J. Phytomol. Pharmacol., 4(1), 20-38, 2025
https://doi.org/10.56717/jpp.2025.v04i01.035
ISSN(Print): 2957-5818, ISSN(Online): 2958-6224

Journal of Phytomolecules & Pharmacology

Review Article

Therapeutic potential of anti-cancer compounds from African medicinal plants: From *in vitro* studies to clinical applications

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Abstract

Cancer remains one of the leading causes of death globally, driving the search for effective and accessible therapeutic agents. African medicinal plants are emerging as a promising source of anticancer compounds due to their long-recognized therapeutic properties. This review evaluates studies published between 2000 and 2024, focusing on the anticancer activity of plant-derived compounds. We searched through PubMed, Google Scholar, Scopus, and African Journals Online. We identified 15 relevant studies investigating the cytotoxic effects of plant extracts from species such as *Aframomum arundinaceum*, *Annona muricata*, *Polyscias fulva*, *Xylopia aethiopica*, among other species. Bioactive compounds were identified as flavonoids (kaempferol), alkaloids, terpenoids, and acetogenins (annonacin). These compounds showed cytotoxicity against various cancer cell lines, including breast, pancreatic, and lung cancers. Commonly observed mechanisms of action included apoptosis induction, cell cycle arrest, and oxidative stress modulation. For instance, annonacin from *Annona muricata* induced apoptosis in pancreatic cancer cells, while kaempferol from *Aframomum arundinaceum* caused G1 phase arrest in breast cancer cells. Polysciasoside A from *Polyscias fulva* showed selective cytotoxicity against lung cancer cells. Despite these promising findings, most studies were limited to in vitro assays, with few advancing to in vivo models. Although the bioactive compounds demonstrate great potential, gaps in preclinical validation, safety profiling, and pharmacokinetic studies hinder their clinical translation. Future research should prioritize in vivo studies, toxicity assessments, and drug delivery systems to improve bioavailability and clinical potential, enabling the development of novel anticancer therapies from African plants.

Article Information
Received: 13 March 2025
Revised: 20 April 2025
Accepted: 22 April 2025
Published: 30 April 2025

Academic Editor
Prof. Dr. Marcello Iriti

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Keywords
Cancer, African medicinal plant, cytotoxic, apoptosis, cell line, therapeutic potential.

1. Introduction

Natural products have long served as a foundation for pharmaceutical innovation, accounting for more than 50% of current drugs across therapeutic areas, including oncology [1, 2]. Historically, plant-derived compounds have yielded some of the most effective anticancer agents, such as paclitaxel from *Taxus brevifolia* [3] and vincristine from *Catharanthus roseus* [4], which shows the unmatched chemical nature and

bioactivity of natural substances. The structural diversity of these compounds often makes them challenging to reproduce synthetically, making plant-derived metabolites an important resource in drug development [5, 6].

African medicinal plants, shaped by vast biodiversity and rich ethnobotanical traditions, are increasingly gaining attention in modern drug discovery. Indigenous knowledge systems across Africa have long employed plant-based remedies to manage a wide array of diseases, including cancer [7]. Scientific investigations are now substantiating these traditional uses, with many species demonstrating cytotoxic effects against various cancer cell lines. For instance, *Annickia chlorantha* has yielded protoberberine alkaloids with DNA-intercalating properties [8], while acylated triterpene saponins from the roots of *Securidaca longepedunculata* are known to induce apoptosis in tumor cells [9]. Similarly, xanthones from *Garcinia gardneriana* [10] and ochnaflavone from *Ochna kibbiensis* have demonstrated promising antiproliferative effects [11]. These findings reflect the chemical diversity inherent in African flora. Major classes of bioactive compounds, including alkaloids, flavonoids, terpenoids, quinones, and xanthones, have been repeatedly linked to mechanisms such as apoptosis induction, cell cycle arrest, and inhibition of angiogenesis [12, 13]. In addition, chemotaxonomic relationships are increasingly being used to prioritize plant species for study, as taxonomic proximity often correlates with shared secondary metabolites and biological activity [14].

Despite growing evidence of in vitro cytotoxicity, there remains limited translation of these findings into clinical applications. Many studies focus on crude extracts or semi-purified fractions, with limited data on pharmacokinetics, toxicity, and target selectivity [15, 16]. Moreover, challenges such as sustainable harvesting, standardization of plant material, and the conservation of medicinal species remain under-addressed, threatening the long-term viability of discovery from natural sources.

Research on the anticancer potential of African medicinal plants remain largely scattered and characterized by methodological variability, limiting the ability to systematically evaluate and prioritize promising therapeutic candidates. This review seeks to bring together existing data on cytotoxic compounds derived from African plants, emphasizing their mechanisms of action, activity against multidrug-resistant (MDR) cancers, and directions for future investigation. It aims to support the translation of preclinical findings into clinical applications while promoting the sustainable utilization of Africa's botanical diversity for cancer treatment.

2. Materials and methods

2. Methods

2.1. Search strategy

This review adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to ensure methodological rigour and transparency in the review process. A comprehensive search strategy was devised using a combination of search concepts and keywords linked by Boolean operators (AND, OR) to identify relevant studies across selected databases, including PubMed, Google Scholar, Scopus, and African Journals Online. These databases were chosen for their extensive coverage of global and region-specific research, particularly studies on African medicinal plants. The following keywords were employed: "medicinal plants", "plant extracts", "African medicinal plants", "African traditional medicine", "herbal medicine Africa", "antineoplastic agents", "neoplasms", "anti-cancer", "anticancer", "cytotoxic", "antitumor", "in vitro techniques", "cell line", "tumour", "in vitro", "cell culture", "tumour cell lines", "drug development", "translational medical research", "clinical application", "drug development", and "translational research". To refine the search results and ensure relevance, filters were applied to restrict the publication period to between 2000 and 2024 and to limit the language to English, ensuring consistency in interpretation. The search focused on literature reporting the anti-cancer properties of African medicinal plants, emphasising in vitro or in vivo studies and their potential for clinical translation. The search results were subsequently uploaded to Rayyan, an online software tool, for systematic screening of articles.

2.2. Eligibility criteria and study selection

The inclusion criteria for this review were designed to

https://doi.org/10.56717/jpp.2025.v04i01.035

capture original primary studies that investigated plant extracts, bioactive fractions, or isolated compounds derived from African medicinal plants, with a focus on their anticancer activity as assessed through in vitro or in vivo models. While studies using crude extracts were considered, priority was given to those employing bioassay-guided fractionation or identifying specific isolated compounds, particularly where mechanisms of action were reported. Studies discussing the translational potential of these compounds, including pharmacological activity or clinical relevance, were also included. Exclusion criteria encompassed review articles, editorials, and non-peer-reviewed publications. The studies were screened and selected independently by three reviewers (CAN, AI, and APN), with any discrepancies resolved through consultation with a third reviewer (CSN). Initial screening was based on titles and abstracts to identify potentially relevant studies, followed by a full-text review of selected articles to confirm their eligibility for inclusion in the data synthesis.

