

REVIEW

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Anticancer activity of Nigerian medicinal plants: a review



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Abstract

Background: Cancer is currently the leading cause of death globally and the number of deaths from cancer is on the rise daily. Medicinal plants have been in continuous use over the years for the management of cancer, particularly, in most developing countries of the world including Nigeria. The use of synthetic drugs for the treatment of cancer is often accompanied by toxic side effects. Thus, the alternative use of readily available and inexpensive medicinal plants is the panacea to the toxic side effects associated with synthetic drugs.

Main body: The present review summarized the anticancer activity of 51 medicinal plants that are widespread in all regions of Nigeria. Furthermore, the proposed anticancer pharmacological actions as well as the anticancer bioactive compounds, the type of cancer cell inhibited, the plant parts responsible for the anticancer activity, and the nature of the extracts used for the studies were discussed in this review. The 51 Nigerian medicinal plants were reported to exhibit anticancer activities of the prostate, cervix, lung, skin, colon, esophagus, blood, ovary, central nervous system/brain, breast, stomach, pancreas, larynx, and kidney. The major classes of bioactive compounds indicated to be responsible for the anticancer activity include the polyphenols, flavonoids, alkaloids, saponins, triterpenes, tannins, and quinones. The major anticancer pharmacological actions of these bioactive compounds were antiproliferative, cytotoxic, cytostatic, antimetastatic, apoptotic, and antioxidative as well as provoked cell cycle arrest, inhibition of angiogenesis and reduction of cancer cell viability.

Conclusion: The Nigerian medicinal plants can be harnessed to provide for readily available and inexpensive anticancer drugs in the future because the plants reported in this review showed promising anticancer activity.

Keywords: Nigeria, Medicinal plants, Anticancer, Antiproliferative, Cytotoxic, Apoptotic

Background

Cancer is currently the leading cause of death globally [1] and the number of deaths from cancer is on the rise daily. The number of recorded deaths of persons as a result of cancer rose by 17% between 2005 and 2015, and therefore, there is the urgent need for more intensive research into the development of new anticancer drugs in addition to the existing ones [2]. Cancer is a disease that is characterized by proliferation of the body cells, due to failures in cellular modulation and obstruction of cell cycle progression, and thereby eliciting malignant tumor

cells formation with the possibility of becoming metastatic [3].

Plant extracts are widely used in Nigeria as important sources of chemotherapeutic agents in spite of the use of synthetic drug by vast majority of the populace. Medicinal plants have been in continuous use over the years for the management of cancer [4], particularly, in most developing countries of the world including Nigeria. The use of synthetic drugs for the treatment of cancer is often accompanied by toxic side effects. Thus, the alternative use of readily available and inexpensive medicinal plants is the panacea to the toxic side effects associated with synthetic drugs [5]. These medicinal plants are made up of bioactive compounds that are responsible for their pharmacological actions in the human body.

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Clinical studies and phytochemical screening have established the antitumor activity of herbal remedies against different types of cancers [6–11].

Notwithstanding the fact that many anticancer agents have been derived from medicinal plants, many plants with anticancer potentials are yet to be discovered. There are over 114,000 plant extracts that are being analyzed for their anticancer activity in various cancer institutes. Accordingly, there is a pressing need to carry out conclusive investigations to establish whether these extracts exhibit anticancer activity and applied as chemotherapeutic agents [12, 13].

One of the major approaches towards new drug discovery is applying the knowledge of ethnobotanical properties of medicinal plants; the so-called ethnobotanical bioprospecting [14–18]. This common approach, which is based on specific traditional uses of herbs in Nigeria, depends majorly on the extent at which the herb was able to cure a particular disease among the populace. Ethnomedicinal practices are usually transferred from one generation to another, and thus, serve as an effective and reliable guide towards the identification of plants that exhibit anticancer activity.

The present review summarized the anticancer activity of Nigerian medicinal plants that have been empirically investigated. The review also highlighted the plant parts and bioactive compounds responsible for the anticancer activity as well as their possible pharmacological actions.

Main text

Information and data acquisition

The information and data used in this review were sourced from scientific databases such as Google Scholar, PubMed, SpringerLink, Medline, ScienceDirect, and Mendeley. Publications from 1972 to 2020 were retrieved from these scientific search engines giving rise to 254 references that were cited in this report.

The Nigerian medicinal plants with promising anticancer activity

This review highlighted 51 anticancer medicinal plants that are widespread in all regions of Nigeria. Furthermore, the proposed anticancer pharmacological actions as well as the anticancer bioactive compounds, the type of cancer cell inhibited, the plant parts responsible for the anticancer activity, and the nature of the extracts used for the studies were reported and are summarized in Table 1.

Acronychia baueri (Rutaceae)

The aqueous bark extract of *A. baueri* has been reported to exhibit remarkable antitumor activity. The antitumor activity of the bark of *A. baueri* was due to the presence of alkaloids (normelicopidine, melicopine, acronycine)

and triterpene lupeol, whereby acronycine exhibited the highest antitumor activity [19].

Ageratum conyzoides (Compositae)

The cytotoxicity of ethylacetate extract of *A. conyzoides* on A549 (lung carcinoma) and P388 (leukemia) cell lines in humans and mouse, respectively, has been reported [20]. The leaf extract of *A. conyzoides* also inhibited the proliferation of SF-767, LNCaP, PC-3, and SF-763 cancer cell lines [21]. The anticancer effect of the leaf extract of *A. conyzoides* was reported to be as a result of the presence of the anticancer compounds: kaempferol, oxygenated terpenes, sesquiterpene hydrocarbons, and monoterpene hydrocarbons [20, 21].

Alchornea cordifolia (Euphorbiaceae)

The methanolic leaf extract of *A. cordifolia* initiated cell death through the activation of caspases, damage of the mitochondrial membrane, and stimulation of reactive oxygen species (ROS) generation in adriamycin-sensitive leukemia (CCRF-CEM cells). The methanolic bark extract of *A. cordifolia* was also reported to have deleterious effects on CCRF-CEM cells [22]. The bioactive compounds isolated from *A. cordifolia* with possible anticancer potentials include the flavonoids, saponins, cardiac glycosides, steroids, anthraquinone, terpenes, xanthenes, alkaloids, and tannins [23].

Allium sativum (Amaryllidaceae)

A. sativum L., also known as garlic, is a rich source of S-allylcysteine and S-allylmercapto-L-cysteine. These bioactive compounds are known to exhibit high radical scavenging activity, which is essential in the inhibition of cancer development. S-allylcysteine also retarded tumor growth [24]. Additionally, *A. sativum* repressed the proliferations of skin, colon, lung, prostate, leukemia, and breast cancer cells in vitro [25, 26].

Aloe barbadensis (Asphodelaceae)

Ethanol extract of *A. barbadensis* (*Aloe vera*) exhibited antitumor activities through the modulation of lipid peroxidation and stimulation of the antioxidant defense system in mice [27, 28]. The anticancer activity of *A. barbadensis* was attributed to aloe-emodin, which was identified in leaf extract of the plant. This bioactive compound exhibited cytotoxicity in hepatoma cell and neuroectodermal tumors, as well as lung squamous cell carcinoma [27]. The cytotoxicity of *A. barbadensis* against HepG2 and HCC cancer cell lines has also been reported [28].

