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Antiproliferative, cytotoxic, and anticancer plants of Nigeria: An updated review

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Abstract
Cancer is a major global cause of death. It arises from deformation of natural cells due to genetic mutations in DNA which then produces an abnormal cell population. Chemotherapy option suffers from the demerits of high cost and non-selectivity, thereby destroying tumor cells in the presence of normal cells. This has paved way for an alternative plant-based medicinal therapy that constitutes natural sources of cytotoxic or antiproliferative compounds, which forms the basis for this review of publications of anti-proliferative, anticancer and cytotoxic research in Nigeria from 2000 to 2023 undertaken using different scientific sources and databases. Cancer incidence in Nigeria is more common in females with breast and cervical cancers having high prevalence. In the males, decreasing prevalence order was: prostate, bladder, skin and colorectal cancers. Ethnobotanical reports of Nigerian natural sources have revealed 116 scientifically-investigated medicinal plants, mostly by *in vitro* (97.34%) found in 50 families largely represented by Fabaceae (14.15%), Euphorbiaceae (10.61%) and Asteraceae (6.19%). Nevertheless, only three plants, *Morinda lucida* (3.28%), *Vernonia amygdalina* (2.63%) and *Persea americana* (2.63%) were the most researched for anti-proliferative potential. The frequently investigated morphological parts included leaf (45.73%), stem/ stem bark (21.70%), root/rootbark (16.27%) and aerial part/ whole plant (7.75%). A limited number, 15 (55.55%) of the 27 frequently occurring plants documented in anticancer ethnobotanical surveys have been scientifically validated. Fully characterized bioactive compounds were derived from extracts of 72.56% of the plants. Interestingly, ten bioactive cytotoxic compounds have been the subject of clinical trials while eight other compounds have been targeted. Various mechanisms of anticancer action including suppression of cancer's stimulating enzymes, DNA repair and stimulation of production of antitumor enzymes, have been postulated. This review has unravelled possibly efficacious folkloric anti-proliferative plants growing in Nigeria and their bioactive compounds some of which are undergoing clinical trials.

Keywords Anticancer activity, fabaceae, euphorbiaceae, *Morinda lucida, Vernonia amygdalina, Persea americana,* bioactive compounds, Nigeria

1. Introduction

Cancer is a complex multifactorial cell disease characterized by abnormal cellular proliferation. Cancer development and progression are dependent on the cellular accumulation of various genetic and epigenetic events [1-3]. It imposes a serious burden on the public health system, and its treatment and cure are scientifically challenging [4]. Cancer is one of the major causes of death in the world starting with the deformation of a natural cell caused by genetic mutations in DNA resulting in an abnormal cell which reproduces in an abnormal way by asexual reproduction to impart changes in surrounding tissues [5]. The disease is a significant health problem worldwide with an average of 182 per 100, 000 sufferers and 102 deaths worldwide every year [6]. According to the World Health Organization, global data indicate 14 million cancer sufferers and 8 million deaths, and it is predicted to exceed 13.1 million deaths globally by 2030 [7]. Notable among treatment options is chemotherapy, which being non-selective often results in destruction of a high percentage of healthy cells with cancer cells. Isolation and testing of cytotoxic or antiproliferative compounds and screening raw plant extracts is crucial in preparing anticancer medicines from natural sources [8-9]. Medicinal plants are important sources of anticancer agents due to their multiple chemical composition and chances of discovering new active compounds [10-14]. Nowadays, more than 60% of anticancer compounds used in chemotherapy are obtained from herbal, marine, and microorganism sources [12]. In this review, an attempt is made to document prevalence of cancer locally, and compile Nigerian medicinal plants that have been scientifically proven for cytotoxicity with their bioactive compounds having potential for cancer treatment.

2. Methods

An extensive literature search was performed using platforms such as PubMed, Google and Google Scholar. The search terms used were "anticancer," "antitumor," "cytotoxic," "bioactive compounds," "ethnobotanical survey" and "Nigerian plants". We focused solely only on reports in English. In addition, information on *in vivo* and *in vitro* studies published in original articles, peer-reviewed journals, books as well as reports on clinical trials were included in the review.

3. Prevalence of cancer in Nigeria

Cancer remains a major source of morbidity and mortality across the globe and about 18.1 million new cases and 9.6 million cancer-related deaths were reported in 2018 [15-16]. Fifty-six percent of newly reported cancer cases occurred in developing countries and it is projected that by 2030, 70% of all new cases of cancer will be found in developing countries due to from population growth, ageing population, westernized lifestyle and socioeconomic development [15].

Despite the threat that cancer poses to public health in sub-Saharan Africa, few countries in this region have 10-20 years' data on cancer incidence mostly based on reports from registries from The Gambia, Zimbabwe and Uganda aside from Nigeria [16], but with difficulties of sustaining cancer registration. Specifically, information on cancer incidence, prevalence and mortality in Nigeria has been based on estimates from case series, medical and mortality records, hospital-based cancer registries and the Ibadan population-based cancer registry (IBCR). The IBCR, at the University College Hospital Ibadan, established in 1962, is the oldest registry in Nigeria that furnished data periodically from 1962 to 1969. Other studies have also provided information on breast cancer in Lagos State, Nigeria mostly prevalent among the 26-45 years old group [17], with women's occupation and profession as major causative factors. Udo-Affah *et al.* [18] also reported similar increase in occurrence of breast cancer in Cross River State of Nigeria attributed to genetic, reproductive and hormonal factors, lifestyle and environment, age, preterm pregnancies and menopause [18-19]. According to the ten-year (1995-2004) study in Kano in northwestern Nigeria, females were more susceptible than males. Breast cancer was most prevalent, followed by cancers of the cervix (19.8%), colorectum (6.8%), connective tissue (6.6%), skin (6.5%), and uterus (5.7%) [20]. The males were characterized by prostate (24.7%), bladder (10.9%), skin (8.2%), colorectal (7.8%), connective tissue (7.5%), and eye (4.8%) cancers. Since 2009, the Nigerian Federal Ministry of Health and the Institute of Human Virology in Nigeria have initiated a program of National System of Cancer Registries to strengthen existing cancer registries and establish new ones through provision of baseline training for newly established registries; continuing education for older registries, mentoring, computer hardware and software provision and support, data management and analysis. According to World Health Organization when Nigeria's population was 195,875,239 in 2018, new cancer cases was 115,950 and deaths 70,327 [21]. According to this survey, prostate cancer was leading in males followed by colorectum, non-Hodgkin lymphoma and liver cancers, while breast and cervix uteri predominate among females.

