



Research paper

Medicinal plants used in management of cancer and other related diseases in Woleu-Ntem province, Gabon

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ARTICLE INFO

Keywords:

Cancer
Medicinal plants
Ethnopharmacological survey
Traditional healers
Anticancer potential
Toxicity

ABSTRACT

Introduction: Despite advances in medical technology, the fight against cancer remains difficult in developing countries. Thus, traditional medicine remains the first choice or sometimes still, the only opportunity for treatment. The purpose of this work was to popularize the medicinal plants used by Gabonese herbal therapists in the treatment of cancers by an ethnopharmacological survey.

Methods: In four localities of the Woleu-Ntem province, traditional healers were interviewed using a semi-structured questionnaire. Collected data were analyzed by descriptive statistical methods and various quantitative indices. The anticancer potential and toxicity of medicinal plants were confirmed by the bibliographic review.

Results: Traditional healers of Woleu-Ntem use 51 species of medicinal plants in cancers management and related diseases. These species are grouped into 49 genera and 29 families, the best-represented being Euphorbiaceae, Annonaceae, Apocynaceae, Myristicaceae and Rubiaceae. Barks are mainly used, followed by leaves. Decoction and maceration were the main methods of preparation. The oral absorption was the main route of administration. Colorectal, breast, cervical and liver cancer were the most cancers treated. The results of the literature search show that most of the plants in the survey have anticancer properties and are non-toxic at dosage and oral use by traditional healers.

Conclusions: The present work is the first study reporting information on the different Gabonese medicinal plants used against cancer. About 16 plant species have been mentioned for the first time as anticancer agents. These species could constitute a scientific database for the research of new bioactive molecules against cancers and other diseases.

1. Introduction

In Africa, the vast majority of the population, especially those living in rural areas, use traditional medicines for their health maintenance,

from the most benign diseases to the most serious ones including cancers. The fight against cancer remains difficult because of the small number of specialists, the lack of technical equipment and the centralization of large health structures in the capital cities of the country's

Abbreviations: 5-LOX, 5-lipoxygenase; Bcl-2, B-cell lymphoma 2; Bcl-xL, B-cell lymphoma-extra large; bFGF, basic fibroblast growth factor; c-FLIP, Cellular FLICE-like inhibitory protein; c-MYC, Avian myelocytomatosis virus oncogene cellular homolog; COX-2, cyclooxygenase 2; CXCR4, C-X-C receptor type 4; DNA, deoxyribonucleic acid; EGF, Epidermal Growth Factor; ELAM-1, leukocyte endothelial cell adhesion molecules; DMBA, 2, 7-dimethylbenz [a] anthracene; FC, frequency citation; FL, fidelity level; GM-CSF, granulocyte-macrophage colony-stimulating factor; *H. pylori*, *Helicobacter pylori*; HIF-1 α , Hypoxia Inducible Factors-1 α ; HPV, Human papillomavirus; HVB, Hepatitis B virus; HVC, hepatitis C virus; ICAM-1, intercellular adhesion-1 molecules; ICF, informant consensus factor; IFNs, interferons; iNOS, nitric oxide synthase; IL1, 6 and 23, Interleukin-1, 6 and 23; LT, T lymphocyte; LB, B lymphocyte; M-CSF, macrophage colony-stimulating factor; MMP-2, -7, -9, matrix metalloproteinase-2, -7, -9; NF-kB, kappa B nuclear factors; PDGF, platelet derived growth factor; RFC, relative frequency citation; RNA, ribonucleic acid; ROS, reactive oxygen species; *S. h.*, *Schistosoma haematobium*; *S. j.*, *Schistosoma japonicum*; *S. m.*, *Schistosoma mansoni*; TGF, transforming growth factor; TLR2, Toll-like receptors; TNF α , tumor necrosis factor α ; TPA, 12-O-tetradecanoylphorbol-13-acetate; UV, use value; VacA, vacuolar cytotoxin; VCAM-1, molecules vascular cell adhesion; VEGF, vascular endothelial growth factor; VEGFR2, vascular endothelial growth factor receptors 2

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<https://doi.org/10.1016/j.eujim.2019.05.010>

Received 20 March 2019; Received in revised form 21 May 2019; Accepted 22 May 2019

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major cities. The weakness of the therapeutic offer in surgery, chemotherapy, radiotherapy, the often-unaffordable costs of drugs and medical care make the therapeutic treatment of patients complicated. At the same time, traditional healers meet the health needs of the majority of the population and take care of the poorest by providing health products quickly available. In remote areas of large cities, traditional medicines are the first choice, and sometimes the only option is to heal. Herbal medicine is a centuries-old activity in Africa that has been maintained for generations and passed on within the family and ethnic group. The plants used often come from the immediate and natural environment of the populations. The selections of the plant type and the associated therapeutic activity have been made by empirical experiments and direct observations over the ages. The plants have been the source of many active molecules that have shown their effectiveness in the treatment of various cancers, such as breast, ovarian and lung treated with taxol (paclitaxel), which comes from barks of *Taxus brevifolia*. Medicinal plants such as *Bidens pilosa* L., native to South America and growing in Cameroon and Madagascar, *Hypoxis hemerocallida* from South Africa, Zimbabwe and Mozambique are known to cure adenoma and prostate cancer [1].

Worldwide, the search for new cancer-fighting molecules remains one of the main concerns of oncology researchers. Simply because, despite advances in biomedical technology in cancer treatments, this pathology remains a real public health problem in the world. In 2012, there were approximately 14 million new cases and 8.2 million disease-related deaths worldwide [2]. In Africa, estimates remain patchy, as many countries lack reliable health data collection systems. But in 2012, International Agency For Research on Cancer (IARC) estimated about 850,000 new cases of cancer, and 600,000 cancer deaths for all of Africa. For the 2030 projections, the figures are: 1.4 million new cases and 1 million deaths [3]. In Gabon, the available data, incomplete due to the lack of a true population cancer register, indicate that the number of new patients is growing steadily, from 183 new patients in 2000 to more than 1000 new patients in 2008 [4]. These data show that cancers are among the leading causes of morbidity and mortality worldwide. One of the hallmarks of cancer is the rapid proliferation of abnormal cells that can invade adjacent parts of the body and then spread into other organs. This is known as metastasis, which is the leading cause of cancer death [2]. Studies have shown that cancer cells are major generators of reactive oxygen species (ROS). ROS which are involved in the progression and proliferation of the cell cycle, cell survival and apoptosis, energy metabolism, cell morphology, cell-cell adhesion, cell mobility, angiogenesis, tumor maintenance and the formation of metastases [5,6]. This suggests that antioxidants can have a beneficial effect in the treatment of cancers. However, other research has shown that medicinal plants are important sources of antioxidants [7–9], antiangiogenic and anti-inflammatory drugs [10]. In order to help in the search for anticancer products from plants, this work aims to popularize the medicinal plants used by Gabon's phytotherapists in the treatment of cancers by an ethnopharmacological study.

2. Materials and methods

2.1. Survey area

The study took place in the Woleu-Ntem province, a traditional territorial entity inhabited by the Fang people. Located in northern Gabon (Central Africa), Woleu-Ntem covers an area of 38,465 km². It is made up of five major cities [Oyem, provincial capital (2°36'0" N, 12°4'0" E), Mitzié (0°46'60" N, 11°34'0" E), Bitam (0°43'0" N, 11°37'60" E), Minvoul (2°9'0" N, 12°7'60" E), Médouneu (0°57'0" N, 10°46'60" E)] and bordered to the North by Cameroon, to West by Equatorial Guinea, to East by Republic of Congo and to South by three other provinces (Ogooué-Ivindo, Moyen-Ogooué and Estuaire) (Fig. 1).

This area belongs to Equatorial phytogeographical sector, characterized by a hot, humid and rainy weather at all times. Average

annual rainfall ranges from 1500 to 2500 mm, temperatures range from 24 to 32 °C and humidity ranges from 70% to 90% [11]. About two-thirds of the flowering plants live in tropical and equatorial zones, of which some 85,000 species (or 50%) are located in Central and South America, 21,000 in tropical Africa, 10,000 in Madagascar and 50,000 in South-East Asia. Some families are only present in this area, such as Myristicaceae [12]. The Fang represent a third of Gabonese population, the current population of Woleu-Ntem is estimated at 154,986 inhabitants including 78,221 men and 76,765 women, which explains its very low population density (4 inhabitants/km²) [13] and its wealth floristic. The Eastern part of the province is practically uninhabited except by small groups of semi-nomadic pygmies who are known to mainly or only utilize traditional medicine. This less industrialized region has a very dense forest biodiversity and a highly developed traditional medicine. The choice of this ethnic group for the study is justified by the absence of ethnobotanical and ethnopharmacological works, especially those specific to medicinal plants.

2.2. Ethnopharmacological surveys

In traditional Gabonese medicine, cancer is defined as an accumulation of mass or hard clods in the body. As a result, natural products that seek to soften or resolve them have long been used to treat cancers. The purpose of ethnopharmacological investigation was to collect information on plants used in traditional medicine to soften and/or resolve mass or hard clods and to collect information on plants used against diseases associated with or precursors of cancer. The investigation was done in several stages.

2.3. Fieldwork

The ethnopharmacological survey was conducted from July 2016 to January 2017 in four localities in the Woleu-Ntem province including: Mebane Endama village (25 km from Oyem), Douala village (74 km from Mitzié), neighborhoods Fek-solé and Miang-si from Mitzié city center.

Semi-structured interviews and discussions with 103 traditional healers and herbal therapists, men and women, known to locals, were preferentially consulted individually. The purpose of this consultation was to show respect for the local tradition and to strengthen the insurance of the herbal therapist. Informed consent (Appendix 1) was obtained from participants after providing them with information explaining the importance of the study, their role in the study and obtain their agreement to participate in the study.

After obtaining consent, the investigators completed a pre-established questionnaire (Appendix 2). The questionnaire consisted of three parts. The first part consisted of age, gender, educational level, address and contact details of the informant with their oral agreement to build a database for Institute of Pharmacopeia and Traditional Medicine (IPHAMETRA). The second part was devoted to all information on the use of plants: names of local plants, organs used, harvesting methods, methods of preparation and administration, treated cancer and other related diseases. In the last part, the investigator had to record the observations and difficulties encountered during the interview or during the investigation.

2.4. Harvesting, herbization and plant identification

The cited plant species were harvested early in the morning with pruning shears, tagged and transported in anti-ultraviolet plastic bags. Digital photographs of the plant and its characteristic organs were made. The plant parts necessary for identification were taken (flowers, fruits and leaves) and planted in a herbarium. Some data on the wearing of the plant were also noted (tree, shrub and grass) and other information useful for its identification (date and place of sampling). After harvest, these samples were deposited at Arboretum of

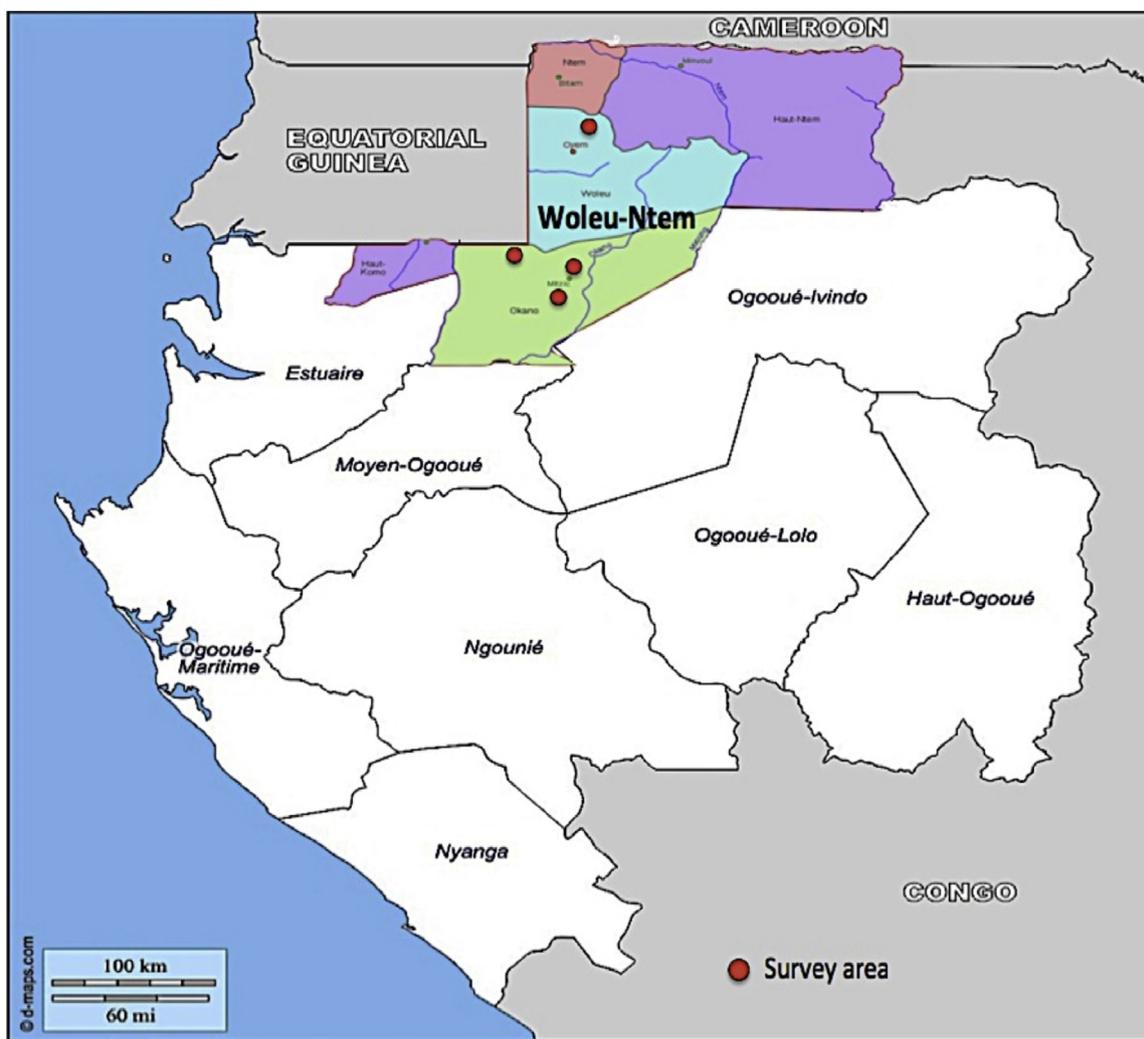


Fig. 1. Map of Gabon showing in red the ethnopharmacological survey areas. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

IPHAMETRA in Libreville for authentication of the plant.

The collected samples were authenticated by the botanists of Gabonese National Herbarium (HNG) using the online databases of international index of plant names (<http://www.ipni.org>), the list of plants (www.theplantlist.org), GRIN taxonomy (<http://www.ars-grin.gov/cgi-bin/npgs/html/queries.pl>) and using the bibliographic support “Checklist of Gabonese Vascular Plants (2006)”.

2.5. Data analysis

Descriptive statistical methods were used to analyze the data from the ethnopharmacological survey and various quantitative indices were also used including informant consensus factor (ICF), use value (UV), relative frequency citation (RFC) and fidelity level (FL). Data were reported in proportions and percentages.

2.5.1. Informant consensus factor (ICF)

The homogeneity of information on the use of medicinal plant species in relation to certain disease categories has been demonstrated by the determination of ICF [14]:

$$ICF = \frac{N_{ur} - N_t}{N_{ur} - 1}$$

“ N_{ur} ” is the number of usage reports for a particular disease category and “ N_t ” indicates the number of taxa used for a particular disease

category.

The ICF value is determined according to the methods reported in the plant species literature and ranges from zero to 1. A value close to 1 indicates that the majority of informants use taxa for a number of conditions related to this species category, while a value close to 0, shows that the choice of taxa is random for one or more reasons or that the informants have not agreed on the use of the plants [15–17].

2.5.2. Fidelity level (FL)

The fidelity level (FL) is the preference for one species by another, to treat a particular disease [18]. The following formula made it possible to calculate the FL:

$$FL = \frac{I_p}{I_u} \times 100.$$

where “ I_p ” is the number of informants certifying the use of a species for a particular disease category, while “ I_u ” is the number of informants in the study area designating the use of that plant for any category of disease. When FL is high, the high use of the plant for a particular disease is confirmed. A low FL indicates a wide range of medicinal uses but with a low frequency for each condition.

2.5.3. Use value (UV)

The use value (UV) indicates the relative importance of plant species uses. It was calculated according to the following formula [19]:

$$UV = \frac{U}{n}$$

where “UV” indicates the use value of individual species, “U” represents the number of uses recorded for that species and “n” represents the number of informants reporting this species. High UV indicates that there are many reports of plant use, implying that the species is important; UV is almost zero if there are few reports related to its use.

2.5.4. Relative frequency citation (RFC)

The RFC indicates the local importance of each species and is calculated by dividing the FC, the number of informants certifying the use of the species divided by the total number of informants contributing to the survey (N), without taking into account use categories [20,21]. The frequency quotation (FC) was obtained using the following formula: FC = (number of citation of a particular species/total citation number of all species) × 100 [22].

$$RFC = \frac{FC}{N} \quad (0 < RFC < 1)$$

2.5.5. Anticancer potential of listed medicinal plants and safety

The anticancer potential of listed medicinal plants was determined by confirming, by published articles, the cytotoxic, antiproliferative, anti-metastatic, anti-migratory properties on cancer cells *in vivo* and *in vitro* without forgetting the antioxidant, anti-inflammatory and anti-angiogenic activities. The safety of the use of medicinal plants was evaluated by studying the published articles of toxicity. For this purpose, bibliographic research has been carried out in databases such as www.scholar.google.fr, www.ncbi.nlm.nih.gov and www.sciencedirect.com.

3. Results

3.1. Demographic data

A total of 103 traditional healers and herbalists participated in the survey. All have already had to treat at least one and up to 20 cancer patients with an average of 2.5 patients per year. These professional healers were classified by sex, age, education, function and experience as traditional healers as shown in Fig. 2.

This survey indicates that male healers outnumbered those of the

female sex (72.8% against 27.2%). The most representative age group of these traditional healers was 41–50 years old (38.8%) followed by the age group of 31–40 years (24.3%).

Regarding the level of education, nearly half of the healers finished primary school or 33%, more than half finished high school or 54.4%. Some of these healers have completed higher, undergraduate and doctoral studies at 4.9%, 2.9% and 1.9%, respectively. Only 2.9% were illiterate.

Based on their experience, traditional healers were classified into five groups: healers with experience less than 2 years (4.9%); healers with experience ranging from 2 to 5 years (12.6%); healers with 6–10 years of experience (23.3%); healers with experience ranging from 11 to 20 years (39.8%) and healers with more than 20 years of experience (19.4%).

3.2. Identified plants and parts used

Exploitation of the survey data made it possible to identify and name 51 species used in traditional medicine by the Fang (Table 1) in the treatment of cancers and related diseases. These species are grouped into 49 genera and 29 families. The species were diversely distributed among botanical families. Thus, some families were more represented than others. The best-represented family are Euphorbiaceae (9.8%), Annonaceae (7.8%), Apocynaceae (7.8%), Myristicaceae (7.8%) and Rubiaceae (5.9%) (Fig. 3). Different organs are taken from the plants to prepare the drugs (Table 1). Bark is mostly used (48.5%); followed by the leaves (36.8%) and the roots (13.2%) (Fig. 4).