Alstonia boonei (Apocynaceae)

The methanol and *n*-hexane stem-bark extracts of *A. boonei* have been established to be cytotoxic to cancer

Table 1 Nigerian medicinal plants and their anticancer activity

Anticancer plant (family)	Part used for study	Extractant used for study	Bioactive compound	Cancer cell type	Pharmacological actions	References
<i>Acronychia baueri</i> (Rutaceae)	Bark	Aqueous	Normelicopidine, mellicopine, acronyicine, and triterpenelupeol	Not specified	Antiproliferative effect	[19]
<i>Ageratum conyzoides</i> (Compositae)	Leaf	Ethylacetate	Kaempferol, oxygenated terpenes, sesquiterpene hydrocarbons, and monoterpene hydrocarbons	Lung, blood, central nervous system and prostate	Cytotoxic and antiproliferative effects	[20, 21]
<i>Alchornea cordifolia</i> (Euphorbiaceae)	Leaf and bark	Methanol	Flavonoids, saponins, cardiac glycosides, steroids, anthraquinone, terpenes, xanthenes, alkaloids, and tannins	Blood	Apoptotic effect	[22, 23]
<i>Allium sativum</i> (Amaryllidaceae)	Bulb	Ethanol	S-allylcysteine, S-allylmercapto-L-cysteine, diallyl disulfide, diallyltrisulfide, and allicin	Skin, colon, lung, prostate, blood, and breast	Cytotoxic and antiproliferative effects	[24–26]
<i>Aloe barbadensis</i> (Asphodelaceae)	Leaf	Ethanol	Aloe-emodin	Liver and lung	Modulation of lipid peroxidation, cytotoxic and antioxidant effects	[27, 28]
<i>Alstonia boonei</i> (Apocynaceae)	Stem-bark, leaf and root	Methanol and n-hexane	Echitamine, eugenol, 1, 2-benzenedicarboxylic acid, and alstiboamine	Pancreas, lung, prostate, colon	Antiproliferative and cytotoxic effects	[29–33]
<i>Anacardium occidentale</i> (Anacardiaceae)	Leaf and stem-bark	Hydroethanol	Agathisflavone, methyl gallate, anacardicin, zoapatanolide A, tannins, alkaloids, saponins, and polyphenols	Laryngeal, blood, and cervical	Cytotoxic and antiproliferative effects	[34–36]
<i>Anogeissus leiocarpus</i> (Combretaceae)	Leaf and root	Ethanol	Ellagic acid, castalagin, and flavogallonic acid	Liver	Antiproliferative effect	[37–41]
<i>Astragalus membranaceus</i> (Fabaceae)	Root	Not specified	Isoflavones, calycosin, ononin, formononetin, and campanulin	Breast	Antiproliferative, apoptotic and cytostatic effects, restoration of deformed T cells	[42, 43]
<i>Atractylis lancea</i> (Compositae)	Root	Ethanol and petroleum ether	Polyacetylenes, sesquiterpenes, and sesquiterpene lactones	Liver and stomach	Cell cycle arrest, antiproliferative and apoptotic effects	[44, 45]
<i>Azadirachta indica</i> (Meliaceae)	Leaves, seeds	Ethanol	flavonoids, phenolics, limonoids, triterpenoids	Skin, prostate, breast, cervical, blood, liver, colon, lung, and stomach	Antiproliferative effects through the induction of autophagy, apoptosis and cell cycle arrest	[28, 46–54]
<i>Boerhaavia diffusa</i> (Nyctaginaceae)	Leaf	Ethanol and methanol	Alkaloids, flavonoids, tannins, saponins, terpenes, anthraquinones, and steroids	Cervical and breast	Cell cycle arrest, antiproliferative effects	[55–57]
<i>Cajanus cajan</i> (Fabaceae)	Leaf	Ethanol	Longistylin C, longistylin A, stilbenoids, and flavonoids	Colorectal, breast, cervical, lung, blood and liver	Antiproliferative effect	[58–63]
<i>Camellia sinensis</i> (Theaceae)	Leaf	Not specified	(+)-galloocatechin, (-)-epigallocatechingallate, and	Colon, lung, breast, and liver	Antiproliferative and cytotoxic effects, cell cycle arrest	[64, 65]

Table 1 Nigerian medicinal plants and their anticancer activity (Continued)

Anticancer plant (family)	Part used for study	Extractant used for study	Bioactive compound	Cancer cell type	Pharmacological actions	References
<i>Carica papaya</i> (Caricaceae)	Leaf	Aqueous	(-)-epigallocatechin Ascorbic acid, quercetin, kaempferol, tetrahydroxyflavone, kaempferol- β -D-glucopyranoside, papain, lycopene, morin, cystatin, fisetin, benzylisothiocyanate, luteolin- β -D-glucopyranoside, luteolin, and myricetin-3-O-rhamnoside	Prostate, lung, blood, pancreas, and liver	Antiproliferative effect	[66–68]
<i>Cassia occidentalis</i> (Fabaceae)	Whole plant	Aqueous	Flavonoids, tannins, alkaloids, anthraquinones, and saponins	Colon, ovary, cervical, breast, and prostate	Antiproliferative effect	[69, 70]
<i>Chromolaena odorata</i> (Compositae)	Leaf	n-Hexane and ethanol	2-hydroxy-4, 4, 5, 6-tetramethoxychalcone, acacetin, kaempferol-3-O-rutinoside, quercetin-3-O-rutinoside, kaempferide, and rhamnazin	Breast, lung, and blood	Cytotoxic effect	[71–77]
<i>Citrus aurantifolia</i> (Rutaceae)	Not specified	Aqueous	Polymethoxyflavones	Colon, pancreas, and breast	Induction of apoptosis, cell cycle arrest, cell lysis, inhibition of metastasis, strengthening immunity	[78–82]
<i>Croton zambesicus</i> (Euphorbiaceae)	Leaf	Dichloromethane	Ent-trachyloban-3- β -ol, ent-trachyloban-3-one, ent-18-hydroxy-trachyloban-3-one, trans-phytol, isopimara-7, and 15-dien-3- β -ol	Cervical	Cytotoxic effect	[73, 83]
<i>Cryptolepis sanguinolenta</i> (Asclepiadaceae)	Root	Aqueous	Cryptolepine, ascriptolepinoic acid, quindoline, and methyl cryptolepinoate	Lung	Antiproliferative effect, reduction of cancer cell viability	[84, 85]
<i>Curcuma longa</i> (Zingiberaceae)	Rhizome	Ethanol	Curcumin	Breast, stomach, colon, lung, and liver	Apoptotic, antiproliferative, antioxidant and anti-inflammatory effects, Cell cycle arrest	[86–90]
<i>Derris scandens</i> (Fabaceae)	Not specified	Ethanol	Glyurallin, derriscandenon B and C, isochandaisone, and derrubone	Colon	Apoptotic effects, inhibition of mitosis	[91, 92]
<i>Enantia chlorantha</i> (Annonaceae)	Stem-bark	Methanol	Columbamine, saponins, pseudocolumbamine, and palmatine	Colorectal, liver, and lung	Antiproliferative and cytotoxic effects	[93–95]
<i>Fagara zanthoxyloides</i> (Rutaceae)	Root	Aqueous	Fagarone	Blood and prostate	Antiproliferative and cytotoxic effects; inhibits cancer cell viability	[96, 97]
<i>Glochidion zeylanicum</i> (Euphorbiaceae)	Stem-bark, leaf and root	Methanol and aqueous	Triterpenoids and megastigmane glycosides	Prostate, colon, and liver	Cytotoxic and antiproliferative effects	[8, 98, 99]
<i>Glycyrrhiza glabra</i> (Fabaceae)	Whole plant	Aqueous	Licochalcone and isoliquiritigenin	Prostate, breast, and colon	Apoptotic and antiproliferative effects, cell cycle arrest	[100–102]
<i>Goniothalamus macrophyllus</i>	Root and stem	Methanol	Goniothalamin	Cervical, breast, and	Cytotoxic and apoptotic	[103, 104]

Table 1 Nigerian medicinal plants and their anticancer activity (Continued)

