income countries [8, 9]. However, these therapies are frequently associated with severe side effects, development of multidrug resistance, and reduced quality of life. This has fueled the growing interest in complementary and integrative oncology approaches that incorporate natural products, particularly those derived from medicinal plants [10, 11]. Notably, the discovery of plant-based anticancer drugs such as vinblastine and vincristine from *Catharanthus roseus*, and paclitaxel from *Taxus brevifolia*, highlights the immense therapeutic potential of phytochemicals [10].

African traditional medicine, which has long served as a primary healthcare resource for over 80% of the population [12], represents a largely untapped reservoir of bioactive compounds with anticancer properties. Rich in chemical diversity alkaloids, flavonoids, terpenoids, phenolics, and steroids—these plants exhibit multiple mechanisms of action including the induction of apoptosis, inhibition of cell proliferation, modulation of oncogenic signaling pathways, and reduction of oxidative stress [13, 14, 15]. Importantly, many of these compounds demonstrate selective cytotoxicity, targeting malignant cells while sparing healthy ones [15].

Despite the widespread ethnomedical use of African plants for cancer treatment and their promising pharmacological profiles, systematic research on their active constituents, molecular mechanisms, and clinical potential remains limited. The variability in regional practices, types of plants used, and extraction protocols further underscores the need for structured investigation and documentation [16].

This review aims to bridge this knowledge gap by critically analyzing existing literature on African medicinal plants with reported anticancer activity. It focuses on their phytochemical constituents, underlying cellular and molecular mechanisms, and outlines future directions for preclinical and clinical studies. By consolidating current evidence, this work advocates for the scientific validation of traditional African medicinal knowledge, with the ultimate goal of contributing to the global fight against cancer through the development of safe, affordable, and accessible plant-derived therapeutics.

Overview of African Medicinal Plants with Anticancer Potential

Natural products have long played a central role in the development of pharmaceutical agents. Remarkably, over 25% of current therapeutics used to treat human diseases are plant-derived, while another 25% are modified forms of natural products [17]. Among these, polyphenols—abundant in fruits and vegetables are particularly valued for their chemopreventive and therapeutic roles in oncology. Many anticancer drugs are either direct plant extracts or semi-synthetic derivatives of plant-based compounds. For instance, etoposide (VP-16), a well-known anticancer agent, is derived semi-synthetically from podophyllotoxin a lignan sourced from *Podophyllum* species [18].

Approximately 60% of currently available anticancer medications are rooted in natural product chemistry, with plants contributing significantly. Notable examples include the vinca alkaloids, taxanes (such as taxol and docetaxel), camptothecin, and combretastatin [19]. The process of identifying these agents typically begins with in vitro screening for cytotoxic or cytostatic activity on cancer cell lines, often guided by traditional medicinal knowledge or ethnobotanical databases [18].

Among African nations, Nigeria stands out as a key contributor to research on medicinal plants with anticancer potential, underscoring the region's rich biodiversity and traditional medicinal heritage.

- ***Dicoma anomala***

A member of the Asteraceae family, *Dicoma anomala* commonly referred to as the fever or stomach bush is a perennial herb native to sub-Saharan Africa. It is widely distributed across various South African provinces and has been traditionally employed to treat ailments such as fevers, ulcers, coughs, and diabetes [20]. The roots and leaves of *D. anomala* contain bioactive compounds including flavonoids, phenolic acids, phytosterols, sesquiterpenes, and triterpenes, many of which exhibit anticancer effects without harming normal cells.

Notably, extracts from *D. anomala* have demonstrated antiproliferative effects against breast cancer cell lines (MCF-7), particularly when sesquiterpenes are conjugated to silver nanoparticles [21]. Similarly, aqueous extracts of *Dicoma capensis*, a related species, have shown anticancer activity against breast cancer lines such as MDA-MB-231 and MCF-12A [22]. These findings validate traditional uses and position *Dicoma* species as valuable candidates for anticancer drug discovery.

