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Review

Traditional West African pharmacopeia, plants and derived compounds for cancer therapy

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ABSTRACT

Traditional pharmacopeia is strongly involved in the continuous search for the well being of African populations. The World Health Organization (WHO) estimates that 80% of the population of developing countries relies on traditional medicine for their primary care needs. Medicinal plants are the major resource of this folk medicine where several species are used for the treatment of diseases with an inflammatory and/or infectious component as it is the case of old wounds, skin diseases and malfunctions affecting internal organs such as liver, lung, prostate and kidney. Many of these pathologies described by practitioners of traditional medicine have similarities with certain cancers, but the lack of training of many of these healers does not allow them to establish a link with cancer. However, ethnobotanical and ethnopharmacological surveys conducted by several researchers allowed to identify plants of interest for cancer treatment. Most scientific investigations on these plants demonstrated an anti-inflammatory or antioxidant effect, and sometimes, antiproliferative and cytotoxic activities against cancer cells were reported as well. The emergence of resistance to cancer chemotherapy has forced researchers to turn to natural products of plant and marine origin. In the West African sub-region, research on natural anti-cancer molecules is still in its infancy stage because of very limited financial resources and the scarcity of adequate technical facilities. However, several plants were investigated for their anticancer properties through north–south or south–south partnerships. In this review, we will review the role of West African traditional pharmacopeia in cancer treatment as well as medicinal plants with anti-cancer properties.

Contents

Abbreviations: CDC2, cell division control protein 2 homolog; CDC25C, M-phase inducer phosphatase 3; DMBA, dimethylbenzen(α)anthracene; DLD1, human colorectal carcinoma; EBV-EA, Epstein-Bar Virus Early Antigen in Raji cell line; GST, glutathione *S* transferase; GSH, glutathione; JNK, Jun N-terminal kinases; MDR, multidrug resistance; NAD(P)H, nicotinamide adenine dinucleotide phosphate-oxidase; PARP, poly(ADP-ribose) polymerase; P-gp, P-glycoprotein; P12, cyclin-dependent kinase inhibitor 1; PI3 kinase/Akt, phosphoinositol-3-kinase; PKC, protein kinase C; PP2A, protein phosphatase 2; p38 MAP kinases, p38 mitogen-activated protein kinases; P450CYP3A2, hepatic expression of cytochrome P450; P450CYP2C11, male-specific P450; TPA, 12-O-tetradecanoylphorbol-13-acetate; TPM4-ALK, tropomyosin alpha-4 chain-anaplastic lymphoma kinase; UDP-GT, glucuronosyl S-transferase; VEGF, vascular endothelial growth factor.

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1. Introduction

The World Health Organization (WHO) has classified cancer among non-communicable diseases, which are responsible for 63% of deaths worldwide [1]. Cancer is characterized by an uncontrolled proliferation of abnormal cells that can affect other organs of the body. This leads to the phenomenon of metastasis, which is the leading cause of death by cancer [2]. The World Bank income groups estimated that the incidence of 12.7 million new cancer cases in 2008 [3] will rise to 21.4 million by 2030, and low or middle-income countries will be the most affected with nearly two thirds of all cancer diagnoses [4]. Already in 2008, WHO had estimated that nearly 70% of cancer deaths occurred in these countries [5]. Particularly in low-income countries, the cancer-associated chronic infections are the cause of 18% of the global cancer burden. The principal infectious agents are human papillomavirus, Hepatitis B virus, Hepatitis C virus and *Helicobacter pylori*, which have been largely stopped through vaccination and awareness among high-income populations, but not in many low-resource countries [5]. West Africa is composed of mostly poor countries where cancer is an emergent disease. In 2008, men in the African Region had more than double of the rate of liver cancer while women in this region had the highest incidence of cancer of the *cervix uteri* worldwide. According to WHO estimates, 80% of the rural population of this region has almost exclusively uses traditional medicine for its needs of primary health care [6]. This massive use of traditional medicine, composed mainly of medicinal plants, is related to cultural and economic reasons. This is why WHO encourages countries of this region to promote and integrate traditional medical practices in their health system [7,8]. The valuation of folk medicine passes necessarily through the initial investigation of phytochemical and pharmacological properties of natural substances and the evaluation of their level of toxicity [9,10]. Secondarily, the traditional healers and herbalists should be educated on the rational use of natural substances in order to preserve species in danger of disappearing. Africa is one of the continents where the highest rate of deforestation in the world was reported [11]. Besides drought and bush fires, uncontrolled exploitation of plants whose therapeutic effect is known represents a threat to species survival. Among these species, we note particularly plants used in cancer treatment. Many of these plants have been studied but there is very little review to assess the level of study of each plant. According to Ameenah [11], the knowledge of African traditional medicine is still poorly recorded, but the rapid loss of the natural habitats of many plants due to anthropogenic activities justifies the fact that the documentation of medicinal uses of African plants is becoming increasingly urgent [11]. This review aims to improve this situation by providing an update on West African plants with anticancer properties whether crude extracts, fractions or isolated and semi-synthesized molecules were investigated.

2. Traditional medicine and cancer treatment

WHO defines traditional medicine as the sum of the knowledge, skills, and practices whether explicable or not, used in the prevention, diagnosis, improvement or treatment of physical and mental illness. It is considered that herbal medicines include herbs, herbal materials, herbal preparations and finished herbal products, which contain as active ingredients parts of plants, or other plant materials, or combinations [12]. The general term "cancer" applies to a large group of diseases that can affect any part of the body. Therefore, cancer is found in several systems (circulatory, lymphatic, digestive, urinary, reproductive) as well as skin [13,14]. Because of technological advances, the diagnosis of cancer is easier in modern medicine but not in the traditional. It is well known that cancer is poorly defined in terms of folklore and traditional medicine [15,16]. According to surveys conducted by Abubakar and his colleagues among the Hausa and Fulani tribes, the concepts and etiology of cancer in traditional medicine are complex and are not always compatible with modern medical practices [17]. This can be justified by the fact that most of the healers of folk medicine are not educated to establish an adequate link between symptoms and type of pathology, which does not allow a proper clinical diagnosis; in addition, diagnostic tools are totally absent. In this context, what may be the contribution of traditional medicine to the treatment of cancer?

2.1. Place and role of West African traditional medicine in cancer treatment

African traditional medicine provided the bulk of the coverage of health needs of populations during the pre-colonial period in the absence of modern Western medicine. According to global statistics in 2008, the West Africa has about 15 physicians per 100,000 inhabitants while in France the ratio is 322 for the same number of inhabitants [18]. Moreover, a resident of West Africa spends between $ 10 and $ 40 for medical care per year, whereas in France this sum is $ 4719 (more than 100 times) [19]. In this context of extreme poverty and severe shortage of health workers in these developing countries, the contribution of traditional medicine in the fight against diseases, especially cancer, is an important asset for the well being of people. Interest in the traditional medicine can be explained by the fact that it is an integral part of the culture of the people who use it [7,8], and also by the economic challenge: on one side, the pharmaceutical drugs are not accessible to the poor and the other side, the richness and diversity of the flora of West Africa are an inexhaustible source of remedies against several diseases. Indeed, on 300,000 plant species recorded in the world, more than 200,000 live in the tropical countries of Africa and elsewhere [20]. The rich flora of West Africa is linked to two different environments: the rain forest along the coast and the savannah in the hinterland [21]. It is well known that plants are significant sources of drugs and particularly antitumor molecules [15,22]. According to WHO, 25% of pharmaceutical drugs are made from plants that were first used in traditional medicine [23]. In several countries of West Africa, traditional healers claim their ability to treat cancer by herbal preparations, mineral or animal substances [7,17,24,25]. The traditional treatment protocol is often influenced by social and cultural habits of the locality of the healer, but in general, this treatment