Anticancer plant (family)	Part used for study	Extractant used for study	Bioactive compound	Cancer cell type	Pharmacological actions	References
(Annonaceae)					effects	
<i>Harungana madagascariensis</i> (Guttiferae)	Stem-bark	Methanol and dichloromethane	Coumarins, anthraquinones, bioflavonoids, anthrone derivatives, and xanthenes	Blood	Cytotoxic effect, activates nitric oxide secretion	[105–107]
<i>Khaya senegalensis</i> (Meliaceae)	Stem-bark	Methanol and hydroethanol	3a, 7a-dideacetylkhivorin, 1-O-deacetylkhayanolide E4, khayanolide B2, 6-dehydroxykhayanolide E5, 1-O-acetylkhayanolide B1, and khayanolide E3	Colon, cervical, liver, and breast	Antiproliferative and apoptotic effects	[108–112]
<i>Lophira alata</i> (Ochnaceae)	Stem-bark	Methanol	Azobechalcone A, flavonoids, isolophirachalcone, lophirone F, lophirone A, triterpenes, sterols, polyphenols, lophirones C, and lophirones B	Liver, lung, breast, skin, and colon	Antiproliferative, antitumor and cytotoxic effects	[93, 113–115]
<i>Mangifera indica</i> (Anacardiaceae)	Stem-bark	Methanol	Galloyl glycosides, lupeol, mangiferin, gallotannins, and gallic acid	Breast, kidney, ovary, and colon	Antiproliferative effect	[116–120]
<i>Millicia excelsa</i> (Moraceae)	Root	Methanol	Neocyclomorusin, cudraxanthone I, betulinic acid, 6-geranylnortocarpetin, and atalantoflavone	Cervical, liver, colon, and brain	Antiproliferative and cytotoxic effects	[121–123]
<i>Morinda lucida</i> (Rubiaceae)	Leaf and stem-bark	Aqueous and methanol	Molucidin, β-sitosterol, stigmasterol, oruwacin, digitoluein, ursolic acid, rubiadin-1-methyl ether, phytol, cycloartenol, oleanolic acid, damnanthra and campesterol	Prostate, stomach, colon and blood	Antiproliferative effect	[124–130]
<i>Newbouldia laevis</i> (Bignoniaceae)	Root-bark	Methanol	2-acetyluro-1, 4-naphthoquinone, tri-terpenoid, tannins, steroids, and quinone derivatives	Pancreas and blood	Antiproliferative and cytotoxic effects	[131–134]
<i>Ocimum gratissimum</i> (Labiatae)	Leaf	Ethanol and aqueous	3, 4-dihydroxycinnamic acid, oleanolic acid, saponins, linalool, eugenol, gerianol, alkaloids, thymol, and citral	Cervical, breast, prostate, lung, colon, pancreas, kidney, and bone	Antiproliferative effect	[135–140]
<i>Panax ginseng</i> (Araliaceae)	Root and rhizomes	Not specified	Ginsenoside Rp1	Breast	Antiproliferative and apoptotic effects, cell cycle arrest	[141, 142]
<i>Picrohiza kurroa</i> (Plantaginaceae)	Root	Hydroalcohol	Apiocynin, cucurbitacinesglycone, caffeic esters, and picrosides	Cervical and breast	Cytotoxic, anti-inflammatory and antioxidant effects	[143–145]
<i>Phyllanthus amarus</i> (Euphorbiaceae)	Whole plant	Methanol	Flavonoids, ellagitannins, polyphenols, triterpenes, sterols, phyllanthin, saponins, and alkaloids	Lung, breast, pancreas, neuron, skin, ovarian, and prostate	Apoptotic, antiproliferative and cytotoxic effects, cell cycle arrest	[146–151]
<i>Phyllanthus emblica</i> (Phyllanthaceae)	Fruit and leaf	Aqueous and ethanolic	Ellagic acid, chebulagic acid, and gallic acid	Cervical and colon	Reduction of cancer cell viability, cytotoxic and	[152–154]

Table 1 Nigerian medicinal plants and their anticancer activity (Continued)

Anticancer plant (family)	Part used for study	Extractant used for study	Bioactive compound	Cancer cell type	Pharmacological actions	References
<i>Psidium guajava</i> (Myrtaceae)	Leaf	Hexane	Cryptonine, tannins, apigenin, dihydrobenzophenanthridine, lycopene, and saponins	Breast, blood cervical, and prostate	antiproliferative effects Antiproliferative and apoptotic effects	[155, 156]
<i>Punica granatum</i> (Lythraceae)	Fruit	Aqueous	Ellagic acid, ellagitannins, punicalagin, and tannins	Colorectal and colon	Cell cycle arrest, antiproliferative and apoptotic effects	[39, 80, 157]
<i>Rauwolfia vomitoria</i> (Apocynaceae)	Root	Ethanol	β-carboline, terpenes, tannins, alkaloids, steroids, saponins, and flavonoids	Pancreas, ovarian, and prostate	Cytotoxic, apoptotic and antiproliferative effects, cell cycle arrest	[158–161]
<i>Scoparia dulcis</i> (Scrophulariaceae)	Leaf	Petroleum ether, ethanol and methanol	Dulcidiol, iso-dulcinol, scopadiol, 4-epi-scopadulic acid B, and scopanolal	Stomach and prostate	Cytotoxic effect	[162–164]
<i>Tabebuia avellanedae</i> (Bignoniaceae)	Bark	Not specified	β-lapachone	Liver	Antiproliferative and apoptotic effects	[165]
<i>Thymus vulgaris</i> (Lamiaceae)	Leaf bulb	Butanol ethanol	Tannins, triterpenes, sterols, flavonoids, and glycosides	Cervical	Cytotoxic effects	[26, 166, 167]
<i>Tinospora cordifolia</i> (Menispermaceae)	Stem	Dichloromethane and methanol	Epoxydiodanedi-terpene, arabinogalactan, berberine, and phenolics	Breast and cervical	Cytotoxic and antiproliferative effects	[168–170]
<i>Tithonia diversifolia</i> (Compositae)	Leaf	Ethanol and methanol	Tagitinin C, 1β-methoxydiversifolin 3-O-methyl ether, and 1β and 2α-epoxytagitinin C	Colon and blood	Antiproliferative effect, cell cycle arrest, inhibition of cancer cell viability, stimulation of cancer cell autophagy	[171–174]
<i>Uvaria chamae</i> (Annonaceae)	Stem-bark and root	Ethanol	Dichamanetin, diuaretin, uvaletin, chamanetin, pinocembrin, isouvaletin, pinostrobin, and isochamanetin	Blood	Antiproliferative effect	[4, 175]
<i>Vernonia amygdalina</i> (Compositae)	Leaf	Chloroform	Steroid glycosides and edotide	Breast and cervical	Antiproliferative effect	[176–178]
<i>Zanthoxylum nitidum</i> (Rutaceae)	Root	Not specified	Nitidine and benzophenanthridine	Lung, cervical, and liver	Cytotoxic and antiproliferative effect	[179–181]
<i>Zingiber officinale</i> (Zingiberaceae)	Whole plant	Ethyl acetate	10-gingerol, 10-shogaol, 6-gingerol, and 6-shogaol	Prostate, liver, breast, and esophageal	Antiproliferative and antimetastatic effects	[182–186]

cells [29]. The bioactive compound, echitamine, present in the stem-bark of *A. boonei* hindered the development and caused the extermination of fibrosarcoma in rat models [30]. Two bioactive compounds, namely, eugenol and 1, 2-benzenedicarboxylic acid isolated from the leaf and root, respectively, of *A. boonei* suppressed the proliferation of MiaPaCa (pancreas), A549 (lung), PC-3 (prostate), and HCT-116 (colon) cancer cell lines [31–33]. Alstiboonine is another bioactive compound from stem-bark of *A. boonei* that has been noted to exhibit deleterious effects on cancer cells [29].

***Anacardium occidentale* (Anacardiaceae)**

Hydroethanolic leaf extract of *A. occidentale* has shown cytotoxicity against leukemia cells. The leaf of this medicinal plant inhibited the proliferation of leukemic cancer cells and was slightly cytotoxic to the cell lines: Hep-2 (laryngeal cancer), HL-60 (leukemia), and Raji (Burkitt lymphoma). These anticancer activities were attributed to the presence of agathisflavone in the hydroethanolic leaf extract of *A. occidentale* [34]. According to Taiwo et al. [35], methyl gallate, anacardicin, zoapatanolide A, and agathisflavone exhibited cytotoxicity against HeLa (cervical cancer) cells. Furthermore, Obembe and Ige [36] noted that the stem-bark and leaves of *A. occidentale* are rich sources of the anticancer compounds such as tannins, alkaloids, saponins and polyphenols.

***Anogeissus leiocarpus* (Combretaceae)**

The inhibition of cancer cell proliferation by leaf and root extracts of *A. leiocarpus* have been reported by Olugbami et al. [37] and Salau et al. [38], respectively. The ethanolic leaf extract of *A. leiocarpus* hindered the proliferation of liver carcinoma HepG2 cell lines [37], whereas the root extract hindered Ehrlich ascites carcinoma cell lines [38]. Ellagic acid, castalagin, and flavogallic acid are bioactive compounds known for their cancer cell proliferation inhibitory activity and have been isolated from *A. leiocarpus* [39–41].

***Astragalus membranaceus* (Fabaceae)**

Root extract of *A. membranaceus* exhibited antitumor activity in vitro and in vivo through its cytostatic activity in myeloid and macrophage-like tumors. This plant also repressed syngeneic tumor development. The potency of root extracts of *A. membranaceus* to restore the functionality of T cells in cancer patients has been ascertained and reported [42]. *A. membranaceus* inhibited the proliferation and induced the apoptosis of breast cancer cell lines (MDA-MB-231, MCF-7, and SK-BR-3). The bioactive compounds, namely, isoflavones, calycosin, ononin, formononetin, and campanulin, have been isolated from *A. membranaceus* and established to be potent anticancer agents [43].

