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# Ethnobotanical survey and biological activities of plants used for cancer treatment in traditional Senegalese medicine

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ABSTRACT

Female breast cancer is known to be one of the leading causes of death in Senegal. In Senegal, the absence of a national cancer control program, the lack of specialized infrastructure and qualified human resources and the exorbitant cost of care have contributed to the extensive use of traditional medecine, particularly in rural areas. This study aims to inventory the medicinal plants used by these healers and to assess the cytotoxic and antioxidant activities of the most widely used one. Data on healers and their use practices and information on plants were collected through the administration of a structured questionnaire. Based on their citation frequencies during the survey, *Antiaris Africana* Engler, *Hymenocardia Acida* Tul. and *Halouf Halal* (local name) were selected for chemical and biological studies. Their hydroalcoholic extracts were analyzed in terms of antioxidant capacity and cytotoxic effects, again, in the human cancer cell line. The study revealed a total of 65 medicinal plants belonging to 35 different families. The plant parts used by traditional healers are leaves (63.89%), roots (11.11%), bark (15.28%), fruits (2.78%), and others (6.94%). Generally, herbal medicine is prepared as a powder and mixed with water by maceration (55.38%) and administered orally. *A. Africana* ranked first with a citation frequency of 5.7% and its hydroalcoholic extract had the highest antioxidant activity in TEAC (6533.64±7 µmol ET/g dry plant) and in ORAC (3745.17±4.8 µmol ET/g dry plant) followed by *H. Acida* in TEAC (3115.6±145 µmol ET/g dry plant) and in ORAC (4105.29±872 µmol ET/g dry plant). The hydroalcoholic extract of *A. Africana* exhibited the highest cytotoxic activity in MCF-7 (Human mammary) and THP-1 (Human acute monocytic leukemia cell line) but had low activity against HTC-116 (Human carcinoma colorectal) and A-375 (Human skin malignant melanoma). The percentages of proapoptotic cells were, respectively, 68.85±6.22, 58.1±1.90 and 48.58±1.4%. These results provide scientific support for the traditional use of medicinal plants in cancer treatment and constitute a database for biological screening to isolate cytotoxic plant-based molecules.

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## 1. Introduction

There are approximately 19.3 million new cases (18.1 million excluding non-melanoma skin cancer) and almost 10 million cancer deaths worldwide in 2020 according to the American Cancer Society and the International Agency for Cancer Research. Breast cancer is the most death-causing tumor-related disease in females [1,2]. In Senegal, an estimated ~11300 new cancer cases occurred in 2020. Female breast cancer and cervical cancer are predominant [3]. This trend is expected to increase in the coming decades, due to insufficient human resources, inadequate technical platform, high cost of cancer care, and lack of a national cancer control program [3]. The high cost of cancer treatment partly explains why most cancer patients end their care in traditional medicine [3]. Therefore, there is a need to explore a therapeutic option. For a long time, mankind has been developing traditional medicine around the world based on the knowledge of medicinal plants. This is attributable to the efficacy, affordability, and perceived safety of these plants [4,5]. In addition, it is a potential source of new pharmaceutical substances. Therefore, the interest and urgency of ethnobotanical research is obvious. Medicinal plants are an important source of antioxidants that increase the antioxidant capacity of plasma and reduce the risk of certain diseases such as cancer, heart disease, and stroke.



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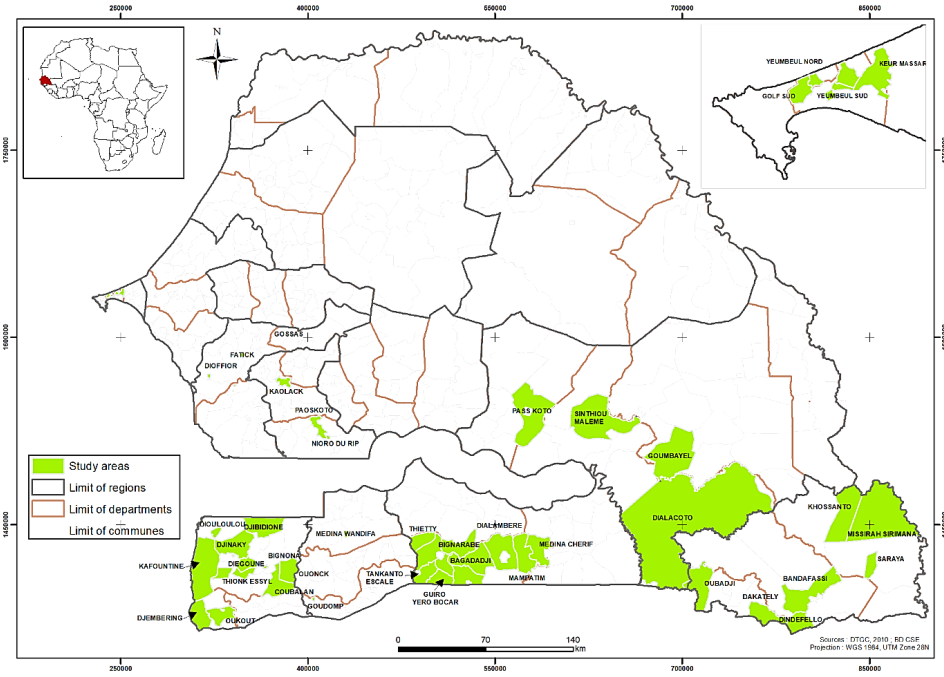


**Figure 1.** Map of the study area.

Many plant extracts and essential oils isolated from plants have been shown to exert biological activity in *vitro* and in *vivo* which justified research on the traditional medicine focused on the antioxidant ant cytotoxic activities of these plants [6].