2.3. Data extraction

Data extraction was performed by CAN, OPE, AI, and NPA, with oversight and review provided by CSN. A structured Google spreadsheet form, developed and piloted by the research team, was used to record study characteristics. The form was designed to capture detailed information from each study, including bibliographic details (e.g., authors, year of publication, title, and country of research) and specific data related to the medicinal plants under investigation. This included the plant species, the part of the plant used, and the methods employed to extract and isolate compounds. Additionally, information on the cancer types studied, the in vitro assays conducted, and the results of these assays were documented. The mechanisms of action of the compounds were recorded, along with any references to clinical trials or potential clinical applications mentioned in the studies. The pilot testing of the form ensured that all relevant data categories were accurately captured for extraction.

2.4. Data synthesis

Extracted data were systematically organized to summarize the therapeutic potential of plant-derived compounds in cancer treatment. Studies were categorized based on cancer models (e.g., breast, lung, colon, leukaemia), bioactive compound classes (e.g., alkaloids, flavonoids, terpenoids), and experimental approaches (e.g., cell lines, animal models). Reported cytotoxic activity, mechanisms of action, and translational relevance were synthesized to highlight key findings. Trends in bioactivity and mechanistic pathways were described to capture commonalities and variations among the studied plant extracts. This synthesis provided a structured overview of the available evidence on plant-derived compounds with cytotoxic effects against cancer.

3. Results

We identified 454 records through a database search: PubMed (n = 112), Google Scholar (n = 228), Scopus (n = 63), and African Journals Online (n = 54). After removing duplicates, 102 unique articles remained. These articles were screened based on their titles and abstracts, resulting in the exclusion of 69 articles. The full texts of the remaining 33 articles were assessed for eligibility, leading to the exclusion of 19 articles due to the absence of cytotoxicity data, unclear or insufficient methodology, or a non-African focus. Ultimately, 14 studies met the predefined inclusion criteria. These studies provided data on medicinal plants with reported cytotoxic activity, the plant parts investigated, the types of in vitro assays performed, and their respective mechanisms of action. Fig. 1 presents the PRISMA flowchart, summarizing the study selection process.

4. Discussion

4.1. Overview of African medicinal plants with anti-cancer potential

African medicinal plants have demonstrated significant anti-cancer potential. They are valuable resources for discovering novel therapeutic agents. Extensive research has been conducted on the cytotoxic activities of indigenous African plants across various regions, including Nigeria [17, 19, 22, 23, 29, 31], Cameroon [18, 20, 21, 26], South Africa [24, 27], Uganda [30], and Tanzania [28]. Detailed information is shown in Table 1.

Among the studied plants, *Macaranga barteri* (family Euphorbiaceae) and *Calliandra portoricensis* (family Leguminosae) exhibited cytotoxic activity against the

https://doi.org/10.56717/jpp.2025.v04i01.035

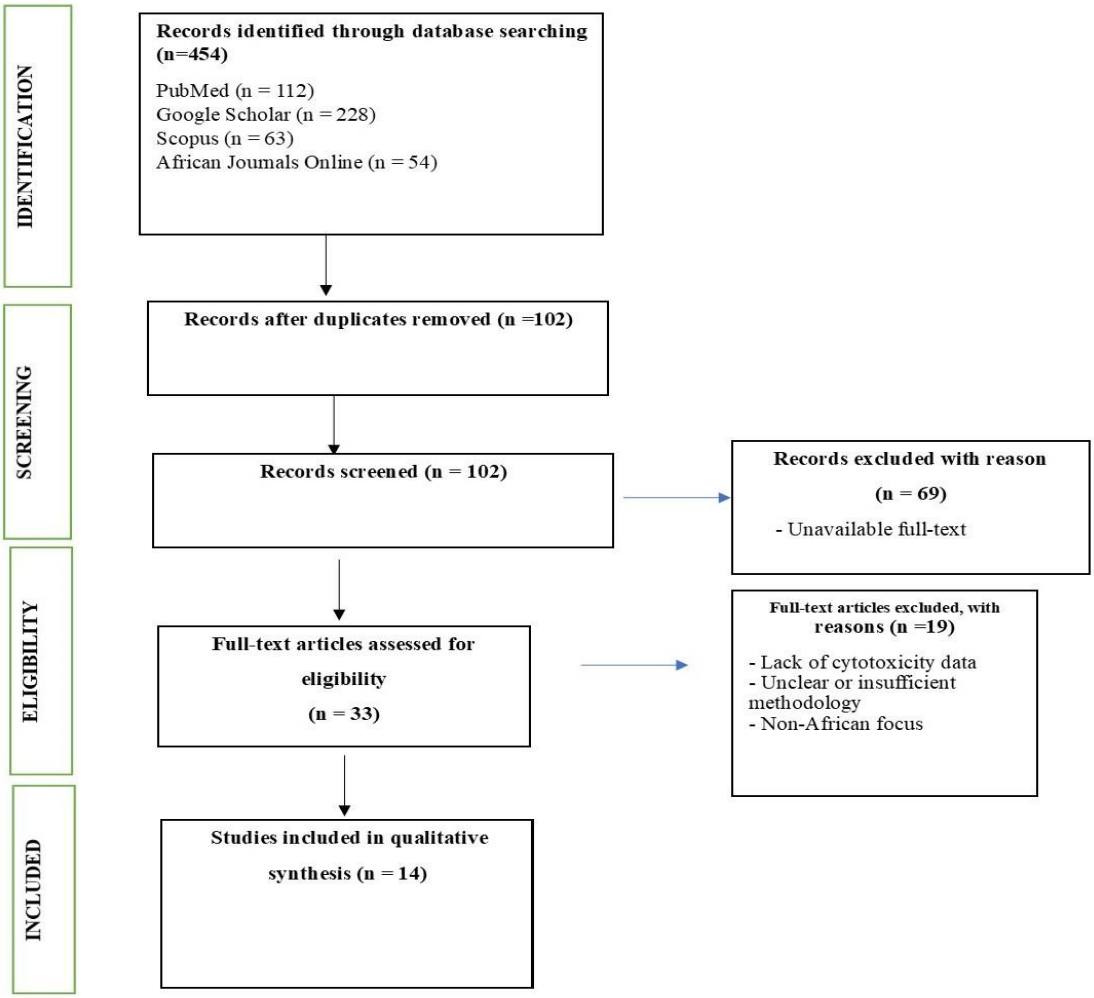

Figure 1. PRISMA (Preferred reporting items for systematic reviews and meta-analyses) flowchart of study selection process.

Rhabdomyosarcoma cancer cell line, as reported by Ogbole *et al.* (17). The leaf extract of *M. barteri* has been shown to possess medicinal properties, including antimicrobial and cytotoxic activities [32,33]. *C. portoricensis*, widely utilised in traditional African medicine, is commonly employed in Nigeria to treat prostate cancer, gonorrhoea, malaria, stomach ulcers, and gastrointestinal disorders [17, 34]. Traditional herbal recipes incorporating its root are specifically formulated to treat breast and prostate cancer. Notably, the methanol root extract of *C. portoricensis* has been shown to significantly inhibit the growth of prostate cancer cell lines [31,35].