4. Traditional anti-proliferative and cytotoxic plants of Nigeria and ethnobotanical surveys

Anticancer research has been a subject of various ethnobotanical surveys in the northeast and southwestern Nigeria. From the survey of Askira/Uba local government area of Borno State, Ngulde *et al.* [22] listed 65 plants found predominantly and sequentially in Caesalpinioideae, Fabaceae, Mimosoideae, Euphorbiaceae and Burseraceae in traditional cancer therapy. *Securidaca longepedunculata, Andira inermis* spp. *rooseveltii, Pterocarpus erinaceus, Carissa edulis, Detarium microcarpum* and *Senna sieberiana* were the frequently mentioned plants. Specific cancers mentioned were the cancers of the breast, skin, flesh/muscle, brain/head, bone, stomach, neck and lungs. In another northeastern survey by Daja and Gidado [23] and twenty-five plant species belonging to 14 different families were identified as potential anticancer sources. The south western Nigeria appears to be the home of ethnobotanical surveys of traditional remedies in cancer therapy. Ashidi *et al.* [24] have documented 45 plant species used by traditional healers in Ijebu, Awori, Ekiti, Yewa, Oyo and Egun communities employed as decoction and infusion for oral route, local application of poultices and bathing with decoctions. *Morinda lucida, Annona senegalensis, Acanthospermum hispidum, Cajanus cajan* and *Nymphaea lotus* were prominent components of the traditional cancer recipes. Also, *Cajanus cajan, Securidaca longepedunculata, Xylopia aethiopica* and *Nymphaea lotus* were implicated in breast cancer therapy. In Abeokuta, Ogun State, 20 plant species predominantly in Fabaceae, and Apocynaceae constitute ingredients of 4 recipes employed mainly as decoction and infusion in treating breast cancer, the leading malignant disease [19]. Six of these plants, *Allium ascalonicum, Calliandra portoricensis, Khaya ivorensis, Lophia alata, Plumbago zeylanica*, and *Xylopia aethiopica* have been scientifically validated. Furthermore, Soladoye *et al.* [25] documented 10 cancer recipes from 73 plants found predominantly in Leguminosae, Liliaceae, Asclepiadaceae, Annonaceae, Apocynaceae amongst others. Alabi *et al.* [26] in the survey of Sagamu in Ogun State, reported five multicomponent folkloric recipes for the treatment of breast cancer. However, only two of the recipes containing *Xylopia aethiopica* and *Uvaria chamae* were cytotoxic against MCF-7 cell lines. Furthermore, 92 plant species belonging mainly to Leguminosae, and to a lesser extent Annonaceae, Apocynaceae and Euphorbiaceae were revealed as ingredients of 38 cancer remedies in the ethnobotanical survey of Iwo and Ibadan towns in Oyo State [27]. Prominent plants were *Citrus limon, Xylopia aethiopica* and *Crotalaria pallida*, while *Jatropha curcas, Khaya ivorensis* and *Kigelia africana* were frequently occurring components of recipes. In Adamasingba and Ogbomoso local government areas of Oyo State, 87 plant species found mainly in Caesalpiniaceae, Meliaceae, Euphorbiaceae, Lamiaceae, Annonaceae and Moraceae were mentioned as traditional remedies for the treatment of five different cancers [28].

5. Reported cytotoxic activity of Nigerian plants

The summary of cytotoxic activities of published works on 116 Nigerian medicinal plants is presented in Table 1. A total of 50 families were covered in this review with Fabaceae (14.15%), Euphorbiaceae (10.61%) and Asteraceae (6.19%) predominating, followed by Combretaceae (3.53%), Meliaceae (3.53%), Rubiaceae (3.53%) and Apocynaceae (3.53%) as the less frequently researched families. Morphological parts frequently investigated ranked as: leaf (45.73%), stem/ stem bark (21.70%), root/rootbark (16.27%), aerial part/ whole plant (7.75%), fruit (3.87%), seed (2.32%) and underground parts (2.32%).

Table 1: Profile of Nigerian plants with anti-proliferative, cytotoxic and anticancer activities

S/No	Plant/ Family	Common name/Morphological part studied	Anti-proliferative and cytotoxic activities	Bioactive compounds	References
1	*Acanthospermum hispidum* DC. (Asteraceae)	Bristly starbur/ shoot	Methanol (MeOH) extract was most active on human cancer cell lines: breast adenocarcinoma (MCF-7), large cell lung carcinoma (COR-L23) and amelanotic melanoma (C-32). (IC_{50} 12-25 µg/mL)	Not specified	[29]
2	*Aframomum melegueta* (Zingiberaceae)	Grains of Paradise /seeds	Cold MeOH extract and n-hexane fraction were active on Rhabdomyosarcoma (RD) and breast (MCF-7) cancer cell lines by MTT assay. Most active 6-shogaol gave CC_{50}, 0.11 and 0.25 ìg/mL against RD and MCF-7, respectively.	6-Shogaol, 6-paradol, 1-dehyro-6-gingerdione	[24]
3	*Ageratum conyzoides* L. (Asteraceae)	Goat weed/ Leaf	Pet-ether, $CHCL_3$ and EtOAc fractions of ethanol (EtOH) extract were cytotoxic to human lung cancer (SK-MES 1) cells.	Not specified	[32]
			EtOAc extract cytotoxic on human non-small cell lung carcinoma (A-549) and mouse leukaemia (P-388) cell lines (IC_{50} 0.68 and 0.0003 mµg/mL, respectively)		[29]
4	*Alafia barteri* Oliv. (Apocynaceae)	Guinea fowl's crest /Leaf, stem	Active against MCF-7, leukaemia (K562), hepatic (WRL68) human cancer cells	Ursane triterpenoids (28-acety-urs-5,20-dien-2,3,24-triol), β-sitosterol, lupeol and α-amyrin, fatty esters. Fatty esters and methyl octanoate, dodec-5-enoic acid, lupeol	[30, 31]
5	*Allanblackia floribunda* Oliv. (Clusiaceae)	Tallow tree	MeOH extract gave growth inhibition (GI) of 66% against breast adenocarcinoma (BT-549) cell line at 20 μg/mL	1,5-dihydroxyxanthone, 1,5,6-trihdroxy-3,7-dimethoxynanthone	[29, 33]
6	*Anacardium occidentale* L. (Anacardiaceae)	Cashew/ leaf	Cytotoxicity against cervical adenocarcinoma cancer (HeLa) cells	Zoapatanolide A (most potent, IC_{50} 36.2 μM) agathisflavone, 1,2-bis (2,6-dimethoxy-4-methoxy carbonylphenyl) ethane (anacardicin), and methyl gallate	[34]
7	*Andrographis paniculata* (Burm. f) Wall. ex Nees (Acanthaceae)	Green chiretta	Aqueous (AQ) and $CHCL_3$ extracts (1:1) were cytotoxic to the murine hepatocytes, thymocytes and splenocytes	Diterpenes (andrographolide)	[35, 36]
8	*Annona senegalensis* Pers. (Annonaceae)	African custard apple/ root	EtOH extract toxic to brine shrimps and caused chromosomal damage in rat lymphocytes.	Mono-tetrahydrofuran acetogenins	[37]
		Stem bark	AQ extract gave complete GI of guinea corn root radicle at 1 mg/mL.		[38]
9	*Anogeissus leiocarpus* (DC.) Guill. & Perr. (Combretaceae)	African birch /root bark	AQ extract and 1:1 mixture of both plants showed anti-proliferative activity on Ehrlich ascites carcinoma cell lines	Resveratrol	[29, 39]
10	*Anthocleista djalonensis* A. Chev (Loganiaceae)	Cabbage tree/ Stem bark, root, leaf	MeOH extract active against brain tumor (ST-57) cell line	Djalonenol, sweroside, and a derivative (1-methoxy sweroside) moderately cytotoxic (ED_{50} 40-70 μg/mL). Derivatization only enhanced cytotoxicity of hydrolytic dimer of sweroside (ED_{50} 4 μg/mL)	[40]
		Stem bark, root	AQ extract gave GI 87.9 and 90% on guinea corn root radicle for root and stem bark, respectively at 1 mg/mL.		[38]
11	*Aristolochia ringens* Vahl. (Aristolochiaceae)	Worm killer/ root	EtOH extract cytotoxic (IC_{50} 3, 20, 22 and 24 μg/mL) for PC-3, A-549, HCT-116 and THP-1 cell lines, respectively. Dichloromethane (DCM)-MeOH extract: (IC_{50} 12, 19.5, 22, 26, 28 and 30 μg/mL for PC-3, HCT-116, THP-1, A-549, A-431 and HeLa, respectively). 2) *in vivo* models-Sarcoma-180: inhibition of tumor growth was 29.45% for EtOH (at 120 mg/kg) and 50.50% for DCM-MeOH (at 110 mg/kg). Leukemia model: 211.11% and 155.56% increase in mean survival time for EtOH and DCM-MeOH extracts, respectively.	Not specified	[41]
12	*Artocarpus altilis* (Parkinson) Fosberg (Moraceae)	Breadfruit/ leaf	MeOH (90%) extract gave GI 98.77% on guinea corn root radicle at 30 mg/mL in 96h.	Quercetin	[42, 43]
13	*Aspilia africana*	Haemorrhagic plant/	AQ and $CHCL_3$ extracts (1:1) were	Not specified	[35]