3.3. Medical practices

According to the results, the decoction was the method most frequently used by traditional practitioners (56.8%). Decoction is a process in which the plant is boiled for a certain amount of time in a solvent. Maceration (24.1%), which involves soaking the plant organ in the solvent for a given time at room temperature was the second most frequent method of preparation (Fig. 5). Water was the most used solvent in the drug development process. Thus, the drink alone (44%) remains the main mode of administration of drugs (Fig. 6).

Traditional healers treat several types of cancer. A total of 12 types of cancer have been listed, classified according to the affected organs including breast, cervical, colorectal, ear, stomach, liver, kidney, nose,

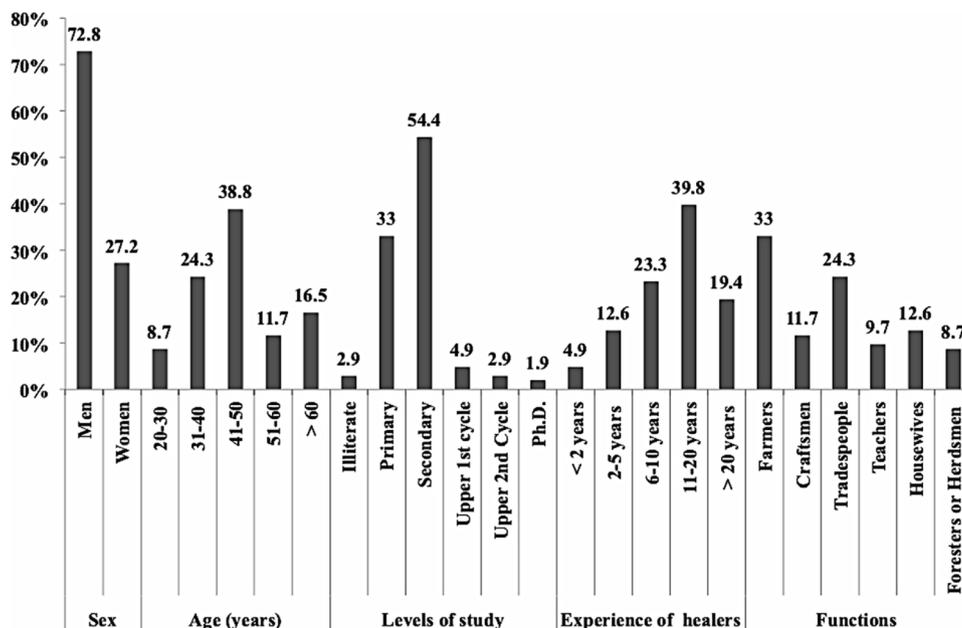


Fig. 2. Demographics of traditional health practitioners.

Table 1
Medicinal plants used by Woleu-Ntem people against cancers and related diseases.

No.	Family	Scientific name (voucher number)	Fang name	Part used	Preparation method	Administration method	Traditional use
1	Anacardiaceae	<i>Mangifera indica</i> L. (Bourobou 513)	Andoc-ntangha	Barks	Maceration	Drink-Enema	Colorectal cancer
				Barks	Maceration	Drink-Enema	Diarrhea
				Barks	Maceration	Drink-Enema	Low back pain
				Barks	Decoction	Seat bath	Hemorrhoids
				Barks	Decoction	Drink-Enema	Sexual asthenia
2	Annonaceae	<i>Anonidium mannii</i> (Oliv.) Engl. et Diek (Bourobou 324)	Ebom	Barks	Maceration	Seat bath	Colic
				Barks	Maceration	Enema	Colorectal cancer
				Barks	Maceration	Enema	Colic
				Barks	Powder	Local application	Abscess
				Barks	Powder	Friction	Antivenom
3	Annonaceae	<i>Annona muricata</i> L. (Dibata 913)	Tsètsobe	Roots	Maceration	Instillation	Nose cancer
				Leaves	Decoction	Drink	Diarrhea
				Barks	Maceration	Drink	Cough
				Barks	Decoction	Drink	Malarial
4	Annonaceae	<i>Xylopiya aethiopica</i> Rich. (A. Issembé 226)	Okala	Leaves	Pilat	Instillation	Nose cancer
				Leaves	Decoction	Drink	Vomitive
				Leaves	Decoction	Drink	Rheumatism
				Leaves	Decoction	Drink	Diarrhea, gastritis
				Barks	Maceration	Drink	Bronchopulmonary disorders
5	Annonaceae	<i>Enantia chlorantha</i> Oliv. (Bourobou 591)	Mfól	Barks	Decoction	Drink	Liver cancer
				Barks	Decoction	Drink	Bile
				Barks	Maceration	Enema	Diarrhea
				Barks	Grated	Local application	Ulcers
				Barks	Decoction	Drink	Malaria
6	Apocynaceae	<i>Tabernaemontana crassa</i> Benth. (not found)	Etsúé	Barks	Decoction	Drink	Unspecified cancer
				Roots	Maceration	Drink	Malaria
7	Apocynaceae	<i>Rauwolfia macrophylla</i> Stapf (not found)	Essôma	Roots	Maceration	Drink	Cervical cancer
				Roots	Maceration	Drink	Intestinal worms
				Roots	Maceration	Drink-Enema	Purgative
8	Apocynaceae	<i>Funtumia africana</i> (Benth.) Stapf (A.M. Louis 431)	Ngông-mebam	Barks	Decoction	Drink	Cervical cancer
				Barks	Decoction	Enema	Diarrhea
				Barks	Latex	Local application	Hemorrhage
				Barks	Decoction	Drink	Diuretic
				Barks	Maceration	Friction	Intercostal pain
9	Apocynaceae	<i>Rauwolfia vomitoria</i> Afzel. (M. Mbembo 81)	Oyomtè	Barks	Decoction	Drink	Cervical cancer
				Leaves	Decoction	Drink	Vomitive, gastritis
				Leaves	Decoction	Local application	Rheumatism
				Leaves	Maceration	Drink	Malaria
				Leaves	Decoction	Drink	Breast cancer
10	Asteraceae	<i>Bidens pilosa</i> L. (Dibata 180)	Mige-me-mbèng, Anyông-élóc	Leaves	Decoction	Drink	Breast cancer
				Leaves	Pilat	Local application	Breast abscess
				Leaves	Pilat	Instillation	Epilepsy
				Leaves	Pilat	Local application	Wounds
				Leaves	Decoction	Drink	Rheumatism
				Leaves	Maceration	Drink	Diarrhea
				Leaves	Decoction	Drink	Aches
				Leaves	Decoction	Drink	Headaches
				Leaves	Decoction	Drink-Enema	Splenomegaly
				Leaves	Decoction	Drink-Enema	Pneumonia
				11	Asteraceae	<i>Vernonia amygdalina</i> Delile (Wieringa 1407)	Nzông-ayól
Leaves	Decoction	Enema-Bath	Varicella and smallpox				
Roots	Decoction	Enema	Dysmenorrhea				
Leaves	Decoction	Drink	Headache				
Leaves	Decoction	Drink	Ascariidiosis, measles				
Leaves	Pilat	Instillation	Conjunctivitis, epilepsy				
Roots	Decoction	Drink-Enema	Splenomegaly, scabiess				
Leaves	Maceration	Drink	Antivenom				
Leaves	Decoction	Enema	Hypertension				
Leaves	Decoction	Drink-Enema	Colorectal cancer				
12	Asteraceae	<i>Tithonia diversifolia</i> (Hemsley) A.Gray (Sosef 882)	Marguerite				
				Leaves	Decoction	Drink	Malaria
				Leaves	Decoction	Drink-Enema	Ascariidiosis, measles
				Leaves	Decoction	Body bath	Splenomegaly, scabiess
				Roots	Maceration	Drink	Hypertension
13	Bombacaceae	<i>Ceiba pentandra</i> (L.) Gaertn. (Sosef 932)	Dum	Leaves	Decoction	Drink	Liver cancer
				Barks	Maceration	Enema	Testicular hernia, gonorrhoea
				Barks	Pilat	Drink	Vomitive
				Barks	Maceration	Friction	Neuralgia
				Leaves	Maceration	Drink	Gastritis, diarrhea
				Fruits	Decoction	Drink	Heart disease, asthma

(continued on next page)

Table 1 (continued)

No.	Family	Scientific name (voucher number)	Fang name	Part used	Preparation method	Administration method	Traditional use
14	Burseraceae	<i>Dacryodes edulis</i> (G.Don) H.J.Lam (Bernard SRFG 274)	Asa	Barks	Maceration	Drink	Stomach cancer, gastritis
				Barks	Grated	Drink	Low back pain
				Barks	Grated	Mouthwash	Tooth decay
				Leaves	Decoction	Drink	Dysmenorrhea
				Barks	Grated	Drink	Diarrhea
15	Burseraceae	<i>Canarium schweinfurthii</i> Engl. (Strijk 259)	Abèl	Roots	Maceration	Drink	Measles
				Barks	Decoction	Local application	Skin cancer
				Barks	Decoction	Body bath	Gangrene
				Barks	Decoction	Drink	Dysentery
				Barks	Decoction	Body bath	Skin cancer
16	Caesalpiniaceae	<i>Sindora klaineana</i> Pellegr. (AM Louis 1758)	Ngom	Barks	Decoction	Body bath	Skin cancer
				Barks	Decoction	Body bath	Scabies, wounds
17	Caesalpiniaceae	<i>Guibourtia tessmannii</i> (Harms) J. Léonard. (Bernard SRFG 328)	Oveng	Barks	Decoction	Drink-Enema	Liver cancer
				Barks	Decoction	Drink-Enema	Wounds, scabs, injuries
				Barks	Decoction	Drink-Enema	Gonorrhea
				Barks	Decoction	Drink-Enema	Talisman of evil spells
18	Caricaceae	<i>Carica papaya</i> L. (Strijk 136)	Alôla	Leaves	Maceration	Body bath	Skin cancer, wounds, ulcers and edemas
				Roots	Maceration	Drink-Enema	Liver disorders
				Leaves	Maceration	Drink	Dysentery
				Roots	Maceration	Drink	Venereal diseases
				Roots	Decoction	Drink	Diabetes
				Roots	Decoction	Drink-Enema	Intestinal disorders
				Barks	Decoction	Drink	Liver cancer, hepatitis
				Barks	Decoction	Enema	Dysentery, anemia
				Barks	Decoction	Instillation	Vision disorders
				Leaves	Decoction	Enema	Malaria
19	Clusiaceae	<i>Harungana madagascariensis</i> Lam. ex Poir. (Bourbou 580)	Atsû	Leaves	Maceration	Drink	Gonorrhea and syphilis
				Barks	Decoction	Seat bath	Hemorrhoids
				Barks	Decoction	Drink-Enema	Liver cancer
				Leaves	Decoction	Body bath	Varicella and smallpox
				Leaves	Decoction	Drink-Enema	Headache
				Leaves	Decoction	Drink-Enema	Ascariidiosis measles
				Leaves	Decoction	Drink-Enema	Splenomegaly
				Leaves	Decoction	Body bath	Scabiess
				Roots	Maceration	Drink-Enema	Diabetes
				Roots	Decoction	Drink	Pulmonary cancer
20	Combretaceae	<i>Combretum micranthum</i> G. Don. (not found)	Ndem ngoghe	Barks	Decoction	Drink	Gonorrhea
				Barks	Decoction	Drink	Tuberculosis, yaws
				Roots	Decoction	Drink	Epilepsy
				Leaves	Decoction	Drink	Asthma bronchitis
				Leaves	Decoction	Drink	Breast cancer
21	Composeae	<i>Vernonia conferta</i> Benth. (AM Louis 2682)	Abingac	Leaves	Decoction	Drink	Cervical cancer
				Leaves	Pilat	Local application	Whitlow
				Leaves	Pilat	Drink	Pain due to spasms of the uterus
				Roots	Maceration	Instillation	Nose cancer
				Leaves	Maceration	Head bath	Migraines
22	Convolvulaceae	<i>Ipomoea batatas</i> (L.) Lam. (not found)	Amôngha	Leaves	Decoction	Drink	Gonorrhea
				Leaves	Decoction	Drink-Enema	Wounds, scabs, injuries
				Leaves	Pilat	Local application	Colorectal cancer
				Leaves	Pilat	Local application	Splenomegaly
				Leaves	Pilat	Local application	Wound healing
23	Cucurbitaceae	<i>Luffa cylindrica</i> (L.) M.Roem. (not found)	ndzic-mvèle	Barks	Grated	Local application	Joint pains
				Barks	Powder	Friction	Rheumatism
				Barks	Powder	Friction	Rheumatism
				Leaves	Decoction	Drink	Cervical cancer, gonorrhea
				Leaves	Decoction	Drink	Mental disorder
24	Euphorbiaceae	<i>Tetrorchidium oppositifolium</i> (Pax) Pax (AM Louis 587)	Nôla	Barks	Decoction	Enema	Destruction of the fetish
				Barks	Decoction	Drink	Pulmonary cancer
				Barks	Decoction	Drink	Chest diseases
				Barks	Maceration	Drink	Increases milk secretion
				Barks	Decoction	Drink	Cervical cancer
25	Euphorbiaceae	<i>Ricinodendron africanum</i> Muell. Arg. (Wilks 807)	Esésang	Leaves	Pilat	Chewing	Gastric disorder
				Leaves	Maceration	Drink	Syphilis
				Barks	Grated	Chewing	Gonorrhea
				Barks	Grated	Chewing	Gonorrhea
				Stalks	Maceration	Drink	Bronchitis
26	Euphorbiaceae	<i>Plagiostyles africana</i> Prain. (Bourbou 42)	Essula	Barks	Grated	Chewing	Hemorrhoids
				Barks	Grated	Chewing	Hemorrhoids
				Barks	Decoction	Drink-Enema	Colorectal cancer
				Barks	Decoction	Drink-Enema	Colic
				Barks	Decoction	Instillation	Nose chancre
27	Euphorbiaceae	<i>Bridelia micrantha</i> (Hochst.) Baill. (Doumenge 225)	Ewologhe	Barks	Decoction	Enema	Joint pains
				Barks	Decoction	Enema	Scabiess
				Barks	Decoction	Body bath	Scabiess
				Barks	Decoction	Body bath	Scabiess
				Barks	Decoction	Body bath	Scabiess
28	Euphorbiaceae	<i>Croton oligandrus</i> Pierre ex Hutch. (not found)	Ongue/Ngèl	Fruits	Poultice	Local application	Skin cancer, epithelioma
				Fruits	Poultice	Drink	Malaria, cough, anemia
				Leaves	Infusion	Friction	Ophthalmia
				Fruits	Poultice	Local application	Skin cancer, epithelioma
				Fruits	Poultice	Drink	Malaria, cough, anemia
29	Fabaceae	<i>Abrus precatorius</i> L. (A.M. Louis 1932)	Ovyang-ndzic	Fruits	Poultice	Local application	Skin cancer, epithelioma
				Fruits	Poultice	Drink	Malaria, cough, anemia
				Leaves	Infusion	Friction	Ophthalmia

(continued on next page)

Table 1 (continued)

No.	Family	Scientific name (voucher number)	Fang name	Part used	Preparation method	Administration method	Traditional use
30	Flacourtiaceae	<i>Oncoba welwitschii</i> (Oliv.) Gilg. (Bourobou 419)	Miam-ngôm	Leaves	Decoction	Drink-massages	Breast cancer
				Leaves	Decoction	Body bath	Meadow; rheumatism
				Leaves	Decoction	Fumigation	Mental disorders
				Leaves	Maceration	Drink	Dysmenorrhea
31	Lamiaceae	<i>Ocimum basilicum</i> L. (Leeuwenberg 12534)	Osim	Leaves	Decoction	Drink	Anti-abortion
				Leaves	Decoction	Drink	Cervical cancer
				Leaves	Pilat	Instillation	Conjunctivitis
				Roots	Maceration	Drink	Gastritis
				Leaves	Maceration	Drink	Icterus
				Leaves	Pilat	Friction	Hyperthermia
32	Lauraceae	<i>Persea americana</i> Mill. (not found)	Avoga	Leaves	Decoction	Drink	Dizziness, headache
				Leaves	Decoction	Drink	Stomach cancer, diarrhea
				Leaves	Pilat	Local application	Anemia
				Leaves	Pilat	Local application	Rashes
				Leaves	Pilat	Local application	Scabies, wounds
				Leaves	Decoction	Drink	Rheumatism
33	Lecythidaceae	<i>Petersianthus macrocarpus</i> (P.Beauv.) Liben (Wilks 808)	Abing	Barks	Decoction	Drink	Cervical cancer
				Barks	Heated	Friction	Joints pains
				Barks	Heated	Local application	Abortive, antiseptic
				Barks	Decoction	Drink	Venereal diseases
				Barks	Decoction	Drink	Pulmonary disorders
				Barks	Decoction	Drink	Gastrointestinal disorders
				Barks	Decoction	Drink-bath	Icterus
				Barks	Decoction	Drink-bath	Wounds, bubbles, boils and chancres
				Barks	Decoction	Drink	Stomach cancer
34	Moraceae	<i>Ficus vogeliana</i> Miq (Wilks 1095)	Tô	Barks	Decoction	Drink	Vomitive
				Barks	Decoction	Drink	Abortive
				Leaves	Maceration	Drink	Cervical cancer, Scabiess
35	Moraceae	<i>Milicia excelsa</i> (Welw.) C.C.Berg (Walters 446)	Abang	Barks	Latex	Local application	Eye pain
				Barks	Decoction	Drink	Promotes lactation
				Barks	Decoction	Drink	Filariasis
36	Moraceae	<i>Ficus asperifolia</i> Miq. (Moungazi 1601)		Leaves	Maceration	Drink	Breast cancer
				Leaves	Pilat	Instillation	Keratitis
				Leaves	Maceration	Drink	Gastritis
				Leaves	Maceration	Drink	Cough
				Leaves	Pilat	Local application	Wounds, ulcers
37	Myristicaceae	<i>Scyphocephalum ochocoa</i> Warb. (Wilks 2240)	Soghe	Barks	Decoction	Local application	Breast cancer
				Barks	Maceration	Drink	Kidney cancer
				Barks	Maceration	Drink	Whooping cough
				Barks	Decoction	Drink-Enema	Gonorrhoea
				Barks	Decoction	Drink-Enema	Ovulation disorders
38	Myristicaceae	<i>Coelocaryon preussii</i> Warb. (Bernard SRFG 293)	Nnom-ètèng	Barks	Decoction	Drink-Enema	Breast cancer
				Barks	Decoction	Drink	Hemoglobinuria
				Barks	Decoction	Drink-Enema	Dysentery, vomitive
				Barks	Maceration	Enema	Hemorrhoids
				Barks	Maceration	Drink-Enema	Dysmenorrhoea
				Barks	Maceration	Drink-Enema	Hemorrhagic disorders
				Barks	Decoction	Drink-Enema	Pulmonary disorders
				Barks	Maceration	Drink	Scabies
				Barks	Latex	Local application	Anesthetic effect
				Barks	Decoction	Friction	Joints inflammation
				Barks	Powder	Vapor bath	Hemorrhage
39	Myristicaceae	<i>Staudtia kamerunensis</i> var. <i>gabonensis</i> (Warb.) Fouilloy (A. Issembé 238)	Mbôn	Barks	Powder	Local application	Wounds
				Barks	Decoction	Drink	Pulmonary cancer, disorders
				Barks	Decoction	Instillation	Eye pain
				Barks	Latex	Local application	Ulcers, wound
				Barks	Latex	Drink	Rheumatism
				Barks	Latex	Drink-Enema	Yaws, gonorrhoea
				Barks	Latex	Drink-Enema	Extended menstruation
				Barks	Decoction	Drink	Dysentery, anemia
40	Myristicaceae	<i>Pycnanthus angolensis</i> (Welw.) Exell (1) (Bois SRFG 827)	Eteng	Barks	Decoction	Drink-Enema	Dysmenorrhoea
				Barks	Decoction	Mouthwash	Oral disorders
				Roots	Decoction	Drink	Stomach cancer, gastritis
				Barks	Decoction	Enema	Cough rebel
				Barks	Decoction	Enema	Psychosomatic disorders
				Barks	Pilat	Local application	Tooth decay
				Barks	Decoction	Drink	Vomitive
Barks	Decoction	Drink	Purifie the milk of nurses				