***Atractylis lancea* (Compositae)**

The ethanol extract of *A. lancea* inhibited the proliferation of Hep-G2 liver cancer cell lines in vitro and induced apoptosis through the restriction of G1-phase cell cycle, disruption of mRNA, and protein synthesis, and thereby retarded telomerase action [44]. The petroleum ether root extract of *A. lancea* was reported to inhibit the growth of gastric cancer cell lines (SGC-7901 and BGC-823) through the blockage of the cell cycle and apoptosis. Polyacetylenes, sesquiterpenes, and sesquiterpene lactones are the major bioactive compounds from petroleum ether root extract of *A. lancea* with potential anticancer activity [45].

***Azadirachta indica* (Meliaceae)**

Leaf and seed extracts of *A. indica* inhibited the proliferation of cancer cells as well as induced the death of cancer cells by autophagy and apoptosis. The inhibition of cancer cell proliferation was achieved and sustained by *A. indica* through obstruction of cell cycle progression [28, 46, 47]. The leaf and seed extracts of *A. indica* stimulated the apoptosis of leukemia, colon, breast, cervical, hepatocarcinoma, choriocarcinoma, stomach, and prostate cancer cells [48, 49, 100, 187–189]. The seed oil of *A. indica* inhibited the proliferation of HeLa cervical and prostate cancer cells [50, 51]. The major classes of bioactive compounds responsible for the anticancer activity of *A. indica* include the flavonoids, phenolics, limonoids, and triterpenoids. The ethanolic leaf extract of *A. indica* repressed the development of PC-3M-luc2 and C4-2B prostate cancer cells in vitro [52]. Generally, *A. indica* has been effective in the repression of skin, prostate, breast, cervical, leukemia, liver, colon, lung and stomach cancers [53, 54].

***Boerhaavia diffusa* (Nyctaginaceae)**

The ethanolic extract of *B. diffusa* has been reported to block the cell cycle at the S-phase as well as destroy HeLa cell lines. *B. diffusa* also hindered the proliferation of cancer cells in mice through free radical scavenging activity [55]. The cytotoxic activity of the methanolic leaf extract of *B. diffusa* against breast cancer (MCF-7) cell lines was established by Muthulingam and Chaithanya [56]. Alkaloids, flavonoids, tannins, saponins, terpenes, anthraquinones, and steroids have been identified to be present in *B. diffusa* extract and are considered to be responsible for the anticancer activity of the plant [57].

***Cajanus cajan* (Fabaceae)**

The ethanolic leaf extract of *C. cajan* repressed CaCo-2 (colorectal), MCF-7 (breast), and HeLa (cervical) cancer cell lines [58]. The bioactive compounds, longistylin C, and longistylin A, from *C. cajan* inhibited the proliferation of A549 (lung), CCRF-CEM, Ehrlich's ascites

carcinoma, and HepG2 cancer cell lines [59–61]. Other bioactive compounds from *C. cajan* with promising anticancer activity include the stilbenoids and flavonoids [62, 63].

***Camellia sinensis* (Theaceae)**

The leaf extracts of *C. sinensis* exhibited antitumor activity against human HT-29 colon carcinoma, UACC-375 melanoma, MCF-7 breast carcinoma, and A-427 lung carcinoma owing to the presence of the following bioactive compounds: (+)-gallicocatechin, (–)-epigallocatechin-3-gallate, and (–)-epigallocatechin [64]. The potency of (–)-epigallocatechin-3-gallate present in *C. sinensis* to induce cell cycle arrest and inhibit the development of cancer cells (hepatocellular carcinoma) has been ascertained and reported [65].

***Carica papaya* (Caricaceae)**

The efficacy of leaf extracts of *C. papaya* in the treatment of prostate cancer has been reported [66]. The aqueous leaf extract of *C. papaya* effectively suppressed the proliferation of plasma cell leukemia (ARH77 cell line), lung cancer (PC14 cell line), pancreatic adenocarcinoma (Capan1 cell line), Burkitt's lymphoma (K562 cell line), pancreatic carcinoma (Panc-1 cell line), large cell lymphoma (Karpas-299 cell line), mesothelioma (JMN cell line), and hepatocellular carcinoma (Huh7 cell line) [67]. Certain bioactive compounds that have been isolated from *C. papaya* leaves are considered to be likely responsible for the anticancer activity. These bioactive compounds include ascorbic acid, quercetin, kaempferol, tetrahydroxyflavone, kaempferol- β -D-glucopyranoside, papain, lycopene, morin, cystatin, fisetin, benzylisothiocyanate, luteolin- β -D-glucopyranoside, luteolin, and myricetin-3-O-rhamnoside [67, 68].

***Cassia occidentalis* (Fabaceae)**

The study done by Bhagat and Saxena [69] elucidated the anticancer activity of aqueous extract of *C. occidentalis*. According to the study by Bhagat and Saxena [69], aqueous extract of *C. occidentalis* inhibited the proliferation of SW-620 (colon cancer), HCT-15 (colon cancer), OVCAR-5 (ovarian cancer), SiHa (cervical cancer), MCF-7 (breast cancer), and PC-3 (prostate cancer) cell lines. However, Bhagat and Saxena [69] did not isolate and identify the specific bioactive compounds responsible for the anticancer efficacy of aqueous extract of *C. occidentalis*. Nevertheless, in general terms, the anticancer activity of *C. occidentalis* have been linked to the presence of the following classes of bioactive compounds isolated from *C. occidentalis*: the flavonoids, tannins, alkaloids, anthraquinones, and saponins [70].

***Chromolaena odorata* (Compositae)**

The *n*-hexane leaf extract of *C. odorata* suppressed MCF-7, MDAMB-468, and CAL51 breast cancer cell lines, whereas the ethanolic leaf extract repressed Lewis lung carcinoma cell (LLC) and HL-60 human leukemia cell lines. The 2-hydroxy-4, 4', 5', 6'-tetramethoxychalcone isolated from *n*-hexane leaf extract of *C. odorata* was noted to be responsible for its anticancer activity [71, 72]. Other anticancer bioactive compounds isolated from *C. odorata* include acacetin, kaempferol-3-O-rutinoside, quercetin-3-O-rutinoside, kaempferide and rhamnazin [73–77].

***Citrus aurantifolia* (Rutaceae)**

C. aurantifolia has been reported to activate the release of caspase-3 for proapoptosis and inhibit the progression of tumor cell cycle at the S-phase [78]. Additionally, *C. aurantifolia* increased the concentration of tumor infiltrating CD8+ T lymphocytes, and thereby strengthened immunity against cancer cells. *C. aurantifolia* also hindered the release of BclxL and Mcl-1 (proteins that inhibit apoptosis) [78]. Polymethoxyflavones, which is present in aqueous extract of *C. aurantifolia*, mitigated cancer cell metastasis through the inhibition of cell adhesion and invasion [79]. These bioactive compounds also initiated the release of NK cells leading to the lysis of cancer cells. *C. aurantifolia* suppressed the action of cyclin-dependent kinases (Cdk) and thereby limited the progression of tumor cell cycle at the G1-phase [79, 80]. *C. aurantifolia* extract repressed colon SW-480, pancreatic Panc-28, and breast MDA-MB-453 cancer cells growth [81, 82].

***Croton zambesicus* (Euphorbiaceae)**

The diterpene, ent-trachyloban-3- β -ol, isolated from dichloromethane leaf extract of *C. zambesicus* has been confirmed to exhibit inhibitory effect on the growth of HeLa cancer cells [83]. Other bioactive compounds with promising anticancer activity from dichloromethane extract of *C. zambesicus* include ent-trachyloban-3-one, ent-18-hydroxy-trachyloban-3-one, trans-phytol, isopimara-7, and 15-dien-3- β -ol [73].

***Cryptolepis sanguinolenta* (Asclepiadaceae)**

The aqueous root extract of *C. sanguinolenta* has shown potency to suppress V79 cell lines (lung fibroblast cells). This effect has been attributed to cryptolepine (an alkaloid), which vastly occurs in *C. sanguinolenta*. Cryptolepine acts by inhibiting the proliferation and viability of cancer cell lines including V79 [84]. Other alkaloids with anticancer activity from *C. sanguinolenta* include ascryptolepinoic acid, quindoline, and methyl cryptolepinoate [85].