	(Pers.) C. D. Adams (Asteraceae)	leaf	cytotoxic to the murine hepatocytes, thymocytes and splenocytes		
14	*Asystasia buettneri* Lindau (Acanthaceae)	CN-/aerial parts	*n*-Hexane and EtOAc extracts were active on leukaemia blood (K-562) and hepatic liver (WRL-68) carcinoma	Hexadecanoic acid, taraxerol, taraxasterol, (*Z*)-9-octadecanoic acid, 5-hexadecenoic acid, 8-methyl tetradec-6-ene	[44]
15	*Azadirachta indica* A. Juss (Meliaceae)	Neem/ leaf	AQ extract inhibited root growth of onion bulb (cytotoxic, EC_{50} 0.6%), mitodepressive effect on cell division and induction of mitotic spindle disturbance	Quercetin-3-*O*-β-glucopyranoside	[45, 46]
16	*Bauhinia galpinii* (N. E. Br.) Schmitz (Fabaceae)	Red bauhinia	Toxicity to brine shrimps	Myricetin-3-*O*-galactopyranoside (LC_{50}, 74.68 and 30.69 μg/mL on Vero cells and bovine dermis cells, respectively)	[47]
17	*Boswellia dalzielii* (Hutch.) (Burseraceae)	Frankincense tree/ Stem bark	$CHCL_3$, EtOAc and Pet-ether fractions of EtOH extract were active against head and neck squamous cell carcinoma of the tongue (AW8507 cell line)	Catechol	[48, 49]
18	*Bryophyllum calycinum* Salisb. (Crassulaceae)	Air plant/ Whole plant	EtOH extract toxic to brine shrimps and caused chromosomal damage in rat lymphocytes.	Bufadienolide (bryophyllin A)	[37, 50]
19	*Byrsocarpus coccineus* Thonn. ex Schum. (Connaraceae)	Children's ear-ring/ bark, leaf	MeOH extract gave GI 54% at 20 μg/mL against breast carcinoma (BT-549), IC_{50} 18.6 and 24.6 μg/mL for leaf and bark, respectively	Not specified	[29]
20	*Caesalpinia bonduc* (L.) Roxb. (Fabaceae)	Fever nut/ leaf, twigs	Petroleum ether, EtOAc and H_2O fractions from EtOH extract exhibited moderate cytotoxic activity against HeLa cells	Flavonoids	[51]
21	*Cajanus cajan* Millsp. (Fabaceae)	Pigeon pea/ leaf	MeOH extract was most active on human cancer cell lines: breast adenocarcinoma (MCF-7), large cell lung carcinoma (COR-L23) and amelanotic melanoma (C-32). DCM fraction was most active (IC_{50} 5-10 μg/mL)	Stilbenes (longistylins A and C, IC_{50} 0.7-14.7 μM)	[29]
22	*Calliandra portoricensis* (Jacq.) Benth (Fabaceae)	Snowflake acacia/ root	DCM fraction exhibited 6-fold activity of cyclophosphamide on Rhabdomyosarcoma cell line. MeOH extract exerted cytotoxicity on prostatic LNCaP, DU-145, lung adenocarcinoma and healthy VERO cells (IC_{50} 2.4, 3.3, 3.6, 17.9 μg/mL, respectively). Also, a 3-fold decreased expression of anti-apoptotic BCL-2 and a 4-fold increase in pro-apoptotic Bax levels at 10 μg/mL in LNCaP cells.	Neurolenin B, nigrosporolide and trans-geranic acid. Polyphenols (gallic acid and afzechelin)	[52] [53]
23	*Calliandra surinamensis* Benth. (Fabaceae)	Surinam powderpuff/ Stem bark	MeOH extract active on human lung adenocarcinoma epithelial (A549) cancer cell lines IC_{50} 106.35 μg/mL,)	xanthone glycoside	[54]
24	*Calophyllum inophyllum* L. (Callophyllaceae)	Beach calophyllum/ Stem bark	Aqueous MeOH (LC_{50} 56.22 μg/mL) and *n*-hexane (LC_{50} 183.55 μg/mL) extracts showed brine shrimp cytotoxicity	Stigmasta-5, 22-dien-3-*O*-β-D-glucoside, macluraxanthone, 1,5-dihydroxyxanthone	[55]
25	*Carica papaya* L. (Caricaceae)	Pawpaw / leaf	AQ extract inhibited root growth of onion bulb (cytotoxic, EC_{50} 0.8%). Mitodepressive effect on cell division and induction of mitotic spindle disturbance	Phytosterols (campesterol, stigmasterol, β-sitosterol)	[45, 56]
26	*Cascabela thevetia* (L.) Lippold (Apocynaceae)	Yellow oleander/ root bark	Optimal GI at 24h: $CHCL_3$ fraction = EtOAc (69%), and AQ fraction = MeOH extract (59%). Tadpole cytotoxicity was LC_{50} 5.3-6.4 mg/mL: EtOAc fraction > AQ fraction > MeOH extract. .	Flavonoids and thevefolin	[57, 58]
27	*Ceiba pentandra* (L.) Gaertn. (Malvaceae)	Kapok tree/ Leaf	GI of guinea corn root radicle at 5 mg/mL in 24h (most active AQ fraction gave GI 86% in 24h. At 48h, inhibition was MeOH extract > AQ fraction = $CHCL_3$ fraction > EtOAc fraction (89-69%). Tadpole cytotoxicity: LC_{50} 4.8-6.0 mg/mL, EtOAc fraction > MeOH extract > $CHCL_3$ fraction > AQ fraction)	3-β-taraxerol, 3-β-taraxerol acetate, all-trans-squalene, β-amyrin	[57, 61]
28	*Celosia trigyna* L. (Amaranthaceae)	Woolflower/ Whole plant	EtOH extract active (GI > 50% at 500 μg/mL) on the HeLa (cervical adenocarcinoma cancer) cell line.	Tetrahydroisoquinoline derivative, 2,3-dimethylheptadecane, 3-octadecane	[62, 63]
29	*Chenopodium*	Mexican tea/ herb	Essential oil showed low cytotoxicity	Ascaridole	[64, 65]