Further studies by Engel et al. identified *Hunteria umbellata*, *Cola lepidota*, *Persea americana*, and *Plukenetia conophora* as exhibiting significant effects on human breast and bone cancer cell lines [19]. *Sansevieria liberica* [23] and *Anacardium occidentale* [22] have demonstrated both in vitro and in vivo anti-cancer activity. Adaramoye et al. investigated *Xylopia aethiopica*, revealing its antiproliferative effects on human cervical cancer cells, thus highlighting its potential as a therapeutic agent [25].

Kuete et al. reported the efficacy of *Annona muricata*, *Alchornea floribunda*, *Euphorbia prostata*, and *Passiflora edulis* against multidrug-resistant cancer cell lines. Furthermore, *Beilschmiedia acuta*, *Clausena anisata*, *Fagara tessmannii*, *Newbouldia laevis*, and *Polyscias fulva* were found to contain bioactive compounds, including anthocyanins, flavonoids, and alkaloids, with potent anti-cancer properties [18]. Mbaveng et al. studied the cytotoxicity of *Curcuma longa*, *Lycopersicon esculentum*, and *Psidium guajava*, highlighting their significant anti-cancer potential [21].

Njoya et al. investigated the cytotoxic effects of

https://doi.org/10.56717/jpp.2025.v04i01.035

Table 1. Reported African medicinal plants with anti-cancer property and plant parts

S/N	Title	Country	Medicinal Plant with cytotoxic activity	Plant Part(s)	Ref.
1	In vitro cytotoxic activity of medicinal plants from Nigeria ethnomedicine on Rhabdomyosarcoma cancer cell line and HPLC analysis of active extracts.	Nigeria	*Macaranga barteri* *Calliandra portoricensis*	Leaves Root	[17]
2	Cytotoxicity of methanol extracts of *Annona muricata*, *Passiflora edulis* and nine other Cameroonian medicinal plants towards multi-factorial drug-resistant cancer cell lines.	Cameroon	*Alchornea floribunda* *Annona muricata* *Euphorbia prostate* *Pachypodanthium staudtii* *Passiflora edulis*	Bark and leaves leaves, seed, pericarp Whole plant Leaves, bark, and roots Fruit and fruit pericarp	[18]
3.	Proliferative effects of five traditional Nigerian medicinal plant extracts on human breast and bone cancer cell lines	Nigeria	*Hunteria umbellata*, *Cola lepidota*, *Persea americana*, *Plukenetia conophora*	Leaves Seeds Leaves Root, Leaves	[19]
4.	Cytotoxicity and modes of action of five Cameroonian medicinal plants against multi-factorial drug resistance of tumor cells.	Cameroon	*Beilschmiedia acuta Kosterm* *Clausena anisata (Willd)* *Fagara tessmannii Engl* *Newbouldia laevis Seem*, *Polyscias fulva* (Hiern) Harms	Roots, leaves, bark Hook, roots, leaves, bark Roots, leaves, bark, Roots, leaves, bark, Roots, leaves, bark	[20]
5	Cytotoxicity of 18 Cameroonian medicinal plants against drug-sensitive and multi-factorial drug-resistant cancer cells.	Cameroon	*Curcuma longa* *Lycopersicon esculentum* *Psidium guajava*	Rhizomes Leaves Bark	[21]
6.	Identification of compounds with cytotoxic activity from the leaf of the Nigerian medicinal plant, Anacardium occidentale L. (Anacardiaceae).	Nigeria	*Anacardium occidentale*	Leaves	[22]
7.	In Vitro and In Vivo Anticancer Activity of Root Extracts of *Sansevieria liberica* Gerome and Labroy (Agavaceae).	Nigeria	*Sansevieria liberica*	Roots	[23]
8.	*Croton gratissimus* leaf extracts inhibit cancer cell growth by inducing caspase 3/7 activation with additional anti-inflammatory and antioxidant activities.	South Africa	Three Croton species (*C. pseudopulchellus*, *C. sylvaticus*, *C. gratissimus*)	Leaves	[24]
9.	Antiproliferative Action of Xylopia aethiopica Fruit Extract on Human Cervical Cancer Cells.	Nigeria	*Xylopia aethiopica*	Fruits	[25]
10.	In vitro cytotoxicity and antioxidant activities of five medicinal plants of Malvaceae family from Cameroon.	Cameroon	*Sida acuta* *Sida cordifolium* *Sida rhombilifolia* *Urena lobata* *Viscum album*	Whole plant	[26]

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Table 1. *(continued)*

S/N	Title	Country	Medicinal Plant with cytotoxic activity	Plant Part(s)	Ref.
11.	In vitro antioxidant and cytotoxicity activities of selected indigenous South African medicinal plants.	South Africa	*Bulbine frutescens* *Bulbine natalensis* *Chlorophytum comosum* *Kniphofia uvaria* *Tulbaghia violacea*	Roots and shoots	[27]
12.	Isolation of a new cytotoxic compound, 3-((Z)-heptadec-14-enyl) benzene - 1-ol from *Rhus natalensis* root extract.	Tanzania	*Rhus natalensis Bernh. ex C. Krauss (Anacardiaceae)*	Root	[28]
13.	Antineoplastic activity of a methanolic extract from Kigelia pinnata DC stem bark.	Bulgaria	*Kigelia pinnata*	Stem bark	[29]
14	Annona muricata silver nanoparticles exhibit strong anticancer activities against cervical and prostate adenocarcinomas through regulation of CASP9 and the CXCL1/CXCR2 genes axis.	Uganda	*Annona muricata*	Fruits and leaves	[30]

three Croton species (*Croton pseudopulchellus*, *Croton sylvaticus*, and *Croton gratissimus*), which demonstrated strong anti-cancer activity through the induction of apoptosis in cancer cells [24]. These plants also exhibited anti-inflammatory and antioxidant properties, enhancing their therapeutic potential.

In a recent study, Vakele et al. [27] evaluated the in vitro antioxidant and cytotoxic activities of selected indigenous South African medicinal plants, including *Bulbine frutescens*, *Bulbine natalensis*, *Chlorophytum comosum*, *Kniphofia uvaria*, and *Tulbaghia violacea*. Collectively, these plants highlight the diverse anti-cancer potential of African medicinal plants, providing a robust foundation for further exploration and development of therapeutic applications. Table 2 presents a detailed report of the *in vitro* assays of these medicinal plants, the results from the assays, and the proposed mechanism of action by which they show cytotoxic effects.

4.2 Selective cytotoxicity of African medicinal plants

One key feature of African medicinal plants with therapeutic potential in cancer treatment is their ability to target cancer cells while selectively sparing normal, healthy tissues. This selective cytotoxicity is crucial in minimizing the collateral damage commonly observed with conventional chemotherapies, which often harm both cancerous and normal cells, leading to severe side effects [36, 37]. In cancer treatment, the capacity to kill malignant cells specifically without affecting healthy cells is a key factor in ensuring both efficacy and safety.

Xylopia aethiopica has shown antiproliferative effects across various human cancer cell lines, inducing cell death in cervical cancer cells while having minimal effects on normal cells. This selectivity is also evident in its action against carcinoma, osteosarcoma, and leukaemia cells, demonstrating its potential for targeted therapy [25, 38, 39].