takes into account the ethical aspects and excludes practices that affect patient's compliance [17,26]. The material used in West African traditional medicine for cancer treatment is of terrestrial origin (mineral, animal or vegetable). Substances of marine origin are almost nonexistent because of weak possibilities of exploring the seabed. In general, medicinal plants are the mainstay of treatment; mineral and organic substances can sometimes be added as supplements [27]. The recipes offered by traditional healers are often multi-components, prepared with two or three plants. The mode of preparation may be by decoction, concoction, infusion, aqueous or alcoholic maceration, and powders added to food or drinks [17,28]. Sometimes poultices are used for external applications in the treatment of some cancers (skin, breast, etc.) [7]. The mode of administration is very varied: oral, anal or dermal washing for aqueous or alcohol extracts, and inhalation for volatile substances [27,29]. Many practitioners of traditional medicine offer herbal recipes that are supposed to treat cancer, but no ethnomedical evidence is established for most of them. This ethnomedical evidence is the result of a randomized clinical study comparing treatment with the traditional recipe to that of modern medicine. Failing to make a comparison, the evolution of health of several patients to healing should be obvious. It requires collaboration between a western trained physician and indigenous healers [30], crucial point that cannot be solved without a clear political will of each country to integrate traditional medicine into their health system. Another palliative strategy is to create an interactive forum between researchers and practitioners of traditional medicine to establish a relationship of mutual trust [7,31]. These forums help to explain to traditional healers, signs and symptoms of cancer and the modern approach to its treatment. Sometimes the recipes offered by traditional healers do not show obvious anticancer properties in the pharmacological assessment and this can be explained by several reasons. To be valid, the pharmacological investigation must meet the mode and period of harvest of the plant, and the method of preparation and administration of the recipe given by the traditional healer. Some recipes are mixed with mystical practices that are not scientifically exploitable [11,26,27]. In addition, the oral administration submits the various substances to the effects of digestive metabolism leading to secondary metabolites that are not available in the in vitro experiment. Another justification, not unimportant, is the ascent of quackery and scams in traditional medicine. Previously, traditional healers did not seek to enrich themselves by practicing traditional medicine; they were a resort for the well being of the population. However, nowadays, many people, claiming healers, are greedy for money and they offer all kinds of recipes that, according to them, can cure any kind of disease. With the emergence of cancer in low-income countries, many false healers make it as an opportunity to get rich on the backs of the sick. These recipes are very expensive but without any relief for the patient. This is why many African countries have taken steps to regulate the practice of traditional medicine in order to integrate it into their health system.

2.2. Integration of traditional medicine in health systems

Since 1978, the WHO at its 31st Assembly has recommended countries to make a complete inventory of medicinal plants, evaluation of their efficacy and safety and a standardization of the active products [32]. WHO has reported some critical problems that impede the integration of traditional medicine in the majority of countries [33]:

- Public demands on folk medicine exceeds the expertise and resources of health authorities.
- Inadequate regulation and registration for herbal products and other traditional therapies.
- Lack of training for research in traditional medicine.

To solve these problems, the traditional medicine team of WHO provided technical guidelines, standards, and methodologies and facilitates the exchange of information among member states in order to enhance traditional medicine integration in each country [33]. Moreover, WHO supports national programs of research and training in order to ensure a comprehensive evaluation of the traditional systems of medicine and to allow an active cooperation with the modern health care system. In this way, the integration of traditional medicine with research and training can lead to a complementary treatment, allowing the patient to benefit from both therapies improved treatment at lower cost. This is a path of development and promotion of traditional medicine products, but cannot succeed without political will of each country to integrate traditional medicine into their national health system. In Ghana (from West Africa) for example, the authorities have decided to introduce a postgraduate diploma course in traditional medicine at its premier medical school at "Korle Bu" in order to formally train doctors and other health professionals in traditional medicine [26]. Another example is Nigeria where the integration of traditional medicine since 1960 is discussed with great interest of traditional healers and doctors [34]. Recent studies have shown that both parties are arranged for collaboration and integration of traditional medicine in the health system of this country [8,35]. In most countries of West Africa, research on medicinal plants has been integrated into the research programs of universities and research center. Some countries like Benin, Burkina Faso, Ghana, Mali and Nigeria have created the center of traditional medicine where research and/or primary care are made with products from local plants. These national commitments have enabled the development and production of herbal medicines, which are authorized for sale by the ministry of health, but these products are generally intended for the treatment of malaria, hypertension and sickle cell disease [36–40]. The cancer research is still in early stage in West Africa [41]. This is due to the scarcity of technical facilities suitable for the realization of anti-cancer tests and limited financial resources allocated to research in West African countries. Thus, most research conducted on the anticancer activity of plants are made in collaboration with laboratories in developed countries. It is therefore evident that the integration of traditional medicine in national health systems is not sufficient to solve the problem of cancer. North–south collaboration is essential at this stage for a recovery and maximum exploitation of the potentialities of traditional medicine in the field of cancer care.

3. West African medicinal plants and their phytochemicals with anticancer properties

Natural compounds exhibit numerous biological activities and recent research provided insight into the cancer hallmarks efficiently inhibited by molecules extracted from various origins [42–47]. Investigation of anti-cancer properties of West Africa medicinal plants can be classified into two levels: the first level involves preliminary research that helped to highlight the anticancer activity of crude extracts or fractions of medicinal plants (Table 1). The second level involves advanced research performed to isolate natural anti-cancer molecules (Table 2).

3.1. Plants with anticancer properties

Approximately twenty-five plants of West Africa, distributed in 18 families, showed an interesting anti-cancer activity (Table 1). The plant families that are most representative are Mimosaceae, Euphorbiaceae and Annonaceae with two plants each. Analysis of the results of our literature search shows that only 30% of these plants have been extensively studied, leading to the isolation of

Table 1
West African medicinal plants with anticancer properties.

Plants	Traditional use	Part used	Extract	Phytochemicals	Anticancer properties	References
Acacia macrostachya (Mimosaceae)	Decoction is used to treat inflammation and cancer	Root barks	Methanol	Di and triterpenes, saponins, tannins, anthraquinones, alcaloids	Antiproliferative effect again KB cells (95% at 10 μg/mL)	[101]
Acalypha wilkesiana (Euphorbiaceae)	Concoction to treat inflammation and breast tumor	Whole plant	Ethyl acetate and hexane	Saponins, tannins, anthraquinones, cardiac glycosides, alkaloids and phlobatannins.	Apoptosis in U87MG and A549 through induction of DNA SSBs and DSBs	[102–104]
Acanthospermum hispidum (Asteraceae)	Poultice and decoction to treat cancer	Flowering shoots	Methanol	Alkaloids, glycosides, flavonoids, tannins, saponins	Significant cytotoxicity on: MCF-7 (IC_{50} = 13.5 ± 1.0 μg/mL), C32 (IC_{50} = 13.5 ± 0.8 μg/mL) and COR-L23 cells (IC_{50} = 8.8 ± 0.9 μg/mL)	[7,105]
Annona senegalensis (Annonaceae)	Skin cancer and leukemia	Stem barks Leaves	Hydro-distillation	Flavonoids, anthocyanosides, saponosides, tannins, triterpenes and steroids	Total essential oil induce a high cytotoxicity effect again: A549 (IC_{50} = 0.3 μg/mL) HT29 (IC_{50} = 10 μg/mL) MCF-7 (IC_{50} = 0.1 μg/mL) RPMI (IC_{50} = 20 ng/mL) U251 (IC_{50} = 0.1 μg/mL)	[106,107]
Balanites aegyptiaca (Balanitaceae)	Treatment of inflammation, diabetes and parasitic diseases	Kernel and galls	Aqueous maceration, Methanol	Cardiac glycosides, tannins, anthraquinons, saponins, triterpenes and steroidal glycosides, alkaloids, flavonoids.	Cytotoxicity effect on a panel of cancer cell lines (A549, U373, PC-3, Bx-PC3, LoVo, MCF-7), strong antioxidant activity	[108–112]
Calotropis procera (Apocynaceae)	Treatment of ulcers, tumor, snake bites, malaria and piles	Root barks and latex	Methanol	Cardenolides, flavonoids, saponins, tannins, alkaloids	High antiproliferative effect on a panel of cancer cell lines (Hs683, U373, HCT-15, LoVo, A549, HL-60, SF295, MDA-MD-435)	[80,113–116]
Cajanus cajan (Fabaceae)	Poultice and concoction to treat cancer	Leaves	Methanol	Steroids, cardiac glycosides, anthraquinones, saponins, flavonoids, alkaloids, tannins	Significant cytotoxicity on: MCF-7 (IC_{50} = 16.08 ± 1.0 μg/mL) and COR-L23 cells (IC_{50} = 9.8 ± 0.9 μg/mL)	[7,117]
Detarium microcarpum (Papilionaceae)	Decoction is used to treat anemia	Stem barks	Methanol	Phenolics, flavonoids, saponins, triterpenes, steroids and glycosides	Inhibition of growth of MDA-MB 231 cells (IC_{50} = 14.8 μg/mL)	[118–120]
Dorstenia psilirus (Moraceae)	Treatment of rheumatism and snakebites	Roots	Methanol	Polyphenol, phenol, flavonoids, saponins, triterpenes and glycosides	Significant cytotoxicity again: MiaPaCa2 (IC_{50} = 9.1 μg/mL) CCRF-CEM (IC_{50} = 7.1 μg/mL) CEM/ADR5000 (IC_{50} = 7.7 μg/mL)	[121,122]
Echinops giganteus (Compositae)	Treatment of heart and gastric troubles	Rhizome	Methanol	Polyphenols, flavonoids, triterpenes, phenols, tannins, anthraquinones, alkaloids, anthocyans	High cytotoxicity again: MiaPaCa2 (IC_{50} = 9.8 μg/mL) CCRF-CEM (IC_{50} = 6.6 μg/mL) CEM/ADR5000 (IC_{50} = 7.9 μg/mL)	[121,123,124]
Holarrhena floribunda (Apocynaceae)	Treatment of snake bites	Stem	Ethanol	Alkaloids, saponins, cardiac glycosides, tannins	Inhibition of growth of: MDA-MB 231 cells (IC_{50} = 9.9 μg/mL) A-549 (IC_{50} = 3.4 μg/mL) KB (IC_{50} = 7.9 μg/mL) SK-MEL28 (IC_{50} = 9 μg/mL)	[118,125]
Imperata Cylindrical (Gramineae)	Treatment of inflammation diseases	Roots	Methanol	Saponins, steroids, terpenoids, cardiac glycosides, alkaloids, tannins and flavonoids	High cytotoxicity again: MiaPaCa2 (IC_{50} = 12.1 μg/mL) CCRF-CEM (IC_{50} = 8.4 μg/mL) CEM/ADR5000 (IC_{50} = 7.1 μg/mL)	[121,126–128]
Jatropha curcas (Euphorbiacea)	Treatment of fever and infectious diseases	Whole plant	n-Hexane, ethyl acetate and methanol	Alkaloids, flavonoids, terpenoids, saponins, tannins, steroids	High inhibition of cancer cells growth by hexane extract: L5178y (IC_{50} = 0.8 ± 0.1 μg/mL) PC12 (IC_{50} = 5.7 ± 0.6 μg/mL) Hela (IC_{50} = 1.7 ± 0.1 μg/mL)	[129–132]