(continued on next page)

Table 1 (continued)

No.	Family	Scientific name (voucher number)	Fang name	Part used	Preparation method	Administration method	Traditional use
41	Nyctaginaceae	<i>Boerhavia diffusa</i> L. (Dibata 1126)		Leaves	Maceration	Local application	Breast cancer
				Roots	Maceration	Enema	Diarrhea
				Leaves	Powder	Anal application	Hemorrhoids
				Leaves	Pilat	Massage	Rheumatism
				Leaves	Maceration	Enema	Ocytocique
				Leaves	Pilat	Massage	Pneumonia
				Leaves	Maceration	Drink	Antipoison
42	Ochnaceae	<i>Lophira alata</i> Banks ex C.F.Gaertn (Alers 146)	Akogha	Roots	Pilat	Enema	Female sterility
				Barks	Decoction	Drink	Breast cancer
				Barks	Decoction	Lotions	Renal pain, dental pain
				Barks	Decoction	Drink	Rheumatism and Lumbago
				Barks	Maceration	Drink	Chronic gonorrhoea
				Barks	Powder	Enema	Purgative
				Roots	Powder	Drink	Sexual asthenia
43	Poaceae	<i>Cymbopogon citratus</i> (DC.) Stapf (not found)	osim-ntangha	Barks	Decoction	Drink-Enema	Gastric ulcer
				Leaves	Decoction	Instillation	Ear cancer
				Leaves	Decoction	Instillation	Suppurative otitis
				Leaves	Decoction	Instillation	Conjunctivitis
44	Rubiaceae	<i>Fleroya ledermannii</i> (K.Krause) Y.F.Deng (Sosef 807)	Otsigé-nzam	Leaves	Decoction	Enema	Measles
				Barks	Decoction	Drink	Colorectal cancer
				Leaves	Decoction	Drink	Stomach cancer
				Barks	Maceration	Drink	Hernia Pneumonia
				Leaves	Maceration	Enema	Metrorrhagia
				Barks	Decoction	Vapor bath	Dysmenorrhoea
				Leaves	Decoction	Drink	Epilepsy
45	Rubiaceae	<i>Coffea mannii</i> (Hook.f.) A.P.Davis (Doumenge 200)	Azèm	Roots	Decoction	Drink	Anti-abortion
				Barks	Grated	Local application	Liver cancer
46	Rubiaceae	<i>Sarcocephalus latifolius</i> (Sm.) E.A.Bruce (Alers 1)	Ntoma-osù	Barks	Decoction	Drink	Wound healing
				Roots	Decoction	Drink-Enema	Liver cancer
				Roots	Decoction	Drink-Enema	Ascites
				Roots	Decoction	Drink-Enema	Gonorrhoea
				Roots	Decoction	Drink-Enema	Renal failure
				Roots	Decoction	Drink-Enema	Epilepsy
47	Rubiaceae	<i>Morinda lucida</i> Benth. (Dibata 358)	Akyang	Roots	Decoction	Drink-Enema	Sexual asthenia
				Roots	Decoction	Drink-Enema	Breast cancer
				Roots	Decoction	Drink-Enema	Liver cancer, Liver cirrhosis
				Leaves	Decoction	Drink-Enema	Stomach cancer, Diarrhea
				Roots	Decoction	Drink	Splenomegaly
				Leaves	Decoction	Drink	Rheumatism
				Roots	Decoction	Instillation	Otitis
				Barks	Decoction	Enema	Veneral diseases
				Barks	Decoction	Drink	Epigastric
				Roots	Grated	Local application	Scabies, wounds, ulcer
				Roots	Decoction	Drink	Digestive disorders
48	Sapotaceae	<i>Tieghemella africana</i> Pierre (Bourobou 936)	Okôla	Barks	Decoction	Drink	Stomach cancer
				Barks	Decoction	Drink	Joints pains
49	Sapotaceae	<i>Omphalocarpum procerum</i> P.Beauv. (M. Mbembo 208)	Mébi-me-ngôn	Barks	Decoction	Drink-Enema	Colorectal cancer
				Barks	Maceration	Drink	Male infertility
				Barks	Decoction	Drink	Wormer
				Barks	Maceration	Enema	Purgative
50	Solanaceae	<i>Solanum americanum</i> Mill. (Bourobou 31)	Anzông	Leaves	Decoction	Drink	Breast cancer
				Leaves	Maceration	Drink	Colorectal cancer
				Leaves	Decoction	Drink	Prostate cancer
				Leaves	Maceration	Instillation	Psychosomatic disorders
				Leaves	Maceration	Instillation	Epilepsy
51	Ulmaceae	<i>Celtis mildbraedii</i> Engler. (Dibata 435)	Engô	Barks	Decoction	Drink-Enema	Colorectal cancer
				Barks	Decoction	Enema	Colic

prostate, lung and skin cancer. The majority of cancers treated are colorectal cancer (18.6%), breast cancer (16.9%), cervical cancer (15.3%), liver cancer (13.6%), stomach cancer (11.9%), skin cancer (6.8%), nose and pulmonary cancer (5.1%) (Fig. 7).

3.4. Informant consensus factor (ICF)

The determination of the ICF required the classification of pathologies into different categories (Table 2). The results show that ICFs range from 0.000 to 0.537. Cancers and other diseases of the digestive system have the highest ICF (0.537), followed by cancers and other diseases of the integumentary system (0.465), followed by cancers and other metabolic diseases (0.444).

3.5. Fidelity level (FL)

FL informs about the preference of traditional healers to use certain plants over others for the treatment of different disease categories (Table 3). The results show that *Celtis mildbraedii*, *Omphalocarpum procerum*, *Mangifera indica*, *Ficus vogeliana*, *Rauvolfia macrophylla*, *Dacryodes edulis*, *Xylopia aethiopica*, *Tetrorchidium oppositifolium*, *Tieghemella africana* and *Anonidium mannii* are the most commonly used plant species for the treatment of cancers and other diseases of the digestive system with FL equal to 100%, 75%, 66.67%, 66.67%, 66.67%, 57.143%, 50%, 50%, 50% and 50%, respectively. Cancers and other diseases of respiratory system are preferentially treated by *Plagiostyles africana*, *Vernonia conferta* and *Annona muricata*, with FL equal to 100%,

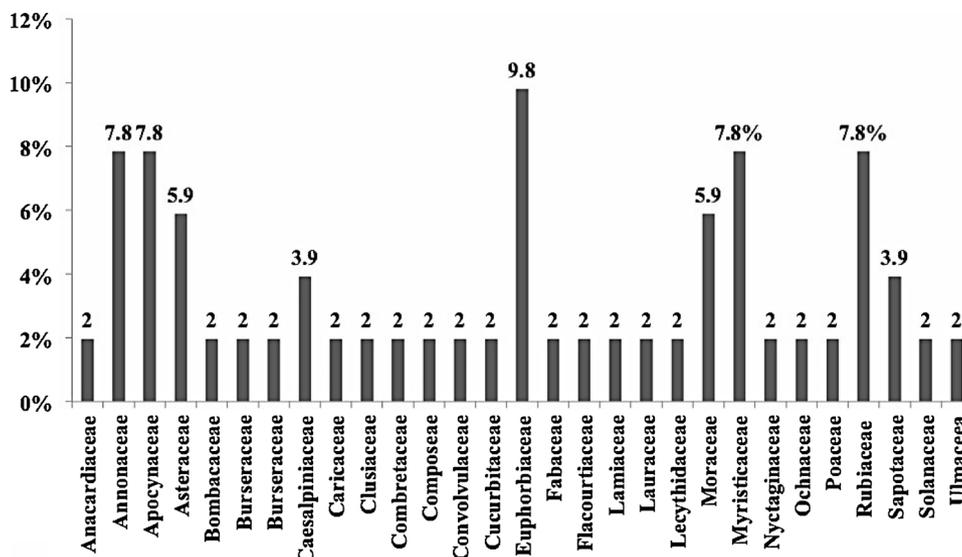


Fig. 3. Different families of plants.

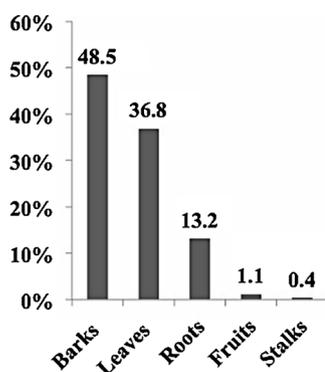


Fig. 4. Different organs used.

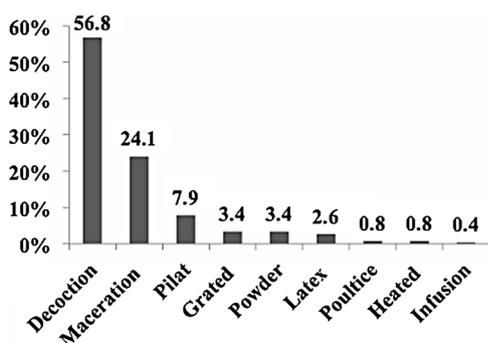


Fig. 5. Different ways of preparing drugs from plants.

57.1% and 50%, respectively. For cancers and other diseases of genital tract, *Bridelia micrantha*, *Ricinodendron africanum* and *Ipomoea batatas* are the most used plants with FL equal to 60%, 50% and 50%, respectively. Cancers and other diseases of integumentary system are preferentially treated by *Canarium schweinfurthii* (FL = 100%), *Sindora klaineana* (FL = 66.7%) and *Coffea mannii* (FL = 50%). *Cymbopogon citratus* (FL = 50%) is most commonly used for the treatment of cancers and other otorhinolaryngological diseases and in the treatment of cancers and other diseases of the nervous system. The plants *Funtumia africana* (FL = 25%) and *Scyphocephalum ochocoa* (FL = 20%) as for them, are more used in the treatment of cancers and other urinary system diseases. Cancers and other metabolic disorders diseases are preferentially treated by *Coffea mannii* (FL = 50%), *Enantia chlorantha*

(FL = 40%), *Sarcocephalus latifolius* (FL = 40%). Cancers and other skeletal diseases were treated by *Tieghemella africana*, *Rauvolfia vomitoria*, *Tetrorchidium oppositifolium* (FL = 50%). The most commonly used by traditional healers for cancer and other diseases of mammary glands are *Ipomoea batatas* (FL = 25%), *Milicia excelsa*, *Oncoba welwitschii*, *Solanum americanum* and *Scyphocephalum ochocoa* (FL = 20%). For cancers and other circulatory diseases, *Tabernaemontana crassa* and *Rauvolfia vomitoria* (FL = 50%) are more used in treatment. *Tabernaemontana crassa* is also the most used herb for unspecified cancer and spiritual diseases (FL = 50%).

3.6. Relative frequency citation (RFC)

The RFC makes it possible to authenticate the frequency of citation of a species of medicinal plant used for various diseases. The RFC has been determined for all plant species (Table 4). It is between 0.006 and 0.04. The RFC is higher for *Bridelia micrantha* (0.04), *Ficus vogeliana* (0.032), *Harungana madagascariensis* (0.029), *Croton oligandrus* (0.028), *Ipomoea batatas* (0.027), *Morinda lucida* (0.027), *Vernonia amygdalina*, *Combretum micranthum*, *Persea americana*, *Coelocaryon preussii*, *Staudtia kamerunensis* var. *gabonensis*, *Pycnanthus angolensis* have RFC = 0.025.

3.7. Use value (UV)

UV, as other indexes RFC, FL and ICF, is an index for selecting potential plant species for pharmacological study and a further guideline for drug development. The use values range from 0.136 to 0.923 (Table 4). *Petersianthus macrocarpus*, *Bidens pilosa*, *Tithonia diversifolia*, *Carica papaya*, *Morinda lucida*, *Vernonia amygdalina*, *Coelocaryon preussii*, *Staudtia kamerunensis* var. *gabonensis* and *Sindora klaineana* have the highest use values with UV = 0.923, 0.833, 0.818, 0.818, 0.778, 0.765, 0.765, 0.765 and 0.750, respectively.

4. Discussion

4.1. Demographic data

In developing countries such as Gabon, the fight against cancer remains difficult because of the late diagnosis, the weakness of the therapeutic capacity in surgery, radiotherapy, chemotherapy and the unaffordable cost of medical care. Thus, traditional knowledge and the use of medicinal plants remain useful for the prevention and treatment of cancers and many other diseases. Traditional medicine is the first

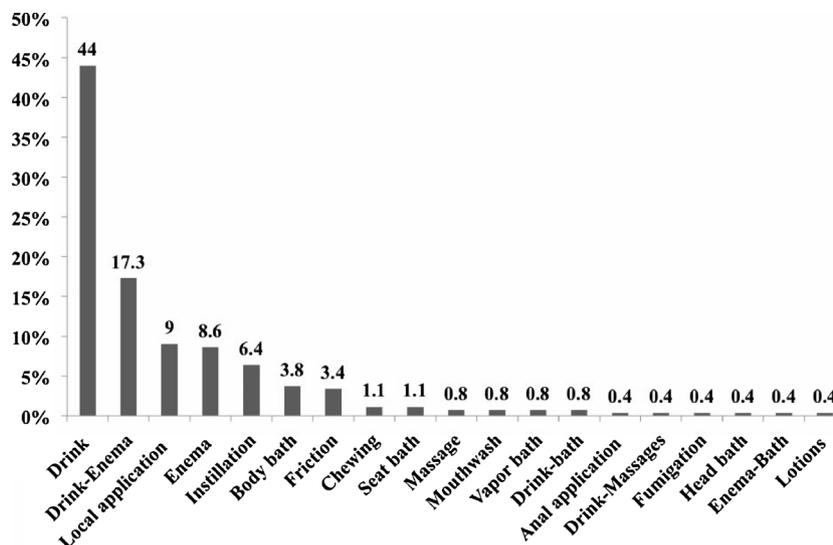


Fig. 6. Different modes of administration of drugs derived from plants.

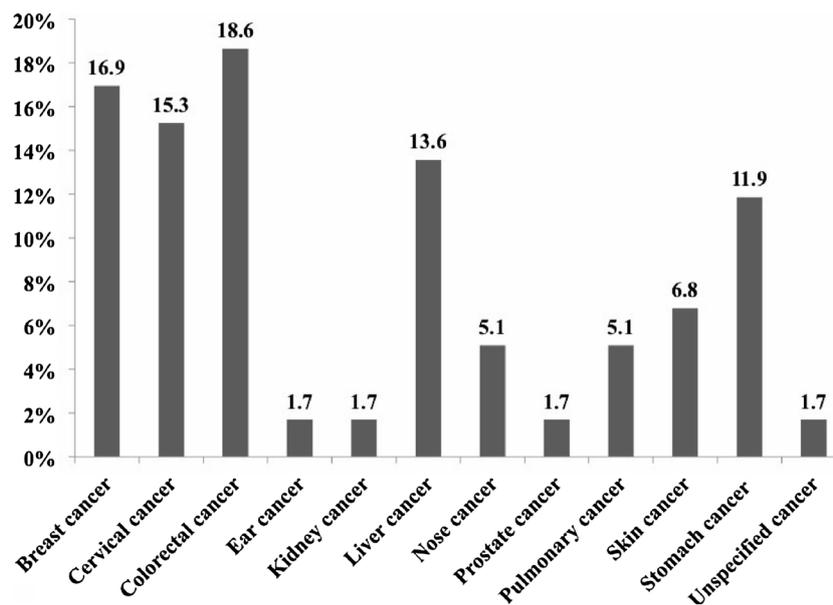


Fig. 7. Types of cancer treated.

choice of treatment for areas where access to appropriate care is difficult and where this medicine is sometimes the only option for the poorest patients to seek treatment. Community health workers in villages often lack commercial medicines, while traditional herbal medicines provided by traditional healers are fast and available at all times when needed.

103 traditional practitioners participated in the present study with a predominance of male healers. Female healers were hesitant, suspicious, and several women herbal therapists refused to participate in the study. Older and illiterate healers had exceptional knowledge of the traditional use of medicinal plant species that young healers did not possess. The transmission of traditional knowledge from one individual to another is done orally. Other authors have also mentioned that many traditional healers have acquired traditional knowledge of medicinal plants from older family members through oral tradition [23]. In several ethnopharmacological or ethnobotanical studies, it has been observed that evolution toward urbanization or modernism is at the origin

of the disinterestedness toward ancestral knowledge on medicinal plants. Knowledge about medicinal plants and their use is in danger of extinction [24]. In general, traditional healers tend to keep secret their knowledge of medicinal plants and herbal preparations and the transmission of their knowledge to the chosen heir is done by oral tradition [23]. Traditional health practitioners hold important information on the medicinal uses of local plant species for treating cancers.

4.2. Identified plants and parts used

The geographical location of the study area, characterized by a still warm, humid and rainy climate, would be the basis for the predominant use of these species [11]. Thus, traditional healers use the plant resources available in their environment for treatment purposes. The present study corroborates with other studies that have reported a predominance of peripheral parts (bark, leaves, roots and fruits) with a variable frequency of use [25,26]. The important use of these

Table 2
Informant consensus factor (ICF).