***Curcuma longa* (Zingiberaceae)**

The rhizome of *C. longa* (turmeric) inhibited the growth of cancer cells and also caused the extermination of lymphoma cells and lymphocytes. The anticancer activity of *C. longa* was attributed to curcumin present in the rhizome [86]. According to Huang et al. [87], *C. longa* repressed the proliferation of cancer cells and prevented forestomach cancerous growth in animals. The antioxidant and anti-inflammatory activity of *C. longa* makes it a suppressor of breast, colon, lung and liver cancer cells. Curcumin has also shown obstructive activity against cancer cell signaling phases [88]. Generally, curcumin stimulated the apoptotic pathway, initiated cell cycle arrest, and hindered the protein tyrosine kinase activity and the manifestation of c-myc mRNA and bcl-2 mRNA [89]. Ahmad et al. [90] reported the anticancer activity of the ethanolic rhizome extract of *C. longa* against MDA-MB-231 human breast cancer cell line.

***Derris scandens* (Fabaceae)**

Ethanolic extract of *D. scandens* was reported to repress human colon cancer HT29 cells in concert with radiosensitization. Furthermore, *D. scandens* provoked HT29 cells death through apoptosis and mitotic inhibition when augmented with γ -irradiation. *D. scandens* also acts by suppression of Erk1/2 activation [91]. Certain isoflavones isolated from *D. scandens* with anticancer potentials include glyurallin, derriscandenon B and C, isochandaisone, and derrubone [92].

***Enantia chlorantha* (Annonaceae)**

The methanolic stem-bark extract of *E. chlorantha* suppressed the proliferation of human colorectal adenocarcinoma (DLD-1 cell line) and human mesothelioma (SPC212 cell line) as well as HepG2 liver cell line [93]. According to Musuyu et al. [94], the stem-bark extract of *E. chlorantha* had deleterious effects on human lung fibroblast cell line. Columbamine, saponins, pseudocolumbamine, and palmatine have been isolated from *E. chlorantha* and were considered to be the anticancer agents in *E. chlorantha* [95].

***Fagara zanthoxyloides* (Rutaceae)**

Root extract of *F. zanthoxyloides* is a rich source of fagaronine. This bioactive compound is cytotoxic to human leukemia [96]. The aqueous root extract of *F. zanthoxyloides* reduced the viability and hindered the proliferation of the following prostate cancer cell lines: PC-3, CWR-22, LNCaP, and DU-145 [97].

***Glochidion zeylanicum* (Euphorbiaceae)**

The triterpenoids and megastigmane glycosides from stem-bark and leaf extracts of *G. zeylanicum*, respectively, inhibited tumor development, whereas the

methanolic root extract was cytotoxic against human cancer cell lines including PC-3. The aqueous root extract of *G. zeylanicum* also suppressed human prostate cancer PC-3 cell line, human colon cancer HT29 cell line, and human liver cancer HepG2 cell line [8, 98, 99].

***Glycyrrhiza glabra* (Fabaceae)**

Licochalcone vastly occurs in *G. glabra*. This bioactive compound exerted apoptotic activity against prostate cancer cells and caused obstruction of the cell cycle through the repression of G2/M cells, cdc2, and cyclin B1. *G. glabra* reduced the levels of cyclin D1 and the transcription factor E2F, raised cyclin E levels and inhibited CDK 4/6 [101]. Another bioactive compound, isoliquiritigenin, isolated from *G. glabra*, suppressed prostate cancer proliferation. Isoliquiritigenin initiated the arrest of S- and G2/M-phases and also induced GADD153 mRNA and protein functions that are involved in cell cycle arrest [100]. The aqueous extract of *G. glabra* exerted anticancer activity against breast cancer (MCF-7) and colon cancer (HT-29) cell lines [102].

***Goniothalamus macrophyllus* (Annonaceae)**

The bioactive compound, goniotalamin, from *G. macrophyllus* exhibited cytotoxic activity against cervical cancer cells (HeLa), through the initiation of DNA fragmentation and damage as well as the activation of caspase-9, leading to apoptosis [103]. The methanolic root and stem extracts of *G. macrophyllus* were highly cytotoxic against breast MCF-7 and colon LS-174T cancer cell lines [103, 104]. These anticancer activities of *G. macrophyllus* were attributed to goniotalamin [104].

***Harungana madagascariensis* (Guttiferae)**

Stem extracts of *H. madagascariensis* induced the release of nitric oxide, which plays major role in cancer chemotherapy [105]. The methanol as well as the dichloromethane stem-bark extract of *H. madagascariensis* suppressed the growth of CCRF-CEM cancer cell lines [106]. The following bioactive compounds with anticancer potentials have been identified in *H. madagascariensis*: coumarins, anthraquinones, bioflavonoids, anthrone derivatives, and xanthonones [107].

***Khaya senegalensis* (Meliaceae)**

Stem-bark extract of *K. senegalensis* induced apoptosis and inhibited the proliferation of the human colon cancer cell lines: HCT-15, HCA-7, and HT-29 [108]. The methanolic and hydroethanolic stem-bark extracts of *K. senegalensis* have been reported to possess anticancer activity, whereas the methanolic extract specifically suppressed HeLa cervical and CaCo-2 colon cancer cell lines [108]. The hydroethanolic extract of *K. senegalensis* exhibited antimetastatic activity against HepG2 liver

cancer cell line [109, 110]. Limonoid compounds such as 3 α , 7 α -dideacetylkhayivorin, 1-O-deacetylkhayanolide E4, khayanolide B2, 6-dehydroylkhayanolide E5, 1-O-acetylkhayanolide B1, and khayanolide E3 have been isolated from *K. senegalensis* and displayed anticancer activity. For instance, 3 α , 7 α -dideacetylkhayivorin inhibited the proliferation of MCF-7 breast, SiHa cervical, and CaCo-2 colon cell lines [111, 112].

***Lophira alata* (Ochnaceae)**

The methanol stem-bark extract of *L. alata* was reported to repress the activity of Epstein-Barr virus (EBV) as well its early antigen, and thereby preventing the development of tumors [113]. The anticancer activity of *L. alata* was attributed to bioactive compounds such as azobechalcone A, flavonoids, isolophirachalcone, and lophirone F, which have been isolated from stem-bark of the plant as described by Murakami et al. [114]. The bioactive compound, lophirone A, which is present in *L. alata* retarded tumor growth [113]. Triterpenes, sterols, and polyphenols isolated from the stem-bark of *L. alata* were also reported to be cytotoxic against HepG2, A549, SPC212, CRL2120, MCF-7, and DLD-1 cell lines [93]. Lophirones C and Lophirones B that occurs in stem-bark of *L. alata* inhibited the proliferation of Ehrlich ascites carcinoma cells [115].

***Mangifera indica* (Anacardiaceae)**

M. indica, popularly called mango, has shown inhibitory effects against the proliferation of cancer cells following the administration of the methanolic stem-bark extract. *M. indica* is a rich source of bioactive compounds such as galloyl glycosides, lupeol, mangiferin, gallotannins, and gallic acid. These bioactive compounds are the major anticancer agents in *M. indica* [116–120]. *M. indica* suppressed the proliferation of MDA-MB-435 (breast cancer), UACC-257 (melanoma), TK-10 (renal cancer), SK-OV-3 (ovarian cancer), and KM 12 (colon cancer) cell lines [116].

***Milicia excelsa* (Moraceae)**

The bioactive compounds, namely, neocyclomorusin and cudraxanthone I, from *M. excelsa* were highly repressive against HeLa cancer cell line [121]. These two bioactive compounds were identified in methanolic root-bark extract of *M. excelsa* [121]. Kuete et al. [122] also reported the deleterious effects of cudraxanthone I on HepG2, HCT-116 and U87MG cell lines. Other anticancer bioactive compounds identified in the root of *M. excelsa* were betulinic acid, 6-geranylornartocarpetin, and atalantoflavone [123].