- ***Fagaropsis angolensis***

Belonging to the Rutaceae family, *Fagaropsis angolensis* is distributed across central and eastern Africa. It is a deciduous tree traditionally used in ethnomedicine and has recently garnered attention for its anticancer properties. Methanol extracts from its root and stem have shown cytotoxic effects against various cancer cell lines including Hep2 (throat), CT26 (colon), DU-145 (prostate), and HCC1395 (breast), with impressive IC_{50} values as low as 5.25 µg/Ml [23,24,25].

However, despite its potent anticancer effects, *F. angolensis* has also shown cytotoxicity against normal Vero cells, indicating a narrow therapeutic index. This underscores the need for further pharmacological studies to isolate, standardize, and optimize the dosage of its active compounds to reduce toxicity while maintaining efficacy.

- ***Withania somnifera***

Widely recognized as Ashwagandha, *Withania somnifera* is a small evergreen shrub found in parts of southern Africa, including Botswana and South Africa. It belongs to the Solanaceae family and is rich in bioactive compounds, particularly withanolide and withaferin A, which are credited for its anticancer properties.

These compounds have been shown to inhibit vimentin, a marker of metastasis, thereby impeding tumor progression, especially in breast cancer models [26]. In vivo studies in murine models revealed that *W. somnifera* modulates apoptosis, autophagy, and oxidative stress pathways [27]. Its ethanol root extracts have been reported to inhibit A549 lung cancer cells by downregulating PI3K, a key player in metastasis [28]. Moreover, earlier findings noted its protective effects against ROS-induced damage and lung adenoma in mice [29].

- ***Prunus Africana***

Prunus africana, a tree found in Southern and Central Africa, has been traditionally used to treat prostate cancer [30, 31]. Studies show its bark extracts reduce prostate cancer growth by inducing apoptosis in prostate cancer cells [24]. Bioactive compounds such as β-amyrin and β-sitosterol contribute to its anticancer effects [32]. However, due to its endangered status, a micropropagation protocol has been developed for future use in drug development [33].

- ***Securidaca longipedunculata***

Securidaca longipedunculata, known for its use in treating cancer in Northern Nigeria, shows antiproliferative effects in vitro and in vivo by inhibiting angiogenesis and inducing apoptosis [34,35]. The active compounds, including xanthones, have been shown to target tumor cells and inhibit cell proliferation [36,37].

- ***Annona senegalensis***

Known as wild soursop, this plant has anticancer effects, particularly in liver cancer, by enhancing liver function and regulating tumor suppressor gene expression [38]. It contains bioactive compounds such as alkaloids, glycosides, and flavonoids, which contribute to its therapeutic properties [39].

- ***Annona muricata***

Annona muricata, widely cultivated in Africa, has been shown to possess significant anticancer properties. Its acetogenins, particularly annonacin, have antitumor activities through apoptosis induction and cell cycle arrest [40,41]. Ethyl acetate extracts from its leaves have been effective against breast cancer cells [42]. The plant's silver nanoparticles (AgNPs) also exhibit anticancer effects by inducing autophagy and apoptosis [43].

- ***Aerva javanica***

Aerva javanica, native to Africa, has shown anticancer activity in breast cancer models. Methanol extracts from its callus and leaves induce DNA fragmentation and cytotoxicity in cancer cells [44,45].

- ***Azanza garckeana***

Azanza garckeana, a semi-deciduous tree from the Malvaceae family, is native to East and Southern Africa. Phytochemical analysis of its seeds reveals the presence of compounds such as tannins, saponins, flavonoids, alkaloids, phenols, glycosides, and carotenoids [46]. Flavonoids, integral to the plant's antioxidant properties, help neutralize free radicals, inhibiting tumor development. The seeds have been noted for their potential in reducing cancer development by interfering with the enzyme oestrogen synthase, responsible for producing estrogen [47]. Furthermore, a complex formed between Mansone G and β-Cyclodextrin, extracted from *A. garckeana*, has shown significant cytotoxic effects against A549 lung cancer cells [48].