Curcumin, derived from *Curcuma longa* (turmeric), is known for its broad anticancer properties and minimal toxicity to normal cells. Its ability to specifically target cancer cells with IC_{50} values as low as 6.25 μg/mL in colon cancer highlights its effectiveness while sparing healthy tissue. Curcumin's action is attributed to its regulation of critical processes like cell cycle progression and critical processes like cell cycle progression and protein kinase activity [21, 40].

Psidium guajava, especially the leaf-derived compounds, has demonstrated potent inhibition of glioblastoma and hepatocellular carcinoma cell lines with minimal effect on normal cells. The presence of bioactive compounds such as guajadial B, D, and F, betulinic acid, avicularin, kaempferol, and betulinic acid in the leaf extract is believed to play a role in this selectivity [21, 41].

https://doi.org/10.56717/jpp.2025.v04i01.035

Table 2. Reported in vitro assays, results, and mechanism of action

S/N	Cancer Type	In vitro Assay Types	Assay Result	Mechanism of Action	Ref.
1	Rhabdomyosarcoma cancer (RD cells)	• Brine Shrimp Lethality Assay (BSLA) • Methyl Thiazolyl Tetrazolium (MTT) Assay • Selectivity Index (SI)	*Macaranga barteri* showed high cytotoxicity (BSLA LC_{50}: 76.3 μg/mL, MTT CC_{50}: 0.22 μg/mL on RD cells) with strong selectivity (SI: 13.7, RD/Vero). Calliandra portoricensis exhibited similar activity (BSLA LC50: 82.4 μg/mL, MTT CC50: 0.82 μg/mL on RD cells, SI: 11.1, RD/Vero).	The extracts exhibited cytotoxic effects through potential mechanisms such as apoptosis induction, disruption of cell membrane integrity, and selective toxicity toward cancer cells, as indicated by high selectivity index values.	[17]
2	Breast cancer Colon cancer Glioblastoma CCRF–CEM leukemia cells	• Resazurin Assay • Cell Cycle Analysis • Apoptosis Detection • Caspase Activity • Mitochondrial Membrane Potential (MMP) Analysis • ROS Measurement	Several extracts (AFB, AMP, AML, AMS, EPW, PSB, PSL, PSR, PEP, PEF) showed IC50 < 20 μg/mL, with potential against resistant hematologic cancers. AML, AMS, and PEP induced apoptosis via MMP loss without caspase activation or ROS increase. *Annona muricata* leaf extract exhibited antiproliferative effects on HL-60 cells (IC50: 14 μg/mL), causing G0/G1 arrest and apoptosis through MMP loss.	MMP loss-induced apoptosis	[18]
3.	Breast and osteocarcinoma	• MTT, Proliferation Assay	*P. americana* root (RPA) extract increased osteosarcoma cell proliferation by 27% at 10 μg/mL. Other extracts showed low activity on non-tumorigenic MCF-12A and POB cells. RPA exhibited the most potent anticancer activity.	Modulated cancer cell growth through selective cytotoxicity and potential apoptotic induction.	[19]
4.	Breast cancer (human cancer cell lines)	• Resazurin assay • Flow cytometry (cell cycle, apoptosis, MMP, ROS) • mRNA microarray	*Beilschmiedia acuta* (leaves and bark) and *Polyscias fulva* (roots) inhibited CCRF-CEM cell growth by >50%. BAL and PFR showed strong cytotoxicity (IC_{50} < 30 μg/mL) across 10 cancer cell lines, including drug-resistant models. BAL had an IC50 < 5 μg/mL in HCT116 (p53−/−) cells. PFR induced apoptosis via ROS increase and mitochondrial dysfunction. Microarray analysis linked activity to alpha-hederin (IC50 < 10 μM in CCRF-CEM and CEM/ADR5000).	Cell cycle arrest (G0/G1 to S phase), apoptosis induction via ROS and mitochondrial disruption	[20]

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Table 2. *(continued).*

S/N	Cancer Type	In vitro Assay Types	Assay Result	Mechanism of Action	Ref.
5.	Leukemia Breast Colon Glioblastoma Hepatocarcinoma	• Resazurin assay • Flow cytometry • Annexin V/PI staining • Caspase assays • MMP integrity • ROS production	13 of 21 extracts (61.9%) showed cytotoxicity (IC50 < 80 µg/mL), with six highly potent extracts (IC50 < 30 µg/mL). *Curcuma longa* (CLR) was most effective (IC50: 6.25–10.29 µg/mL), followed by *Psidium guajava* (PGB) (IC50: 1.29–62.64 µg/mL) and *Lycopersicon esculentum* (LEL) (IC50: 9.64–57.74 µg/mL).	CLR and PGB induced apoptosis via caspase activation, mitochondrial dysfunction, and ROS production. LEL also triggered cell death through similar mechanisms.	[21]
6.	Cervical cancer (HeLa cell line)	Alamar Blue cell viability assay	*Anacardium occidentale* extracts showed concentration-dependent reductions in HeLa cell viability with varying potencies.	Cell viability reductions and corresponding morphological damage were noted for each extract.	[22]
7.	A549 (lung), HCT-116 (colon), PC3 (prostate), A431 (skin), HeLa (cervix), THP-1 (leukemia), Sarcoma-180 (S-180) ascites & solid tumor, L1210 leukemia	SRB cytotoxicity assay, S-180 and L1210 in vivo models	*Sansevieria liberica* hydroalcohol extract (SL-A002) showed strong cytotoxicity (IC50: 23 µg/mL, HeLa), distilled water extract (SL-A003) was most potent for HCT-116 (IC50: 22 µg/mL), and methanol extract (SL-A004) for A549 (IC50: 23 µg/mL) and THP-1 (IC50: 18 µg/mL). In vivo, SL-A002 reduced tumor growth by 89.36% (S-180 ascites) and 47.40% (S-180 solid tumor), and extended survival in L1210 leukemia by 158.33%, comparable to 5-FU.	Induced apoptosis, inhibited tumor proliferation, and prolonged survival in leukemia models.	[23]
8.	MCF-7 (Breast), HeLa (Cervix), Caco-2 (Colorectal), A549 (Lung)	Antioxidant (DPPH, ABTS), Anti-inflammatory (NO inhibition, 15-LOX inhibition), Cytotoxicity (MTT, Caspase 3/7 activation)	C. pseudopulchellus and C. sylvaticus extracts showed high toxicity to non-cancerous cells (LC50: 7.86–48.19 µg/mL). C. gratissimus extracts were more selective (LC50: 152.30–462.88 µg/mL, SI: 1.56–11.64). C. pseudopulchellus acetone extract showed strong NO inhibition (IC50: 34.64 µg/mL) and 15-LOX inhibition (IC50: 0.57 µg/mL). Caspase 3/7 activation was highest (1.83-fold) in HeLa cells treated with C. gratissimus acetone extract.	Induced apoptosis via caspase-3/7 activation	[24]