Categories	Number of used reports	Number of taxa	IFC
Cancers and other digestive system diseases	68	32	0.537
Cancers and other integumentary system diseases	44	24	0.465
Cancers and other metabolic disorders diseases	19	11	0.444
Cancers and other genital apparatus diseases	48	31	0.362
Cancers and other otorhinolaryngological diseases	4	3	0.333
Cancers and other circulatory system diseases	31	22	0.300
Cancers and other skeletal diseases	27	20	0.269
Cancers and other respiratory system diseases	22	18	0.190
Cancers and other glands breast diseases	14	12	0.154
Cancers and other nervous system diseases	21	18	0.150
Cancers and other urinary system diseases	4	4	0.000
Unspecified cancer and Spiritual diseases	3	3	0.000

Cancers and other digestive system diseases: colorectal cancer, stomach cancer, colic, hemorrhoids, diarrhea, splenomegaly, purgative, intestinal worms, gastric ulcer, digestive disorders, gastrointestinal disorders, gastritis, vomitive, wormer, epigastric, ascariasis. Cancers and other integumentary system diseases: skin cancer, scabies, ulcer, wound healing, keratitis, scabies, epithelioma, gangrene, edemas, yaws, varicella, smallpox, scabs, measles, boils, bubbles, abscess, antiseptic, rashes, whitlow. Cancers and other metabolic disorders diseases: liver cancer, liver disorders, diabetes, liver cirrhosis, ascites, icterus, bile, hepatitis, antipoison, hyperthermia. Cancers and other genital apparatus diseases: prostate cancer, cervical cancer, male infertility, sexual asthenia, syphilis, gonorrhoea, venereal diseases, female sterility, ovulation disorders, dysmenorrhoea, ocytocique, abortive, extended menstruation, pain due to uterus spasms, anti-abortion, metrorrhagia, venereal diseases, chancres, testicular hernia. Cancers and other otorhinolaryngological diseases: ear cancer, otitis, suppurative otitis, oral disorders. Cancers and other circulatory system diseases: hypertension, anemia, hemorrhagic disorders, wounds, heart disease, hemorrhage, injuries, malaria, antivenom, filariasis. Cancers and other skeletal diseases: rheumatism, lumbago, dental pain, intercostal pain, tooth decay, joints pains, joints inflammation, headaches, aches, low back pain. Cancers and other respiratory system diseases: nose cancer, pulmonary cancer, bronchitis, pneumonia, pulmonary disorders, asthma bronchitis, tuberculosis, hernia pneumonia, bronchopulmonary disorders, nose chancre, cough rebel, cough, chest diseases, whooping cough. Cancer and other glands breast diseases: breast cancer, breast abscess, purifies the milk of nurses, promotes lactation. Cancers and other nervous system diseases: psychosomatic disorders, mental disorders, migraines, epilepsy, anesthetic effect, neuralgia, eye pain, conjunctivitis, ophthalmia, vision disorders, dizziness. Cancers and other urinary system diseases: kidney cancer, renal pain, hemoglobinuria, diuretic. Unspecified cancer and spiritual diseases: unspecified cancer, talisman of evil spells, and destruction of the fetish.

peripheral parts is related to their easy accessibility and the fact that they constitute the storage places for secondary metabolites. Unlike what the results unveiled, a study of plants used against malaria in Zimbabwe showed a predominant use of roots (55.5%) followed by barks (13.7%) [27]. Alone or associated, these parts of plants are involved in the development of several medicinal recipes.

4.3. Medical practices

As in this study, other studies have also reported that decoction is the most used method of preparation [28]. Water is the most used solvent in the drug development process. Thus, the oral intake alone remains the main mode of administration of drugs. These results are consistent with several other studies that have shown that the beverage is the predominant drug delivery mode [27]. Traditional healers often use solvents that are accessible and available in their environment. Thus, substances that are less dangerous for consumption are made available to patients. Traditional healers treat several types of cancer. A total of 12 types of cancer have been listed, classified according to the affected organs including breast, cervical, colorectal, ear, stomach, liver, kidney, nose, prostate, lung and skin cancer.

4.4. Diagnosis of cancer by traditional healers

Empirically, traditional healers define cancer as the accumulation of mass or hard clods in the body. Nowadays they recognize different types of cancers by specific signs. Briefly, in addition to hard bumps, when a traditional healer receives a patient, he asks him a number of questions about his illness. Two questions are frequently asked: The first question is to know what changes the patient has been observing on his body since he feels sick. The second question is how the disease was discovered. According to these traditional healers, almost all the patients they treat have been diagnosed with cancer in the hospital. However, because of the unaffordable cost of medical care and conventional medicines, these poor patients are unable to follow the treatment of modern medicine and they then resort to traditional

medicine.

With the information these patients bring back from the hospital, traditional healers know that it is cancer and know the type of cancer. And with the information patients give about changes in their bodies, traditional healers record the signs of each cancer. Three doctors oncologists have confirmed these clinical signs described by traditional healers. The cancers diagnosed by traditional healers were:

Breast cancer is diagnosed by the appearance of a non-painful ball or mass of irregular contours in one breast. Breast skin becomes like the orange peel; the narrowed breast; blushes and a lot of heat are present in the breast.

Liver cancer is determined by the appearance of a mass in liver region to the right of the belly just under the ribs. The skin and whites of the eyes are yellow; the urine is dark; the stools are pale and itchy on the skin; an effusion of fluid that fills and inflates the belly.

For stomach cancer, patient has a mass in the abdomen that can be palpated; nodule in the navel region; blackening of skin in body folds and abdominal bloating after meals.

Skin cancer is defined by the presence of lesion that does not heal or reappears after healing; pale white or yellow flat areas that resemble scars raised and scaly red plaques; small smooth and shiny masses of pearly white, pink or red. Pink mass whose edges are raised and the center is recessed; mass whose surface has small blood vessels; bleeding lesion; mass or itchy area.

Nose cancer is diagnosed by the presence of bump or mass in the face, on the palate or inside the nose. Swelling of the face in the upper part of the cheek.

Kidney cancer is defined by the appearance of palpable abdominal mass and swelling of the legs and ankles.

The predominance of breast, colorectal, cervical, liver, stomach, skin, nose and pulmonary cancer may reveal a high incidence of these types of cancer in this region. Unfortunately no studies on the prevalence of cancers have been done in this area to date. Nevertheless, a study has shown that the most common cancers in Gabon, of all genders, are in order of importance: cervical cancer 19.4%, otorhinolaryngology cancer 17.6%, breast cancer 11% and non-Hodgkin's

malignant lymphoma 12.9% [4]. One study reported good cytotoxic effects of human cancerous strains of medicinal plants [29], showing once again that medicinal plants are rich in bioactive compounds. Traditional medicine is all the more complex because secret knowledge is transmitted orally from father to son or from the owners who communicate it laboriously. To this is added the experiences of the traditional healers acquired during the exercise of his profession. In addition, various rituals associated with recipes make traditional medicine, including incantations during harvesting, during the development or administration of the drug, but also the time of harvest, the mode and the amount of sampling more complicated of the plants.

4.5. Informant consensus factor (ICF)

The determination of the ICF made it possible to observe the homogeneity of information on the use of medicinal plant species in relation to certain categories of diseases. The homogeneity of

information on the use of medicinal plant species in relation to certain categories of diseases is average. The elevation of ICF in the categories of disease could be due to the ability of traditional healers to easily diagnose these conditions and to ensure better management of patients. These results could inform about the prevalence of these disease categories in study area. Some studies have previously reported that diseases of the digestive system have the maximum ICF, including studies conducted in Morocco [30], Italy [31] and Algeria [32]. However, these results are contradictory to those obtained in Turkey where gastrointestinal diseases were almost unregistered with the lowest IFC (0.01) [33].

4.6. Fidelity level (FL)

The fidelity level, expressed as a percentage, which indicates the preference of traditional healers to use some plants over others for the treatment of different disease categories. As in the present study, a

Table 3
Fidelity level (FL).

Categories	Medicinal species	FL (%)
Cancers and other digestive system diseases	<i>Annona muricata</i> L.	25
	<i>Anonidium manni</i> (Oliv.)	50
	<i>Bidens pilosa</i> L.	18.2
	<i>Boerhavia diffusa</i> L.	25
	<i>Bridelia micrantha</i> (Hochst.) Baill.	20
	<i>Ceiba pentandra</i> (L.) Gaertn.	44.4
	<i>Celtis mildbraedii</i> Engler.	100
	<i>Coelocaryon preussii</i> Warb.	20
	<i>Petersianthus macrocarpus</i> (P.Beauv.) Liben	10
	<i>Combretum micranthum</i> G. Don.	28.6
	<i>Croton oligandrus</i> Pierre ex Hutch.	33.3
	<i>Dacryodes edulis</i> (G.Don) H.J.Lam	57.1
	<i>Enantia chlorantha</i> Oliv.	20
	<i>Ficus asperifolia</i> Miq.	16.7
	<i>Ficus vogeliana</i> Miq	66.7
	<i>Funtumia africana</i> (Benth.) Stapf	25
	<i>Harungana madagascariensis</i> Lam. ex Poir.	12.5
	<i>Lophira alata</i> Banks ex C.F.Gaertn	22.2
	<i>Mangifera indica</i> L.	66.7
	<i>Tieghemella africana</i> Pierre	50
	<i>Fleroya ledermannii</i> (K.Krause) Y.F.Deng	28.6
	<i>Morinda lucida</i> Benth.	38.5
	<i>Ocimum basilicum</i> L.	28.6
	<i>Omphalocarpum procerum</i> P.Beauv.	75
	<i>Persea americana</i> Mill	28.6
	<i>Pycnanthus angolensis</i> (Welw.) Exell (1)	42.9
	<i>Rauvolfia macrophylla</i> Stapf	66.7
	<i>Solanum americanum</i> Mill.	20
	<i>Tetrorchidium oppositifolium</i> (Pax) Pax	50
	<i>Tithonia diversifolia</i> (Hemsley)	42.9
	<i>Vernonia amygdalina</i> Delile	27.3
	<i>Xylopia aethiopica</i> Rich.	50
	Cancers and other respiratory system diseases	<i>Abrus precatorius</i> L.
<i>Annona muricata</i> L.		50
<i>Bidens pilosa</i> L.		9.1
<i>Boerhavia diffusa</i> L.		12.5
<i>Bridelia micrantha</i> (Hochst.) Baill.		20
<i>Coelocaryon preussii</i> Warb.		10
<i>Petersianthus macrocarpus</i> (P.Beauv.) Liben		10
<i>Croton oligandrus</i> Pierre ex Hutch.		16.7
<i>Ficus asperifolia</i> Miq.		16.7
<i>Luffa cylindrica</i> (L.) M.Roem.		14.3
<i>Fleroya ledermannii</i> (K.Krause) Y.F.Deng		14.3
<i>Plagiostyles africana</i> Prain.		100
<i>Pycnanthus angolensis</i> (Welw.) Exell		14.3
<i>Scyphocephalum ochocoa</i> Warb.		20
<i>Staudtia Kamerunensis</i> var. <i>gabonensis</i> (Warb.) Fouilloy		10
<i>Vernonia conferta</i> Benth.		57.1
<i>Xylopia aethiopica</i> Rich.		33.3

(continued on next page)

Table 3 (continued)

Categories	Medicinal species	FL (%)	
Cancers and other genital apparatus diseases	<i>Boerhavia diffusa</i> L.	25	
	<i>Bridelia micrantha</i> (Hochst.) Baill.	60	
	<i>Carica papaya</i> L.	11.1	
	<i>Ceiba pentandra</i> (L.) Gaertn.	22.2	
	<i>Coelocaryon preussii</i> Warb	10	
	<i>Petersianthus macrocarpus</i> (P.Beauv.) Liben	40	
	<i>Croton oligandrus</i> Pierre ex Hutch.	16.7	
	<i>Dacryodes edulis</i> (G.Don) H.J.Lam	14.3	
	<i>Ficus vogeliana</i> Miq	33.3	
	<i>Funtumia africana</i> (Benth.) Stapf	25	
	<i>Guibourtia tessmannii</i> (Harms) J. Léonard.	14.3	
	<i>Harungana madagascariensis</i> Lam. ex Poir.	25	
	<i>Ipomoea batatas</i> (L.) Lam.	50	
	<i>Lophira alata</i> Banks ex C.F.Gaertn	22.2	
	<i>Luffa cylindrica</i> (L.) M.Roem.	14.3	
	<i>Mangifera indica</i> L.	16.7	
	<i>Milicia excelsa</i> (Welw.) C.C.Berg	20	
	<i>Fleroya ledermannii</i> (K.Krause) Y.F.Deng	42.9	
	<i>Morinda lucida</i> Benth.	7.7	
	<i>Ocimum basilicum</i> L.	14.3	
	<i>Omphalocarpum procerum</i> P.Beauv.	25	
	<i>Oncoba welwitschii</i> (Oliv.) Gilg.	40	
	<i>Rauvolfia macrophylla</i> Stapf	33.3	
	<i>Ricinodendron africanum</i> Muell. Arg.	50	
	<i>Sarcocephalus latifolius</i> (Sm.) E.A.Bruce	40	
	<i>Scyphocephalum ochocoa</i> Warb.	40	
	<i>Solanum americanum</i> Mill.	20	
	<i>Staudtia Kamerunensis</i> var. <i>gabonensis</i> (Warb.) Fouilloy	30	
	<i>Vernonia amygdalina</i> Delile	9.1	
	<i>Vernonia conferta</i> Benth.	14.3	
	Cancers and other integumentary system diseases	<i>Abrus precatorius</i> L.	33.3
		<i>Anonidium mannii</i> (Oliv.) Engl. et Diek	25
		<i>Canarium schweinfurthii</i> Engl.	100
		<i>Carica papaya</i> L.	44.4
		<i>Coelocaryon preussii</i> Warb.	10
		<i>Petersianthus macrocarpus</i> (P.Beauv.) Liben	20
		<i>Combretum micranthum</i> G. Don.	28.6
		<i>Croton oligandrus</i> Pierre ex Hutch.	16.7
		<i>Enantia chlorantha</i> Oliv.	20
		<i>Ficus asperifolia</i> Miq.	33.3
		<i>Guibourtia tessmannii</i> (Harms) J. Léonard.	28.6
<i>Ipomoea batatas</i> (L.) Lam.		25	
<i>Luffa cylindrica</i> (L.) M.Roem.		28.6	
<i>Milicia excelsa</i> (Welw.) C.C.Berg		20	
<i>Morinda lucida</i> Benth.		15.4	
<i>Persea americana</i> Mill.		28.6	
<i>Coffea mannii</i> (Hook.f.) A.P.Davis		50	
<i>Sindora klaineana</i> Pellegr.		66.7	
<i>Staudtia Kamerunensis</i> var. <i>gabonensis</i> (Warb.) Fouilloy		20	
<i>Tithonia diversifolia</i> (Hemsley) A.Gray		28.6	
<i>Vernonia amygdalina</i> Delile		18.2	
<i>Vernonia conferta</i> Benth.		14.3	
Cancers and other otorhinolaryngological diseases		<i>Cymbopogon citratus</i> (DC.) Stapf	50
		<i>Morinda lucida</i> Benth.	7.7
		<i>Staudtia Kamerunensis</i> var. <i>gabonensis</i> (Warb.) Fouilloy	10
Cancers and other urinary system diseases		<i>Coelocaryon preussii</i> Warb.	10
	<i>Funtumia africana</i> (Benth.) Stapf	25	
	<i>Lophira alata</i> Banks ex C.F.Gaertn	11.1	
Cancers and other metabolic disorders diseases	<i>Scyphocephalum ochocoa</i> Warb.	20	
	<i>Boerhavia diffusa</i> L.	12.5	
	<i>Carica papaya</i> L.	33.3	
	<i>Ceiba pentandra</i> (L.) Gaertn.	11.1	
	<i>Combretum micranthum</i> G. Don.	28.6	
	<i>Enantia chlorantha</i> Oliv.	40	
	<i>Guibourtia tessmannii</i> (Harms) J. Léonard.	14.3	
	<i>Harungana madagascariensis</i> Lam. ex Poir.	25	
	<i>Morinda lucida</i> Benth.	15.4	
	<i>Ocimum basilicum</i> L.	14.3	
	<i>Coffea mannii</i> (Hook.f.) A.P.Davis	50	
	<i>Sarcocephalus latifolius</i> (Sm.) E.A.Bruce	40	

(continued on next page)

Table 3 (continued)

Categories	Medicinal species	FL (%)	
Cancers and other skeletal diseases	<i>Bidens pilosa</i> L.	36.4	
	<i>Boerhavia diffusa</i> L.	12.5	
	<i>Coelocaryon preussii</i> Warb.	10	
	<i>Petersianthus macrocarpus</i> (P.Beauv.) Liben	10	
	<i>Combretum micranthum</i> G. Don.	14.3	
	<i>Croton oligandrus</i> Pierre ex Hutch.	16.7	
	<i>Dacryodes edulis</i> (G.Don) H.J.Lam	28.6	
	<i>Funtumia africana</i> (Benth.) Stapf	25	
	<i>Lophira alata</i> Banks ex C.F.Gaertn	33.3	
	<i>Mangifera indica</i> L.	16.7	
	<i>Tieghemella africana</i> Pierre	50	
	<i>Ocimum basilicum</i> L.	14.3	
	<i>Oncoba welwitschii</i> (Oliv.) Gilg.	20	
	<i>Persea americana</i> Mill	14.3	
	<i>Pycnanthus angolensis</i> (Welw.) Exell (1)	14.3	
	<i>Rauvolfia vomitoria</i> Afzel.	50	
	<i>Staudtia Kamerunensis</i> var. <i>gabonensis</i> (Warb.) Fouillooy	10	
	<i>Tetrorchidium oppositifolium</i> (Pax) Pax	50	
	<i>Vernonia amygdalina</i> Delile	9.1	
	<i>Xylopia aethiopica</i> Rich.	16.7	
	Cancer and other breast diseases	<i>Bidens pilosa</i> L.	18.2
		<i>Boerhavia diffusa</i> L.	12.5
		<i>Coelocaryon preussii</i> Warb.	10
<i>Ficus asperifolia</i> Miq.		16.7	
<i>Ipomoea batatas</i> (L.) Lam.		25	
<i>Lophira alata</i> Banks ex C.F.Gaertn		11.1	
<i>Milicia excelsa</i> (Welw.) C.C.Berg		20	
<i>Morinda lucida</i> Benth.		7.7	
<i>Oncoba welwitschii</i> (Oliv.) Gilg.		20	
<i>Pycnanthus angolensis</i> (Welw.) Exell (1)		14.3	
<i>Scyphocephalum ochocoa</i> Warb.		20	
<i>Solanum americanum</i> Mill.		20	
Cancers and other circulatory system diseases		<i>Abrus precatorius</i> L.	33.3
		<i>Annona muricata</i> L.	25
	<i>Anonidium mannii</i> (Oliv.) Engl. et Diek	25	
	<i>Bidens pilosa</i> L.	9.1	
	<i>Carica papaya</i> L.	11.1	
	<i>Ceiba pentandra</i> (L.) Gaertn.	11.1	
	<i>Coelocaryon preussii</i> Warb.	10	
	<i>Petersianthus macrocarpus</i> (P.Beauv.) Liben	10	
	<i>Enantia chlorantha</i> Oliv.	20	
	<i>Ficus asperifolia</i> Miq.	16.7	
	<i>Guibourtia tessmannii</i> (Harms) J. Léonard.	28.6	
	<i>Harungana madagascariensis</i> Lam. ex Poir.	25	
	<i>Luffa cylindrica</i> (L.) M.Roem.	28.6	
	<i>Milicia excelsa</i> (Welw.) C.C.Berg	20	
	<i>Morinda lucida</i> Benth.	7.7	
	<i>Persea americana</i> Mill	28.6	
	<i>Rauvolfia vomitoria</i> Afzel.	50	
	<i>Sindora klaineana</i> Pellegr.	33.3	
	<i>Staudtia Kamerunensis</i> var. <i>gabonensis</i> (Warb.) Fouillooy	10	
	<i>Tabernaemontana crassa</i> Benth.	50	
	<i>Tithonia diversifolia</i> (Hemsley) A.Gray	28.6	
	<i>Vernonia amygdalina</i> Delile	18.2	
	Cancers and other nervous system diseases	<i>Abrus precatorius</i> L.	16.7
<i>Bidens pilosa</i> L.		9.1	
<i>Ceiba pentandra</i> (L.) Gaertn.		11.1	
<i>Coelocaryon preussii</i> Warb.		10	
<i>Cymbopogon citratus</i> (DC.) Stapf		50	
<i>Harungana madagascariensis</i> Lam. ex Poir.		12.5	
<i>Luffa cylindrica</i> (L.) M.Roem.		14.3	
<i>Milicia excelsa</i> (Welw.) C.C.Berg		20	
<i>Fleroya ledermannii</i> (K.Krause) Y.F.Deng		14.3	
<i>Ocimum basilicum</i> L.(2)		28.6	
<i>Oncoba welwitschii</i> (Oliv.) Gilg.		20	
<i>Pycnanthus angolensis</i> (Welw.) Exell (1)		14.3	
<i>Ricinodendron africanum</i> Muell. Arg.		25	
<i>Sarcocephalus latifolius</i> (Sm.) E.A.Bruce		20	
<i>Solanum americanum</i> Mill. (2)		40	
<i>Staudtia Kamerunensis</i> var. <i>gabonensis</i> (Warb.) Fouillooy		10	
<i>Vernonia amygdalina</i> Delile (2)		18.2	
<i>Vernonia conferta</i> Benth.		14.3	
Unspecified cancer and spiritual diseases		<i>Guibourtia tessmannii</i> (Harms) J. Léonard.	14.3
	<i>Ricinodendron africanum</i> Muell. Arg.	25	
	<i>Tabernaemontana crassa</i> Benth.	50	

Table 4
Relative frequency citation (RFC) and use value (UV).