	ambrosioides L. var *anthelminticum* (L.) A. Gray (Chenopodiaceae)		against bovine erythrocytes (haemagglutination titre 9.16)		
30	*Chromolaena odorata* (L.) R. M. King & H. Rob (Asteraceae)	Siam weed/ leaf	Brine shrimp cytotoxicity (LC_{50} 324 and 392 ppm for AQ and EtOH extracts, respectively)	Kaempferide (a flavonoid)	[29, 66]
31	*Citrus aurantium* L. (Rutaceae)	Bitter orange/ Stem bark	DCM fraction showed significant cytotoxicity, with its highest activity against lung (A549) cancer cells (IC_{50} 3.88 μg/mL), and the least activity on liver (HepG2) cells (IC_{50} 5.73 μg/mL). Isolated compounds gave IC_{50} 12.65-50.74 μM.	Acridone alkaloids: citrusinine-I, citracridone-I, 5-hydroxynoracronycine, natsucitrine-I, glycofolinine, citracridone-III.	[67]
32	*Cnidoscolus acontifolius* (Mill.) Johnst (Euphorbiaceae)	Tree Spanish/ leaf	MeOH extract at 100 μg/mL inhibited growth of lung (NCI-H460) and breast (MCF-7) cancer cell lines. Active $CHCL_3$ fraction gave GI_{50}, TGI_{50} and LC_{50} of 22.5, 43.75 and 68.75 μg/mL, respectively against breast cancers and GI_{50} and TGI_{50} of 35.4 and 55.8 μg/mL, respectively against lung cancer cells.	Longipinane, longiverbanone, caryophyllene oxide	[68, 69]
33	*Combretum paniculatum* Vent. (Combretaceae)	Burning bush/ Leaf	Active against HT-29 (colon), MCF-7 (breast) and HeLa (cervix adenocarcinoma) cancer cell lines (GI > 50% at 500 µg/mL)	Pheophorbide A, pheophorbide A methylester	[70]
34	*Commiphora africana* (A. Rich.) Engl. (Burseraceae)	African myrrh/ Stem bark	MeOH extract active against human cancer cell lines	Resveratrol derivatives: (*E*)-resveratrol 3-*O*-rutinoside (showed highest anti-proliferative effect, with IC_{50} 16.80, 21.74, 17.89 and 17.44 μM, against MCF-7, A-549, PC-3 and HepG2 human cancer cell lines, respectively). 5-Methoxy-(*E*)-resveratrol 3-*O*-rutinoside, pinostilbene and 3-hydroxy-5-methoxy benzoic acid	[71]
35	*Conyza sumatrensis* Retz. (Asteraceae)	Broad-leaved fleebane /leaf	AQ and $CHCL_3$ fractions of MeOH extract active against breast (MCF-7), lung cancer (NCI-H460), mouse embryonic fibroblast normal cell line (NIH3T3). Extract (250 µg/mL) and $CHCL_3$ fraction (100 µg/mL) active against breast (MCF-7) and lung (NCI-H460) cancer cells	Stigmasterol 3-*O*-β-glucoside, 2,3-dihydroxypropyl hexacoanoate	[42, 72]
36	*Corchorus olitorius* L. (Malvaceae)	Nalita jute/ leaf	Bioactive compounds from MeOH extract at up to 1.6 mM gave mild cytotoxic activity against HeLa cells at ⩾800 μM.	Polyphenolic compounds-Methyl-1,4,5-tri-*O*-caffeoyl quinate and trans-3-(4-hydroxy-3-methoxyphenyl) acrylic anhydride. The latter compound was found to be related to curcumin, known to have anti-cancer activity.	[73]
37	*Cyathula achyranthoides* (Kunth.) Moq. (Amaranthaceae)	Cadillo/ Whole plant	EtOH extract active (GI 40-50% at 500 μg/mL) on the HeLa (cervical adenocarcinoma cancer) cell line.	Not specified	[62]
38	*Cyathula prostata*. (L.) Blume (Amaranthaceae)	Rat's burgrass/ whole plant	MeOH extract (100 mg/ kg) increased survival period of mice induced with Dalton's lymphoma ascites cells, decreased the body weight and also altered many hematological markers and also restored the antioxidant enzymes	Pheophorbide A (more toxic), pheophorbide A-methyl ester	[74]
39	*Cymbopogon citratus* (DC.) Stapf. (Poaceae)	Lemongrass/ leaf	Inhibition of onion root growth by the AQ extracts with mitodepressive effects on cell division and induced mitotic spindle disturbance	Citral	[29, 45]
40	*Cyperus articulatus* L. (Cyperaceae)	Jointed flatsedge/ Rhizome	Essential oils loaded Chitosan nano particles more cytotoxic against MDA-MB-231 breast cancer cells after 48 h	nootkatone, 6-methyl-3,5-heptadien-2-one, retinene, nopinone, cycloeucalenol, anozol, toosendanin, furanone, ethanone and vitamin A	[75]
41	*Delonix regia* (Boj. ex Hook) Raf. (Fabaceae)	Flame tree/ stem bark	$CHCL_3$ fraction of MeOH extract most active in inhibiting growth of guinea corn root radicle (GI 95.3%). Tadpole cytotoxicity: most active $CHCL_3$ fraction	Lupeol, epilupeol, β-sitosterol, p-methoxy benzaldehyde	[76, 77]

			(LC_{50}, 6.0 mg/mL).		
42	*Detarium microcarpum* Guill. & Perr. (Fabaceae)	Sweet detar/ stem bark	MeOH and AQ extracts active against breast (MCF-7) cancer cells.	syringin, serpyllin, alpinumisoflavone, procyanidin B3 and gallic acid	[60]
43	*Drymaria cordata* (L.) Willd. (Caryophyllaceae)	Chickweed/ Whole plant	EtOH extracts active (GI < 50% at 500 µg/mL) on the HeLa (cervical adenocarcinoma cancer) cell line	Stigmasteryl glucoside	[62, 78]
44	*Elaeophorbia drupifera* (Thonn) Stapf (Euphorbiaceae)	Jordan's jungle/ leaf	Active on lung, colon and lympnocytic leukaemia system (P-388)	Lupeol	[79, 80]
45	*Enterolobium cyclocarpum* (Jacq.) Griseb. (Fabaceae)	Monkey-ear tree/ Leaf	MeOH extract cytotoxic (IC_{50} 2.07 and 11.84 μg/mL for HeLa and MCF-7, respectively)	Not specified	[81]
46	*Erythrophleum suaveolens* (Guill. & Perr.) Brenan (Fabaceae)	Forest ordeal tree/ Leaf	EtOH extract was toxic to brine shrimps and caused chromosomal damage in rat lymphocytes. MeOH extract was potent against five human carcinoma cell lines (IC_{50} 0.2-1.3 μg/mL), GI of breast carcinoma (BT-549), (breast carcinoma (BT-20) and prostate adenocarcinoma (PC-3) cell lines = 100%	Not specified	[29, 37]
47	*Eugenia uniflora* L. (Myrtaceae)	Pitanga/ leaf	EtOH extract active against human prostate (DU-145), breast (JIMT-1), and pancreatic (BxPC-3) cancer cell lines	Not specified	[82]
48	*Euphorbia deigtonii* Croizat (Euphorbiaceae)	Leper's burton	Active on sarcoma, squamosal, and P388	Not specified	[79]
49	*Euphorbia desmondi* Keay & Milne-Redh. (Euphorbiaceae)	CN/-	Active on melanoma, colon, P-388AQ and $CHCL_3$ fractions of MeOH extract active against MCF-7, lung cancer (NCI-H460), mouse embryonic fibroblast normal cell line (NIH3T3)	Not specified	[79]
50	*Euphorbia graminea* Jacq. (Euphorbiaceae)	CN/-		Diterpenoid (abietane-11,23-diene-16-oic-14-ones)	[83]
51	*Fagara zanthoxyloides* Lam. (Rutaceae)	Senegal prickly-ash / root bark	IC_{50} 25-44 μg/mL for androgen-dependent (PC-3, DU-145) and androgen independent (LNCap) cancer cells	Fagaronine	[29]
52	*Ficus coronata* Spin. (Moraceae)	Sandpaper fig/ leaf	GI of guinea corn root radicle: $CHCL_3$ fraction > MeOH extract > AQ fraction. $CHCL_3$ fraction tadpole cytotoxicity: LC_{50}, 6.5 mg/mL	Phenols and flavonoids	[84]
53	*Garcinia kola* Heckel (Clusiaceae)	Bitter kola/ root	EtOH extract active in brine shrimp lethality test, inhibition of telomerase activity and induction of chromosomal aberrations *in vivo* in rat lymphocytes.	Not specified	[37]
		stem bark	In the Allium test, extract produced significant decreases in root growth and also significant cytotoxicity as evidenced by decreased mitotic index		[85]
54	*Gliricidia sepium* (Jacq.) Kunth ex Walp. (Fabaceae)	Quick stick/ stem bark	MeOH extract (GI of guinea corn root radicle: 61-81% at 24-72 h) and AQ fraction (71-79.8%., LC_{50}, 6.8 mg/mL, on tadploes).	Phenols and flavonoids	[88]
55	*Globimetula braunii* (Engl.) Van Tiegh (Loranthaceae)	Maloney/ leaf	EtOH extract (80%) active against human prostate (DU-145), breast (JIMT-1) and pancreatic (MiaPaCa-2/ BxPC-3). (CC_{50} 105.1 μg/mL) against breast cancer cells. EtOAc fraction was most active on pancreatic cancer cell lines (CC_{50} 70.4 μg/mL)	Triterpenoid esters (globrauneines)	[89, 90]
56	*Gongronema latifolium* Benth. (Asclepiadaceae)	Bush buck/ Leaf	MeOH (80%) active against human leukemia HL-60 cells and gave apoptotic response. Cytotoxic against human cancer cell lines: myeloid leukemia HL-60, hepatocellular carcinoma, lung carcinoma, breast adenocarcinoma and colon.	A new pregnane glycoside: iloneoside (3-*O*-[6-deoxy-3-*O*-methyl-β-D-allopyranosyl-(1→14)-β-D-oleandropyranosyl]-11,12-di-*O*-tigloyl-17β-marsdenin)	[86, 87]
57	*Guiera senegalensis* J. F. Gmel. (Combretaceae)	Moshi medicine	MeOH and AQ extracts active against breast (MCF-7) cancer cells.	Isorhamnetin and eupatorin	[60]