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Table 2. *(continued).*

S/N	Cancer Type	In vitro Assay Types	Assay Result	Mechanism of Action	Ref.
9.	C-33A (cervical), KB (oral), MCF-7 (breast), A549 (lung), NIH3T3 (fibroblast)	SRB assay, Flow cytometry, Propidium iodide staining, RT-PCR	*Xylopia aethiopica* fruit extract showed dose-dependent cytotoxicity, with the strongest effect on C-33A cells (IC50: 30.8 μg/mL). It induced cell cycle arrest at sub-G0/G1 and G2/M phases and promoted apoptosis via Bax upregulation and Bcl-2 downregulation.	Induced apoptosis through the mitochondrial pathway, increasing the Bax/Bcl-2 ratio and activating p53-mediated cell cycle arrest at G2/M.	[25]
10.	HepG-2 (human hepatoma)	MTT assay, Antioxidant enzyme assays (SOD, CAT, GST, GR)	Sida acuta (IC50: 461.53 ± 0.23 μg/mL) and Urena lobata (IC50: 454.93 ± 0.12 μg/mL) exhibited strong antiproliferative effects. At 250 μg/mL, both reduced cell growth significantly over 72 hours. Sida cordifolia and Viscum album showed notable effects after 48 hours, while Sida rhombifolia displayed weak cytotoxicity.	Enhanced antioxidant enzyme activities (SOD, CAT, GST), reducing oxidative stress in HepG-2 cells.	[26]
11.	Caco-2 (colon), HeLa (cervical), HepG2 (liver)	DPPH (antioxidant), MTT (cytotoxicity)	*Bulbine natalensis* and *B. frutescens* showed the highest antioxidant activity (33.2% and 26.3%, respectively). Ethanol extracts of *Chlorophytum comosum*, *Kalanchoe uvaria*, and *Tulbaghia violacea* induced >80% cytotoxicity in HepG2 and Caco-2 cells. The most potent extracts were *Bulbine frutescens* shoot (IC50: 10.43 μg/mL), *Kalanchoe uvaria* shoot (IC50: 23.0 μg/mL), and *Chlorophytum comosum* root (IC50: 23.77 μg/mL).	ROS induction, apoptosis, cell cycle arrest, mitochondrial membrane disruption.	[27]
12.	HeLa cervical cancer cells	Brine shrimp lethality assay (BSLA), Cytotoxicity assay, Cytotoxicity (Hoechst/PI staining), Cell cycle analysis, Caspase 3/8 activation, PS translocation, Antioxidant (FRAP, DPPH)).	*Rhus natalensis* ethyl acetate extract showed high toxicity (BSLA LC50: 7.2 μg/mL) and strong anticancer activity (IC50: 17.2 μg/mL on HeLa cells). A newly isolated compound, 3-((Z)-heptadec-14-enyl) benzene-1-ol, exhibited weaker activity (IC50: 35.24 μg/mL). The extract also demonstrated antioxidant activity (DPPH EC50: 83.05 μg/mL, FRAP: 58.75 μmol Fe^{2+}/g dry weight).	Apoptosis induction via caspase 3 activation and PS translocation.	[28]

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Table 2. *(continued).*

S/N	Cancer Type	In vitro Assay Types	Assay Result	Mechanism of Action	Ref.
13.	Leukemia (SKW-3, REH, HL-60, K-562), B-cell lymphoma (DOHH-2), Hodgkin lymphoma (HD-MY-Z), Breast cancer (MCF-7), Murine lung cancer	MTT assay, Apoptosis assay (DNA fragmentation)	*Kigelia pinnata* extract showed strong cytotoxicity, with the lowest IC50 values in MCF-7, SKW-3, and Lewis lung cancer cells. Fractionation yielded two active chloroform fractions (CF3, CF7) with lower potency. Apoptosis was confirmed via DNA laddering in SKW-3 cells.	Apoptotic cell death induction, likely mediated by quinone compounds.	[29]
14.	Prostate (PC3) and Cervical (HeLa) adenocarcinomas	Resazurin assay, Cell migration assay, Colony formation assay, Gene expression analysis	Annona muricata silver nanoparticles (AgNPs-F, AgNPs-L) showed strong antiproliferative effects. AgNPs-F had the highest selectivity (SI: 7.8) and colony suppression, outperforming 5-FU. AgNPs-L exhibited higher cytotoxicity on normal cells.	Inhibited cell migration, reduced colony formation, and increased cell death, suggesting anti-metastatic potential.	[30]

Croton sylvaticus, *Bulbine natalensis*, and *Tulbaghia violacea* have also shown promising anticancer effects with minimal toxicity to non-cancerous cells, particularly in hepatocellular and colorectal cancer models [24, 27]. *Sansevieria liberica* was observed to reduce tumour size with negligible impact on healthy tissues [23]. *Fagara tessmannii*, rich in alkaloids, induces apoptosis specifically in breast cancer cells [18].

Generally, bioactive compounds present in these plants, including alkaloids [42 ,43], flavonoids [44, 45], terpenoids [46], and anthocyanins [47], contribute to their ability to target cancer cells selectively. This ability is an important factor in considering them as leads for the development of anticancer agents, making them valuable for future clinical studies.

4.3. Anticancer mechanisms of phytochemical derivatives from African medicinal plants

The anticancer mechanisms of African medicinal plants largely involve apoptosis induction and cell cycle arrest, which are vital for limiting cancer growth. Studies have shown how plant-derived phytoconstituents can effectively target and regulate these pathways.

4.3.1. Apoptosis induction

Apoptosis, or programmed cell death, is a key defense against cancer development. It eliminates damaged or dysfunctional cells without triggering inflammation [48]. However, in cancer cells, this process is often disrupted, leading to uncontrolled cell proliferation [49]. Medicinal plants have been shown to restore apoptotic pathways, either through the intrinsic (mitochondrial) pathway or the extrinsic (death receptor) pathway.

4.3.1.1. Intrinsic pathway activation

The intrinsic apoptotic pathway is primarily triggered by mitochondrial dysfunction resulting from cellular stress, such as oxidative damage or DNA lesions. A central event is the loss of mitochondrial membrane potential (MMP), which is vital for ATP production and mitochondrial integrity. Stress signals activate pro-apoptotic proteins such as Bax and Bak, causing membrane permeabilization and MMP depolarization. This leads to the release of cytochrome

https://doi.org/10.56717/jpp.2025.v04i01.035

c into the cytosol, where it binds to Apaf-1 to form the apoptosome. The apoptosome activates caspase-9, which in turn activates caspase-3 and caspase-7, driving DNA fragmentation, chromatin condensation, and apoptotic cell death [50].

Several African medicinal plant extracts exert their anticancer effects by engaging this pathway. *Xylopia aethiopica* induces apoptosis in cervical cancer cells by upregulating Bax and downregulating Bcl-2, thereby increasing the Bax/Bcl-2 ratio, disrupting MMP, and promoting cytochrome c release and caspase-9 activation [25, 51]. Similarly, the root extract of *Polyscias fulva* contains triterpene saponins, particularly dammarane-type glycosides such as polysciasoside A and hederagenin derivatives, which disrupt MMP, trigger cytochrome c release, and activate the caspase cascade, resulting in apoptosis.