- ***Phyllanthus amarus* (Euphorbiaceae)**

Phyllanthus amarus is a widely distributed herb across tropical regions, including Africa, Asia, and the Americas. The plant’s extracts are known for their anticancer properties, particularly in initiating apoptosis in cancer cells. Research shows that *P. amarus* can induce cell cycle arrest in the G0/G1-phase and S-phase of different cancer cell lines, including PC-3 and MeWo, and hinder their migration, invasion, and adhesion [49]. In addition to its anticancer effects, *P. amarus* contains various phytochemicals such as flavonoids, ellagitannins, triterpenes, and alkaloids, which have been linked to its anticancer properties [44]. Studies have also highlighted its role in treating conditions like tubercular ulcers, wounds, and scabies, underlining its broad medicinal value.

- ***Thymus vulgaris* (Lamiaceae)**

Thymus vulgaris, commonly known as thyme, is a plant native to Southern Europe, the Mediterranean, and parts of Africa and Asia. The cytotoxic activity of extracts from T. vulgaris has been demonstrated in various cancer cell lines, including human breast cancer MCF-7 cells [41]. Active compounds like diallyl disulfide, diallyl trisulfide, and allicin have also shown strong anticancer potential, particularly in suppressing cancer cell proliferation [43]. These bioactive compounds make T. vulgaris a promising candidate for the development of natural anticancer agents.

- ***Spondias mombin***

This tropical plant possesses a diverse range of phytochemicals that contribute to its anticancer activity. Carotenoids from S. mombin promote cancer cell death and suppress tumor growth, particularly in breast cancer. Quercetin, a key flavonoid, triggers apoptosis, inhibits Bcl-2 proteins, suppresses NF-κB activation, and modulates PI3K/Akt and MAPK pathways. Kaempferol reduces angiogenesis by lowering VEGF levels and blocking Akt activation. Additionally, antioxidants like astaxanthin and β-carotene derivatives help reduce oxidative stress and DNA damage [50–55].

- ***Xanthosoma sagittifolium***

Known as tannia or malanga, this plant exhibits anticancer effects through induction of apoptosis, cell cycle arrest, and inhibition of angiogenesis. Its hydroethanolic extract is cytotoxic to leukemia cells, modulates NF-κB and STAT3 signaling, and acts through PTEN-related pathways [56–60].

- ***Elaeis guineensis***

Commonly referred to as oil palm, it contains tocotrienols and phenolic compounds with strong anticancer activity. Its methanol extract induces apoptosis and reduces cancer cell viability. Tocotrienols also arrest the cell cycle at G1 phase and inhibit key signaling pathways like NF-κB and MAPK [61–65].

- ***Irvingia gabonensis***

Also known as African mango, its bioactive components such as gallotannins, flavonoids, and terpenoids provide antioxidant, pro-apoptotic, and anti-inflammatory effects. The extracts activate mitochondrial apoptosis pathways and inhibit protein tyrosine phosphatases, helping regulate metabolism and immune responses [66,67].

- ***Blighia sapida***

Ackee contains saponins, alkaloids, and flavonoids that suppress ERK5—a pathway involved in breast cancer. It also displays antioxidant and anti-inflammatory properties, and promotes apoptosis in vitro [68–72].

- ***Talinum triangulare***

Waterleaf contains compounds like quercetin, apigenin, and lycopene that inhibit cancer cell growth and heat shock protein activity. It enhances immune response, reduces oxidative stress, and interferes with lipid peroxidation [73–78].

- ***Launaea taraxacifolia***

African lettuce exhibits strong antioxidant activity due to its phenolics and flavonoids. It induces cell cycle arrest and apoptosis, notably in esophageal cancer cells [79–82].