58	*Heliconia psittacorum* L. f. (Heliconiaceae)	Heliconia/ leaf	GI of guinea corn root radicle at 48 and 72h: (MeOH extract > AQ fraction > $CHCL_3$ fraction). $CHCL_3$ fraction was most cytotoxic against tadpole (LC_{50}, 5.0 mg/mL)	Phenols and flavonoids	[84]
59	*Hymenocardia acida* Tul. (Phyllanthaceae)	Heart-fruit/ stem bark	$CHCL_3$ fraction of MeOH extract (GI 78-90% on guinea corn root radcle) was most potent. AQ and EtOAc fractions showed similar tadpole cytotoxicity (LC_{50}, 4.1-4.3 mg/mL). EtOH extract was toxic to brine shrimps and caused chromosomal damage in rat lymphocytes.	Hymenocardine	[37, 88]
60	*Hyptis suaveolens* L. (Lamiaceae)	CN /leaf volatile oil	Cytotoxic on human breast (AU 565) and cervical (HeLa) cancers at 50 μg/mL by MTT assay with 86.74% and 21.8% inhibitions, respectively. Tadpole mortality (LC_{50} 8 µg/mL) and brine shrimp mortalities ((LC_{50} 188.67 μg/mL))	Sabinene (10.64%), (-)-4-terpineol (7.27%)	[91]
61	*Icacina trichantha* Oliv (Icacinaceae)	CN-/tuber	Cytotoxic on human melanoma (MDA-MB-435) cancer cells (IC_{50} 0.66-6.44 μM) for pimaranes, and IC_{50} 3.00-4.94 μM on HT-29 cells for norpimaranes	Three (9βH)-pimaranes and two (9βH)-17-norpimaranes	[92]
62	*Ipomoea batatas* (L.) Lam (Convulvulaceae)	Sweet potato /peel	n-Hexane fraction of EtOH extract showed the most promising anticancer activity (IC_{50} 24.75, 47.91, 52.37, 34.17, 46.07, and 25.89 μg/mL against breast, colon-1, colon-2, ovary, lung, and head/neck cancer cell lines, respectively).	Glucocerebroside	[93]
63	*Jatropha curcas* L. (Euphorbiaceae)	Physic nut/ root	Extracts (hexane and EtOAc) were highly active against L5178y mouse lymphoma cells and HeLa human cervix carcinoma cells. EtOH extracts showed dose-dependent inhibition (IC_{50} 23-38 μg/mL) of human epithelial breast (MCF-7) cancer cells Light petroleum ether fraction of MeOH (80%) extract gave IC_{50} 159 μg/mL against human lung adenocarcinoma (A-549) cancer cell line	Diterpenoids (curcusone C, curcusone D, multidione, 15-epi-4*Z*-jatrogrossidentadion, 4*Z*-jatrogrossidentadion, 4*E*-jatrogrossidentadion, 2-hydroxyisojatrogrossidion, and 2-*epi*-hydroxyiso jatrogrossidion)	[29, 94]
64	*Jatropha gossypiifolia* L (Euphorbiaceae)	Bellyache bush/ Root bark	-	Lathyrane diterpenoid, abiodone	[95]
65	*Khaya senegalensis* (Desr) A. Juss. (Meliaceae)	African mahogany	extract was mitotoxic in liver (HepG2) cell lines	Limonoid (3α, 7α-dideacetylkhivorin)	[29, 96]
66	*Kigelia pinnata* (Lam.) Benth. (Bignoniaceae)	Sausage tree/ Leaf	cytotoxicity on rhabdomyosarcoma cell line	3-Hydro-4,8-phytene showed lower cytotoxicity (rhabdomyosarcoma) potential (IC_{50} 171.7 *ng*/mL). (9*Z*, 12*Z*)-methyl octadeca-9,12-dienoate (IC_{50} 153.3 *ng*/mL) from EtOAc extract was highly cytotoxic	[97]
67	*Landolphia dulcis* (R. Br.) Pichon (Apocynaceae)	Sabine	MeOH extract gave GI 83-91% at 20 µg/mL against breast carcinoma (BT-549) cell line	Not specified	[29]
58	*Larportea aestuans* (L.) Chew. (Urticaceae)	West Indian wood nettle/ whole plant	EtOH extract active against human prostate (DU-145), breast (JIMT-1), and pancreatic (BxPC-3) cancer cell lines	Not specified	[82]
69	*Lippia multiflora* Moldenke (Verbenaceae)	Tea bush/ bark	MeOH extract gave brine shrimp cytotoxicity (LC_{50} 1.1 μg/mL).	Not specified	[98]
70	*Lophira alata* Banks & Gaertn. (Ochnaceae)	Red ironwood tree/ Stem bark	MeOH extract (0.1 μg/mL) significantly reduced the viability of Ehrlich ascites carcinoma cells	Flavonoids (lophirones B and C). Azobechalcone A and isolophirachalcone	[29]
71	*Macaranga barteri* Mull. Arg. (Euphorbiaceae)	Good leaf for nanny-goats/ Leaf	EtOAc fraction exhibited 4-fold activity of cyclophosphamide on Rhabdomyosarcoma (RD) cell line. Anti-proliferative activity against human cancer cell lines	3,5 dicaffeoylquinic acid, acteoside, kampferol-7-*O*-glucoside and bastadin 11. Stilbenes: macabartebenes A-C (1-3, IC_{50} 0.60-0.79 μM). Prenylated stilbenes: vedelianin (IC_{50} 0.32-0.54 μM), schweinfurthin G, and mappain. Prenylated flavonols: 8-prenyl	[52, 99]