In addition, *Bulbine frutescens* and *Lycopersicon esculentum* induce apoptosis via oxidative stress. Extracts from *B. frutescens* elevate reactive oxygen species (ROS) levels, causing mitochondrial dysfunction and apoptosis [27, 52]. Likewise, rhizome extracts of *Curcuma longa* and bark extracts of *Psidium guajava* enhance ROS generation and activate caspases, reinforcing the critical role of oxidative stress and mitochondrial damage in intrinsic apoptotic signaling [21].

4.3.1.2. Extrinsic pathway activation

The extrinsic apoptotic pathway begins when external ligands like FasL, TNF-α, or TRAIL bind to death receptors such as Fas, TNFR1, or DR4/DR5 on the cell surface. This activates the death-inducing signaling complex (DISC), which in turn activates caspase-8. Caspase-8 then triggers effector caspases like caspase-3 and caspase-7, leading to apoptosis [53].

Several plant extracts have been shown to induce apoptosis through this pathway. These include acetone and ethanol leaf extracts of *Croton gratissimus*, the ethyl acetate fraction of *Rhus natalensis*, and methanol extracts of *Annona muricata* and *Passiflora edulis*. These extracts activate caspase-3 and caspase-7, promoting apoptosis in various cancer cell lines such as MCF-7 (breast), HeLa (cervical), Caco-2 (colorectal), and A549 (lung) adenocarcinoma cells [18, 24, 28].

4.3.2. Cell cycle arrest

In addition to apoptosis, the arrest of cancer cells at specific phases of the cell cycle is another mechanism. Cancer cells often bypass critical checkpoints that regulate cell division, leading to unchecked proliferation [54]. Plant extracts of African origin can modulate these checkpoints, leading to cell cycle arrest and inhibition of tumour growth.

4.3.2.1. G0/G1 phase arrest

G0/G1 phase arrest occurs when the cell cycle is halted at the G0/G1 phase, where cells are either in a quiescent state (G0) or preparing for DNA replication and division (G1). During the G1 phase, cells grow and accumulate the necessary proteins for DNA synthesis [55]. Arresting the cell cycle at this point prevents the transition to the S-phase, where DNA replication occurs, effectively stopping further cell division. This blockage is a critical mechanism for regulating uncontrolled cell proliferation, especially in cancer.

Several plant extracts show activity in inducing G0/G1 phase arrest, thereby blocking the early stages of cell division. Annona muricata leaf extracts, rich in acetogenins, which are a group of naturally occurring polyketide compounds, particularly annonacin, cause G0/G1 arrest in leukemia cells (HL-60) by downregulating cyclins and cyclin-dependent kinases (CDKs), which are essential for cell cycle progression [18]. Acetogenins, chemically characterized by a long aliphatic chain attached to a polyketide backbone, have been found to inhibit mitochondrial function, contributing to their cytotoxic and cell cycle-arresting properties [56].

Similarly, extracts from *Polyscias fulva* roots, containing dammarane-type glycosides such as polysciasoside A and hederagenin, induce both G0/G1 and S-phase arrest in breast cancer cells. These compounds are triterpene saponins characterized by a steroid-like structure consisting of a dammarane or hederagenin backbone. They can interact with cell membrane components and modulate the cell cycle by affecting cyclin and CDK activity [20].

Additionally, high-performance liquid chromatography (HPLC) analysis of the dichloromethane fraction of *Macaranga barteri* extract revealed the presence of bioactive compounds, including acteoside, 3,5-dicaffeoylquinic acid, kaempferol-7-O-glucoside, and bastadin 11 [17]. Among these, acteoside, a phenylpropanoid glycoside, stands out for its potent anticancer, cytotoxic, anti-

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inflammatory, and antimetastatic activities. Chemically, acteoside consists of a hydroxytyrosol core linked to a glucose and rhamnose moiety, along with a caffeic acid group, forming a highly bioactive structure. Studies indicate that it inhibits the growth of human promyelocytic leukemia (HL-60) cells by causing cell cycle arrest at the G0/G1 phase and encouraging their differentiation into monocytes. This shows its relevance in cancer therapy [17].

4.4. Role of medicinal plants in combating multidrug-resistant (MDR) cancers

Multidrug resistance (MDR) poses a formidable challenge in cancer therapy, often rendering chemotherapy ineffective due to the survival and proliferation of drug-resistant cancer cell subpopulations [57]. MDR commonly arises from mechanisms such as the overexpression of ATP-binding cassette (ABC) efflux transporters like P-glycoprotein (P-gp/ABCB1), mutations in oncogenes (e.g., EGFR), and dysregulation of apoptotic signaling pathways [58]. These adaptations enable cancer cells to evade cytotoxic drugs, leading to relapse and poor prognosis.

In evaluating the activity of medicinal plants against MDR cancers, researchers often use the degree of resistance (D.R.), defined as the ratio of the IC_{50} value (concentration inhibiting 50% of cell viability) in the resistant cell line to that in the corresponding sensitive cell line [20]. A D.R. < 1 suggests collateral sensitivity, i.e., the extract is more toxic to resistant cells, while a D.R. > 1 implies some level of cross-resistance [20]. Values approaching or below 1 indicate the potential of the tested agent to overcome or bypass conventional resistance mechanisms.

A growing body of evidence now supports the role of African medicinal plants in overcoming MDR, primarily through mechanisms such as efflux inhibition, modulation of apoptosis, and disruption of oncogenic signaling [59]. These plants' efficacy is closely tied to their rich repertoire of bioactive phytochemicals, many of which belong to well-characterized chemical classes such as flavonoids, terpenoids, and alkaloids.

4.4.1. Inhibition of drug efflux and collateral sensitivity

One major avenue through which medicinal plants counter MDR is by inhibiting the P-gp efflux pumps, thereby increasing intracellular drug accumulation. Several plant extracts also exhibit collateral sensitivity, selectively targeting resistant cancer cells over their drug-sensitive counterparts.

Aframomum arundinaceum is particularly noteworthy for its activity against resistant phenotypes such as leukaemia (CEM/ADR5000) and EGFR-mutated glioblastoma (U87MG.ΔEGFR), with D.R. values below 0.51 [20]. The phytochemical analysis identified galanals A and B and naingenin, among others. Galanals A and B are cyclic sesquiterpenoid dialdehydes with fused rings and reactive aldehydes. They induce cytotoxicity by disrupting mitochondrial membranes and activating caspase-mediated apoptosis, targeting resistant cells selectively [60]. Naringenin, a flavanone from A. arundinaceum, downregulates P-gp and inhibits PI3K/Akt and MAPK/ERK pathways, thus boosting drug retention and pro-apoptotic signaling in MDR cancers [61].

Similar mechanisms are evident in *Anonidium mannii*, which displayed potent antiproliferative effects on CEM/ADR5000 and U87MG.ΔEGFR cells, with D.R. values below 1 [62]. Its phytochemicals include terpenoids, alkaloids, and flavonoids, which modulate drug efflux and signaling pathways [63]. *Xylopia aethiopica* and Piper capense have likewise demonstrated activity against CEM/ADR5000 cells, which are a multidrug-resistant subline of CCRF-CEM leukemia cells. *X. aethiopica* had an IC_{50} as low as 3.91 µg/mL in leukemia CCRF-CEM cells, outperforming conventional agents like doxorubicin, which had resistance indices above 40-fold in the same model [39].