Medicinal species	Citation	FC	RFC	U	UV
<i>Petersianthus macrocarpus</i> (P.Beauv.) Liben	13	1.973	0.019	12	0.923
<i>Bidens pilosa</i> L.	12	1.821	0.018	10	0.833
<i>Tithonia diversifolia</i> (Hemsley) A.Gray	11	1.669	0.016	9	0.818
<i>Carica papaya</i> L.	11	1.669	0.016	9	0.818
<i>Morinda lucida</i> Benth.	18	2.731	0.027	14	0.778
<i>Vernonia amygdalina</i> Delile	17	2.580	0.025	13	0.765
<i>Coelocaryon preussii</i> Warb.	17	2.580	0.025	13	0.765
<i>Staudtia kamerunensis</i> var. <i>gabonensis</i> (Warb.) Fouillouy	17	2.580	0.025	13	0.765
<i>Sindora klaineana</i> Pellegr.	4	0.607	0.006	3	0.750
<i>Vernonia conferta</i> Benth.	9	1.366	0.013	6	0.667
<i>Oncoba welwitschii</i> (Oliv.) Gilg.	9	1.366	0.013	6	0.667
<i>Ceiba pentandra</i> (L.) Gaertn.	14	2.124	0.021	9	0.643
<i>Enantia chlorantha</i> Oliv.	8	1.214	0.012	5	0.625
<i>Sarcocephalus latifolius</i> (Sm.) E.A.Bruce	10	1.517	0.015	6	0.600
<i>Fleroya ledermannii</i> (K.Krause) Y.F.Deng	12	1.821	0.018	7	0.583
<i>Boerhavia diffusa</i> L.	14	2.124	0.021	8	0.571
<i>Lophira alata</i> Banks ex C.F.Gaertn	14	2.124	0.021	8	0.571
<i>Ricinodendron africanum</i> Muell. Arg.	7	1.062	0.010	4	0.571
<i>Omphalocarpum procerum</i> P.Beauv.	7	1.062	0.010	4	0.571
<i>Mangifera indica</i> L.	11	1.669	0.016	6	0.545
<i>Luffa cylindrica</i> (L.) M.Roem.	11	1.669	0.016	6	0.545
<i>Ficus asperifolia</i> Miq.	11	1.669	0.016	6	0.545
<i>Dacryodes edulis</i> (G.Don) H.J.Lam	13	1.973	0.019	7	0.538
<i>Combretum micranthum</i> G. Don.	17	2.580	0.025	8	0.471
<i>Ocimum basilicum</i> L.	15	2.276	0.022	7	0.467
<i>Harungana madagascariensis</i> Lam. ex Poir.	20	3.035	0.029	9	0.450
<i>Xylopia aethiopica</i> Rich.	14	2.124	0.021	6	0.429
<i>Guibourtia tessmannii</i> (Harms) J. Léonard.	14	2.124	0.021	6	0.429
<i>Abrus precatorius</i> L.	14	2.124	0.021	6	0.429
<i>Funtumia africana</i> (Benth.) Stapf	12	1.821	0.018	5	0.417
<i>Milicia excelsa</i> (Welw.) C.C.Berg	12	1.821	0.018	5	0.417
<i>Scyphocephalum ochocoa</i> Warb.	12	1.821	0.018	5	0.417
<i>Persea americana</i> Mill.	17	2.580	0.025	7	0.412
<i>Pycnanthus angolensis</i> (Welw.) Exell (1)	17	2.580	0.025	7	0.412
<i>Anonidium mannii</i> (Oliv.) Engl. et Diek	10	1.517	0.015	4	0.400
<i>Coffea mannii</i> (Hook.f.) A.P.Davis	5	0.759	0.007	2	0.400
<i>Celtis mildbraedii</i> Engler.	5	0.759	0.007	2	0.400
<i>Canarium schweinfurthii</i> Engl.	8	1.214	0.012	3	0.375
<i>Rauvolfia vomitoria</i> Afzel.	14	2.124	0.021	5	0.357
<i>Tetrorchidium oppositifolium</i> (Pax) Pax	15	2.276	0.022	5	0.333
<i>Solanum americanum</i> Mill.	15	2.276	0.022	5	0.333
<i>Rauvolfia macrophylla</i> Stapf	9	1.366	0.013	3	0.333
<i>Tabernaemontana crassa</i> Benth.	6	0.910	0.009	2	0.333
<i>Cymbopogon citratus</i> (DC.) Stapf	14	2.124	0.021	4	0.286
<i>Annona muricata</i> L.	15	2.276	0.022	4	0.267
<i>Croton oligandrus</i> Pierre ex Hutch.	19	2.883	0.028	5	0.263
<i>Plagiostyles africana</i> Prain.	12	1.821	0.018	3	0.250
<i>Bridelia micrantha</i> (Hochst.) Bail.	27	4.097	0.040	6	0.222
<i>Ipomoea batatas</i> (L.) Lam.	18	2.731	0.027	4	0.222
<i>Tieghemella africana</i> Pierre	11	1.669	0.016	2	0.182
<i>Ficus vogeliana</i> Miq	22	3.338	0.032	3	0.136

study in Ghana also mentioned *Xylopia aethiopica* in the treatment of stomach cancer, one of cancers of digestive system [34]. As in this study, *Vernonia conferta* is mentioned in the treatment of stomach, liver, breast and prostate cancers in another study [34]. A study in Kakamega County, Kenya also mentioned *Bridelia micrantha* in the treatment of cervical cancer, a cancer of genital tract as in this study [35]. In addition to being used in the treatment of cancers and other urinary system diseases, *Scyphocephalum ochocoa*, has been mentioned in another study for the treatment of skin, stomach, liver and breast cancers [10]. In addition to being used in the treatment of cancers and other skeletal diseases, Agyare et al.; are reported that *Rauvolfia vomitoria* is used in the treatment of genital and skin cancer [34].

4.7. Relative frequency citation (RFC) and use value (UV)

In this study, the RFC is between 0.006 and 0.04. It makes it possible to authenticate the frequency of citation of a species of medicinal plant

used for various diseases. The high value of RFC for certain species could be explained by the fact that these taxa are the most known and widespread in the region are therefore the most appropriate.

The value of UV use, like the other indices, is an index of selection of potential plant species for a pharmacological study for the development of new drugs. The utilization values range from 0.1 to 0.9. The UV value for species such as *Petersianthus macrocarpus*, *Bidens pilosa*, *Tithonia diversifolia*, *Carica papaya*, *Morinda lucida*, *Vernonia amygdalina*, *Coelocaryon preussii*, *Staudtia kamerunensis* var. *gabonensis* and *Sindora klaineana* indicate that these plants are used intensively to treat the different diseases indicated in this study. The low UV values recorded for some plants, such as: *Ficus vogeliana*, *Tieghemella africana* and *Ipomoea batatas* may be due to limited knowledge of the uses of these plants to cure diseases other than cancer.

4.8. Summary of the biological mechanism of cancer and the mode of action of medicinal plants

To better understand the modes of action of medicinal plants in anticancer therapy, it is important to recall briefly the biological mechanisms of cancer (Fig. 8).

Carcinogenesis is under the control of two types of carcinogens: initiators and tumor promoters. The initiators initiate oncogenesis by causing new genetic mutations on tumor-promoting oncogenes and tumor-suppressor genes that stop this progression. Initiators can be classified into three categories.

Biological carcinogens, such as human papillomavirus (HPV), which causes cervical cancer; hepatitis B and C viruses that cause liver cancer; Gram-negative bacterium *Helicobacter pylori* (*H. pylori*), the cause of stomach cancer; *Schistosoma japonicum* (*S. j.*) or *Schistosoma mansoni* (*S. m.*) parasites predisposing to colorectal cancer and *Schistosoma haematobium* (*S. h.*) may lead to bladder cancer [36–38]. Chemical carcinogens such as asbestos, components of tobacco smoke, aflatoxin (food contaminant) or arsenic (pollutant of drinking water), other chemicals are used experimentally to induce cancer [39]. Physical carcinogens such as ultraviolet radiation and ionizing radiation can induce deoxyribonucleic acid (DNA) damage [40,41]. These biological, chemical and physical carcinogens produce reactive oxygen species (ROS) that will damage DNA by causing irreversible mutations and activate the Ras and c-MYC proteins that promote the recruitment of immune cells (neutrophils, dendritic cells, macrophages, eosinophils and mast cells and lymphocytes). These cells produce pro-inflammatory and pro-angiogenic cytokines and chemokines and thus initiate oncogenesis [42,43].

Pro-inflammatory factors such as cytokines (IL1, IL6 and IL23, TNF α , TGF β , EGF), chemokines, prostaglandins, cytotoxic mediators, serine and cysteine proteins and interferons (IFNs), derived from immune cells and cyclooxygenase 2 (COX-2) will activate inflammation which is a powerful promoter of cancer. The inflammation will generate the formation of cancer progenitor cells. The latter can also be derived from epigenetic mutations, modification of gene expression without affecting the genetic information they carry. These cells should normally be eliminated by the mechanisms of programmed cell death called apoptosis. However, they will escape apoptosis thanks to anti-apoptotic factors such as B-cell lymphoma 2 (Bcl-2), c-FLIP, GM-CSF and M-CSF. Thanks to Cyclin D1, cell proliferation factor and the oncogene c-MYC, these cells will multiply to a size of 2 mm in diameter, at which size the intratumoral cells become necrotic and secrete the ROS that will have the goal is to activate pro-angiogenic factors to induce angiogenesis [5,44].

Angiogenesis is a multi-stage process of formation of new vessels from the arterial vasculature created by endothelial cells. It is important for the development of solid tumors beyond 2 mm in diameter because it supplies the tumor cells with oxygen and nutrients [45]. The ROS will induce several signaling pathways to induce angiogenesis and promote the dissemination of metastases into the bloodstream. The ROS will act

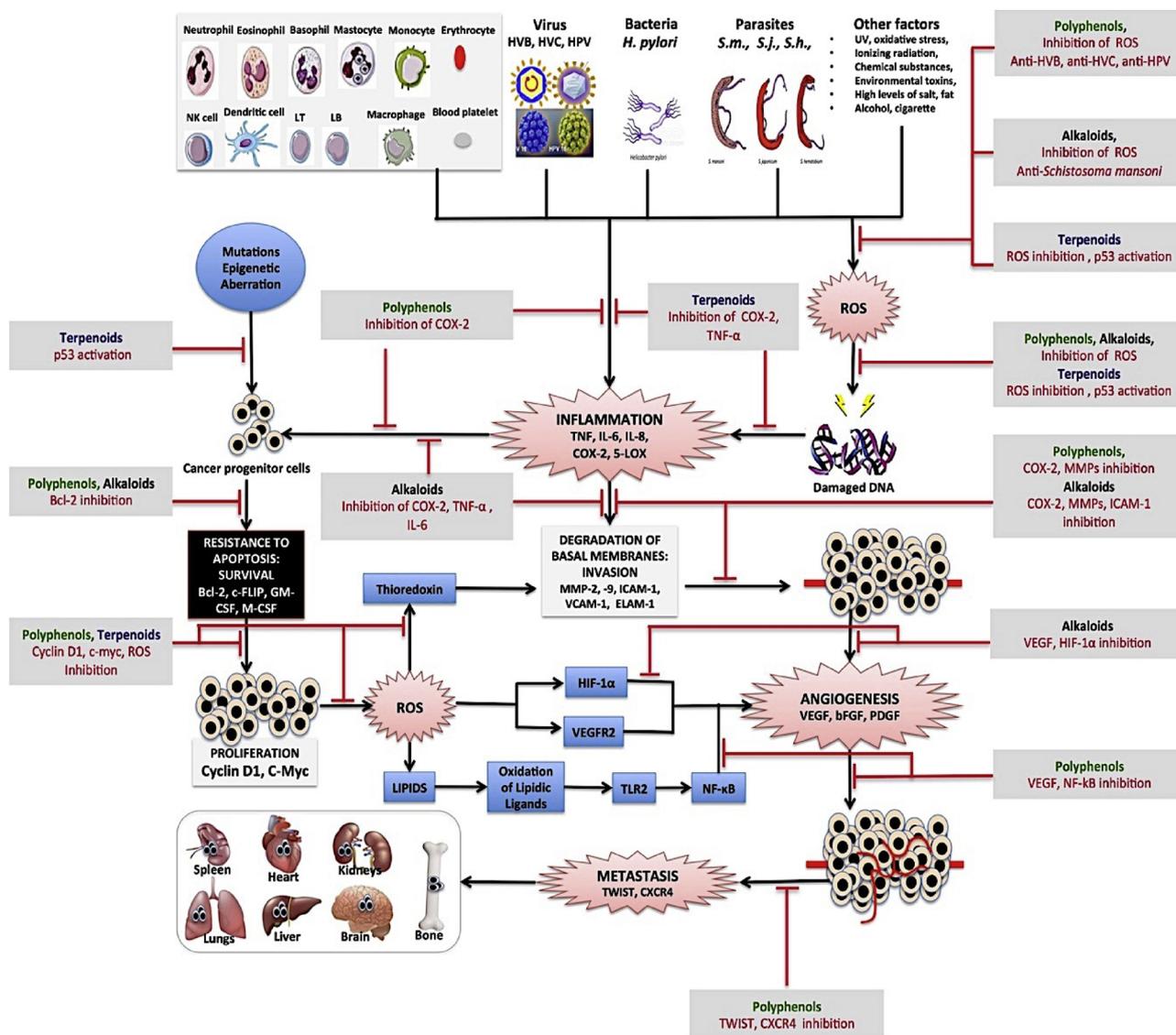


Fig. 8. Summary of the biological mechanism of cancer and mode of action of bioactive compounds of medicinal anticancer plants. 5-LOX: 5-lipoxygenase; Bcl-2: B-cell lymphoma 2; Bcl-xL: B-cell lymphoma-extra large; bFGF: basic fibroblast growth factor; c-FLIP: Cellular FLICE-like inhibitory protein; c-MYC: Avian myelocytomatosis virus oncogene cellular homolog; COX-2: cyclooxygenase 2; CXCR4: C-X-C receptor type 4; DNA: deoxyribonucleic acid; EGF: Epidermal Growth factor; ELAM-1: leukocyte endothelial cell adhesion molecules; GM-CSF: Granulocyte-macrophage colony-stimulating factor; *H. pylori*: *Helicobacter pylori*; HIF-1 α : Hypoxia Inducible Factors-1 α ; HPV: human papillomavirus; HVB: Hepatitis B virus; HVC: Hepatitis C virus; ICAM-1: intercellular adhesion-1 molecules; IL1, 6 and 23: Interleukin-1, 6 and 23; LT: T lymphocyte; LB: B lymphocyte; M-CSF: macrophage colony-stimulating factor; MMP-2, 9: matrix metalloproteinase-2, 9; NF- κ B: kappa B nuclear factors; PDGF: platelet derived growth factor; ROS: reactive oxygen species; *S. h.*: *Schistosoma haematobium*; *S. j.*: *Schistosoma japonicum*; *S. m.*: *Schistosoma mansoni*; TGF: transforming growth factor; TLR2: Toll-like receptors; TNF α : tumor necrosis factor α ; VCAM-1: molecules vascular cell adhesion; VEGF:vascular endothelial growth factor; VEGFR2:vascular endothelial growth factor receptors 2.

either with the inducing factor of hypoxia (HIF-1 α) and its cofactor p300 which will lead on the one hand the expression of vascular endothelial growth factor (VEGF) whose role is to stimulate the proliferation and migration of endothelial cells and increase microvascular permeability [46,47]. This VEGF will interact with its receptors (VEGFR2) and induce neovascularization. On the other hand, the HIF-1 α associated with inflammation, will induce the expression of matrix metalloproteinase-2 and 9 (MMP-2 and 9), intercellular adhesion-1 molecules (ICAM-1), molecules vascular cell adhesion (VCAM-1), leukocyte endothelial cell adhesion molecules (ELAM-1) [48]. ROS can also directly interact with VEGFR2 receptors and induce angiogenesis. ROS can also induce oxidation of lipids that will interact with Toll-like receptors (TLR2) and activate kappa B nuclear factors (NF- κ B) [49]. The cancer cells will end up in the bloodstream and affect other organs of the body: this is metastasis, which according to the WHO is the

leading cause of death related to cancer [2].

Medicinal plants have beneficial effects in anticancer therapy, through their antioxidant activity, their anti-inflammatory capacity, their anti-angiogenic potential and their anti-metastatic effect (Fig. 8). Indeed medicinal plant extracts are rich in bioactive compounds such as polyphenols, alkaloids and terpene compounds [8,9,50].

The polyphenols are grouped into phenolic acids, stilbenes, lignans and flavonoids. The flavonoids are subdivided into flavonols, flavones, isoflavones, flavanones, anthocyanidins and flavanols (catechins and proanthocyanidins). The anticancer efficacy of polyphenols lies in their involvement in various mechanisms of oncogenesis. Polyphenols have been reported to protect against DNA damage and tumor initiation by modulating the metabolizing enzymes of phase I and II xenobiotics and also protect against carcinogenesis by promoting apoptosis, decreasing proliferation cell and inhibiting inflammation. In addition, recent

research shows that polyphenols are potent epigenetic modulators capable of restoring the proper structure of the epigenome. Indeed, disorders of carcinogenesis, well before genetic mutations [51]. Polyphenols inhibit cancer cell proliferation and angiogenesis by inhibiting NF- κ B-regulated gene products, such as cyclin D1, c-MYC, Bcl-2, Bcl-xL and apoptosis, protein-1, COX -2, MMPs and VEGF [52]. In addition, the polyphenols have anti-*Helicobacter pylori* effects by inhibition of vacuolar cytotoxin VacA, which is one of the factors expressed by *Helicobacter pylori* to allow colonization of the stomach and plays a role in the pathogenesis [53]. Polyphenols have anti-hepatitis B virus, anti-hepatitis C virus activity and thus prevent cancer of the stomach and liver [54,55].