Khaya senegalensis (Meliaceae)	Treatment of inflammation diseases	Stem barks	Methanol	Alkaloids, flavonoids, anthraquinones, cardiac glycosides, saponins, steroids, tannins, terpenoids	Strong antioxidant and anti-inflammatory activities, High inhibition of growth of: HT-29 (IC_{50} = 1.0 μg/mL) HCT15 (IC_{50} = 0.3 μg/mL) HCA7 (IC_{50} = 0.2 μg/mL) after 24 h treatment with strong inhibition of the expression of anti-apoptotic protein Bcl-2 in these cell lines. The extract blocks cell cycle progression and inhibits selectively COX-2 expression levels in HCA7 and HT29	[133–137]
Lantana ukambensis (Verbenaceae)	Decoction is used to treat cancer	Whole plant	Methanol and Methylene chloride	Saponins, tannins, triterpenoids, steroids, anthraquinons, alkaloids	Antiproliferative effect again KB cells (94% at 10 μg/mL)	[101]
Ozoroa insignis (Anacardiaceae)	Decoction to treat inflammation, Infusion to increase lactation in women after childbirth	Stems and Roots	Methanol	Saponins, tannins, triterpenoids, steroids, flavonoids	Inhibition of growth of MDA-MB 231 cells (IC_{50} = 14.8 μg/mL)	[101,118]
Parkia biglobosa (Mimosaceae)	Infusion to treat dental caries	Stem barks	Methanol	Cardiac glycosides, tannins, alkaloids, triterpenes and steroids	Inhibition of growth of MDA-MB 231 cells (IC_{50} = 13.5 μg/mL)	[118,138,139]
Piper capense (Piperaceae)	Sleep inducing and anthelmintic	Seeds	Methanol	Alkaloids, phenols, saponins, tannins, sterols, triterpenes	Significant cytotoxicity again: MiaPaCa2 (IC_{50} = 8.9 μg/mL) CCRF-CEM (IC_{50} = 7.03 μg/mL) CEM/ADR5000 (IC_{50} = 6.56 μg/mL)	[121,123]
Trichelia emetica (Meliaceae)	Treatment of abdominal pains, dermatitis, inflammation, Breast pain	Leaves, root and stem barks	Methanol, ethanol, Aqueous decoction	Steroids, triterpenoids, coumarins	Growth inhibition effect toward S180 and MCF-7 cell lines	[50,140,141]
Vitellaria paradoxa (Sapotaceae)	Treatment of scabies, ulcers and wounds	Seeds, root and stem barks	Methanol	Saponins, steroids, alkaloids, tannins, cardiac glycosides, anthraquinones	Cytotoxicity effect against T98G, MDA-MB231, A375 and HCT116 cell lines.	[74,137,142,143]
Ximenia americana (Olacaceae)	Internal wounds, gastric ulcer, uterine cancer, dermatitis	Root barks	Aqueous decoction	Alkaloids, anthraquinones, cardiac glycosides, flavonoids, saponins, tannins, terpenoids	High cytotoxicity again: MCF-7 (IC_{50} = 1.7 μg/mL) BV173 (IC_{50} = 1.8 μg/mL) CC531 (IC_{50} = 3.3 μg/mL) U87-MG (IC_{50} = 9 μg/mL) K562 (IC_{50} = 11 μg/mL) SKW3 (IC_{50} = 20 μg/mL)	[25,138,144,145]
Xylopia aethiopica (Annonaceae)	Wounds and skin infections	Seeds	Methanol	Alkaloids, phenols, saponins, tannins, triterpenes	High cytotoxicity again: MiaPaCa2 (IC_{50} = 6.86 μg/mL) CCRF-CEM (IC_{50} = 3.91 μg/mL) CEM/ADR5000 (IC_{50} = 7.4 μg/mL)	[121,123]
Zinziber officinalis (Zingiberaceae)	Treatment of cancer and infectious diseases	Rhizome	Methanol	Alkaloids, glycosides, saponins, phenols, tannins, flavonoids, triterpenoids, steroids	Significant cytotoxicity again: MiaPaCa2 (IC_{50} = 16.3 μg/mL) CCRF-CEM (IC_{50} = 8.8 μg/mL) CEM/ADR5000 (IC_{50} = 6.8 μg/mL)	[121,146,147]

Table 2
Anticancer molecules isolated from West African plants.