4.4.2. Disruption of oncogenic signaling and cell cycle regulation

Some plant-derived compounds exhibit their anti-MDR effects by targeting dysregulated signaling pathways and inducing cell cycle arrest (Table 3), mechanisms that are hijacked by resistant cancer cells. Kaempferol-3,7,4′-trimethylether, a methylated flavonol isolated from *A. arundinaceum*, enhances both lipophilicity and membrane permeability due to its methyl groups. Flavonols are known to inhibit kinases involved in tumor progression. This compound has been linked to G2/M cell cycle arrest and suppression of oncogenic kinase activity, providing a good mechanism for its effect against resistant cells [20].

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Ferutinin, a sesquiterpene ester derived from *Ferula hermonis,* is another notable example. Structurally, it contains a drimane skeleton and esterified phenolic groups. It has been shown to induce over 50% inhibition in MDR cell lines, including pancreatic (MiaPaCa-2), breast (MCF-7), and leukaemia (CEM/ADR5000) cells. Ferutinin exerts its activity through mitochondrial disruption and modulation of calcium homeostasis, triggering apoptosis even in cells resistant to classical agents [64].

4.4.3. Selective cytotoxicity and p53-independent apoptosis

Some medicinal plants demonstrate broad-spectrum activity while exhibiting selective cytotoxicity toward cancer cells, particularly those with mutations in tumor suppressors like p53, which are frequently associated with resistance to apoptosis.

Extracts from *Beilschmiedia acuta* and *Polyscias fulva* have shown strong activity in p53-deficient colon carcinoma cells (HCT116 p53−/−), with D.R. values of 0.23 and 0.41, respectively [20]. These low values indicate hypersensitivity in mutant cells, suggesting the activation of alternative apoptotic pathways. The cytotoxicity of both extracts was higher in hepatocarcinoma (HepG2) than in normal AML12 hepatocytes. This speaks to their tumor-selective potential.

In addition, *Garcinia quaesita, Voacanga soyauxii,* and *A. mannii* have all demonstrated IC_{50} values below 30 µg/mL in a variety of resistant cell lines [62]. These effects are attributed to their phytochemical compositions, rich in terpenes and alkaloids, which interact with multiple molecular targets. Alkaloids can induce DNA fragmentation and oxidative stress, and terpenes often act through membrane destabilization or receptor modulation. Similarly, extracts from *Crataegus sinaica, Carthamus tenuis, Bidens pilosa,* and *Haplophyllum tuberculatum* demonstrated activity against CEM/ADR5000 cells. These plants contain a mix of flavonoids, lignans, and phenolic acids, many of which have been linked to ROS generation, apoptosis induction, and efflux pump inhibition [64].

4.5. Future directions and clinical research potential for anti-cancer molecules from African medicinal plants

The clinical potential of anti-cancer molecules from African medicinal plants offers promising opportunities to translate *in vitro* findings into therapeutic applications. Moving forward, key investigations should focus more on *in vivo* studies to determine the efficacy, safety, and pharmacokinetic profiles of these bioactive compounds. Although substantial research has been conducted using cell lines and animal models, advancing to well-designed clinical trials will be important to assess the therapeutic effects, optimal dosing regimens, and potential adverse effects in human subjects.

Compounds with strong preclinical promise, such as galanals A and B and naringenin from *Aframomum arundinaceum*, flavonoid glycosides and xylopic acid from *Xylopia aethiopica,* and acetogenins like annonacin from *Annona muricata*, should be prioritized for further in vivo testing. Other notable plants include *Polyscias fulva*, which contains dammarane-type glycosides such as polysciasoside A and hederagenin; *Beilschmiedia acuta*, known for its alkaloids and flavonoids; *Garcinia quaesita,* rich in potent terpenes and alkaloids; and *Piper capense*, which is abundant in flavonoids. Animal models of human cancers, such as xenograft or syngeneic mouse models, would be valuable for these investigations, with endpoints including tumor growth inhibition, survival rates, and the assessment of any off-target toxicities.

Additionally, studies should focus on the synergistic potential of African plant-derived compounds in combination with established chemotherapeutic agents. This combination strategy holds promise for enhancing therapeutic efficacy while reducing the toxicities often associated with conventional treatments. For instance, early studies have shown that *Polyscias fulva* and *Annona muricata* extracts may enhance the efficacy of standard chemotherapy agents [65].

A promising avenue for the identification and optimization of bioactive compounds is the application of advanced scientific methodologies, such as high-throughput screening, genomics, and proteomics. These tools are indispensable for rapidly identifying potential anticancer agents and providing mechanistic insights into their therapeutic actions [66]. Complementing these approaches, Structure-Activity Relationship (SAR) studies and computational techniques like molecular docking and Quantitative Structure-Activity Relationship (QSAR) modeling are

https://doi.org/10.56717/jpp.2025.v04i01.035

Table 3. Medicinal plants activity against MDR cancers, categorized by cancer type, phytochemicals, and mechanisms

Cancer type (MDR cell line)	Plant species	Key phytochemicals	Compound class	Mechanism of action
Leukaemia (CEM/ADR5000)	*Aframomum arundinaceum*	Galanals A & B	Sesquiterpenoid dialdehydes	Mitochondrial disruption; Caspase-dependent apoptosis; selective cytotoxicity (D.R. < 1)
	A. arundinaceum	Naringenin	Flavanone (Flavonoid)	Downregulates P-gp; Inhibits PI3K/Akt and MAPK/ERK signaling
	A. arundinaceum	Kaempferol-3,7,4′-trimethylether	Methylated flavonol	Kinase inhibition; G2/M cell cycle arrest
	Xylopia aethiopica	Not specified	Alkaloids, terpenoids	Collateral sensitivity (D.R. ~1.9); enhanced mitochondrial stress
	Piper capense	Not specified	Terpenoids, phenolics	D.R. < 1; Efflux inhibition
	Zingiber officinale	Gingerols, shogaols	Phenolic ketones	P-gp modulation; oxidative stress induction
	Imperata cylindrica	Not specified	Saponins, flavonoids	ROS generation; apoptosis induction
	Anonidium mannii	Not specified	Terpenoids, alkaloids, flavonoids	P-gp inhibition; collateral sensitivity (D.R. < 1)
	Crataegus sinaica, Bidens pilosa	Flavonoids, phenolic acids	Polyphenols	P-gp inhibition; ROS-mediated apoptosis
	Ferula hermonis	Ferutinin	Sesquiterpene ester	Mitochondrial Ca^{2+} disruption; apoptosis (IC_{50} < 30 μg/mL)
	Voacanga soyauxii	Indole alkaloids	Alkaloids	DNA intercalation; apoptotic activation
Glioblastoma (U87MG.ΔEGFR)	*Aframomum arundinaceum*	Galanals A & B	Sesquiterpenoids	Disruption of EGFR-linked survival pathways
	Anonidium mannii	Not specified	Alkaloids, terpenoids	EGFR modulation; selective cytotoxicity
Colon Carcinoma (HCT116 p53−/−)	*Polyscias fulva*	Not specified	Triterpenoids	Selective cytotoxicity to p53-deficient cells (D.R. 0.41)
	Beilschmiedia acuta	Not specified	Alkaloids, flavonoids	Apoptosis induction in p53-mutant cells (D.R. 0.23)
Hepatocarcinoma (HepG2)	*Beilschmiedia acuta, Polyscias fulva*	Not specified	Alkaloids, flavonoids	More cytotoxic to HepG2 than to normal hepatocytes
Breast Cancer (MCF-7, MDA-MB-231/BCRP)	*A. polyanthum*	Not specified	Not specified	Cytotoxic to BCRP-expressing MDR cells
	Ferula hermonis	Ferutinin	Sesquiterpene ester	Apoptosis via mitochondrial stress; P-gp independence
Pancreatic Cancer (MiaPaCa-2)	*Ferula hermonis*	Ferutinin	Sesquiterpene ester	Broad MDR cytotoxicity (inhibition > 50%)
General MDR-Sensitive Cell Lines (Multiple)	*Garcinia quaesita*	Xanthones, flavonoids	Polyphenols	P-gp inhibition; apoptosis
	Carthamus tenuis, Haplophyllum tuberculatum, Vitis vinifera	Flavonoids, phenolic compounds	Polyphenols	Efflux pump inhibition; oxidative stress