Alkaloids are a group of very diverse natural organic compounds, heterocyclic with nitrogen as a heteroatom and more or less complex molecular structure. Their anticancer activity lies in their ability to inhibit the expression of COX-2, TNF- α , inducible nitric oxide synthase (iNOS), IL-6, HIF-1 α , MMPs, VEGF, ICAM-1, Bcl-2, NF- κ B [56]. Alkaloids have the anti-*Schistosoma mansoni* properties allowing them to prevent the onset of colorectal cancer [57].

Terpenoids are the largest class of natural products with 25,000 chemical structures elucidated today. On the basis of their structures, terpenoids are subdivided into monoterpenoids, sesquiterpenoids, diterpenoids, triterpenoids and tetraperpenoids. The efficacy of terpenoid in anticancer therapy lies in their ability to intervene in several levels of oncogenesis. By their ability to neutralize ROS and maintain the integrity of the p53 protein, terpenoid drugs prevent lipid peroxidation and damage to DNA. They possess anti-inflammatory activity due to inhibition of TNF- α expression. They prevent tumor invasion and protect the basement membrane by inhibiting MMP-2, MMP-7 and MMP-9. They prevent the proliferation of cancerous cells by inhibition of c-MYC. Terpenoids are antiangiogenic by their ability to inhibit NF- κ B and VEGF [58].

4.9. Anticancer potential of listed plants

The anticancer potential of plants listed can be estimated from their ability to neutralize reactive oxygen species (antioxidant activity), their anti-inflammatory activity, their ability to inhibit the formation of new blood vessels (antiangiogenic activity) and their ability to inhibit the proliferation of several cancer cell strains and inhibited the progression of cancer types *in vivo* and *in vitro* (Table 5).

4.9.1. Promyelocytic leukemia, lung carcinoma, stomach and colon cancer

Bidens pilosa: Three compounds isolated from *Bidens pilosa*, namely: 1,3-dihydroxy-6(E)-tetradecene-8,10,12-triylne (Fig. 9a), 1,2-dihydroxytrideca-5,7,9,11-tetrayn (Fig. 9b) and 1,2-dihydroxy-5(E)-tridecene-7,9,11-triylne (Fig. 9d), showed good antiangiogenic activity marked by inhibition of significant cell proliferation of D cells. Primary human umbilical vein endothelium (HUVEC) with IC₅₀ values of 12.5 μ M, 1.73 μ M and 12.4 μ M, respectively [66]. It has been reported that the extract fraction of *Bidens pilosa* methanol stops the progression of rat-induced breast cancer and reduces oxidative stress [187]. A flavonoid isolated from *Bidens pilosa*, centaauridine (Fig. 9c), also showed anticancer activity in B lymphoma cells. The cytotoxicity of centaauridine was further analyzed using 60 human tumor cell lines from American National Cancer Institute (NCI). The cytotoxicity of centaauridine, expressed as GI₅₀ (growth inhibition of 50% in the panel of NCI tumor lines), was 0.24 μ M [188]. In addition, 1,2-dihydroxy-5(E)-tridecene-7,9,11-triylne also isolated from *Bidens pilosa* (Fig. 9d) showed elevated IC₅₀ values against A549 lung carcinoma cells and keratinocytes HACAT but also could inhibit cell proliferation of HUVECs. Butine (Fig. 9e) is also a flavonoid from the medicinal plant *Bidens pilosa*, which has shown a cytotoxic effect on the proliferation of human colon adenocarcinoma cells with an IC₅₀ value of 1.75 μ M at 2 μ M. Butine acts on the incorporation of leucine, thymidine and uridine labeled with [¹⁴C], can lead to the inhibition of deoxyribonucleic acid (DNA),

ribonucleic acid (RNA) and of protein synthesis of cancer cells of the human colon. In addition, butine also exhibited non-toxic inhibition of 1-chloro-2,4-dinitrobenzene (CDNB) in glutathione S-transferase (GST) activity. Tumor resistance was correlated with elevated levels of GST, thus, the proliferation of cancer cells inhibited by butene [189].

Tithonia diversifolia: One study reported that tagitinin C (Fig. 9f) and 1 β , 2 α -epoxytagitinin C (Fig. 9g), two compounds were isolated from *Tithonia diversifolia*. The potential as cancer chemopreventive agents of these compounds was evaluated by measuring the antiproliferative activity of Col2 colon cancer cells and the induction of cell differentiation in human promyelocytic leukemia cells (HL-60). These compounds were then investigated for their ability to inhibit pre-neoplastic lesions *in vivo* induced by 7,12-dimethylbenz[a]anthracene in a mammary mouse organ culture assay. These isolates showed significant antiproliferative activity [190].

Mangifera indica: It has been demonstrated that a methanol extract of the bark of *Mangifera indica* has the ability to inhibit the survival of human pancreatic PANC-1 cells without apparent toxicity under normal nutrient-rich conditions [191]. Other researchers have shown that the polyphenols of *Mangifera indica* and their main microbial metabolite, pyrogallol, inhibit the proliferation of breast cancer cells through the upregulation of AMPK and the downregulation of the AKT pathway mTOR [192]. Magiferin (1,3,6,7-tetrahydroxyxanthone C2- β -D-glucoside) is a compound isolated from *Mangifera indica* (Fig. 9h). In one study, the effects of mangiferin were examined in carcinogenesis of the colon in rats induced by a chemical carcinogen, azoxymethane (AOM). The experiments were performed according to two tests: a short-term test to study the effects of mangiferin on the development of pre-neoplastic lesions by AOM, aberrant crypt foci (ACF), and the long-term test to study the effect of the injection of mangiferin on the tumorigenesis induced by AOM. In the short-term test, mangiferin in a diet significantly inhibited the development of ACF in treated rats compared to rats treated with AOM alone. In the long-term test, the group treated with 0.1% of mangiferin, in the initiation phase of the experimental protocol had a significantly lower incidence and multiplicity of intestinal neoplasia induced by AOM (47.3 and 41.8% reduction in the group treated with AOM alone for incidence and multiplicity, respectively). This proliferation of cells in the mucosa of the colon was reduced in rats treated with mangiferin (65 \pm 85% reductions in the AOM-treated group). These results suggest that mangiferin has potential as a natural chemopreventive agent [193].

Ipomoea batatas: A study reported that 3,4,5-tri-O-caffeoylquinic acid (Fig. 9i), isolated from this plant had anticancer activity on cancer cells of the stomach (Kato III), colon (DLD-1) and promyelocytic leukemia (HL-60). Indeed, Kurata et al. have studied the suppression of the proliferation of human cancer cells by phenolic compounds isolated from the sweet potato leaf. Human cancer cells used in their research included stomach cancer cells (Kato III), colon cancer (DLD-1) and promyelocytic leukemia cells (HL-60). 3,4,5-Tri-O-caffeoylquinic acid effectively reduced the growth of three types of cancer cells. In trying to clarify the mechanism of growth suppression with the addition of the apoptotic inhibitor N-ethylmaleimide, they were observed that nuclear granulation in HL-60 cells treated with 3,4,5-tri-O-caféoylquinique suggested the induction of apoptosis. This effect was confirmed by DNA fragmentation, increased caspase-3 activity, and c-Jun expression. The suppression of growth of HL-60 cells by 3,4,5-tri-O-caffeoylquinic acid was determined to be the result of apoptotic cell death. These results indicate that 3,4,5-tri-O-caffeoylquinic acid may have a potential for cancer prevention [194].

Sarcocephalus latifolius: β -sitosterol (Fig. 9j) is a compound isolated from the medicinal plant *Sarcocephalus latifolius*. The anti-carcinogenic property *in vivo* of β -sitosterol in 1,2-dimethylhydrazine-induced colon carcinogenesis (DMH) was studied because of its antioxidant properties and its ability to suppress the impaired expression of β -catenin and proliferation of mucosal cell antigen from DMH treated rats in short-term colon carcinogenesis. Studies suggest that β -sitosterol exerts a

Table 5
Anticancer potential, toxicity and phytochemical composition of the listed plants.

No.	Scientific name Family (voucher number)	Anticancer activity and other therapeutics activities	Toxicity	Phytochemical composition
1	<i>Mangifera indica</i> L. Anacardiaceae (Bouroubou 513)	Analgesic and anti-inflammatory effect [59]. Cytotoxic effect of human lung cancer cells (A-549), human leukemia (Molt-4) and prostate cancer (LnCap) [60]. Significant cytotoxic activities on MCF 7, MDA-MB-435 and MDA-N breast cancer cell lines, as well as colon cancer (SW-620) [61]. Cytotoxic and antiproliferative effect on breast cancer cells (MDA-MB-231 and MCF-7) [62]. Anticancer, immunomodulatory, anti-angiogenic, apoptotic effect and gene regulatory effects of mangiferin from <i>Mangifera indica</i> L. [63].	Studies indicated that acute and subchronic toxicities of mangiferin for oral exposure are low [64]	The preliminary phytochemical screening of methanolic extract of the peel of <i>M. indica</i> revealed the presence of flavonoids, saponins, tannins, steroids, terpenoids, glycosides and alkaloids [65].
2	<i>Anonidium mannii</i> (Oliv.) Engl. et Dielk Annonaceae	No pharmacological studies were found on this plant.	No toxicity study was found on this plant.	No studies found on this plant showing its chemical composition.
3	<i>Annona muricata</i> L. Annonaceae (Dibata 913)	Anticancer, anti-inflammatory, antioxidant, hepatoprotective, antihypertensive, antinociceptive, antidiabetic, hypolipidemic, gastroprotective anticonvulsant and bilirubin-lowering, antiparasitic, anti-arthritis, antiplasmodial, insecticidal, molluscicidal and wound healing activities [66]; cytotoxic effect of breast cancer cell lines (MCF-7, MDA-MB-231, and 4 T1) [72]; antiangiogenic effect on chicken chorioallantoic membrane (CAM) [67].	Doses higher than 5 g/kg of aqueous extract can cause kidney damage and acute toxicity possible at a dose of 211 mg/kg per day, or 71 cups of tea per day therefore this plant is very weakly toxic [68].	This plant is rich in alkaloids, megastigolans, flavonol triglycosides, phenolics, cyclopeptides and essential oils [66].
4	<i>Xylofia aethiopia</i> Rich. Annonaceae (A. Isembe 226)	Cytotoxic, antiproliferative, anti-inflammatory, antioxidant, antihelminthic, anti-anaphylactic and antimicrobial effects [69]; Cytotoxic activity against cancer (MCF-7) [70]; Antioxidant activity and cytotoxicity activity against human myeloid leukemia (HL-60), human hepatocellular carcinoma (SMMC-7721), human lung carcinoma (A-549), human breast adenocarcinoma (MCF-7) and colon cancer (SW480) cell lines [71]; Antioxidant, antiangiogenic and antiproliferative potentials of methanol extract [72]	Long-term use in concentrations greater than 20 g/kg can cause kidney problems [73]	Cyanogenetic glycosides, flavonoids, tannins, sterols, carbohydrates [74]
5	<i>Enanitia chlorantha</i> Oliv Annonaceae (Bouroubou 591)	Testiculo-protective effect of stem bark extract on lead induced toxicity in adult wistar rat [75]. Anti- <i>Helicobacter pylori</i> , antimalarial, antimicrobial, antibacterial, antioxidant, anticonvulsion, anti-inflammatory, analgesic, antipyretic, antiviral activities, gastro protective effect and enhancing male fertility [76]. Cytotoxic effect on human mesothelioma cells (SPC212), human non-small cell lung cancer cells (A549) (NSCLC), HepG2 hepatocarcinoma cells, ATCC and MCF-7 breast adenocarcinoma cells, colorectal adenocarcinoma DLD-1 [77]. No pharmacological studies were found on this plant.	The 1000, 2000 and 3000 mg/kg extract caused congestion in the heart and kidneys of experimental rats. These results suggest that oral administration of this plant can produce severe toxic effects at relatively high doses. It is therefore necessary to be cautious in its use [78]. This plant extract can be taken safely up to a dose of 500 mg/kg body weight [76].	Phytochemical screening of the ethanolic extract of <i>E. chlorantha</i> stem bark revealed the presence of alkaloid, saponins and reducing sugar [78].
6	<i>Tabernaemontana crassa</i> Benth. (not found)	No pharmacological studies were found on this plant.	No toxicity study was found on this plant.	No studies found on this plant showing its chemical composition.
7	<i>Rauwolfia macrophylla</i> Stapf Apocynaceae (not found)	No pharmacological studies were found on this plant.	No toxicity study was found on this plant.	No studies found on this plant showing its chemical composition.
8	<i>Funtumia africana</i> (Benth.) Stapf Apocynaceae (A.M. Louis 431)	Anti-inflammatory and larvicidal activities were found on leaf and stem [79].	No toxicity study was found on this plant.	No studies found on this plant showing its chemical composition.

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Table 5 (continued)

No.	Scientific name Family (voucher number)	Anticancer activity and other therapeutics activities	Toxicity	Phytochemical composition
9	<i>Rauvolfia vomitoria</i> Alzel. Apocynaceae (M. Mbembo 81)	Cytotoxicity effect on Human ovarian cancer cell lines OVCAR-5 and OVCAR-8 [80]; antitumor effect in an orthotopic pancreatic cancer mouse model PANC-1 [81]; cytotoxicity effect on human hepatocarcinoma HepG2 cell line and anthelmintic activities [82].	Administration of leaf and root extract to rats does not have any untoward effect on kidney and liver [83]; administration of very high doses may be toxic to the liver and kidneys [84].	Several alkaloids have been isolated from this plant, in particular: αYohimbine, Reserpine, Rescinamine, Aricin, Reserpinine, Isoreserpinine, Sarpagine, Ajmalin, Sandwicine, Mitrodidine, Seredamine, Suaveolin, Tetraphyllicin Yomalidine, Serpentine, Alstonine, Rauvoxin [80].
10	<i>Bidens pilosa</i> L. Asteraceae (Dibata 180)	<i>In vivo</i> antitumoral, antioxidant effect and <i>in vitro</i> cytotoxicity effect on murine-derived Ehrlich ascites carcinoma (EAC) cell line [85]; cytotoxicity effect on human oral (KB), liver (HepG2), colon (CaCo2) and breast (MCF-7) cancer cell lines [86]; anticancer, anti-inflammatory, antidiabetic, antioxidant, antimicrobial, hypotensive, vasodilator activities [87]; favorable antiproliferation activity against the four human cancer cell lines: human lung cancer cell line A549, liver cancer cell line HepG-2, nasopharyngeal carcinoma cell line CNE-2 and malignant melanoma cell line B16 [88].	The set of studies carried out on toxicity of this plant shows that oral administration of the aqueous extract of this is almost safe [87].	Flavonoids, phenylacetyleins, alkaloids, steroids, triterpenoids and tannins [89]; saturated carbohydrate, aliphatic carboxylic acids, acetylenic 38 hydrocarbons, phenols, chalcones, flavonols, porphyrines [90].
11	<i>Vernonia amygdalina</i> Delile Asteraceae (Wieringa 1407)	Antiproliferative effect and inhibition of DNA synthesis of human ductal carcinoma cell line (BT-549) [91]; cytotoxicity effects in human breast cancer cell lines (MCF-7 and MDA-MB-231 cells) [92]; cytotoxicity effect on androgen-independent human prostate tumor cell line PC-3 [93].	A study has shown that the toxicity of aqueous extract of this plant is shown from a concentration of 5000 mg/kg body weight [94]; another recent study concluded that the aqueous extracts of this plant have a high hepatotoxicity [95].	Oxalate, phytate, tannins, saponins flavonoid, cyanogenic glycoside, alkaloids, anthraquinone, steroid, phenol [96].
12	<i>Tithonia diversifolia</i> (Hemsley) A. Gray Asteraceae (Sosef 882)	Antiangiogenic activity and cytotoxicity effect on WiDr: cancer cell [97]; cytotoxicity effect on cervical cancer cell line (HeLa), myeloma and SiHa cell lines (LPPT-UJGM), breast cancer (T47D, MCF7 and EVSAT), colon cancer (WiDr) and melanoma (M19) cell lines [98]; antioxidant, anti-inflammatory, antinociception, antidiarrheal, antihypertensive, analgesic, and cancer chemopreventive effects [99].	Study report toxicity from 400 mg/kg in rats [100]; the toxicity of aqueous extracts by oral administration is estimated above 10,000 mg/kg in rats [101].	Polyphenol, flavonoid, saponins, quinone, triterpenoid/steroid, alkaloids, saponins, tannins, terpenoids flavonoids and phenols [102].
13	<i>Catha pentandra</i> (L.) Gaertn. Bombacaceae (Sosef 932)	Angiogenesis, anti-inflammatory, anti-ulcer, anti-fungal, anti-diarrhoeal, hepatoprotective, anthelmintic, hypoglycaemic, hypolipidaemic activities [103]; aqueous extract (400 and 800 mg/kg) of this plant has significant anti-inflammatory and analgesic activity in rats and mice [104]; bark extracts from this plant showed a cytotoxic effect of <i>in vitro</i> Ehrlich ascites carcinoma (EAC), MCF-7 and B16F10 cells and <i>in vivo</i> on the model EAC (liquid tumor) and ascites model of Dalton lymphoma (DLA or solid tumor) [105].	A study has shown that this plant has no toxic effect at a dose of 2000 g/kg in rats [106]; a other study has shown that the toxicity of this plant can only be observed at a dose higher than 5000 mg/kg in rats [107].	Carbohydrates, glycosides, steroids, tannins, flavonoids, saponins, resins, fats and oils [108].
14	<i>Dacryodes edulis</i> (G.Don) H.J.Lam Bursaceae (Bernard SRFG 274)	Antioxidant, antibacterial, antimicrobial, antimalarial, haemopoietic, cardiovascular and antidrepanocytary [109].	Isolated products of this plant have been shown to be non-toxic against LLC-MK2 monkey kidney epithelial cells [110].	Essential oils rich in monoterpenes, sesquiterpenes, diterpens, triterpens, phellandrène et β-caryophyllène [111].
15	<i>Canarium schweinfurthii</i> Engl. Bursaceae (Strijk 259)	Anticancer, antioxidant, analgesic, antimalarial, anti-diabetic, antimicrobial, antibacterial, growth promoting, nephroprotective, food preservative, anthelmintic and termiticidal activities [112].	No toxicity study was found on this plant	Alkaloids, saponins, total polyphenols, flavonoids, tannins, anthocyanins, leuco-anthocyanins, quinones, terpenes and steroids [113]
16	<i>Sindora klaineana</i> Pellegr. Caesalpinaceae (AM Louis 1758)	No pharmacological studies were found on this plant.	No toxicity study was found on this plant.	No studies found on this plant showing its chemical composition
17	<i>Gulbourtia tessmannii</i> (Harms) J. Léonard. Caesalpinaceae (Bernard SRFG 328)	Antioxidant activity of aqueous and hydroethanolic extracts of this plant [114]; methanolic extract of this plant improves sexual parameters in obese rats [115].	One study has shown that this plant has low intraperitoneal toxicity (LD ₅₀ = 328.78 mg/kg) and no subacute toxicity by oral ingestion (LD ₅₀ = 5000 mg/kg) [116].	Phenols, flavonoids, tannins and terpenoids, glucoiside [115].