Molecule	Nature and origin	Pharmacological properties	References
Acetoxyjatropholone	Diterpene from *Jatropha curcas*	Cytotoxic on L5178y cells with IC_{50} of 2.5 μg/mL	[67,129]
Balanitin-6/7	Steroidal saponin from *Balanites eagyptiaca*	Significant growth inhibition of: A549 (IC_{50} = 0.3 μg/mL), U373 (IC_{50} = 0.5 μg/mL), PC-3 (IC_{50} = 0.9 μg/mL), Bx-PC3 (IC_{50} = 1.2 μg/mL), LoVo (IC_{50} = 1.5 μg/mL), MCF-7 (IC_{50} = 2.6 μg/mL), depletion of (ATP)i leading to major disorganization of the actin cytoskeleton in A549 and U373 cells.	[109,148]
Butyrospermol acetate and cinnamate	Triterpenes from *Butyrospermum parkii* or *Vitellaria paradoxa* (Sapotaceae)	Significant inhibition of EBV-EA activation induced by TPA. High inhibition of topic inflammation with ID_{50} of 0.7 and 0.2 μmol/ear respectively.	[74]
Curcusone A, B, C, D	Diterpene from *Jatropha curcas*	Cytotoxic on L5178y cells with IC_{50} of 0.2 μg/mL for curcusone A and B, 0.08 for curcusone C and 0.1 μg/mL for curcusone D.	[66,129]
15-Epi-4E-jatrogrossidentadion	Diterpene from *Jatropha curcas*	Cytotoxic on L5178y cells with IC_{50} of 0.8 μg/mL	[67,129]
2-Hydroxy-isojatrogrossidion and 2-epi-hydroxy-isojatrogrossidion	Diterpenes from *Jatropha curcas*	Cytotoxic on L5178y cells with IC_{50} of 0.2 μg/mL for each compound.	[67,129]
Jatropholone	Diterpene from *Jatropha curcas*	Cytotoxic on L5178y cells with IC_{50} of 7.5 μg/mL	[67,129]
4Z and 4E-jatrogrossidentadion	Diterpenes from *Jatropha curcas*	Cytotoxic on L5178y cells with IC_{50} of 0.6 and 2.1 μg/mL respectively	[67,129]
Kurubasch aldehyde	Sesquiterpenoid from *Trichilia emetic* (Meliaceae)	High inhibition of the proliferation of murine sarcoma S180 cancer cells with IC_{50} of 7.4 μM. Reduction of breast cancer cells (MCF-7) proliferation with IC_{50} of 78 μM.	[50]
Longistylin A	Hydroxyl stylbene from *Cajanus cajan*	High cytotoxicity again: MCF-7 (IC_{50} = 5.2 μg/mL), C32 (IC_{50} = 3.3 μg/mL), COR-L23 (IC_{50} = 5.0 μg/mL), HepG2 (IC_{50} = 0.7 μg/mL), 16HBE40 (IC_{50} = 2.5 μg/mL), AR42J-B13 (IC_{50} = 0.7 μg/mL), CCR-CEM (IC_{50} = 9.8 μg/mL), CEM/ADR5000 (IC_{50} = 10.3 μg/mL)	[7]
Longistylin C	Hydroxyl stylbene from *Cajanus cajan*	High cytotoxicity again: MCF-7 (IC_{50} = 4.4 ± 0.3 μg/mL), C32 (IC_{50} = 4.1 ± 0.4 μg/mL), COR-L23 (IC_{50} = 2.8 ± 0.3 μg/mL), HepG2 (IC_{50} = 1.6 ± 0.4 μg/mL), 16HBE40 (IC_{50} = 2.4 ± 0.05 μg/mL), AR42J-B13 (IC_{50} = 4.5 ± 0.2 μg/mL)	[7]
Lupeol acetate and cinnamate	Triterpenoid saponins from *Vitellaria paradoxa*	Significant inhibition of EBV-EA activation induced by TPA. High inhibition of topic inflammation with ID_{50} of 0.54 and 0.15 μmol/ear respectively.	[74]
Multidione	Diterpene from *Jatropha curcas*	Cytotoxic on L5178y cells with IC_{50} of 5.5 μg/mL	[67,129]
2″-Oxovoruscharin	Cardenolide from *Calotropis procera*	High antiproliferative effect on: Hs683 (IC_{50} = 8 nM) U373 (IC_{50} = 15 nM) HCT-15 (IC_{50} = 16 ± 5 nM) LoVo (IC_{50} = 10 nM) A549 (IC_{50} = 74 nM) Inhibition of the Na^+/K^+-ATPase pump with IC_{50} of 75 nM.	[80]
Pinostrobin	Flavanone from *Cajanus cajan*	Significant cytotoxicity again: CCRF-CEM (IC_{50} = 10.2 ± 1.1 μg/mL) Low cytotoxicity on Vero cells (CC_{50} > 100 μg/mL)	[7,149]
Parkioside B	Triterpenoid saponin from *Vitellaria paradoxa*	Antiproliferative effect again: T98G (IC_{50} = 2.9 μg/mL) MDA-MB231 (IC_{50} = 9.6 μg/mL) A375 (IC_{50} = 2.7 μg/mL) HCT116 (IC_{50} = 14.1 μg/mL)	[142]
Riproximin	Lectin from *Ximenia Americana*	High cytotoxicity on HeLa cell lines with IC_{50} of 1.1 pM	[150]
UNBS1450	Semi-synthetic derivative of 2-oxovoruscharin from *Calotropis procera*	Inhibitory potential on Na^+/K^+-ATPase isozymes. Induction of apoptotic cell death (K562, U937, Jurcat) at low dose (nM). Inhibition of NFkB pathway activation	[81,151]
Uscharin and voruscarin	Cardenolides from *Calotropis procera*	High antiproliferative effect on: Hs683 (IC_{50} = 4 nM) U373 (IC_{50} = 40 and 32 nM) HCT-15 (IC_{50} = 28 and 27 nM) LoVo (IC_{50} = 10 and 17 nM) A549 (IC_{50} = 25 and 9 nM) Inhibition of the Na^+/K^+-ATPase pump by uscharin with IC_{50} of 68 nM.	[80]

A375: human malignant melanoma cell line, A549: Lung carcinoma cell line, AR42J-B13: rat pancreatic cell line, B16F1: mousse melanoma, BV173: human chronic myeloid leukemia cell line, Bx-PC3: pancreas cancer cell line, C32: amelanotic melanoma cell line, CC531: rat colon cancer cell line, CCRF-CEM: leukemia cell line, CEM/ADR5000: leukemia cell multidrug resistant, COR-L23: large cell of lung carcinoma, DLD1: human colorectal carcinoma, EBV-EA: Epstein-Bar Virus Early Antigen in Raji cell line, HCA7: human colonic carcinoma cell line, HCT116: human colon carcinoma cell line, HCT15: human colon adenocarcinoma cell line, Hela: human cervix carcinoma cell line, HepG2: human hepatocellular liver carcinoma cell line, HL-60: human promyelocytic leukemia cell line, HS683: human neuronal glioma cell line, HT29: human colon adenocarcinoma grade II cell line, 16HBE40: human bronchiolar cell line, Jurcat: human T-cell leukemia cell line, K562: human chronic myeloid leukemia cell line, KB: human nasopharynx carcinoma cell line, L5178y: mousse lymphoma cell line, LoVo: colon cancer cell line, MCF-7: breast adenocarcinoma cell line, MDA-MB231: mammary carcinoma cell line, MiaPaCa2: human pancreatic carcinoma cell line, PC-3: prostate cancer cell line, PC12: rat adrenal medulla pheochromocytoma cell line, RPMI: human multiple myeloma cell line, S180: murine sarcoma cell line, SF295: central nervous system cancer cell line, SK-Mel28: melanoma cell line, SKW3: human acute lymphoblastic leukemia cell line, T98G: human glioblastoma multiforme cell line, TPA: 12-O-tetradecanoylphorbol-13-acetate, U251: human glioma cell line, U373: glioblastoma cell line, U87MG: grade IV human glioblastoma cell line, U937: histiocytic lymphoma cell line.

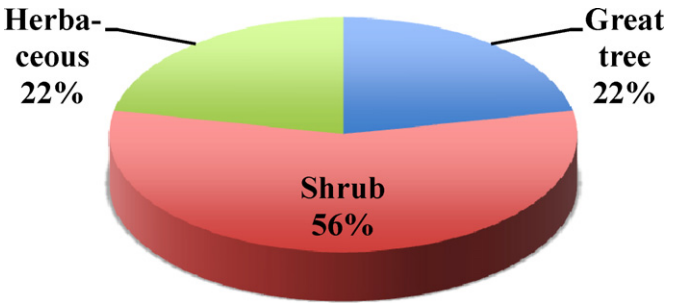


Fig. 1. Distribution of West African anticancer plants. Anticancer plants of West Africa have been classified into three groups according to their size: high tree, shrub and herbaceous. The percentage of each class was calculated based on the number of plants contained in this class compared to the total number of plants reported in Table 1. This classification allows to see the class that is most exploited in the search for anticancer drugs.

anticancer molecules. *Jatropha curcas* (Euphorbiacea) remains the most studied, where twelve diterpenes with anticancer properties were isolated. Thus, the majority of these plants are at the stage of preliminary investigation carried out on crude extracts or fractions.

56% of these anticancer plants are shrubs and most used organs of these plants are the roots and stem barks (50%) (Figs. 1 and 2). This could justify the risk of extinction of certain shrubs, as harvesting of the stem barks is traumatic for the plants and anarchic harvest of roots contributes significantly to their disappearing. To contribute to the conservation of the environment, research on anticancer plants could focus on herbaceous that represent 22% of West African anticancer plants (Fig. 1) and also to the leaves and seeds whose harvest is not a danger to the survival of the species.

The type of extract that is the most investigated is the methanolic one with 60% of use (Fig. 3) in contrast to traditional protocols that typically uses the aqueous extracts by decoction or maceration.

Among the cancer cells investigated, the most commonly used and the most sensitive to plant extracts are the leukemia cell lines followed respectively by breast, colon and lung cancer (Fig. 4). This trend responds moderately to health needs of African populations. In fact, the most common types of cancers in Africa are: uterine cervix, liver cancer, breast, and prostate cancer [48], and according to WHO, in 2011, breast cancer was the top cancer in women both in the developed and the developing world [49]. Unfortunately,

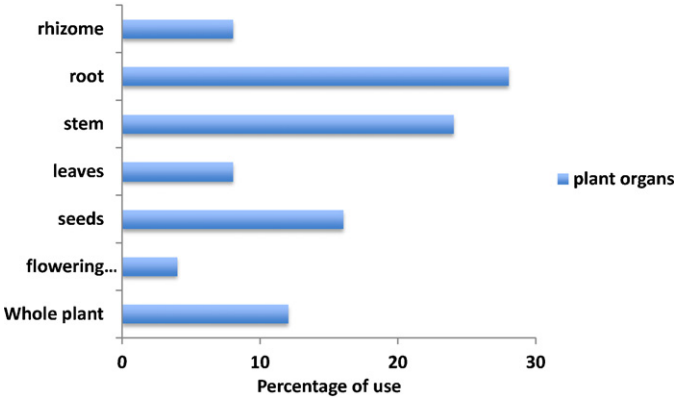


Fig. 2. Plant parts used in the investigation of West African anticancer plants. Overview of the plant parts that are most used for research of anticancer drugs in West Africa. The percentage of use of each organ was calculated from the number of times that the organ was used compared to the total number of use of all organs in the studies of West African anticancer plants reported in Table 1.