Definitions: D.R. < 1 = Collateral sensitivity (more toxic to resistant cells); IC_{50}= Inhibitory Concentration 50%; P-gp (ABCB1) = Drug efflux pump contributing to MDR; EGFR = Epidermal Growth Factor Receptor, often mutated in resistant glioblastoma; ROS = Reactive Oxygen Species, involved in apoptosis induction.

https://doi.org/10.56717/jpp.2025.v04i01.035

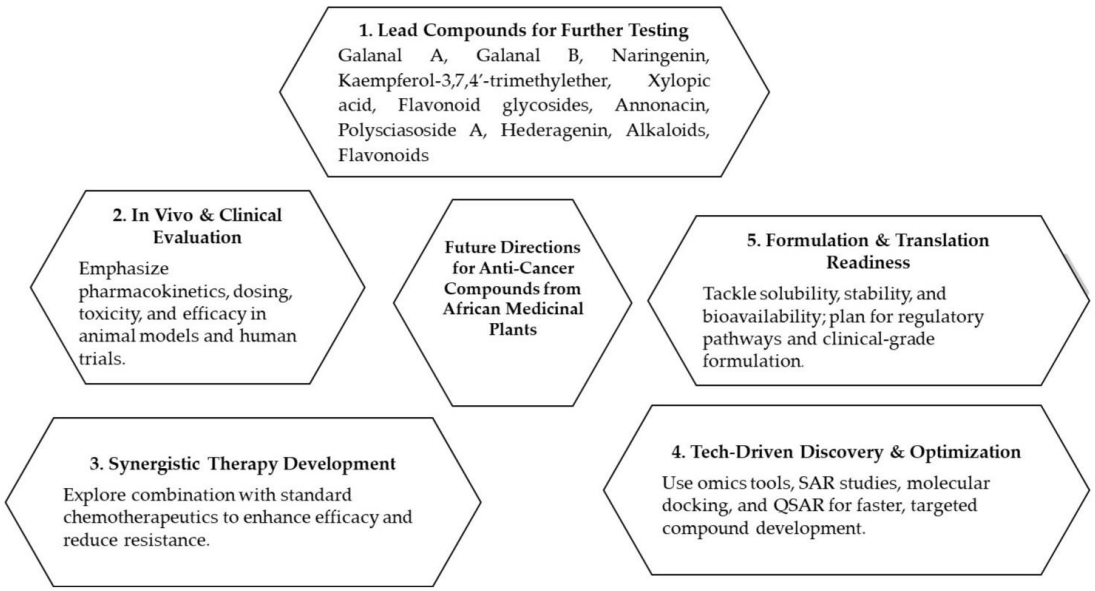

Figure 2. Summary of future directions for anti-cancer compounds from African medicinal plants

invaluable for guiding the optimization of lead compounds. These computational methods can enhance potency, selectivity, and pharmacokinetic properties, which are essential for their progression toward clinical application [67].

Moreover, the path to clinical translation must also address formulation and regulatory challenges. Issues such as solubility, stability, and bioavailability of plant-derived compounds are significant hurdles. Strategies to improve the bioavailability of poorly soluble compounds, such as the development of nanoformulations, liposomal delivery systems, or prodrugs, will be critical. Furthermore, regulatory considerations, including ensuring the consistency and safety of plant-based formulations, will require rigorous clinical evaluation and adherence to regulatory standards.

A collaborative approach between traditional healers and modern researchers is essential. Traditional knowledge, passed down through generations, can guide the selection of promising plant species for scientific investigation. Integrating this indigenous wisdom with contemporary techniques will help optimize the therapeutic potential of these plant-derived compounds, ensuring that they are both effective and safe for human use. Fig. 2 presents a summary of future directions for anti-cancer compounds from African medicinal plants.

5. Conclusions

The anticancer potential of African medicinal plants is evident in their cytotoxic effects against various cancer cell lines, mediated through mechanisms such as apoptosis induction, cell cycle arrest, and oxidative stress modulation. These activities are largely attributed to diverse classes of bioactive compounds, including alkaloids, flavonoids, terpenoids, and phenolics, many of which possess unique structural scaffolds that could serve as promising leads for anticancer drug development. The rich biodiversity of African flora presents a valuable reservoir of such compounds with therapeutic promise. However, clinical translation remains limited due to gaps in preclinical validation, toxicity profiling, and pharmacokinetic studies. Moreover, the heavy reliance on crude extracts in many studies limits mechanistic insight and hinders the identification of active principles. To advance the field, future studies should prioritize the isolation, characterization, and structural optimization of lead molecules, supported by bioassay-guided fractionation and structure–activity relationship (SAR) analyses. Standardization of extraction methods, bioassay protocols, and mechanistic investigations is essential to ensure reproducibility and comparability across studies. In addition, emerging technologies such as metabolic engineering, synthetic biology, and nanoformulation

https://doi.org/10.56717/jpp.2025.v04i01.035

may enhance the yield, bioavailability, and target specificity of promising plant-derived anticancer agents.

Authors' contributions

Conceptualized the study, C.A.N., C.S.N.; Study selection, resolving discrepancies, C.A.N., A.I., A.P.N.; Data extraction, C.A.N. O.P.E., A.I., N.P.A.; Prepared the original draft, C.A.N., O.P.E., A.I., N.P.A.; Supervision, consultation and reviewed the final draft of the manuscript, C.S.N.

Acknowledgements

The authors sincerely appreciate the Department of Pharmacology and Toxicology, University of Nigeria, Nsukka, for their invaluable support in providing access to the database for sourcing relevant literature. Their guidance and resources were instrumental in the successful completion of this review.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Availability of data and materials

All data will be made available on request according to the journal policy.

Conflicts of interest

The authors declare no conflict of interest.

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