- ***Solanum macrocarpon***

African eggplant shows cytotoxicity against MCF-7 and HeLa cells. Glycoalkaloids like solamargine, along with flavonoids and phenolics, contribute to its antioxidant and immunomodulatory anticancer properties [83–88].

- ***Chrysophyllum albidum***

African star apple is rich in phenolics and flavonoids, particularly in its leaf and fruit extracts. These compounds scavenge free radicals, induce apoptosis, and downregulate VEGF, which inhibits angiogenesis. Its extract has shown cytotoxic effects against breast cancer cells (MCF-7), suggesting potential as an antiangiogenic agent [89–91].

Common Bioactive Compounds From African Medicinal Plants and Their Anticancer Mechanism

Alkaloids: Over recent years, several plant-based alkaloids have demonstrated cytotoxicity against various cancer cell lines. Proto-alkaloids differ from typical alkaloids in that their nitrogen atom originates from amino acid residues but is not part of a heterocyclic ring. Colchicine, a well-known proto-alkaloid from *Colchicum* species, has traditionally been used for inflammation [92]. Beyond this, it has shown anticancer properties: inducing apoptosis in breast cancer cells through p53, Bax, and caspase activation [93], suppressing β-catenin signaling in colon cancer cells [94], and promoting cell death in oral cancer via increased cytosolic calcium triggered by phospholipase C [95].

Neopapillarine, a coumarin-alkaloid conjugate found in *Neocryptodiscus papillaris*, exhibited selective cytotoxicity against renal cancer cell lines, although further studies are needed to elucidate its mechanism [96].

Indole alkaloids such as vinblastine and vincristine, used clinically in cancer therapy. New indole alkaloids like reflexin A from *Rauvolfia reflexa* have been shown to induce apoptosis via caspase pathways in colon cancer cells [97]. Acetoxytabernosine from *Alstonia yunnanensis* caused G1 phase arrest and apoptosis in liver cancer cells [98]. Chaetocochin J from *Chaetomium globosum* inhibited colorectal cancer cell growth via AMPK activation and autophagy induction. Caulerpin, extracted from *Halimeda cylindracea*, reduced migration and promoted apoptosis in lung and colon cancer cells with minimal toxicity to normal fibroblasts [99,100]. Another indole derivative, 3,10-dibromofascaplysin from *Fascaplysinopsis reticulata*, suppressed proliferation in drug-resistant prostate cancer cells by weakening androgen receptor activity [101].

Quinoline-based structures serve as scaffolds for various anticancer agents [102]. Alkaloids such as coclaurine and related benzylisoquinolines from *Annona squamosa* inhibited growth in colon, breast, and liver cancer cells, with coclaurine showing superior potency due to more hydroxyl groups [103]. Neferine from *Nelumbo nucifera* triggered ROS generation and apoptosis in cervical cancer cells [104]. Other isoquinolines like palmatine and 6-methoxydihydroavicine disrupted glycolysis and mitochondrial functions in various cancers [105,106], while crebanine N-oxide from *Stephania hainanensis* caused G2/M arrest and apoptosis [107]. Camptothecin, a pyrroloquinoline alkaloid from *Camptotheca acuminata*, inhibits topoisomerase I, disrupting DNA replication and inducing cell death [108]. Its derivative, 10-hydroxycamptothecin, isolated from *Xylaria* fungi, inhibits BDR4 in triple-negative breast cancer cells [109].

Flavonoids: Flavonoids, a group of polyphenolic compounds abundantly present in plants, have gained considerable attention for their anticancer potential due to their natural origin, low toxicity, and multi-targeted action. Unlike conventional chemotherapeutic agents which often have significant side effects and limited selectivity, flavonoids exhibit cancer-preventive and therapeutic properties by interfering with carcinogenic processes such as cell proliferation, angiogenesis, apoptosis evasion, and metastasis [110–113]. For instance, quercetin a dietary flavonoid found in berries and green tea has been extensively studied for colorectal cancer, where it promotes apoptosis, cell cycle arrest, and modulates estrogen receptors and oxidative stress pathways [114]. Similarly, luteolin and kaempferol demonstrate pro-apoptotic activity in hepatocellular carcinoma by targeting specific molecular regulators like miR-6809-5p and oxidative stress pathways [115,116].