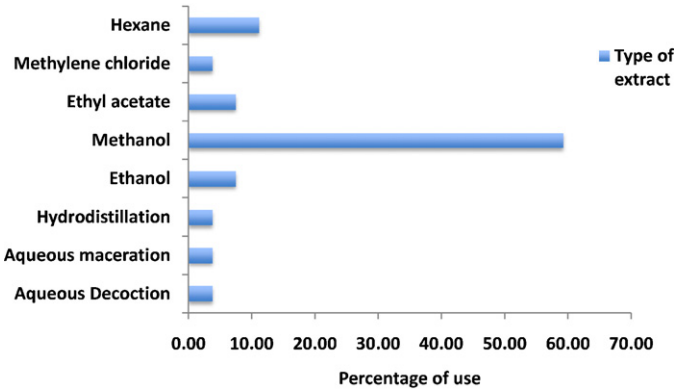


Fig. 3. Extracts used in the screening of West African anticancer plants. Different types of extraction used in the evaluation of anticancer properties of West African plants and the percentage of use of each extract. Each percentage was calculated from the number of times that the solvent was used compared to the total number of use of all solvents in the studies of West African anticancer plants reported in Table 1.

uterine cervix cancer, which is the most common among women in Africa, and liver cancer commonly found in both men and women are poorly investigated. In fact, liver and uterine cervix cancers are about eight times less studied compared to breast cancer (Fig. 4).

3.2. Phytochemicals with anticancer properties

Very few anticancer molecules were isolated from medicinal plants of West Africa. Only about twenty-six showed strong cytotoxicity against a panel of cancer cell lines (Table 2 and Fig. 6). 46% of these molecules are diterpenes followed by triterpenes that represents 19% (Fig. 5). This preponderance of terpenes (65%),

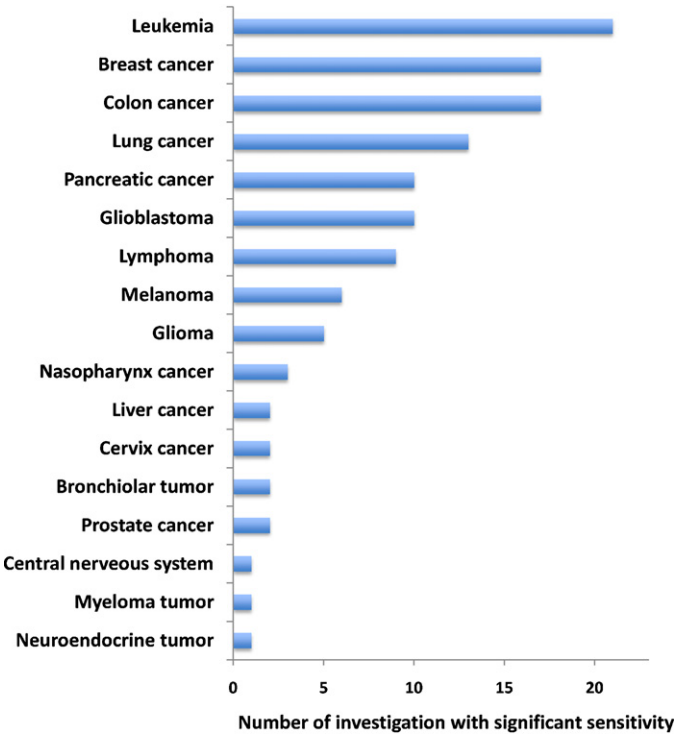


Fig. 4. Frequency of sensitivity of cancer cells to West African plant products. Overview of cancer cell lines sensitive to extracts or molecules isolated from West African medicinal plants and the frequency of sensitivity of each cell line. The frequency represents the number of times that each cell line gave a high sensitivity to plant products at dose less than 10 μg/mL.

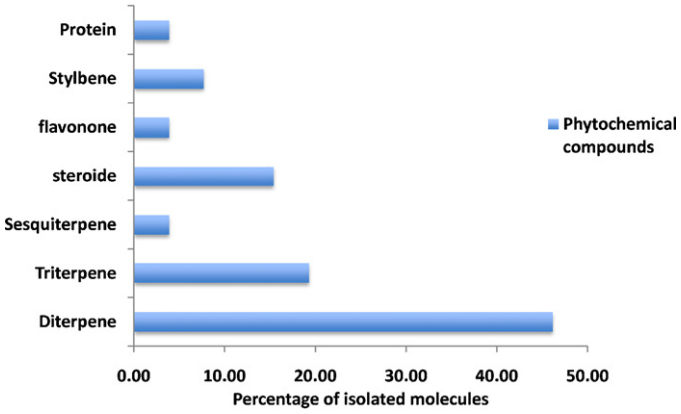


Fig. 5. Anticancer molecules isolated from West African plants. Phytochemical families from West African plants, which showed a significant anticancer activity against cancer cell lines. The percentage of each phytochemical family was calculated based on the number of active molecules in this family compared to the total number of active molecules reported in Table 2.

which are non-polar compounds, could justify the wide use of methanol in the extraction of West African anticancer plants.

These molecules open a wide field of prospects for preclinical and clinical studies with the aim of producing natural anti-cancer drugs.

3.2.1. Sesquiterpenes

Sesquiterpenes are mainly present in higher plants and are known as the group of C15 compounds resulting from the assembly of three isoprenoid units. They are found in essential oils of plants with a large structural variety with several cyclic, mono, bi, tri and tetracyclic systems. These diversities lead to various pharmacological properties including antimalarial, antibacterial, antiviral, anti-inflammatory and anti-tumor activities. Among anticancer molecules isolated from West African plants, one sesquiterpenoid is Kurubasch aldehyde from *Trichillia emetica* (Table 2, Fig. 6) that exhibited a high level of inhibition of the proliferation rate of murine sarcoma S180 cancer cells (IC_{50} of 7.4 μM) and a moderate reduction of breast cancer cell (MCF-7) proliferation (IC_{50} of 78 μM) [50]. Several papers were published on the anticancer properties of sesquiterpenes that revealed their potential mechanisms of action. The investigation of isodihydrocostunolide, a sesquiterpene isolated from *Saussurea lappa* Clarke (Compositae), conducted by Robinson et al. [51] showed the involvement of the *exo*-methylene group of the sesquiterpene chemical structure in the observed cytotoxicity. When a methoxy group substitutes the *exo*-double bond, the cytotoxic activity decreases drastically. Another sesquiterpene, namely curcuphenol isolated from *Baccharis genistelloides*, demonstrated an inhibition of DNA replication and induction of apoptosis through the stimulation of caspase-3 activity [52]. Dall'Acqua et al. [53] reported the antiproliferative and proapoptotic properties of sixteen isolated sesquiterpenes from the essential oils of three Italian plants *Ferula communis*, *Ferula glauca* and *Ferulago campestris*. All of them are cytotoxic at least against one of the tested cancer cell lines highlighting the interest of sesquiterpenes in cancer therapy. The most active compounds namely 2α-acetoxy-6α-p-methoxybenzoyl-10β-acet-oxy-jaeschkeanadiol and pallinin (6α,10α-diangeloyl-jaeschkeanadiol) are able to induce apoptosis in a time and dose-dependent manner. The preliminary investigation of structure–activity relationship suggested that the *trans* fusion of the penta- and hepta-atomic cycles and lipophilic ester groups of position 6 enhances the cytotoxic effect. In addition, the β orientation for the ester group in position 2 is essential for their cytotoxicity (Fig. 7).

Recently, two sesquiterpenes isolated from *Artemisia douglasiana* Besser, dehydroleucodine and dehydroparishin-B were found to be able to block selectively migration and proliferation of B16 melanoma cells in a dose-dependent manner [54]. The pharmacological effects of these compounds are suggested to be linked to the presence of two alkylating groups: the α-methyl γ-lactone and the α,β-unsaturated ketone. The dehydroleucodine that contains these two groups exhibited a most higher activity in contrast of dehydroparishin-B in which only one group (α,β-unsaturated ketone) is present. Five other sesquiterpenes (artemisinin, artemether, artesunate, artemotil, dihydroartemisinin) isolated from the genus *Artemisia* which were previously used in malaria treatment are in preclinical or clinical trial for anticancer activity with satisfactory results [55]. It is demonstrated that these antimalarial sesquiterpenes do not act by the same mechanism of action in cancer therapy showing the diversity of their pharmacological properties [56,57]. Other way of action of sesquiterpenes is their ability to inhibit the nuclear factor κB (NF-κB), which is well known to be involved in cancer and inflammatory diseases [58].

3.2.2. Diterpenes

Diterpenes are C20 phytochemicals derived from geranylgeranyl pyrophosphate [59]. They are characterized by fascinating variations in their skeletons leading to several series of molecules with diverse biological properties. The chemical structures responsible for the pharmacological activity are often unsaturated α-β-ketones, phenols groups and carbon–carbon double bonds.