***Morinda lucida* (Rubiaceae)**

Two major bioactive compounds, namely, β -sitosterol and molucidin, have been isolated from *M. lucida* leaves and noted to possess anticancer activity [124]. The β -sitosterol repressed LNCaP, PC-3, and DU-145 (prostatic carcinoma) cell lines, while molucidin had deleterious actions on stomach cancer (KATO-3) and colon cancer (LoVo) cell lines [124]. The aqueous and methanolic leaf extracts of *M. lucida* hindered the proliferation of human leukemia HL-60 cell line and damaged kidney epithelial cells of monkeys, respectively [125, 126]. The stem-bark extract of *M. lucida* was also reported to exert anticancer activity in mice [127]. Other anticancer bioactive compounds present in *M. lucida* include stigmasterol, oruwacin, digitolutein, ursolic acid, rubiadin-1-methyl ether, phytol, cycloartenol, oleanolic acid, damacantha, campesterol, and molucidin [128–130].

***Newbouldia laevis* (Bignoniaceae)**

The root-bark extract of *N. laevis* is a rich source of 2-acetylfuro-1, 4-naphthoquinone [131]. This bioactive compound suppressed MiaPaCa-2 and CCRF-CEM cancer cell lines [131]. The methanolic leaf extract of *N. laevis* has also been established to exhibit slight inhibitory proliferative action against CCRF-CEM cells [132]. Other anticancer bioactive compounds isolated from *N. laevis* include triterpenoid, tannins, steroids, and quinone derivatives [133, 134].

***Ocimum gratissimum* (Labiatae)**

Caffeic acid (3, 4-dihydroxycinnamic acid) and oleanolic acid from *O. gratissimum* exhibited promising anticancer activity. Report also showed that 3, 4-dihydroxycinnamic acid from *O. gratissimum* suppressed HeLa cervical cell line [135], whereas oleanolic acid from ethanolic leaf extract of *O. gratissimum* repressed breast carcinoma, prostate adenocarcinoma, lung carcinoma, colon adenocarcinoma, pancreatic carcinoma, and renal carcinoma in humans [136]. Crude extract of *O. gratissimum* hindered tumor proliferation and suppressed breast cancer development [137]. The aqueous extract of *O. gratissimum* repressed A549 (human lung carcinoma) cell line and as well hindered the development of osteosarcoma cells and bone cancer in humans [138, 139]. Other anticancer bioactive compounds from *O. gratissimum* are saponins, linalool, eugenol, gerianol, alkaloids, thymol, and citral [140].

***Panax ginseng* (Araliaceae)**

Ginsenoside Rp1 from *P. ginseng* inhibited the insulin-like growth factor 1 receptor and thereby prevented human breast cancer cells from multiplying as well as disrupted the anchorage of cells colony. This bioactive compound also induced cell cycle arrest and repressed the growth of cells through apoptosis [141]. The roots

and rhizomes of *P. ginseng* have also been reported by Kim et al. [142] to inhibit the proliferation of MCF-7 breast cancer cell lines.

***Phyllanthus amarus* (Euphorbiaceae)**

P. amarus extracts have been reported to initiate apoptosis of cancer cells. *P. amarus* caused obstruction of the G0/G1-phase and S-phase in PC-3 and MeWo cell lines, respectively, and hindered the invasion, migration, and adhesion of these cell lines [143, 144]. Generally, the methanolic extract of *P. amarus* was cytotoxic to lung, breast, pancreas, neuroblastoma, skin, ovarian, glioblastoma, and prostate cancer cell lines. Flavonoids, ellagitannins, polyphenols, triterpenes, sterols, phyllanthin, saponins, and alkaloids have been isolated from *P. amarus* and have been reported to promote anticancer activity [145].

***Phyllanthus emblica* (Phyllanthaceae)**

The aqueous extract of *P. emblica* was cytotoxic against human fibrosarcoma cells (HT1080) by interrupting the invasion, movement, adhesion, and growth of the cells at low level of IC₅₀ [146]. Ellagic acid, chebulagic acid, and gallic acid were among the most studied anticancer bioactive compounds from *P. emblica* and are known to exhibit antioxidant properties [147–149]. The ethanolic fruit and leaf extracts of *P. emblica* inhibited cancer cell proliferation as well as reduced the viability of HT-29 colon cancer cell line [150]. Mahata et al. [151] reported the efficacy of the fruit extract of *P. emblica* against cervical cancer cells in vitro.

***Picrorhiza kurroa* (Plantaginaceae)**

P. kurroa root extract is known to be cytotoxic against cancer cells. The anticancer activity of *P. kurroa* root extract was attributed to the bioactive compounds, namely, apiocynin, cucurbitacines aglycone, and caffeic esters [152]. Picrosides isolated from *P. kurroa* was reported to possess anticancer activity by its anti-inflammatory and antioxidant actions [153]. The hydroalcoholic extract of *P. kurroa* was reported to be cytotoxic against cervical HeLa, SiHa, and breast MCF-7, MDA-MB 231 cancer cell lines [154].

***Psidium guajava* (Myrtaceae)**

The study carried out by Ryu et al. [155] revealed the anticancer potency of *n*-hexane leaf extract of *P. guajava*. The extract induced cell death in prostate PC-3 cancer cell lines through the interruption of the signaling activity associated with tumor formation. The inhibition of the proliferation of breast MCF-7, leukemia P388, prostate DU-145, cervical KB, and HeLa cell lines by the leaf extract of *P. guajava* has also been reported [156]. The anticancer potency of *P. guajava* has been

linked to the bioactive compounds, namely, cryptonine, tannins, apigenin, dihydrobenzophenanthridine, lycopene, and saponins present in the plant [156].

***Punica granatum* (Lythraceae)**

P. granatum is rich in ellagic acid and ellagitannins. These bioactive compounds are metabolically transformed to urolithins in the gut microbiota. Urolithins disrupted the cell cycle, prevented cancer cell proliferation, and stimulated apoptosis [80]. The ellagitannin in *P. granatum* extract repressed colorectal cancer in patients [157]. The aqueous fruit extract of *P. granatum* inhibited the proliferation of colon cancer cell lines including HT29, SW620, SW480, and HCT116 [39]. The anticancer activity was attributed to the presence of ellagic acid and punicalagin as well as tannins in *P. granatum* [39].

***Rauvolfia vomitoria* (Apocynaceae)**

Ethanolic root extract of *R. vomitoria* has been reported to be cytotoxic to pancreatic, prostate, and ovarian cancer cells [158–160]. The ethanolic root extract of *R. vomitoria* initiated apoptosis and hindered the expansion of tumors in pancreatic cells according to the study done by Yu and Chen [160]. This anticancer activity was attributed to the presence of β -carboline in *R. vomitoria*. Furthermore, *R. vomitoria* extract repressed the proliferation as well as induced cell cycle arrest in prostate cancer cells [158]. Additionally, ethanolic root extract of *R. vomitoria* inhibited the development of ovarian cancer cell lines (OVCAR-8, OVCAR-5, SHIN-3) and also initiated apoptosis of cancer cells [159]. Other anticancer bioactive compounds identified in *R. vomitoria* include terpenes, tannins, alkaloids, steroids, saponins, and flavonoids [161].

***Scoparia dulcis* (Scrophulariaceae)**

The petroleum ether leaf extract of *S. dulcis* repressed NUGC-4 and KATO-3 cell lines. Reports showed that dulcidiol, iso-dulcinol, scopadiol, 4-epi-scopadulcic acid B, and scopanolal were identified to be responsible for its anticancer activity [162]. The ethanolic and methanolic leaf extracts of *S. dulcis* suppressed DU-145 prostate and AGS (human gastric adenocarcinoma) cell lines [163, 164].

***Tabebuia avellanedae* (Bignoniaceae)**

β -Lapachone is a bioactive compound present in the stem-bark of *T. avellanedae* and has shown high efficacy to ameliorate cancer. Specifically, β -lapachone hindered the development of HepG2 hepatoma cell line in vivo through DNA fragmentation and the synthesis of apoptotic bodies. This bioactive compound repressed the proteins Bcl-2 and Bcl-XL and also stimulated the action

of Bax, thus supporting apoptosis. β -Lapachone from *T. avellaneda* also caused the activation of poly (ADP-ribose) polymerase protein and caspase-3 and caspase-9 [165].

***Thymus vulgaris* (Lamiaceae)**

El-khamissi et al. [166] reported the cytotoxic activity of ethanol peel extract of *T. vulgaris* bulb in human breast cancer MCF-7 cell lines. Other bioactive compounds such as diallyl disulfide, diallyl trisulfide, and allicin isolated from *T. vulgaris* have also shown high potency in the suppression of cancer cells [26].