(continued on next page)

Table 5 (continued)

No.	Scientific name Family (voucher number)	Anticancer activity and other therapeutics activities	Toxicity	Phytochemical composition
18	<i>Carica papaya</i> L. Caricaceae (Strijk 136)	Anti-tumor activity and immunomodulatory effects of aqueous extract of this plant [117]; cytotoxicity of ethanolic extract on breast cancer cell lines (MCF-7) [118]; antiproliferative effect on prostate cancer (PC) using PC-3 cell line [119].	One study suggested that daily oral administration of leaf extracts from this plant to rats for 13 weeks at a dose up to fourteen times the levels used in the practice of traditional medicine had not caused significant toxic effects [120].	Folic acids, vitamin B12, alkaloids, saponins, glycosides, tannins, anthraquinones, flavonoids [121].
19	<i>Harungana madagascariensis</i> Lam. ex Poir. Clusiaceae (Bourboul 580)	Antioxidant properties of stem bark extracts [122]; antibacterial activities of methanol extracts, fractions and compounds from this plant [123]; cytotoxic activity of CCRF-CEM leukemia cells [35].	It has been shown that at relatively high doses (≥ 200 mg/kg), the extract can induce liver injury, inflammation of the parenchyma and portal vein, and that cell necrosis [124].	Flavonoids, alkaloids, saponins, glycosides, tannins [125].
20	<i>Combretum micranthum</i> G. Don. Combretaceae (not found)	Antiviral activity against herpes simplex virus type 1 and type 2 (HSV-1 and HSV-2) methanolic extracts of this plant [126]; cytotoxic effect against cell line of T24 bladder, HeLa cervical and MCF7 breast cancer [127]; anti-inflammatory, immunostimulant, hypoglycemic, antifungal, antibacterial and antimalarial activities [128].	Aqueous extract of natural origin is moderately toxic with lethal dose 50% equal to 1258 ± 72.84 mg/kg body weight and 1500 ± 89.12 mg/kg [129].	Leaf extracts contain flavonoids including vitexin, isovitexin, orientin homoorientin, alkaloids including stachydrine, hydroxyl-stachydrine and choline; sugar alcohols including m-inositol and sorbitol; flavan-alkaloids including kinkéloïds A, B, C and D [130]; tannins, saponins, steroids, terpenoids and phenols [131].
21	<i>Vernonia conferta</i> Benth. Compositae (AM Louis 2682)	Cytotoxic activity of crude methanolic extracts against human cancer cell lines. DLD-1 (colon), MCF-7 (breast) and M14 (melanoma) [132].	No toxicity study was found on this plant.	No studies found on this plant showing its chemical composition.
22	<i>Ipomoea batatas</i> (L.) Lam. Convolvulaceae (not found)	Anticancer potential inhibits proliferation and induces apoptosis of prostate cancer cells <i>in vivo</i> and <i>in vitro</i> and inhibitory effect on growth of cancer cell lines of MCF-7 (breast cancer) and SNU-1 (gastric cancer); anti-oxidant activities, anti-inflammatory potential, anti-ulcer potential, antimicrobial effects, effect on cardiovascular system, effect on immune system, hematological effects [133].	It has been shown that the tuber extract of this plant has no toxic or deleterious oral effects up to 2000 mg/kg indicating low toxicity at high doses. The LD ₅₀ value for oral tuber extract was not determined because no mortality was observed up to a dose of 2000 mg/kg [134].	Triterpenes, steroids, alkaloids, flavonoids anthraquinones, coumarins, saponins, tannins and phenolic acids [135].
23	<i>Luffa cylindrica</i> (L.) M.Roem. Cucurbitaceae (not found)	Cytotoxic effect of α -luffin (a protein isolated from this plant) on JEG-3 (human placental choriocarcinoma cell line), HepG2 (human hepatoma cell line), and MCF-7 cells (human breast cancer cell line) [136].	Oral administration of aqueous extracts up to concentrations of 5000 mg/kg body weight does not induce acute toxicity in mice [137].	Carbohydrates, sterols, saponins, flavonoids, alkaloid and phenols [138].
24	<i>Tetrorchidium oppositifolium</i> (Pax) Euphorbiaceae (AM Louis 587)	Antioxidant and antiangiogenic properties [7].	No toxicity study was found on this plant.	Reducing sugar, coumarins, digitoxins, anthracenics, flavonoids, proanthocyanidins, alkaloids, tannins, polyphenols, saponosides [7].
25	<i>Ricinodendron africanum</i> Muell. Arg. Euphorbiaceae (Wilks 807)	No pharmacological studies were found on this plant.	No toxicity study was found on this plant.	No studies found on this plant showing its chemical composition.
26	<i>Plegioxyles africana</i> Prain. Euphorbiaceae (Bourboul 42)	No pharmacological studies were found on this plant.	No toxicity study was found on this plant.	No studies found on this plant showing its chemical composition.
27	<i>Bridelia micrantha</i> (Hochst.) Baill. Euphorbiaceae (Doumenge 225)	Cytotoxic effect on human cervical adenocarcinoma (Hela) cells, human breast cancer cells (MCF-12A), lymphocytes (both at rest and stimulated) and primary porcine hepatocytes [139]; cytotoxic effect on CCRF-CEM leukemia cell line of dichloromethane and methanol extract of leaves and stem bark [140]; antioxidant, anthelmintic, antimicrobial, anticonvulsant and sedative, antidiabetic, antidiarrhoeal, antinociceptive, antiplasmodial, antischistosomal, hepatoprotective, insecticidal and β -lactamase inhibitory activities [141].	Oral administration of this plant extract shows no clinical signs of toxicity at a dose of 2000 mg/kg [142].	Alkaloids, steroids, tannins, flavonoids, and saponins [143].
28	<i>Croton oligandrus</i> Pierre ex Hutch. Euphorbiaceae (not found)	Cytotoxic effect on adenocarcinoma human alveolar basal epithelial cell 211 line (A549), human breast adenocarcinoma cell line (MCF7), human prostate cancer cell line (PC3) and human normal prostate epithelium cell line (PNT2 212) [144].	No toxicity study was found on this plant	Crotonoligaketone, lupeol, beta-sitosterol, crotonadiol, 7-acetoxytrachiloban-18-oic acid, imbricatadiol, crotonzambeturan B, 3-O-acetylauritic acid and stigmasterol [145].

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Table 5 (continued)

No.	Scientific name Family (voucher number)	Anticancer activity and other therapeutics activities	Toxicity	Phytochemical composition
29	<i>Abrus precatorius</i> L. Fabaceae (A.M. Louis 1932)	The isolated compound abrin from the seeds of <i>Abrus precatorius</i> showed <i>in vitro</i> and <i>in vivo</i> antitumor properties by the induction of apoptosis [146]; aqueous leaf extract exhibits cytotoxic activity on the MDAMB-231 human breast cancer cell line with [147]; antiproliferative, anticancer, tumor inhibiting, antioxidant, anti-inflammatory, antimicrobial, anti-diabetic, anti-fertility, anti-allergic, antispermatogenic, bronchodilator activity, anti-arthritis, immunomodulating, immunostimulatory, memory enhancer effects [148].	One study showed that no mortality or adverse effects were observed in laboratory animals during the acute oral toxicity study period. The study therefore concluded that the LD ₅₀ of the crude hydro-methanolic extract of this plant is greater than 2000 mg/kg body weight [149].	Alkaloids, flavonoids, phenols, saponins, glycosides, tannins, carbohydrate and terpenoids [150].
30	<i>Oncoba welwitschii</i> (Oliv.) Gilg. Flacourtiaceae (Bouroubou 419)	Antioxidant and antiangiogenic properties [7].	No toxicity study was found on this plant.	Reducing sugar, coumarins, digitoxins, anthracenics, flavonoids, proanthocyanidins, alkaloids, tannins, polyphenols, saponosids [7].
31	<i>Ocimum basilicum</i> L. Lamiaceae (Leeuwenberg 12534)	Cytotoxic activity of breast cancer cells (MCF-7 and MDA-MB-231) [151]; antioxidant and anticancer activities of <i>Ocimum basilicum</i> L. [152]; antiangiogenic property of <i>Ocimum basilicum</i> ethanolic leaf extract [153].	The results of the acute study indicate that the LD ₅₀ of <i>Ocimum basilicum</i> is greater than 5 mg/kg [154].	Flavonoids, polyphenolics and alkaloids [155].
32	<i>Persia americana</i> Mill Lauraceae (not found)	Antioxidant, analgesic and anti-inflammatory, hypotensive, anticonvulsant, antiviral, wound healing, antiulcer, vasorelaxant, antihypertoxic, hypoglycemic, antifungal activities [156]; a new alkene lactone (4-hydroxy-5-methylene-3-undecyclidenedio-hydruran-2 (3H)-one), isolated from this plant, significantly inhibits the proliferation of MCF-7 breast cancer cells at a concentration of 10 µg/mL [157]; a triterpenoid compound isolated from the ethanolic extract inhibited cell proliferation of the MCF-7 and HepG2 cell line with IC ₅₀ values of 62 µg/mL and 12 µg/mL, respectively, and is safe for the cells normal [158].	Study showed that all extracts of <i>P. americana</i> leaf showed no toxic effect, no lethality or toxic reaction was found at a selected dose of 2000 mg/kg throughout the experiment, no mortality had not been observed when extracts were used to treat rats. Regarding the OEDC recommendation, the LD ₅₀ values offered by <i>P. americana</i> extract are greater than 5000 mg/kg [159].	Alkanols, terpenoid glycosides, flavonoids, coumarin, 1,2,4-trihydroxyheptadec-16-ene, 1,2,4-trihydroxyheptadec-16-yne and 1,2,4-trihydroxyundecane from the unripe fruits of <i>P. americana</i> , 1,2,4-trihydroxyheptadec-16-ene (1) and related compounds 2–8, purified from the seeds of <i>P. americana</i> [156].
33	<i>Peterianthus macrocarpus</i> (P. Beauv.) Liben Lecythidaceae (Wilks 808)	No pharmacological studies were found on this plant.	No toxicity study was found on this plant.	No studies found on this plant showing its chemical composition.
34	<i>Ficus vogeliana</i> Miq Moraceae (Wilks 1095)	No pharmacological studies were found on this plant.	No toxicity study was found on this plant.	No studies found on this plant showing its chemical composition.
35	<i>Militia excelsa</i> (Welw.) C.C.Berg Moraceae (Walters 446)	Antiproliferative activity of three compounds isolated from <i>M. excelsa</i> root bark (cudraxanthone I, neocyclomorusine and (9βH)-3β-acetoxylanosta-7,24-diene) on cervical cancer cell lines (HeLa) [160].	The results of one study showed that the administration of ethanol extract of <i>M. excelsa</i> does not cause untoward effects on laboratory animals. The extract is neither hepatotoxic nor nephrotoxic at the doses studied. Extracts of <i>M. excelsa</i> could be used at a maximum dose of 750 mg/kg body weight [161].	Flavonoids, saponins, cardiac glycoside, terpenoid, tannins, alkaloids, polyphenol, phenol and triterpenes [161].
36	<i>Ficus asperifolia</i> Miq. Moraceae (Moungazi 1601)	Cytotoxic activity of crude methanolic extracts against human cancer cell lines, DLD-1 (colon), MCF-7 (breast) and M14 (melanoma) [131]; antioxidant activity and hepatoprotective effect [162].	Aqueous extract of <i>F. asperifolia</i> (Miq.) shows no adverse effects after oral administration of doses up to 3500 mg/kg [162].	Sterols and triterpenes, flavonoids and saponosides, alkaloids and polyphenol [163,164].
37	<i>Scyphocophalium ochocoa</i> Warb. Myristicaceae (Wilks 2240)	Antioxidant, anti-inflammatory and antiangiogenic activities of <i>S. ochocoa</i> [10].	No toxicity study was found on this plant.	Polyphenols, tannins, flavonoids, proanthocyanidins, saponosides, alkaloids, anthracenics, digitoxigenins, flavonols, flavanols, digitoxins, sterol, triterpenes, oses and holosides [10].
38	<i>Coelocaryon preussii</i> Warb. Myristicaceae (Bernard SRFG 293)	No pharmacological studies were found on this plant.	No toxicity study was found on this plant.	No studies found on this plant showing its chemical composition.

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Table 5 (continued)

No.	Scientific name Family (voucher number)	Anticancer activity and other therapeutics activities	Toxicity	Phytochemical composition
39	<i>Staudia kamerunensis</i> var. <i>gabonensis</i> (Warb.) Fouillloy Myristicaceae (A. Iseembé 238)	No pharmacological studies were found on this plant.	No toxicity study was found on this plant.	No studies found on this plant showing its chemical composition.
40	<i>Pycnanthus angolensis</i> (Welw.) Exell (1) Myristicaceae (Bois SRFG 827)	Anticancer effects <i>in vitro</i> [29]; potent cytotoxic activity of <i>Pycnanthus angolensis</i> extracts against HeLa human cervical adenocarcinoma cells <i>in vitro</i> [165]. Three compounds isolated from the bark of <i>Pycnanthus angolensis</i> , three-4,4'-dihydroxy-3-methoxyline, butinolactone himokinin and talaumidine showed inhibitory effects of cancer cells lungs [166]. Anticancer, anti-inflammatory, antioxidant, immunostimulatory, immunosuppressive, antidiabetic and hypoglycemic, antifibrinolytic, diuretic and renal, hepatoprotective, antimicrobial, spasmolytic, antiasthmatic, anticonvulsant activities [168].	One study has shown that oral administration of <i>P. angolensis</i> extract (5000 mg/kg) produces no visible signs or symptoms of toxicity, abnormal behavior and mortality after 24 h and seven days of observation [167].	Glycosides, alkaloids, saponins, steroids, tannins, flavonoids and terpenoids [165].
41	<i>Boerhavia diffusa</i> L. Nyctaginaceae (Dibata 1126)	Anticancer, anti-inflammatory, antioxidant, immunostimulatory, immunosuppressive, antidiabetic and hypoglycemic, antifibrinolytic, diuretic and renal, hepatoprotective, antimicrobial, spasmolytic, antiasthmatic, anticonvulsant activities [168].	One study reported that oral administration of <i>B. diffusa</i> leaves aqueous extract showed no toxic effects up to 2000 mg/kg in albino rats [169].	Alkaloids, anthraquinones, flavonoids, saponosides, tannins, steroids and terpenoids and polyphenols [170].
42	<i>Lophira alata</i> Banks ex C.F.Gaertn Ochnaceae (Alers 146)	Cytotoxic effect on human melanoma cells (SPC212), human non-small cell lung cancer cells (A549) (NSCLC), HepG2 hepatocarcinoma cells, ATCC and MCF-7 breast adenocarcinoma cells, colorectal adenocarcinoma DLD-1 [77]; antioxidant, anti-inflammatory and antiangiogenic properties [171].	No toxicity study was found on this plant	Saponosides, polyphenols, triterpenes, oses, holosides, tannins, alkaloids, sterols flavonoids, proanthocyanidins, coumarins, reducing sugar and gixtoxins [171].
43	<i>Cymbopogon citratus</i> (DC.) Steuf Poaceae (not found)	Antioxidant and antiproliferative effects of extracts of <i>Cymbopogon citratus</i> . These extracts have one out of five different cancer cells: human colon carcinoma (HCT-116), breast carcinoma (MCF-7 and MDA-MB 231), ovarian carcinoma (SKOV-3 and COAV) [172].	One study reported that oral administration of essential oil of <i>Cymbopogon citratus</i> has no toxic effects up to a dose of approximately 3000 mg/kg [173].	Favonoids, phenol, tannins, steroids, sterols, carbohydrate, glycosides, protein and amino acids and anthraquinone [174].
44	<i>Fleroya ledermannii</i> (K.Krause) Y.F.Deng Rubiaceae (Sosef 807)	Arjunolic acid, a compound isolated from <i>Fleroya ledermannii</i> , exhibited an <i>in vivo</i> antitumor effect on the mouse-induced cancer model, using dimethyl-benz [a] anthracene (DMBA) as the initiator and 12-O-tetradecanoylphorbol-13-acetate (TPA) as a promoter [175].	No studies on the oral toxicity of this plant have been found.	No studies found on this plant showing its chemical composition.
45	<i>Coffea mannii</i> (Hook.f.) A.P.Davis Rubiaceae (Doumenge 200)	No pharmacological studies were found on this plant.	No toxicity study was found on this plant.	No studies found on this plant showing its chemical composition.
46	<i>Sarcocephalus latifolius</i> (Sm.) E.A.Bruce Rubiaceae (Alers 1)	β -sitosterol, a compound derived from <i>Sarcocephalus latifolius</i> , has a chemoprotective effect in the experimental carcinogenesis induced by 1,2-dimethylhydrazine (DMH), indicating its potential as anticancer drug [176].	It has been shown that water extract of this plant is toxic at concentrations ranging from 250 to 583 mg/kg [177].	Carbohydrate, saponosides, terpenoid, flavonoids, alkaloids, tannins, carotenoids, leuco-anthocyanane, anthracene, coumarins, cardiotonic heteroside, reducing compound [178].
47	<i>Morinda lucida</i> Benth. Rubiaceae (Dibata 358)	A study revealed antineoplastic activity in a rat model [179]; in addition, the methanolic extract of <i>Morinda lucida</i> bark combined with <i>Lippia multiflora</i> leaves showed a cytotoxic effect <i>in vitro</i> on cancer cells [180]; in addition, <i>Morinda lucida</i> had shown anticancer activity on human breast adenocarcinoma stem cells and on large cell lung carcinoma cell lines [29].	It has been shown that the lethal dose, LD ₅₀ of the methanolic extracts of the fruit, leaf, bark and <i>Morinda lucida</i> root was greater than 5000 mg/kg. Rats tolerate the extracts even at higher doses without any sign of acute toxicity [181].	Steroids, saponins, tannins, alkaloids, flavonoids, phenols and carbohydrate [182].
48	<i>Teghemella africana</i> Pierre Sapotaceae (Bouroubou 936)	No pharmacological studies were found on this plant.	No toxicity study was found on this plant.	No studies found on this plant showing its chemical composition.
49	<i>Omphalocarpum procerum</i> P.Beauv. Sapotaceae (M. Mbembo 208)	No pharmacological studies were found on this plant.	No toxicity study was found on this plant.	No studies found on this plant showing its chemical composition.