Anticancer properties of natural compounds include chemopreventive and chemotherapy aspects. Chemopreventive agents may inhibit the initiation, promotion or progression stages of carcinogenic process. The blocking agents are compounds that act at the initiation stage by inhibition of the formation and stimulation of the detoxification of procarcinogen products (electrophilic and oxidant metabolites). The result leads to the decrease of DNA damage enhancing the blocking of tumor initiation [60]. Two diterpenes from coffee (cafestol and kahweol) were found to prevent the DNA-binding of carcinogen agents such as benzo(a)pyrene and 2-amino-1-methyl-6-phenylimidazo(4,5-b)pyridine implicated in the initiation of breast, prostate, cancer of lymphatic system and colon cancers. This anticarcinogenic effect acts through several key mechanisms such as the induction of phase II enzymes (GST, UDP-GT, NAD(P)H) involved in carcinogen detoxification, reduction in the expression of phase I enzyme (P450CYP3A2, P450CYP2C11) of carcinogen activation or specific inhibition of P450 enzymatic activity and stimulation of intracellular antioxidant mechanisms by the increase of GSH intracellular concentration; as it is well known that GSH is a major antioxidant which plays a crucial role in the detoxification of activated xenobiotics [60–62].

The chemotherapeutic effect of diterpenes is due to their cytotoxicity enhancing by their protonophoric activity. Moreover their lipophilicity allows them to target potentially the biological membranes. Several investigation revealed the key mechanisms of diterpene cytotoxicity such as DNA damage by covalent bindings, topoisomerase I and II inhibitory activities and mitochondria dependent apoptosis [63]. The non-specific targeting of these molecules is causing serious side effects and is a major hurdle for the development of anticancer drugs.

Two jatrophane diterpenes (A and B) isolated from *Euphorbia dendroides* were found to decrease vascular endothelial growth factor (VEGF) secretion that is an anti-angiogenic effect. It is known that the up-regulation of VEGF expression in tumors is associated with poor prognosis in patients and probably development of metastasis that is the major cause of cancer-related death [64,65]. Among the diterpenes isolated from West African anticancer plants, the most antimetastasic one remains curcusone B belonging to the class of crotophorbolanes [66]. In fact, this compound

showed a high anti-metastasic effect at non-toxic doses to chlolangiocarcinoma cell lines. The suppression of 90% of cell invasion was observed at 10 μM of curcusone B through the suppression of cell mobility and matrix metalloproteinase-2 activities in the culture medium. This effect of the compound leads to disruption of actin cytoskeleton, reduction of the phosphorylation of myosin regulatory light chain and activation of PI3 kinase/Akt signaling [67].

Some diterpenes showed a significant inhibitory effect against the function of ATP binding cassette (ABC) protein called commonly multidrug resistance (MDR) that is responsible for most failure of cancer chemotherapy. The most known is the transporter P-glycoprotein (P-gp) that is overexpressed in many cancer cells enhancing the efflux mechanism of anticancer drugs with the consequence of cell survival. The investigation on anti-MDR effect of six diterpenes isolated from *Euphorbia lathyris*

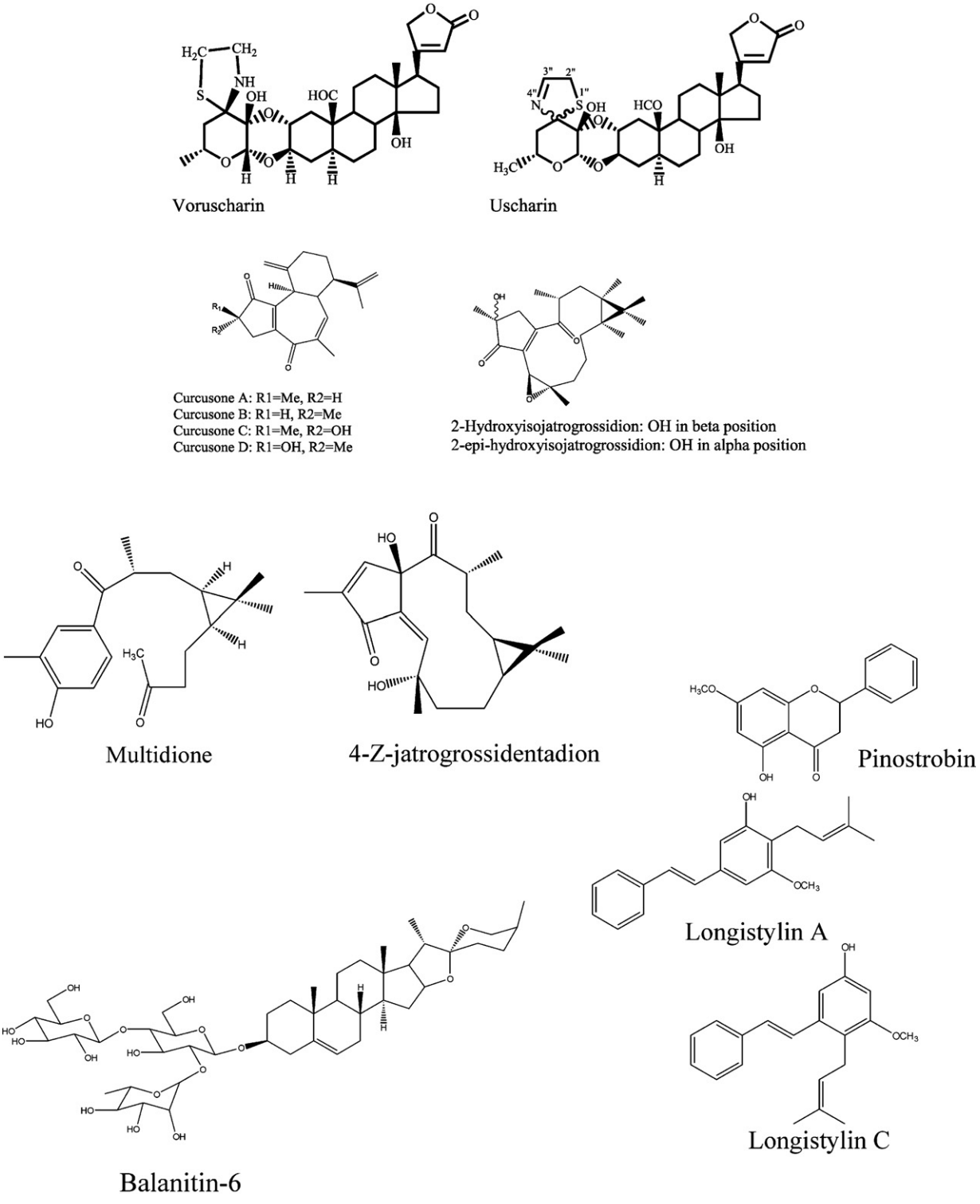
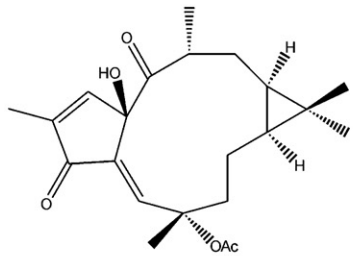
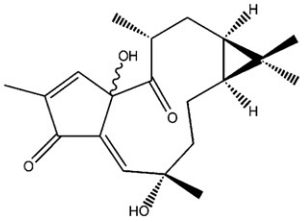


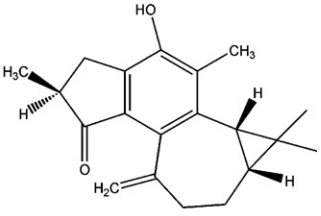
Fig. 6. Chemical structure of anticancer molecules isolated from West African plants. Chemical structure of each anticancer molecule isolated from extracts of West Africa plants has been drawn using the software "*Chemical Structure Drawing Standard (CS ChemDraw, 1998, Cambridge Soft Corporation)*". Each chemical structure is in conformity with the original published in the scientific literature.