T. vulgaris oils stimulated the extermination of cancer cells by controlling interferon signaling and the biosynthesis of N-glycan as well as the extracellular signal-regulated kinase 5 signaling [167]. According to the study by Soomro et al. [190], the butanol leaf extract of *T. vulgaris* exhibited slight anticancer activity against HeLa cervical cancer cell lines. This anticancer activity of *T. vulgaris* was attributed to the bioactive compounds such as tannins, triterpenes, sterols, flavonoids, and glycosides isolated from this plant.

***Tinospora cordifolia* (Menispermaceae)**

T. cordifolia has been used in vitro to exterminate HeLa cancer cells, which confirms the anticancer activity of *T. cordifolia* [168]. The dichloromethane extract of *T. cordifolia* exhibited high efficacy against cancer cells in mice [168]. The methanolic stem extract of *T. cordifolia* elicited cytotoxicity and inhibited the proliferation of human breast cancer cell line (MDA-MB-231) in the study carried out by Ahmad et al. [169]. The anticancer bioactive compounds identified in *T. cordifolia* include epoxycedanediene, arabinogalactan, berberine, and phenolics [170].

***Tithonia diversifolia* (Compositae)**

The ethanolic and methanolic leaf extracts of *T. diversifolia* inhibited the proliferation of HL-60 and U373 cancer cell lines, respectively [171, 172]. Bioactive compounds such as tagitinin C, 1 β -methoxydiversifolin 3-O-methyl ether, 1 β and 2 α -epoxytagitinin C are the major anticancer agents present in *T. diversifolia* and were involved in the inhibition of human Col2 colon cancer cells proliferation and cell death [173]. The methanolic leaf extract of *T. diversifolia* contains tagitinin C, which suppressed G2/M, reduced cancer cell viability, and stimulated cancer cell autophagy. Tagitinin C was also reported to be responsible for the anticancer activity of methanolic leaf extract of *T. diversifolia* [174].

***Uvaria chamae* (Annonaceae)**

The ethanolic stem-bark extract of *U. chamae* exhibited anticancer activity through the repression of lymphocytic

leukemia proliferation, whereas the ethanolic root extract mitigated tumor marker levels in rats [175]. The bioactive compounds isolated from *U. chamae* with anticancer potentials include dichamanetin, diuvaretin, uvaretin, chamanetin, pinocembrin, isouvaretin, pinostrobin, and isochamanetin [4].

***Vernonia amygdalina* (Compositae)**

Studies showed that *V. amygdalina* extracts inhibited the proliferation of BT-549 and MCF-7 breast cancer cell lines [176]. Steroid glycosides have been linked to the anticancer agent of *V. amygdalina* [176]. The chloroform extract of *V. amygdalina* suppressed KB cell lines. The peptide known as edotide in the leaves of *V. amygdalina* inhibited breast cancer [176–178].

***Zanthoxylum nitidum* (Rutaceae)**

The root of *Z. nitidum* is a rich source of nitidine. Nitidine is an anticancer agent that acts as an inhibitor of topoisomerases I and II activities [179, 180]. Benzophenanthridine isolated from *Z. nitidum* roots was reported to exert cytotoxic and antiproliferative activities against lung (A549), cervical (HeLa), and liver (SMMC-7721) cancer cell lines [181].

***Zingiber officinale* (Zingiberaceae)**

The anticancer bioactive compounds, namely, 10-gingerol, 10-shogaol, 6-gingerol, and 6-shogaol are present in *Z. officinale*. These bioactive compounds hindered the proliferation of PC-3 prostate cancer cell line [182]. 6-shogaol inhibited the proliferation of Huh7, HepG2, and SMMC-7721 (human hepatocellular carcinoma) cell lines [183, 184]. 10-gingerol was reported to inhibit metastasis [185]. The ethyl acetate extract of *Z. officinale* has been reported by Li et al. [186] to suppress the proliferation of MCF-7 breast, HepG2 liver, and KYSE-150 esophageal cancer cell lines.

Classifications of bioactive compounds with anticancer activity

The major classes of bioactive compounds from medicinal plants with anticancer activity include the polyphenols, flavonoids, alkaloids, saponins, triterpenes, tannins, and quinones. These bioactive compounds exerted antiproliferative, cytotoxic, cytostatic, antimetastatic, apoptotic, and antioxidative actions as well as provoked cell cycle arrest, inhibited angiogenesis and reduced cancer cell viability.

Polyphenols

Polyphenols have been reported to possess antioxidant and cytotoxic activities against cancer cells [191–193]. The anti-carcinogenicity of the polyphenols is hinged on their capabilities to initiate apoptosis. Polyphenols

regulate the assemblage of copper ions on chromatin. The copper ions assemblies on chromatin, engendered by the polyphenols such as resveratrol, elicit DNA disintegration [191].

Plant polyphenols also interacted and interfered with cancer cells proteins and thereby inhibited the growth of these cells. Polyphenols bonded directly with cancerogens disrupted their cancer promoting activities through acetylation, phosphorylation, and methylation mechanisms. For instance, a polyphenol-curcumin was reported to suppress the actions of tumor necrosis factor (TNF) in cell lines [194]. Curcumin also stimulated the apoptotic pathway, initiated cell cycle arrest and hindered the protein tyrosine kinase activity as well as the manifestation of c-myc mRNA and bcl-2 mRNA [89].

Flavonoids

The flavonoids were reported to be toxic to cancer cells and exhibited high free radical scavenging activity [195]. The following flavonoids, alpinumisoflavone and 4'-methoxy licoflavanone, initiated the apoptosis of human leukemia via extrinsic and intrinsic signaling pathways; the mitochondria of the cell were destroyed in the process, and thereby lead to cell death [196]. Xia et al. [197] reported the high anticancer efficacy at low concentrations of the flavonoids.

The flavonoids hindered NF- κ B expression. NF- κ B is a protein complex that is required for the angiogenesis, proliferation and survival of cancer cells [198]. The flavonoid, isoliquiritigenin, induced the obstruction of S-phase and G2/M-phase as well as activated GADD153 mRNA and protein functions involved in cell cycle arrest [100].

Alkaloids

These bioactive compounds disrupted tumorigenesis as well as the progression of tumor cell growth [199–201]. The alkaloids inhibited cancer cells proliferation through the initiation of cell apoptosis and by stimulating the termination of cancer cell cycle at G1-phase or G2/M-phase [199, 202, 203]. The alkaloids induced cancer cell autophagy and endoplasmic reticulum damage [202, 204]. The alkaloids elicited their anticancer efficacy majorly by acting as inhibitor of tumor invasion and metastasis [205, 206]. Jie et al. [207] and Hamsa and Kuttan [208] reported the ability of alkaloids to inhibit tumor angiogenesis. These bioactive compounds reduced cellular glutathione (GSH) levels by interacting directly with GSH and thus stimulated the generation of ROS [209–212]. The alkaloids are also involved in the inhibition of NF- κ B activation [199, 202].

Saponins

Saponins exhibited immunomodulatory activities through cytokine interplay [199]. Cytotoxic and cytostatic actions

were among the major anticancer mechanisms of saponins [213, 214].

The triterpene saponins repressed the growth of cancer cells and activated apoptosis [215]. Saponins exerted antiproliferative activity by clustering in the S-phase and causing G2/M-phase obstruction, as well as the inhibition of the expression of p21 and the cyclin-dependent kinase activity. Saponins activate cancer cell apoptosis through the stimulation of caspase-3 and caspase-9, and the disintegration of poly (ADP-ribose) polymerase accompanied by DNA fragmentation and condensation of nuclear chromatin [216, 217]. The steroidal saponins promoted cancer cell cycle arrest and induced apoptosis, as well as acted as antitumor agents [218]. The saponins, ginsenoside Rp1, induced cancer cell cycle arrest through the repression of G2/M cells, cdc2, and cyclin B1 [102].

Triterpenes

Triterpenes such as 3-O-acetyl-11-keto- β -boswellic acid initiated tumor cell apoptosis through the stimulation of the death receptor DR-5 signaling pathway [219, 220]. Triterpenes also initiated apoptosis of tumor cells through the upregulation and downregulation of Bax (proapoptotic protein) and Bcl-2 (antiapoptotic protein) secretion [221–225]. Triterpenes have also induced apoptosis by raising the levels of intracellular Ca²⁺ and stimulating the release of P53 [226].