				kaempferol, and broussoflavonol F, and the geranylated flavonol, isomacarangin	
72	*Mangifera indica* L. (Anacardiaceae)	Mango/ stem bark	Inhibition of onion root growth by the AQ extracts with mitodepressive effects on cell division and induced mitotic spindle disturbance	Polyphenolics	[45]
73	*Markhamia tomentosa* (Benth) K. Schum ex. Engl. (Bignoniaceae)	Sour sweat-sugary plant/ Leaf-derived fungi	MeOH extract of endophytic fungal strain, *Syncephalastrum racemosum* showed anti-proliferative effect on HeLa cancer cell line (IC_{50} 43.56 μg/mL)	Mollic acid	[100]
74	*Massularia acuminata* (G. Don) Bullock ex Hoyl. (Rubiaceae)	"Pako Ijebu" chewing stick/ stem bark	EtOH extract active against human prostate (DU-145), breast (JIMT-1), and pancreatic (BxPC-3) cancer cell lines.	Acuminatoside [4-(3', 3'-dihydroxy-1-mercaptopropyl)-phenyl glucosylpyranoside]	[82] [89]
		Leaf, stem and root	EtOH (80%) extract active on human prostate (DU-145), leaf extract being most active (CC_{50}, ≥ 135.05 μg/mL)	acuminatoside (75.28% reduction in viable cancer cells at 250 μg/mL)	
75	*Melastomastrum capitatum* Fern. (Melastomataceae)	CN-/ leaf	EtOAc fraction of MeOH extract was active on breast (MCF-7), ovarian (OV-7) and woman vagina melanoma (HMVII) cancer cells	Saturated fatty acid esters and phthalate acid derivatives	[101]
76	*Morinda lucida* Benth (Rubiaceae)	Brimstone tree /stem bark	Brine shrimp cytotoxicity at LC_{50} 2.6 μg/mL	Not specified	[98]
		Leaf	MeOH extract was most active on human cancer cell lines: breast adenocarcinoma (MCF-7), large cell lung carcinoma (COR-L23) and amelanotic melanoma (C-32). (IC_{50} < 50 μg/mL)	Not specified	[29]
		Root bark	EtOH extract active in brine shrimp lethality test, inhibition of telomerase activity and induction of chromosomal aberrations *in vivo* in rat lymphocytes Inhibition of anti-apoptotic BCL-XL, BCL-2, and MCL-1).	Not specified	[37]
			Inhibition of onion root growth by the AQ extracts with mitodepressive effects on cell division and induced mitotic spindle disturbance	Triterpenes (ursolic acid and oleanolic acid) and phytosterols (cycloartenol, campesterol, stigmasterol, and β-sitosterol) have higher binding affinities for anti-apoptotic B cell lymphoma 2 (BCL-2) proteins	[45, 102]
77	*Moringa oleifera* Lam. (Moringaceae)	Horse-raddish tree/ Leaf	EtOH extract (0.2 mL of 100 mg/mL, i.v) gave antileukemic activities on benzene-induced leukemic rats	Ten phenolic compounds (including quercetin)	[103]
78	*Nymphaea lotus* L. (Nymphaeaceae)	White Egyptian lotus/ Whole plant	MeOH extract was most active on human cancer cell lines: breast adenocarcinoma (MCF-7 and large cell lung carcinoma (COR-L23) (IC_{50} 0.38 and 0.47 μg/mL, respectively). EtOH extract active in brine shrimp lethality test, inhibition of telomerase activity and induction of chromosomal aberrations *in vivo* in rat lymphocytes.	Not specified	[29, 37]
79	*Ocimum gratissimum* L (Lamiaceae)	Mosquito plant/ leaf	EC_{50} 2.46-3.47 μg/mL against human cancer cell lines: breast carcinoma (MCF-7). lung carcinoma (A-549), colon adenocarcinoma (HT-29), renal carcinoma (PC), pancreatic carcinoma (PACA-2)	Oleanolic acid	[29]
80	*Olax subscorpioidea* Oliv. (Olacaceae)	CN-/ root	In the *Allium* test, extract produced significant decreases in root growth and also significant cytotoxicity as evidenced by decreased mitotic index.	Not specified	[85]
81	*Oncoba spinosa* Forssk. (Salicaceae)	Fried egg tree/ Leaf	*n*-Hexane fraction of MeOH (95%) extract showed brine shrimp cytotoxicity (LC_{50} < 1000 μg/mL)	Flacourtin (3-hydroxy-4-hydroxymethylphenyl-6-*O*-benzoyl-β-d-glucopyranoside)	[104]
82	*Parkia biglobosa* (Jacq.) Benth. (Fabaceae)	African locust bean/ stem bark Seed	Pet-ether fraction was cytotoxic to human lung cancer (SK-MES 1) cells AQ extract was cytotoxic to Hep-G2 (IC_{50} 1.3 mg/mL) and HeLa (IC_{50} 0.6 mg/mL) cells	Not specified	[32] [105]
83	*Parquetina nigrescens* (Afzel)	Bullock/ leaf	MeOH extract inhibited growth of lung cancer cells at 100 μg/ml. DCM fraction	Not specified	[106]

	Bullock (Apocynaceae)		cytotoxicity at 50 µg/ml: (GI_{50} 14, TGI_{50} 30 and LC_{50} 45 µg/mL).		
84	*Pentaclethra macrophylla* Benth. (Fabaceae)	African oil bean/ Leaf, stem bark seed, fruit pericarp	Fruit pericarp > stem bark > seed > leaf (haemagglutination titre 71.4, 25.6, 5.3, 0.5) for the AQ extract	Not specified	[107]
85	*Persea americana* Mill (Lauraceae)	Avocado pear/ leaf, stem and root barks	GI of guinea corn root radicle: AQ fraction > $CHCL_3$ fraction (100% inhibition at 20 mg/ mL).	Triterpenids	[108]
		Root bark	MeOH extract (10 µg/mL) gave antiproliferative activity against breast (MCF-7) cancer cell lines		[109]
		Leaf and seed	AQ fraction of MeOH extract more active than $CHCL_3$ fraction, and inhibited growth of guinea corn root radicle at 20 mg/mL		[110]
		Leaf	Tadpole cytotoxicity of $CHCL_3$ fraction: Isolated compound > VLC faction 4 > VLC fraction 5 (LC_{50} 3.33, 4.67, 18.0 µg/mL)		[111]
86	*Picralima nitida* Stapf Th.& H. Dur. (Apocynaceae)	Run-run	Increased β1-integrin expression and strengthened the cortical actin cytoskeleton.	Not specified	[29]
87	*Piliostigma thonningii* (Schum.) Milne-Redh. (Fabaceae)	Camel’s foot tree/ stem bark	MeOH extract, $CHCL_3$ and AQ fractions at 0.25-5.0 mg/mL inhibited growth of guinea corn root radicle. AQ fraction was most active (GI 62.6% at 5 mg/mL in 72h.).Tadpole cytotoxicity: most active $CHCL_3$ fraction (LC_{50}, 5.0 mg/mL)	Not specified	[76]
88	*Piper guineense* Schum. (Piperaceae)	Ashanti pepper/ Leaf	Cytotoxic against human cancer cell lines: myeloid leukemia (HL-60), hepatocellular carcinoma, lung carcinoma, breast adenocarcinoma and colon.	Not specified	[87]
89	*Pseudocedrela kotschyii* (Schweinf.) Harms (Meliaceae)	Dry zone cedar/ root	IC_{50} 12-20 µg/mL for PC-3, DU-145 and LNCap cells	Limonoid (7-deacetoxy-7-oxogedunin)	[29]
90	*Pycnanthus angolensis* (Welw.) Warb. (Myristicaceae)	African nutmeg/ leaf	MeOH extract was active on human cancer cell lines: breast adenocarcinoma (MCF-7), large cell lung carcinoma (COR-L23) and amelanotic melanoma (C-32).	Isoflavones (irilone, tectorigenine, formononetin, genistein, 2’ hydroxybiochanin) and flavanone (liguiritigentin)	[29]
91	*Pyrenacantha staudtii* (Engl.) Engl. (Icacinaceae)	CN-	EtOH extract active on human epithelial breast (MCF-7) cancer cells	Not specified	[29]
92	*Raphia hookeri* G. Mann. & H. Wendl. (Arecaceae)	Ivory Coast raffia palm/ fruit	n-BuOH fraction exhibited greater cytotoxicity than the AQ fraction against brine shrimps, and tadpoles (LC_{50} 0.83 ppm)	Not specified	[112]
93	*Ricinodendron heudelotii* (Baill.) Pierre (Euphorbiaceae)	African wood-oil nut tree/ Leaf	EtOAc fraction of EtOH extract was active on HL-60, SMMC-7721, A-549, MCF-7, SW-480, and normal lung epithelial (BEAS-2B) cell lines	gallic acid, gallic acid ethyl ester, corilagin, quercetin-3-*O*-rhamnoside, myricetin-3-*O*-rhamnoside, 1,4,6-tri-*O*-galloyl glucose, 3,4,6-tri-*O*-galloyl glucose, 1,2,6-tri-*O*-galloyl glucose, and 4,6-di-*O*-galloyl glucose. Corilagin was most cytotoxic (IC_{50} 33.18 µg/mL against MCF-7 cells)	[113]
94	*Rutidea parviflora* DC. (Rubiaceae)	CN-/ Stem bark	AQ extract and n-BuOH fraction showed cytotoxicity (IC_{50} < 10 µg/mL) and induction of apoptosis in human ovarian cancer cells (OVCAR-4, OVCAR-8, A2780 and cisplatin resistant A2780)	Palmatine (IC_{50} 5.5-7.9 µM)	[114]
95	*Sapium ellipticum* (Krauss.) Pax. (Euphorbiaceae)	Jumping seed tree/ leaf	EtOH extracts active (GI > 50% at 500 µg/mL) on the HeLa (cervical adenocarcinoma cancer) cell line.	Not specified	[62]
96	*Sarcocephalus latifolius* (J. E. Smith) E. A. Bruce (Rubiaceae),	African peach/ Leaf and root bark	MeOH extract (leaf and root bark at 400 µg/mL gave tadpole mortality of 33.30% and 100%, respectively in 24h.). Both samples were equipotent on guinea corn root radicle (GI 95-98.6%) at 30 mg/mL in 24h.	Not specified	[115]
97	*Securidaca*	Rhodes’s violet/ root	AQ extract showed *in vitro* activity	Bis (2-ethylhexyl) phthalate	[116, 117]