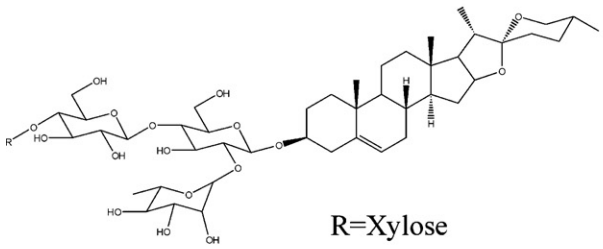
4-E-jatrogrossidentadion



15-epi-4E-jatrogrossidentadion

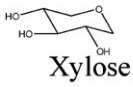


Jatropholone

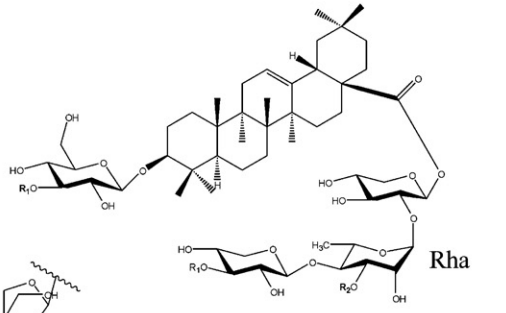


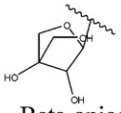
R=Xylose

Balanitin-7



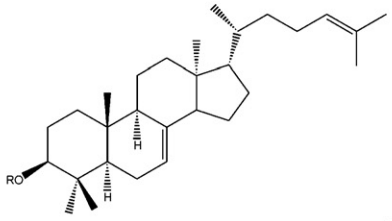
Xylose

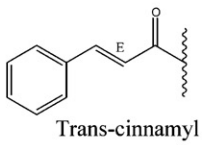




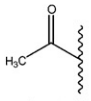
Beta-apiose

Parkioside B
R1=Beta-apiose and
R2=Alpha-L-Rhamnopyranosyl



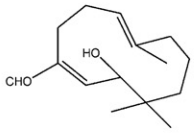


Trans-cinnamyl

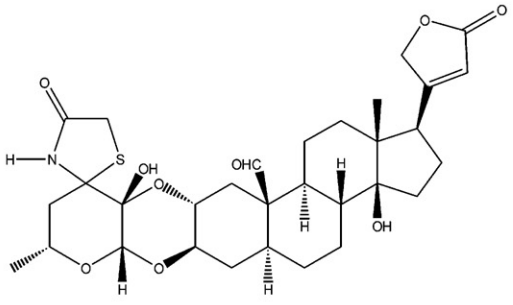


Acetyl

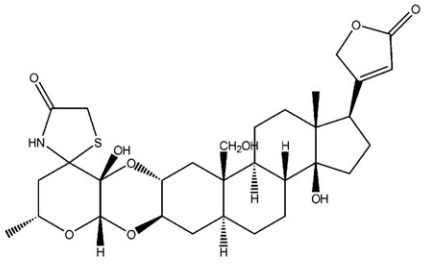
Butyrospermol acetate: R=Acetyl
Butyrospermol cinnamate: R=trans-cinnamyl



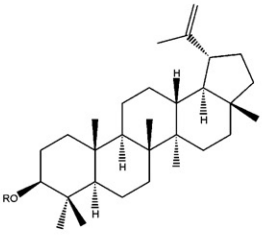
Kurubasch aldehyde

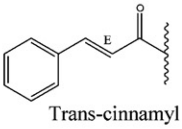


2''-Oxovoruscharin

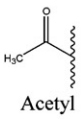


UNBS1450





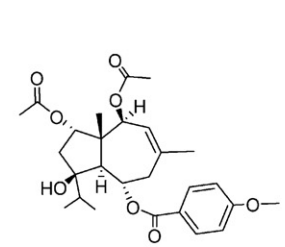
Trans-cinnamyl



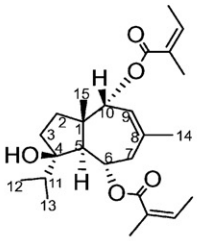
Acetyl

Lupeol acetate: R=Acetyl
Lupeol cinnamate: R=trans-cinnamyl

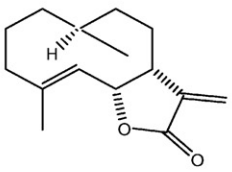
Fig. 6. (*Continued*).



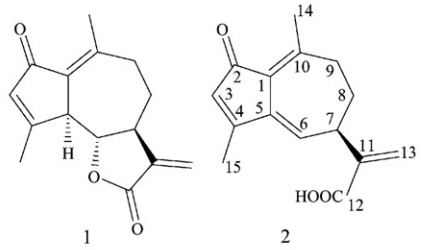
2α-acetoxy-6α-p-methoxybenzoyl-10β-acet- oxy-jaeschkeanadiol



Pallinin or 6α,10α-diangeloyl-jaeschkeanadiol

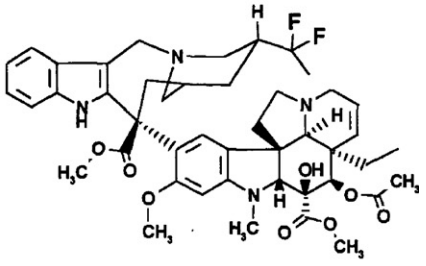


Isodihydrocostunolide

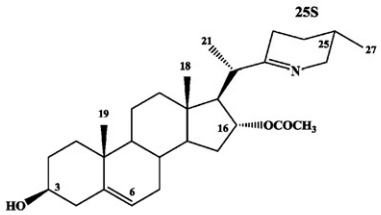


1 2

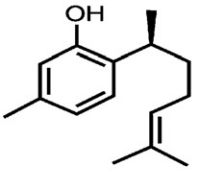
Dehydroleucodine (1) and dehydroparishin-B (2)



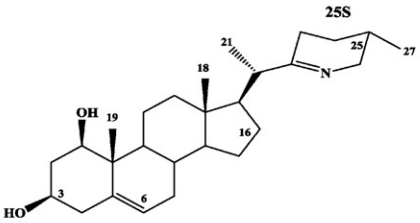
Vinflunine



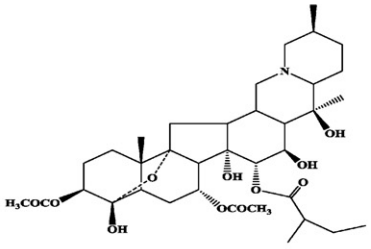
Veralosinine



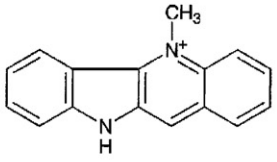
Curcuphenol



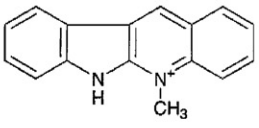
Veramigrine



Neogermitrine



Cryptolepine



Neocryptolepine

Fig. 7. Chemical structure of other anticancer molecules. Chemical structure of anticancer molecules discussed in this report has been drawn using the software "*Chemical Structure Drawing Standard (CS ChemDraw, 1998, Cambridge Soft Corporation)*". Each chemical structure is in conformity with the original published in the scientific literature.

(chemical structure similar to that of diterpenes isolated from *J. curcas*) showed that the activity is depended to the position of the carbon–carbon double bound in the different skeletons and the group containing nitrogen is benefit to the inhibition of P-gp [68]. An other study conducted by Pesic et al. showed that the jatrophane diterpenes (euphodendrophane A and B) from *E. dendroides* have an inhibitory effect against P-gp with a significant difference between the two diterpenes due to the presence of isobutyl group in the skeleton of euphodendrophane B that is favorable to the inhibitory ability of this molecule [64].

3.2.3. Triterpenes

Triterpenes are C30 phytochemicals derived from squalene, a triterpene that is formed by condensation of two units of farnesyl

pyrophosphate. Many triterpenes occur free, but others occur as glycosides namely saponins. Diversity of their structure leads to multiple pharmacological effects including anti-cancer properties that are reported by several authors. According to Lin et al. [69], triterpenes enriched fraction from *Ganoderma lucidum* exhibit a significant inhibition of hepatoma cell growth through key mechanisms including down regulation of protein kinase C (PKC) activity, activation of c-Jun N-terminal kinases (JNK) and p38 mitogen-activated protein kinases (p38 MAP kinases) and G2-phase cell cycle arrest. It is well known that PKC is involved in cell cycle control; especially its inhibitors are responsible for inhibition of hepatoma cell growth. JNK and p38 are also specific kinases responsible of cellular stresses and their activation is one of the triterpene cytotoxic mechanisms. The recent investigations on triterpenes from *G. lucidum* using a proteomic method allowed to highlight 12 proteins of Hela cell line that may be target-related proteins of ganodermic acids [70]. The mechanism of action of these triterpenes is not well known. It has been demonstrated that *Ganoderma* triterpenes increase ROS levels that can cause damage to proteins [70–72]. In addition, sesquiterpene lactones may exert their cytotoxic activity by interaction of the α-methylene γ-lactone moiety with thiol groups of macromolecules leading to their damage [73]. Thiol groups are important for the stability and function of proteins. That kind of action can be a probable mechanism used by triterpenes to interact with their protein targets.

These proteins are known to play important roles in cell proliferation and cell death (translation initiation factor 5A, ubiquilin 2, 14-3-3 beta/alpha, PP2A of subunit A PR65-alpha isoform, heterogeneous nuclear ribonucleoprotein K), in carcinogenesis (interleukin-17E, TPM4-ALK fusion oncoprotein type 2), in oxidative stress (peroxiredoxin 2, Cu/Zn-superoxide dismutase, chain A of DJ-1 protein) and in calcium signaling and endoplasmic reticulum stress (nucleobindin-1, reticulocalbin-1). Triterpenes such as ganodermic acids might exert their cytotoxic effect by altering these proteins.