Recent investigations have highlighted various flavonoids with notable anticancer mechanisms. Hesperidin-loaded nanoparticles have shown cytotoxic effects against glioma cells with reduced polymer toxicity [117,118], while aurones and their analogues target a range of cellular proteins including kinases and histone deacetylases [119]. Myricetin, another bioactive flavonoid, exerts antimitotic effects in liver cancer cells by disrupting mitochondrial metabolism [120]. Several plant extracts rich in flavonoids, such as those from *Matricaria recutita* and *Gastrocotyle hispida*, demonstrate dose-dependent cytotoxicity against hepatocellular and other cancer cell lines by modulating VEGF expression and other critical molecular targets [121,122]. Prenylated flavonoids, including those from *Sinopodophyllum hexandrum*, show potent cytotoxic activity with IC_{50} values under 10 μmol/L, indicating strong anticancer efficacy [123].

While many of these compounds remain in preclinical evaluation, a few have entered advanced clinical trials. Notably, icaritin (ICT), a prenylated flavonoid, is in phase III trials for hepatocellular carcinoma, showing immune-enhancing properties and targeting key pathways like STAT3 and NFκB [124]. Isoquercetin has also progressed to clinical trials for reducing thrombosis in cancer patients by inhibiting protein disulfide isomerase activity [125].

These studies underscore the therapeutic potential of flavonoids as safer, plant-based anticancer agents. Given my interest in drug discovery and plant natural products, the integration of such bioactive compounds into modern oncology could lead to innovative and less toxic treatment strategies.

Terpenoids and Triterpenes: Terpenoids, a diverse and structurally rich class of natural compounds primarily found in medicinal plants, have shown immense promise in cancer therapy. Their biosynthesis, derived from isoprene units, contributes to a wide range of bioactive molecules that exert cytotoxic effects on various cancer cell lines. These compounds function through mechanisms such as inducing apoptosis, inhibiting angiogenesis, and suppressing metastasis, making them attractive candidates for anticancer drug development. Notably, diterpenoids like taxol and triterpenoids such as ursolic acid have been extensively studied and utilized in chemotherapeutic formulations [126,127].

The anticancer effects of terpenoids are mediated through multiple molecular targets and pathways, including modulation of oxidative stress, interference with the cell cycle, and inhibition of pro-survival signaling cascades like PI3K/Akt and NF-κB. For instance, monoterpenes such as limonene and perillyl alcohol have demonstrated significant efficacy in both in vitro and clinical settings, showing their ability to sensitize tumor cells to conventional therapies (128). Moreover, some sesquiterpenes have shown potential in overcoming multidrug resistance, a major hurdle in cancer treatment, by altering membrane permeability and drug efflux pump expression (129).

Recent research continues to highlight the therapeutic relevance of plant-derived terpenoids in oncology, reinforcing their role not just as cytotoxic agents but also as chemopreventive molecules. With a strong basis in traditional medicine and modern pharmacological validation, these natural compounds are being explored for formulation into novel drug delivery systems to enhance bioavailability and selectivity. This aligns with the growing scientific interest in integrating ethnopharmacological knowledge with molecular oncology to develop safer, plant-based anticancer therapeutics (130, 131).