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Table 5 (continued)

No.	Scientific name Family (voucher number)	Anticancer activity and other therapeutics activities	Toxicity	Phytochemical composition
50	<i>Solanum americanum</i> Mill. Solanaceae (Bourboubou 31)	Stem methanol extract inhibits the growth of the cervical cancer cell line (Hela-a) and prostate cancer (PC3) at 91.11 and 80.49% respectively, compared with the control positive 89.07%. Follow-up of methanol leaf extract on Hela-a and PC3 cell line where growth inhibition percentages were 84.86 and 74.28%, respectively [183]; anticancer, anti-inflammatory, hepatoprotective, immunostimulant, antimicrobial, anti-HCV, cardioprotective, analgesic, anti-hyperlipidemic, anti-diarrhoeal, antitoxic, cytotoxic, anti-gastritis and antiulcerogenic activity [184]. No pharmacological studies were found on this plant.	The average lethal dose by oral administration of the extract is 3129 mg/kg body weight showing this plant has a weakly toxic [185].	Alkaloids, flavonoids, steroids, tannins, phlobatannins, phenols, steroids and tannins [186].
51	<i>Celtis mildbraedii</i> Engler. Ulmaceae (Dibata 435)	No pharmacological studies were found on this plant.	No toxicity study was found on this plant.	No studies found on this plant showing its chemical composition.

chemoprotective effect in experimental DMH-induced carcinogenesis, indicating its potential as an anticancer drug [176].

Anonidium mannii: Extracts from this plant have been reported to induce apoptosis in leukemic cells by loss of mitochondrial membrane potential [195]. *Bridelia micrantha*, *Harungana madagascariensis* and *Futunia africana* have a cytotoxic activity of CCRF-CEM leukemia cells [196]. *Luffa cylindrica*: It has been discovered that this plant has anticancer activities on two strains of colon cancer cells (HT-29 and HCT-15) [197].

4.9.2. Human cervical adenocarcinoma

Pycnanthus angolensis is a plant that has been shown to have anticancer effects *in vitro* [29]. Another study reported potent cytotoxic activity of *Pycnanthus angolensis* extracts against HeLa human cervical adenocarcinoma cells *in vitro* [165]. Stem bark extracts of dichloromethane and ethyl acetate from *Pycnanthus angolensis* are rich in bioactive compounds including glycosides, alkaloids, saponin, steroids, tannins, flavonoids and terpenoids. Both extracts showed *in vitro* cytotoxicity against human cervical adenocarcinoma cells (HeLa) using a resazurin assay with the emetin reference drug. The ethyl acetate extract of *Pycnanthus angolensis* showed significant cytotoxicity with $CC_{50} = 90.27 \mu\text{g/mL}$. The dichloromethane extract demonstrated a higher cytotoxic activity with $CC_{50} = 26.66 \mu\text{g/mL} < 30 \mu\text{g/mL}$ a recommended limit for the cytotoxicity of the extract [162]. Three compounds isolated from *Pycnanthus angolensis* bark, three-4,4'-dihydroxy-3-methoxyline (Fig. 9k), butinolactone hinokinin (Fig. 9l) and talaumidine (Fig. 9m) showed inhibitory effects of cancer cells lungs [166].

Milicia excelsa: A study has shown that three compounds isolated from methanolic extract of the root bark of this plant namely cudraxanthone I (Fig. 9n), neocyclomorusine (Fig. 9o) and (9 β H)-3 β -acetoxylanosta-7,24-diene (Fig. 9p) had cytotoxic effects on the growth of human cervical cancer cells (HeLa). The compounds cudraxanthone I and neocyclomorusine had more excellent activities ($IC_{50} < 10 \mu\text{g/mL}$). In addition to these compounds, neocyclomorusine showed the highest radical scavenging activity ($IC_{50} = 0.73 \pm 0.01 \text{ mg/mL}$) [160].

4.9.3. Breast, human prostate and liver cancer

Annona muricata: The crude extracts of this plant show different levels of cytotoxicity of breast cancer cell lines by reducing the size and weight of the tumor in female mice [198]. The leaves of *Annona muricata* produced Annonaceae acetotonin, muricatocin C (Fig. 9q). The absolute configuration of muricatocin C suggests relative stereochemistry and significantly improves cytotoxicity against A-549 human lung solid tumor cell lines and MCF-7 human breast solid tumor cell lines [199]. It has been reported that another compound, Muricatocin (Fig. 9r), isolated from the seeds of *Annona muricata* exhibited a toxicity against lung A549, breast MCF7, colon HT-29 cancer cells [66].

Persea americana: Triterpenoids from the seeds of this plant inhibited cell proliferation of the MCF-7 and HepG2 cell line [158]. A study carried out on the root bark of *Persea americana* in Canada allowed to isolate and characterize the chemical constituent and also to determine the anticancer property of a new alkene lactone derived. The alkene lactone is 4-hydroxy-5-methylene-3-undecyclidenediohydruran-2(3H)-one (Fig. 9s). At a concentration of $10 \mu\text{g/mL}$, a significant reduction in the proliferation of MCF-7 breast cancer cells was induced with an IC_{50} of $20.48 \mu\text{g/mL}$. Apoptosis rates of MCF-7 cells were significantly increased. At the final concentration of $10 \mu\text{g/mL}$, 80% of the breast cancer cells were dead. This compound causes a stimulating effect on non-tumorigenic MCF-12A cells with respect to cell adhesion, while tumorigenic MCF-7 cells are detached continuously [157].

Fleroya ledermannii: A compound arjunolic acid (Fig. 9t) was isolated and arjunolic acid derivatives were tested *in vivo* on a two-step carcinogenesis test on mouse skin, using dimethylbenz [a] anthracene

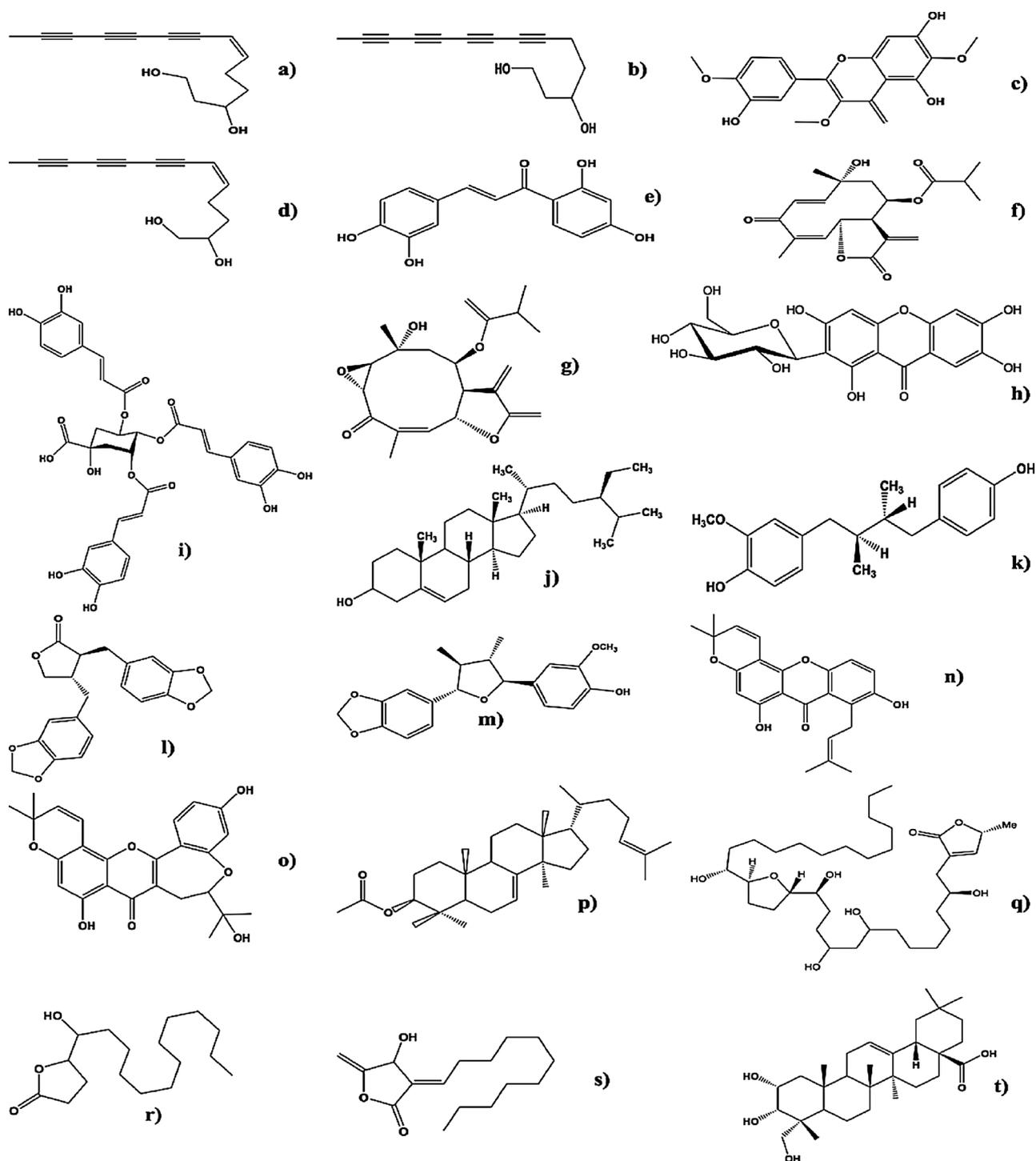


Fig. 9. Anticancer compounds isolated from medicinal plants from the ethnopharmacological survey. (a) 1,3-Dihydroxy-6(E)-tetradecene-8,10,12-tri-ene; (b) 1,2-dihydroxytrideca-5,7,9,11-tetra-ene; (c) centaauridine; (d) 1,2-dihydroxy-5(E)-tridecene-7,9,11-tri-ene; (e) butine from *Bidens pilosa*; (f) tagitinin C; (g) 1 β , 2 α -epoxytagitinin C isolated from *Tithonia diversifolia*; (h) magiferin (1,3,6,7-tetrahydroxyxanthone C2- β -D-glucoside) isolated from *Mangifera indica*; (i) 3,4,5-tri-O-cafeoylquinic acid isolated from *Ipomoea batatas*; (j) β -sitosterol isolated from *Sarcocephalus latifolius*; (k) threo-4,4'-dihydroxy-3-methoxyline; (l) butinolactone hinokinin; (m) talaumidine isolated from *Pycnanthus angolensis*; (n) cudraxanthone I; (o) neocyclomorusine; (p) (9 β H)-3 β -acetoxyxanosta-7,24-diene isolated from *Milicia excelsa*; (q) muricatocin C; (r) muricatacin isolated from *Annona muricata*; (s) 4-hydroxy-5-methylene-3-undecyclidenedio-hydruran-2 (3H)-one isolated from *Persea americana*; (t) arjunolic acid isolated from *Mitragyna ciliata*.

(DMBA) as initiator and 12-O-tetradecanoylphorbol-13-acetate (TPA) as a promoter. The activities were evaluated by both the rate (%) of mice carrying papilloma and the mean number of papillomas per mouse and compared to the control. In the group of treated mice, the appearance of papillomas was delayed in relation to the results of the control. These results suggest that arjunolic acid derivatives could be

compounds of interest as antitumor promoters.

Rauvolfia vomitoria: Extracts inhibited the growth and progression of the human LNCaP prostate cancer cell cycle *in vitro* and *in vivo* [200]. Other researchers have found that this plant has the ability to decrease the cell growth of three ovarian cancer cell lines and to inhibit tumor growth in mice [80].

Morinda lucida: A study revealed antineoplastic activity in a rat model [179]. In addition, the methanolic extract of *Morinda lucida* bark combined with *Lippia multiflora* leaves showed a cytotoxic effect *in vitro* on cancer cells [180]. In addition, *Morinda lucida* had shown anticancer activity on human breast adenocarcinoma stem cells and on large cell lung carcinoma cell lines [29].

Xylopiya aethiopica: Researchers have shown that this plant could be a potential therapeutic agent against cancer since it inhibits cell proliferation and induces apoptosis and cell cycle arrest in C-33A cells [201]. *Enantia chlorantha* and *Nauclea latifolia* showed their cytotoxic capacity on four cancer cell lines [202].

Vernonia amygdalina: This plant has been shown to arrest the cell cycle by an independent p53 pathway and induce apoptosis in both human breast cancer cell lines (MCF-7 and MDA-MB-231 cells) [92].

Ceiba pentandra: Extracts have been shown to have cytotoxic and antitumor activity [105]. *Carica papaya*: Leaf extract was shown to have selective antiproliferative and anti-metastatic properties against prostate cancer [203]. *Abrus precatorius*: Research has validated the anticancer properties of this plant on breast cancer cells [204].

Ocimum basilicum: The extract has been shown to exhibit cytotoxic activity against MCF-7 breast cancer cells [205].

Boerhavia diffusa: It has been discovered that this plant has anti-metastatic, cytotoxic properties on cancer cells of the breast, cervix, liver and colon [206–208]. *Cymbopogon citratus*: The antiproliferative potential of extracts has been demonstrated on human colon carcinoma (HCT-116), breast carcinoma (MCF-7 and MDA-MB 231), ovarian carcinoma (SKOV-3 and COAV) and a normal liver cell line (WRL 68) [172,209]. *Solanum americanum*: a study has shown that this plant has anticancer properties marked by cytotoxicity of MCF-7 breast cancer cells [210].

4.10. Safety of use of listed plants

The determination of the safety of use of the listed medicinal plant extracts is based on the study of their toxicity, which corresponds to the capacity, or property of a substance to cause a change in the physiological functions or in the structure of the cells. These can lead to diseases or health problems: adverse effects. A toxic dose refers to the specified amount of a substance that can, under particular conditions, produce damage to a particular living organism. The bibliographic data on the toxicity of the study plants are summarized in Table 5. The clinical signs of toxicity are manifested by the friction of the nose and mouth on the floor of the cage, weaknesses and vertigo, loss of appetite and agitation. The most common toxicities are: renal toxicity or nephrotoxicity and liver toxicity or hepatotoxicity. Some plants from the ethnopharmacological investigation have been studied for hepatotoxicity, nephrotoxicity, cardiotoxicity and splenotoxicity.

Sarcocephalus latifolius: A study has reported that oral administration of the aqueous leaf extract of *Sarcocephalus latifolius* to albino rats is toxic at doses ranging from 500 to 2000 mg/kg body weight during prolonged treatment and causes hepatic and renal lesions [177].

Morinda lucida: The histological effects of leaf, bark, stem and root extracts on certain visceral organs and muscles of Albino Wistar mice were studied and compared. No adverse effects have been observed on the kidneys, muscles, stomach and colon, indicating that these different extracts are not toxic to the dosage and oral route used by traditional healers. However, caution should be exercised in case of overdose [211].

Annona muricata: A study has reported that *Annona muricata* leaf extract, administered orally to mice at a dose of 2000 mg/kg body weight, does not cause degeneration or necrosis of glomeruli, tubules and interstitium. On the kidneys and the liver does not show either degeneration or necrosis. This result indicates that the extract is virtually non-toxic and does not damage the liver and kidneys [212].

Enantia chlorantha: Effects of stem bark ethanolic extract on changes in body weight, biochemical and hematological parameters, and

histology of vital organs (heart, kidneys and liver) were evaluated in rats at doses of 1000, 2000 and 3000 mg/kg body weight by oral administration. The results showed that the extracts caused congestion of the heart and kidneys of experimental rats. *Enantia chlorantha* can produce severe toxic effects at high doses. It is therefore necessary to be cautious in its use [78].

Rauvolfia vomitoria: Study of the toxicity in mice showed no tissue lesions on the liver, kidneys and spleen, no clinical signs of toxicity were observed [80].

It is assumed that herbal medicines have fewer side effects than allopathic medicines. These results show that most of the plants from the ethnopharmacological survey are non-toxic for the dosage and oral route used by local traditional healers. However, like any drug, these plant extracts can be toxic to the liver, kidneys, heart, stomach, colon and spleen if overdosed. Therefore, it would be important to be careful in case of overdose.

5. Conclusions

The present work is the first study reporting information on the different species of medicinal plants used against Gabon cancer by the Fang population of Woleu-Ntem province in particular. This study identified 51 species of medicinal plants that are used for the treatment of cancer. 16 species of plants have been mentioned for the first time, as entering the anticancer therapy they are: *Anonidium mannii*, *Celtis mildbraedii*, *Coelocaryon preussii*, *Coffea mannii*, *Ficus vogeliana*, *Omphalocarpum procerum*, *Oncoba welwitschii*, *Plagiostyles africana*, *Rauvolfia macrophylla*, *Ricinodendron africanum*, *Scyphocephalus ochocoa*, *Sindora klaineana*, *Staudtia kamerunensis* var. *gabonensis*, *Tabernaemontana crassa*, *Tetrorchidium oppositifolium* and *Tieghemella africana*. In addition, 18 species of medicinal plants listed have antitumor properties *in vivo*, including: *Abrus precatorius*, *Annona muricata*, *Bidens pilosa*, *Boerhavia diffusa*, *Canarium schweinfurthii*, *Carica papaya*, *Ceiba pentandra*, *Fleroya ledermannii*, *Ipomoea batatas*, *Mangifera indica*, *Morinda lucida*, *Ocimum basilicum*, *Persea americana*, *Rauvolfia vomitoria*, *Sarcocephalus latifolius*, *Solanum americanum*, *Tithonia diversifolia* and *Vernonia amygdalina*. 29 plants have cytotoxic activities in several cancer cell lines *in vitro* and *in vivo*. 28 plants were tested for toxicity *in vivo* and found to be non-toxic to different organs such as the liver, kidneys, lungs and heart. Through the valuable information obtained during the ethnopharmacological survey, the traditional practitioners of the study area showed that they had significant knowledge of the large number of registered plant species and the description of clinical signs to distinguish different types of cancers. In order to promote the fight against cancer, these species could constitute a very good scientific database for the research of new bioactive molecule against cancers but also against other cancer precursor diseases. It is therefore necessary to preserve this heritage through documentation and scientific studies.

Ethics approval

This ethnopharmacological study was approved by the Ethics Committee of Gabon No. 009 March 2013. All the traditional practitioners have passed the study to their consent. Before the start of the survey, Woleu-Ntem Water and Forests Department was met to have their agreement for the collection of plant organs in the study area.

Author's contributions

NMMRL is the lead author, designed the study, developed the protocols, analyzed the data and drafted the manuscript. SOC participated in all the experiments and the manuscript. NJDLC reviewed the protocols, provided material support, and made corrections to the manuscript. NAGR and OJP participated in the interpretation and analysis of the data. OAF is Head of Laboratory of Biochemistry and Mixed Unit for Biomedical Research, University of Health Sciences, Libreville, Gabon.

OELC, Head Laboratory of Research in Biochemistry, oversaw this work and made the necessary editorial corrections and gave final approval for the submission of the revised version. All authors have read and approved the final version.

Funding

This research received no external funding.

Conflicts of Interest

The authors declare no conflict of interest.

Acknowledgements

The authors are very grateful to Shell Gabon for material support at the Laboratory of Research in Biochemistry, University of Sciences and Technology of Masuku, Franceville, Gabon. We are very grateful to local informants who have agreed to share their knowledge on the use of medicinal plants with us. We also thank Mr. Meye Misso Paul-Edouard, our guide for the investigation and during the harvest.

Appendices

1. Informed consent.
2. Ethnopharmacological survey sheet on medicinal plants used in the treatment of cancer.

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