Among the triterpenes isolated from West African anticancer plants, lupeol seems to be the most representative as its derived compounds exhibited some interesting anticancer properties. In fact, lupeol cinnamate isolated from shea nuts showed a significant inhibitory effect on Epstein-Barr virus early antigen (EBV-EA) activation induced by 12-O-tetradecanoylphorbol-13-acetate (TPA), the latter is considered to be a potent tumor promoter. TPA induces activation of ornithine decarboxylase that is a biomarker of skin carcinogenesis and the administration of TPA leads to activation of kinases that activate cell proliferation pathway and alter the expression of anti-apoptotic Bcl-2 and pro-apoptotic Bax proteins. Moreover, lupeol cinnamate exhibits an inhibitory effect in a two-stage carcinogenesis tested on mouse skin using 7,12-dimethylbenzen(α)anthracene (DMBA) as an initiator and TPA as a promoter [74]. Thus, lupeol cinnamate can be a lead to anticancer drugs development. Gauthier et al. [75] reported that the glycosidation of lupeol at 3-O-β-D enhances its cytotoxicity by 7–12-fold against A549, DLD1 and B16F1 cell lines.

3.2.4. Steroids

Steroids are derivatives of triterpenes with 26 or more carbon atoms that have undergone a characteristic type of rearrangement. Among the steroids isolated from West African plants, cardenolides are the most representative with 2″-oxovoruscharin and uscharin both isolated from roots of *Calotropis procera*. The general term of cardenolide regroups steroids compounds characterized by the presence of a five-membered unsaturated lactone ring at C-17, which are responsible of cadiotonic activity [76,77]. The mechanism of this cardiotonic effect acts through the high specific inhibition of the Na^+/K^+-ATPase [78]. The anticancer activity of steroids is due to the induction of apoptosis through induction of variation in intracellular levels of Na^+, K^+, Ca^{2+} and H^+, inhibition of NF-κB pathway and inhibition of glycolysis [79]. The anticancer activity of the two cardeloides (uscharin and 2″-oxovoruscharin) isolated from *C. proceras* is improved by chemical structure modification. The most active semi-synthesized compounds present a formyl or a hydroxyalkyl-moiety on C10 and a free 14-β-hydroxy on the steroid skeleton, which allowed the greatest in vitro antitumor activity and marked inhibition of Na^+/K^+-ATPase activity. In these cardenolides, the presence of free hydroxyl in the steroid skeleton is necessary for the antiproliferative effect and inhibition of sodium pump [80]. The reduction of the ketone moiety of 2″-oxovoruscharin resulted in the promising anticancer molecule UNBS1450 that is significantly less toxic than its origin compound and proved to be even more potent in cancer therapy [81]. This molecule provokes disorganization of the actin cytoskeleton leading to non-apoptotic cell death mechanisms and overcomes major MDR pathways. UNBS1450 is in a phase I clinical trial since 2008.

3.2.5. Alkaloids

Alkaloids are a group of compounds that contain mostly basic nitrogen atoms in their chemical structure. This group is largely present in the stem and root barks or rhizomes of the plants giving a bitter taste to these plant organs. These compounds are well known to possess antiparasitic (antimalarial), antimicrobial and antibacterial properties. Some of them exhibited a significant anticancer activity in preclinical and clinical trials [82,83]. Some alkaloids like vinflunine (tested on murine P388 cells) induces cell death through apoptosis leading to DNA fragmentation. This induction of apoptosis is mediated through activation of caspase-3 and/or caspace-7. In addition, this alkaloid exhibit its cytotoxic effect by stimulating c-Jun N-terminal kinase (JNK) triggered by cellular stress [82]. Two other plant alkaloids namely cryptolepine and neocryptolepine isolated from the roots of *Cryptolepis sanguinolenta* were investigated by Dassonneville et al. [84] for their anticancer properties. Their chemical structures are similar except the respective orientation of their indole and quinolone rings. The authors reported that the cytotoxicity of these two alkaloids acts through an apoptotic pathway by caspase-3 activation but one of them, cryptolepine, was found to be four times more toxic than its isomer proving that the positions of the indole and quinolone rings are crucial to the activity of these alkaloids. Another alkaloid, ellipticine, exhibits its anticancer activity through a covalent binding to DNA leading to its damage [85]. Finally some alkaloids are able to inhibit multidrug resistance (MDR) that is considered to be one of the major reasons of chemotherapy failure. Ivanova et al. [86] reported the effect of three alkaloids, neogermitrine, veralosinine and veramigrine, which were able to increase the intracellular concentration of the reference compound rodamine 123 by 87, 93 and 88 times respectively compared to untreated cancer cells [86]. This kind of alkaloid is relevant to resolve the problem of drug resistance and then to improve the efficacy of anticancer drugs.

3.2.6. Polyphenols

Polyphenols are characterized by the presence of multiple phenol groups. This category includes chalcones, flavonoids, tannins, curcuminoids, gallocatechins, stilbenes and anthocyanidins [87,88] presenting a wide range of pharmacological properties. These compounds are particularly known for their antioxidant activity that is useful for cancer management. In fact, the ability of polyphenols to scavenge free radicals is considered to be a chemopreventive effect of these compounds. In addition polyphenols are able to interact with the cytochrome P450 CYP1 family enzymes that are promoters of the initiation stage of carcinogenesis. These

interactions act in two pathways: to inhibit the procarcinogen activation and to be a substrate for the release of inhibitors of tumor cell growth. For example, resveratrol is an inhibitor of CYP1, but the conversion product of resveratrol metabolism by CYP1B1 namely piceatanol is a known tyrosine kinase inhibitor [89]. Several studies showed that plant polyphenols such as flavonoids or tannins [90,91] cause oxidative strand breakage in DNA in the presence or absence of metal ion such as copper [87]. It is suggested that polyphenols can act as prooxidants catalyzing DNA degradation in the presence of transition metal ions such as copper. Cancer cell lines are well known to contain high amount of copper and then will be more subject to redox reactions with polyphenols leading to the generation of reactive oxygen species (ROS) and phenoxyl radicals that are involved in cell death through DNA, lipid or other biological macromolecule damages [92]. This redox reaction leads to antioxidant and pro-oxidant characteristics of many polyphenols. For example, the reduced form of flavonoids acts as an antioxidant whereas the oxidized form leads to phenoxyl radicals with pro-oxidant activities [92]. Recently, Park and co-workers published the ability of flavonoids to induce G2/M cell cycle arrest through regulation of proteins such as cyclin B1, cdc2, cdc25c and p21. Moreover, these compounds induce apoptosis by up-regulation of the ratio of Bax/Bcl-xL, caspase-3 activity and cleaved PARP, and by down-regulation of pro-caspase-3, -6, -8 and -9 [93]. Interestingly, chalcones also present interesting anticancer potential by inhibiting NF-κB cell signaling pathways and by interfering with epigenetic regulation [94–96]. Polyphenol diversity, availability and multiple pharmacological properties justify the enthusiasm of researchers to investigate this group of compounds.

4. Concluding remarks

This literature review, although not exhaustive, confirms the embryonic stage of research on anticancer properties of West Africa plants. All research on these plants leading to the isolation of anti-cancer molecules were performed in collaboration with laboratories of developed countries. North–south cooperation is proving indispensable for enhancing and exploiting the therapeutic potential of West African medicinal plants. In this cooperation, the south provides ethno-pharmacological knowledge and plant materials and the northern countries provide a technical platform suitable for phytochemical and biological studies, and mobility scholarships for the exchange of researchers, a very crucial aspect for intellectual capacity building and technology transfer to developing countries.

It is not easy to raise recipes from traditional healers for cancer treatment unlike other diseases such as malaria, because of their lack of real knowledge on cancer. In addition, people who have recipes do not want to give because of lack of trust between researchers and traditional healers. To facilitate dialog with traditional healers and increase the chances of getting useful information, inflammation can be used as a keyword to reach cancer. It is now well known that chronic inflammation leads to cancer in the affected organs [97–100]. In addition, Products of medicinal plants that are able to heal old wounds are likely to possess anticancer activity. Even if the receipts given by the healers are often active, this should not hide the risks related to the lack of hygiene, overdose and chronic toxicity of some of these recipes. Some products relieve the patient but causes long-term damage to certain organs like stomach, intestines and kidneys. This is why the WHO strategy for traditional medicine requires an evaluation of the toxicity level of products from medicinal plants [10,12,23].

In conclusion, the research on anticancer plants remains a vast field waiting to be explored. Many resources exist in the flora of West Africa to deal with emergent diseases such as cancer. Rational exploitation of these resources is only possible through political will of African countries and financial or technical support from developed countries.

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