	longepedunculata Fres. (Polygalaceae)	bark	against Ehrlich Ascites carcinoma cells (IC_{50} 67 μg/mL), and *in vivo* activity (i.p) (decrease in angiogenesis and volume of ascitic fluid) in mice. EtOH extract active against brain tumour (U-87) cell line (IC_{50} 20.53 μg/mL)		
98	*Securinega virosa* (Roxb. Ex. Willd) Baill (Euphorbiaceae).	Common bush weed/ leaf and root bark	MeOH extract of leaf and root bark gave 100% and 56.7% tadpole mortality, respectively at 400 μg/mL in 24h.	Virosecurinine and viroallosecurinine	[118]
99	*Senna nigricans* Vahl (Fabaceae)	CN-/ Leaf	Brine shrimp cytotoxicity (LC_{50} 42.77 μg/mL) of EtOAC extract	Emodin	[59]
100	*Senna siamea* (Lam.) Irwin et Barneby (Fabaceae)	Siamese tree	MeOH and AQ extracts active against breast (MCF-7) cancer cells.	Serpyllin, friedelin, emodin, cassiamin B	[29, 60]
101	*Setaria megaphylla* (Steud.) T. Dur. & Schinz. (Poaceae)	Broad-leaved bristle grass/ leaf	*n*-Hexane fraction active against HeLa cancer cells (GI 28.8, TGI 44.3 μg/ mL)	Not specified	[29]
102	*Sida acuta* F. (Malvaceae)	Common wireweed	MeOH extract gave GI 83-91% at 20 µg/mL against breast carcinoma (BT-549) cell line	Not specified	[29]
103	*Solanum erianthum* D. Don (Solanaceae)	Potato tree/ Leaf	Volatile oil demonstrated potent inhibitory activity against Hs 578T and PC-3 human breast, and prostate tumor cells respectively.	α-terpinolene, *p*-cymene, β-pinene, α-phellandrene	[29]
104	*Spondias mombin* Linn (Anacardiaceae)	Spanish plum/ Leaf	MeOH (80%) extract active on oral cancer (KB), cervical cancer (C-33A), breast cancer (MCF-7) and lung cancer (A-549) cell lines. DCM fraction gave best antiproliferative activity.		[119]
			Essential oil from fresh leaf was more active than dried sample (LC_{50} from brine shrimp lethality assay: 0.01 and 4.78 μg/mL, respectively)	Monoterpenoids, sesquiterpenoids and non-terpenoids derivatives. Principal components were β-caryophellene (27.9-30.9%) and γ-cadinene (9.7-12.3%)	[120]
		Stem bark	$CHCL_3$ fraction (GI 61.5-83.3%) and EtOAc fraction (65.7-71.7%) showed activity on guinea corn root radicle at 5 mg/mL. Tadpole cytotoxicity: $CHCL_3$ fraction (100% mortality at 20 mg/mL, LC_{50} 5.1 mg/mL) equivalent to chloramphenicol positive control tested at 0.5 mg/mL.		[121]
105	*Spondiathus preussii* Engl. & Pax. (Euphorbiaceae)	Preuss strophanthus/ Stem bark	Active on melanoma. EtOH extract toxic to brine shrimps and caused chromosomal damage in rat lymphocytes.	3-β-Hydroxy-20 (29)-lupen-28-oic acid (ED_{50} 24 mg/mL)	[37, 79]
106	*Struchium sparganophora* (Linn) O. Ktze (Asteraceae)	Bush bitter leaf/ Leaf	MeOH extract, $CHCL_3$ and aqueous fractions gave 47.81, 32.51 and 43.81% inhibitions of guinea corn root radicle. LC_{50} on tadpoles (26, 6.25 and 5 μg/mL, respectively)	Vernodalin showed cytotoxic activity on the melanoma and ovarian cancer cell lines, while the conjugated 3 methyl, 2, 6 hexacosedienol and luteolin caused cell death after 48h reculture	[122, 123]
107	*Terminalia avicennioides* Guill et Perr. (Combretaceae)	Crocodile's ear	AQ extract showed anti-proliferative activity on Ehrlich ascites carcinoma cell lines	Not specified	[29]
108	*Tapinanthus bangwensis* (Engl. & K. Krause) Danser (Loranthaceae)	African mistletoe/ leaf	EtOH extract (80%) active against human prostate (DU-145), breast (JIMT-1) and pancreatic (MiaPaCa-2/ BxPC-3).	Not specified	[89]
109	*Tapinanthus globiferus* (A. Rich) van Tiegh (Loranthaceae)	Eastern Nigeria mistletoe	EtOH extract (80%) active against human prostate (DU-145), breast (JIMT-1) and pancreatic (MiaPaCa-2/ BxPC-3).	Not specified	[89]
110	*Tetrapleura tetraptera* (Schum & Thonn.) Taub. (Fabaceae)	Aridan/ fruit	MeOH extract gave GI 66% at 20 μg/mL against breast carcinoma (BT-549) cell line	Tetraterpenoid glucopyranosides	[2, 29]
111	*Turraea vogelii* Hook. f. ex. Benth. (Meliaceae)	CN-/Leaf, stem	$CHCL_3$ leaf extract cytotoxic against myelogenous leukemia cell K-562 (IC_{50} 14.27 μg/mL), while $CHCL_3$, EtOAc and MeOH stem extracts also active (IC_{50} 19.50, 24.10, 85.40 μg/mL respectively)	$CHCL_3$ leaf: triterpenoids-oleana-12,15,20-trien-3β-ol, and oleana-11,13-dien-3β,16α, 28-triol, and six fatty esters. Stem: Tetradecane and four fatty acids: hexadecanoic acid, tetradecanoi acid,	[124]