Triterpenes induced cell cycle arrest at the G2/M-, G1-, and S-phases by mitigating cyclin Bi/cdc2 action, upregulation of P21 effect and the repression of cyclin A expression, respectively [221, 224, 227]. Triterpenes hindered the proliferation of tumor cells through the obstruction of the Akt/mTOR signaling pathway [228, 229]. Triterpenoids hindered the invasion and migration of cancer cells by mitigating the expression of the proteins MMP-2 and MMP-9 as well as gelatinase activity [230]. This class of bioactive compounds suppressed tumor angiogenesis by inhibiting the secretion of the angiogenic factors: bFGF and VEGF-A and the vascular endothelial growth factor [231, 232].

Tannins

The anticancer pharmacological actions of the tannins, such as ellagiatannin, have been reported to be involved in cyclin E upregulation and cyclins A and B1 downregulation, cell cycle obstruction at the S-phase, and apoptosis activation through the intrinsic pathway by downregulating bcl-XL accompanied by the cytosolic mitochondrial secretion of cytochrome C, as well as induction of caspase-3 and caspase-9 [233].

According to Jia et al. [234], tannins such as corilagin exhibited anti-inflammatory action, inhibited the growth of cancer cells by obstructing the TGF- β /AKT/ERK/Smad

signaling pathways, as well as induced cell cycle arrest at the G2/M-phase. Tannins also elicited apoptosis of cancer cells through the stimulation of sub-G1 fraction and condensation of chromosome as well as DNA disintegration [235].

Quinones

Quinones such as aloe-emodin inhibited the proliferation of cancer cells through the obstruction of the following cell cycles: G1-, G2/M- or S-phases [236–240]. Quinones stimulated DNA damage by inducing ROS [241]. Quinones activated cancer cell apoptosis by stimulating c-Jun N-terminal kinase, caspases, the Fas pathway and p53 pathway [236, 240, 242, 243].

The anticancer activity of the quinones has also been attributed to the ability of these bioactive compounds to mitigate the expression of urokinase, MMP-2 and MMP-9 proteins as well as nuclear translocation inhibition [139, 244, 245]. The quinone, β-lapachone, was reported to induce DNA fragmentation and the synthesis of apoptotic bodies, repressed the proteins Bcl-2 and Bcl-XL and stimulated the action of Bax, and thereby promoted cancer cell

apoptosis, activated poly (ADP-ribose) polymerase protein and caspase-3 and caspase-9 [165].

Anticancer drugs derived from Nigerian medicinal plants after undergoing research and clinical trials

Drugs derived from medicinal plant in the form of herbal remedies are preferred to synthetic drugs for the treatment of cancer because; for the most part, they are associated with fewer side effects, inexpensive, and readily available. These herbal remedies can be easily consumed as components of the patient’s dietary intake [246, 247]. The anticancer activity of medicinal plants are dependent on their bioactive compounds, although some of these bioactive compounds such as lectins, some taxanes, cyanogenic glycosides, and lignans are less tolerated and toxic to humans [248, 249]. Nevertheless, research has also shown that plants derived drugs exhibited anticancer activity with little or no toxic effects on normal cells and have been subjected to clinical trials for the development of therapeutics [247].

The anticancer drugs derived from Nigerian medicinal plants that have undergone various stages of

Table 2 Anticancer drugs derived from Nigerian medicinal plants after undergoing research and clinical trials

Anticancer drug	Plant source	Bioactive compound involved	Pharmacological actions
Paclitaxel (Taxol)	<i>Taxus brevifolia</i> (Taxaceae)	Taxane	Disruption, polymerization, and stabilization of the microtubules stimulate cancer cell apoptosis, hinder translational machinery, interfere with the synthesis of the spindle, and inhibit mitosis.
Vinblastine, Vinflunine Vinorelbine, Vindesine, Vincristine,	<i>Catharanthus roseus</i> (Apocynaceae)	Vinca alkaloids	Antitumor effects, proapoptotic activity, and obstruction of the cell cycle inhibits mitosis, attaches to β-tubulin, and interferes with microtubule activity.
Pomiferin	<i>Maclura pomifera</i> (Moraceae); <i>Derris malaccensis</i> (Leguminosae)	Isoflavonoid	Inhibitor of histone deacetylases induces DNA fragmentation, cytotoxic to cancerous cells, and causes proapoptosis.
Epigallocatechin-3-gallate	<i>Camellia sinensis</i> (Theaceae)	Catechin	Inhibits the action of certain kinases, hinders the proliferation of cancer cells, exerts antioxidant effects, and inhibits carcinogenesis caused by chemicals and UV radiations.
Sulphoraphane	<i>Brassica rapa</i> (Brassicaceae)	Isotiocyanate	Hinders the development of breast tumors, inhibits the proliferation of cancer cells, and stimulates phase 2 enzymes for detoxification.
Flavopiridol	<i>Dysoxylum binectariferum</i> (Meliaceae)	Synthetic flavonoid derivative, rohitukine	Inhibits cell growth, immune system modulation, exerts tyrosine kinase activity, and ameliorates inflammation.
Epipodophyllotoxin	<i>Podophyllum peltatum</i> (Berberidaceae)	Podophyllotoxin isomer	Disrupts cell cycle and causes proapoptosis of cancer cells.
Combretastatin A-4 phosphate	<i>Combretum caffrum</i> (Combretaceae)	Water-soluble analog of combretastatin	Inhibits angiogenesis, vascular shutdown, and necrosis of tumor cells.
Noscipine	<i>Papaver somniferum</i> (Papaveraceae)	Noscipine alkaloid	Inhibition of cancer cells proliferation hinders the growth of tumors and interferes with microtubules.
Roscovitine	<i>Raphanus sativus</i> (Brassicaceae)	Olomucine	Inhibits the continuation of the cell cycle and inhibits cyclin-dependent kinases.

Sources: [6, 7, 10, 198, 246–254]

research and clinical trials include paclitaxel (Taxol), vinblastine, vinflunine, vinorelbine, vindesine, vincristine, pomiferin, epigallocatechin-3-gallate, sulphoraphane, flavopiridol, epipodophyllotoxin, combretastatin A-4 phosphate, noscapine, and roscovitine. The Nigerian plants from which anticancer drugs are derived, the bioactive compounds that exert the anticancer activity as well as the associated pharmacological actions are presented in Table 2.

Conclusion

In this review, the 51 Nigerian medicinal plants were reported to exhibit anticancer activity of the prostate, cervixes, lung, skin, colon, esophagus, blood, ovary, central nervous system/brain, breast, stomach, pancreas, larynx, and kidney, indicating the possible use of these medicinal plants as anticancer drug agents. The major classes of bioactive compounds indicated to be responsible for the anticancer activity include the polyphenols, flavonoids, alkaloids, saponins, triterpenes, tannins, and quinones. The major anticancer pharmacological actions of these bioactive compounds were antiproliferative, cytotoxic, cytostatic, antimetastatic, apoptotic, and antioxidative as well as provoked cell cycle arrest, inhibition of angiogenesis and reduction of cancer cell viability. This review also reported 14 anticancer drugs derived from Nigerian medicinal plants that have undergone various stages of research and clinical trials. These anticancer drugs include paclitaxel (Taxol), vinblastine, vinflunine, vinorelbine, vindesine, vincristine, pomiferin, epigallocatechin-3-gallate, sulphoraphane, flavopiridol, epipodophyllotoxin, combretastatin A-4 phosphate, noscapine, and roscovitine.

The present review showed that leaf, root, and stem-bark extracts of the Nigerian medicinal plants were principal sources of vast majority of bioactive compounds that exhibited anticancer activity. Therefore, further emphases on the investigations of anticancer activity of these Nigerian medicinal plants parts, namely, the leaf, root, and stem-bark extracts is recommended. Nigerian medicinal plants can be harnessed to provide for readily available and inexpensive anticancer drugs in the future because the plants reported in this review showed promising anticancer activity.

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Studies involving plants statement

Not applicable

Authors' contributions

FOO/PCC conceived and designed the scope of the report. FOO/PCC/CMC/CCE contributed in writing the paper. FOO/PCC revised and edited the manuscript draft. CMC/CCE authors were the resource persons who provided all the necessary materials for writing the manuscript. All authors have read and approved the manuscript in the present form and gave the permission to submit the manuscript for publication.

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