Tannin: Tannins, a class of polyphenolic compounds found abundantly in many medicinal plants, have exhibited notable cytotoxic and antiproliferative activities against cancer cells. In particular, aqueous leaf extracts from various *Cornus* species such as *C. mas*, *C. alba*, and *C. officinalis* demonstrated strong inhibitory effects on MCF-7 breast cancer cells, with survival rates dropping to nearly 11% after 72 hours of treatment. These effects correlated closely with high tannin content, although other polyphenols such as flavonoids and hydroxycinnamic derivatives also contributed modestly to cytotoxicity [132, 133]. Similarly, extracts from *Crateva adansonii*, an African ethnomedicinal plant, significantly reduced tumour volume and oxidative stress in a rat breast cancer model, largely attributed to its gallotannin and flavonoid content [134].

Further evidence of tannins' anticancer potential comes from *Caesalpinia spinosa* (P2Et), a Peruvian medicinal plant rich in gallotannins. Its ethanolic extract induced apoptosis in breast tumour cells and triggered immunogenic cell death (ICD) markers like calreticulin and ATP release [135, 136]. These immunomodulatory effects enhanced anti-tumour immunity, as seen in the increased activation of CD4+ and CD8+ T cells. Moreover, this extract reduced lung and spleen metastases in vivo and demonstrated a synergistic effect with doxorubicin in combating cancer stem cells (CSC) in resistant breast cancer models [137–139]. These findings support the integration of tannin-rich plant extracts as potent adjuvants in cancer therapy, particularly for resistant and metastatic cancers.

Quinones: Quinones, a diverse class of natural compounds found in many medicinal plants, exhibit significant anticancer potential by targeting multiple pathways involved in tumor progression. Compounds like aloe-emodin have been shown to disrupt cancer cell proliferation by arresting the cell cycle at various checkpoints including G1, S, and G2/M phases [140–141]. These bioactive molecules also induce oxidative stress by generating reactive oxygen species (ROS), which in turn cause DNA damage [145]. Additionally, quinones can activate intrinsic and extrinsic apoptotic mechanisms through the modulation of caspases, the Fas signaling pathway, the tumor suppressor protein p53, and c-Jun N-terminal kinase, ultimately promoting programmed cancer cell death [140, 144, 146, 147].

Beyond inducing apoptosis, quinones exert their anticancer effects by suppressing metastasis-related proteins and signaling pathways. They have been found to inhibit the expression of urokinase-type plasminogen activator as well as matrix metalloproteinases MMP-2 and MMP-9, which are critical for tumor invasion and metastasis [150, 151, 152]. One notable quinone, β-lapachone, has been reported to cause DNA fragmentation and apoptotic body formation, while downregulating anti-apoptotic proteins like Bcl-2 and Bcl-XL. It simultaneously enhances the expression of pro-apoptotic protein Bax and activates poly (ADP-ribose) polymerase along with caspases-3 and -9, further reinforcing its potential as a promising anticancer agent [153]. These findings underscore the therapeutic relevance of quinones in the development of plant-based anticancer drugs.

Conclusion

Traditional African medicinal plants possess vast potential as sources of anticancer agents due to their diverse bioactive compounds and long-standing use in indigenous healthcare systems. This review underscores the therapeutic promise of these plants in combating various cancers through mechanisms such as apoptosis induction, anti-proliferation, and metastasis inhibition. While numerous in vitro and in vivo studies have demonstrated promising results, challenges remain in terms of clinical validation, toxicity profiling, and standardization. Bridging the gap between traditional knowledge and modern scientific research is essential for harnessing the full therapeutic potential of African botanicals.

Future Directions

- Phytochemical Standardization: Development of standardized extraction and formulation protocols to ensure consistency in bioactive content.
- Mechanistic Studies: Advanced molecular studies to elucidate precise mechanisms of action of plant-derived compounds.

- Preclinical and Clinical Trials: Comprehensive in vivo studies followed by human clinical trials to validate safety and efficacy.
- Bioprospecting and Conservation: Sustainable harvesting and conservation strategies to protect biodiversity while exploring novel anticancer compounds.
- Ethnopharmacological Integration: Strengthening collaboration between traditional healers and scientific researchers to validate and preserve indigenous knowledge.

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