				(*Z*)-9-eicosenoic acid, and ethyl tetradec-7-enoate. EtOAc: 1,2,3-propanetriyl tris (heptadecanoate, (*Z*)-9-octadecenoic acid, (*Z*)-7-tetradecenoic acid. MeOH stem: (*Z*)-5-pentadecenoic acid.	
112	*Uvaria chamae* P. Beauv (Annonaceae)	Bush banana/ root	In the *Allium* test, extract produced significant decreases in root growth and also significant cytotoxicity as evidenced by decreased mitotic index.	c-benzylflavanones (uvaretin, isouvaretin)	[85]
		leaf	Oral administration of MeOH extract to mice showed dose-dependent cytotoxicity. At 750 mg/kg, mitotic index was less than that of cyclophosphamide control, chromosomal aberration was greater than control (genotoxic activity).		[102]
113	*Vernonia amygdalina* Del. (Asteraceae)	Bitter leaf / leaf	Active fraction (100 μg/mL) of EtOH extract inhibited DNA synthesis on human breast cancer (MCF-7) cell line (GI 97%).	Steroid glucosides	[29]
			MeOH extract cytotoxic on skin melanoma (HT-144) cell line (GI 86 μg/mL)		[125]
			Different concentrations (10, 100 and 1000 μg/mL) inhibited BT-549 growth by 14, 22 and 50%, respectively.	Sesquiterpene lactone (epivernodalol, GI 1.73 μg/mL) mechanism due to inhibition of DNA synthesis and cell proliferation	[29]
			DCM extract showed cytotoxic activity against human cancer cell lines: myeloid leukemia (HL-60), hepatocellular carcinoma, lung carcinoma, breast adenocarcinoma and colon (IC_{50} 5.85-8.84 μg/mL)		[87]
114	*Waltheria indica* L. (Malvaceae)	Sleepy morning/ leaf	AQ extract gave GI 100% of guinea corn root radicle at 1 mg/mL.	Not specified	[85]
115	*Xylopia aethiopica* (Dunal.) A. Rich (Annonaceae)	Ethiopian pepper/ fruit	Essential oil was cytotoxic on carcinoma cells (Hep-2 cell line) at 5 mg/mL	3,4',5-trihydroxy-6",6"-dimethylpyrano {2,3-g} flavone, and an alkaloid (isotetrandrine)	[126]
		Fruit	Pet ether fraction showed greatest activity (GI 37.2%) at 75 μg/mL against JIMT-1		[82]
116	*Zingiber officinale* Roscoe (Zingiberaceae)	Ginger/ rhizome volatile oil	Cytotoxic on human breast (AU 565) and cervical (HeLa) cancers at 50 μg/mL by MTT assay with 43% and 50% inhibitions, respectively. Tadpole mortality (LC_{50}, 8 μg/mL) and brine shrimp mortalities (LC_{50}, 157.75 μg/mL)	α-Citral (11.68%), β-citral (10.18%)	[127]

Morinda lucida (3.28%), *Vernonia amygdalina* (2.63%) and *Persea americana* (2.63%) (Table 1) were the most researched plant species. Antiproliferative activities were reported for the leaf, root bark and stem bark of *Morinda lucida*, plus an *in-silico* study [102] to unravel potent bioactive compounds. Most of the investigation on *Vernonia amygdalina* focused on human cell lines leading to the isolation of potent steroid glycosides [29]. All studies except one in the case of *Persea americana* were preliminary and the cytotoxic principles were identified as triterpenes [109, 111].

In the Nigerian cancer research, the *in vitro* model using various cancer cell lines is often the preferred methodology (97.34%) (Table 1). Nonetheless, the uncommon *in vivo* model has been extended to *Morinda lucida*, *Cyathula prostata*, *Moringa oleifera* and *Uvaria chamae* using mice or rats. Furthermore, it is noteworthy that remarkable progress has been recorded in anticancer research in Nigeria with extracts of 72.56% of the plants in Table 1 fully characterized for bioactive compounds. Out of the 27 frequently occurring plants documented in Nigerian anticancer ethnobotanical surveys, only 15 (55.55%) have been scientifically validated.

6. Current clinical trials of useful cytotoxic compounds

A substantial number of chemical moieties of plant origin are currently at various stages of clinical trials according to the review of Osafo *et al* [129]. The authors have documented progress of clinical trials of ten bioactive cytotoxic compounds from medicinal plants including betulinic acid isolated from the northern Nigeria traditional cancer remedy, *Parinari curatellifolia* which has been shown to be cytotoxic to neuroectodermal and brain tumor cells [129]. An ointment formulation of betulinic acid is currently undergoing Phase I/II clinical trial for the treatment of dysplastic nevi with moderate to severe dysplasia [129]. A phase II clinical trial of curcumin from *Curcuma longa* in patients with advanced pancreatic cancer showed a brief but significant tumor regression with no toxicities observed. Also, clinical studies of curcumin alone or in combination with other chemotherapeutic agents (gemcitabine, 5-fluorouracil and oxaliplatin) have been carried out in the United States and Israel for patients with colorectal and pancreatic cancers [129]. Lycopene from tomato is currently in Phase II clinical trials in the United States for the prevention and treatment of prostate cancer. Resveratrol from various plants including *Arachis hypogaea* is now undergoing Phase I/II clinical trials for the prevention and treatment of colon cancer in the United States [129]. UNBS1450 is a reduction product of the cardenolide, 2"-oxovoruscharin from *Calotropis procera* which has entered

Phase I clinical studies in Europe for patients with solid tumors and lymphomas.

Others include combretastatin A4 isolated from the South African tree, *Combretum caffrum*, being assessed in a phase II trial with regard to ovarian, anaplastic thyroid, gastric, and other solid tumors; perillyl alcohol from the essential oil yielding *Lavandula* species is undergoing phase I/II clinical trials in patients with breast cancer, ovarian cancer, and glioblastoma multiform [129]. 1-Methylisoindigo (an indole alkaloid) from *Indigofera* species, *Isatis* species and *Polygonum* species is under clinical trial in the China for chronic myelogenous leukemia.

7. Mechanism of action of cytotoxic compounds

It is believed that anticancer effects of plants develop by suppressing cancer's stimulating enzymes, repairing DNA, stimulating production of antitumor enzymes in cell, increasing body immunity, and inducing antioxidant effects [130]. A review of cytotoxic plants of the Indian subcontinentwith reference to their mechanisms of action has been published [128]. Pereyra *et al* [131] have documented the diverse mechanisms of anticancer potential of the naphthoquinones.

8. Conclusion

The review provides a remarkable diversity of new natural products on which to base the discovery and development of anticancer drugs. The considerable structural diversity is represented in the 30 relevant structures presented. Several potent antiproliferative natural products have been described, and those belonging to steroids class have high anticancer activity. Most of the active compounds described here have only been evaluated by *in vitro* assays for cytotoxicity, and fewer have been assayed *in vivo*. The compounds listed have been included based on the potency and/or selectivity of their biological properties, and reflect the tremendous effort that is being devoted to recognizing the potential of natural products as lead compounds in the treatment of cancer in Nigeria and mechanisms of their action. The cancer prevalence in Nigeria which is based on the data provided calls for urgent attention by the stakeholders.

9. References

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