African traditional medicine abounds in medicinal plants and tribal people, wherever they exist, still rely mainly on herbal medicines. In many parts of Africa, herbal medicine still plays a vital role in health care delivery systems, especially in remote places where clinics and hospitals are sparsely located. In these communities, traditional healers operate closer to the people, taking advantage of the biodiversity of plant species in these areas to cure various diseases. Although herbal medicine is well established in many cultures and traditions of Africans and is still a way of life for almost 80% of people in Africa. In Senegal, plants and herbal medicine continue to play a critical role as an alternative and affordable healthcare for various diseases such as cancer. Unfortunately, not much information has been documented in the scientific literature and is therefore in danger of being lost in favor of modern medicine. The information on herbal medicine in this part of the world has been dominated by oral tradition. For this purpose, an ethnobotanical survey and biological investigations were carried out to describe the different uses of medicinal plants by the local population and to establish a catalog of medicinal plants and their therapeutic uses, particularly for the treatment of cancer. The present study aims to investigate, inventory, and document medicinal plants used in traditional cancer treatment in Senegal and to evaluate the antioxidant activities of the most widely used. The results of this study may play a role in the conservation of knowledge of traditional medicine. Furthermore, the study could reveal uninvestigated or scarcely investigated plants that could serve as potential sources of new anticancer agents [7].

## 2. Experimental

### *2.1. Study area*

Senegal is a West African country bordered by the Atlantic Ocean to the west, Mauritania to the north, Mali to the east, and Guinea and Guinea-Bissau to the south. The Gambia forms an enclave in southern Senegal, open to the Atlantic. Senegal is a flat country with a fairly dry tropical climate (most of Senegal belongs to the Sahel). The population, made up of various groups (the wolof being the dominant ethnic group) and mostly Islamic, is concentrated in the West of the country. Two-thirds of the working population is engaged in agriculture (groundnuts, rice, millet, livestock) and fishing. Industries are located on the Cape Verde Peninsula. The country is divided into fourteen regions: Dakar, Ziguinchor, Diourbel, Saint-Louis, Tambacounda, Kaolack, Thiès, Louga, Fatick, Kolda, Matam, Kaffrine, Kédougou, and Sédhiou. The study area is shown on the map below and included 57 rural communities in 15 departments of 8 regions (Dakar, Tambacounda, Kaolack, Fatick, Kolda, Kédougou, Ziguinchor, and Sédhiou) (Figure 1).

### *2.2. Data collection and statistical analyses*

The ethnopharmacological survey was conducted with 193 traditional healers with the help of guides chosen based on their knowledge of local languages and plants. An initial individual interview was conducted with traditional healers to briefly explain the objectives of the study and the importance of the information provided to obtain their consent. In a second interview, data on use practices in traditional cancer treatment were collected with a questionnaire divided into two parts. The first part focuses on the description of cancer by traditional healers and the second part is on medicinal plants used in its treatment. Samples and photos of declared plants were taken based on their local names and herbaria were made for their identification, which was carried out at the Laboratory of Pharmacognosy and Botany of Cheikh Anta Diop University, Dakar, Sénegal. The taxonomy of medicinal plants was confirmed using data available in the African Pharmacopoeia [8]. The scientific name, botanical family, and therapeutic uses of medicinal plants were compiled in an MS Excel sheet. The citation frequency of each plant was determined using the following formula: FC = n/N×100, where n = Number of respondents stating its use to treat cancer; N = Total number of informants interviewed. Data collected included also methods

of preparation of medicinal products and identification of the way in which these products were applied.

### 2.3. Solvents used for extraction

The solvents (ethanol, methanol, DMSO) used in this study were of analytical grade and were purchased from Sigma-Aldrich (St Louis, USA).

### 2.4. Reagents for chemical tests

2,2′-Azino-*bis*-(3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt (ABTS), Trolox: (±)-6-hydroxy-2,5,7,8 tetramethylchromane-2-carboxylic acid, potassium persulfate, 2,2′-azo-*bis*(2-methylpropionamidine) dihydrochloride (AAPH) and fluorescein were purchased from Sigma-Aldrich (Steinheim, Germany). The phosphate buffer solution (PBS) was prepared as follows: 137 mM sodium chloride, 2.7 mM potassium chloride, 10 mM di-sodium hydrogen phosphate dihydrate, 1.76 mM monopotassium phosphate dissolved in 1 L of Milli-Q water.

### 2.5. Material and reagents for biological tests

Roswell Park Memorial Institute Medium (RPMI-1640) was purchased from Sigma (St Louis, USA) and Fetal bovine serum (FBS) was purchased from Life Technologies (Paisley, UK). Gibco Dulbecco's modified eagle medium (DMEM) was purchased from Sigma Dominique Dutscher (Brumath, France). The Trypsin-EDTA (1X) 0.05%, PBS pH = 7.2 (1X) and the antibiotic-antimycotic solution were purchased from Gibco Invitrogen (Grand Island, USA). The cells used for the toxicity tests were human carcinoma colorectal (HTC-116, ATCC® CCL-247™), human skin malignant melanoma (A-375, ATCC®CRL-CRL-1619), human mammary (MCF-7, ATCC® HTB-22, 227™) and human acute monocytic leukemia cell line (THP-1, ATCC® TIB-202). They were purchased from the American Type Culture Collection (ATCC, LGC Standards, Molsheim, France).

### 2.6. Plant material

The leaves of *A. Africana*, *H. Acida* and *H. Halal* were harvested manually in May 2018 in the Department of Bignona (Ziguinchor/Senegal). A specimen of each plant was deposited for identification at the Laboratory of Pharmacognosy and Botany of the Cheikh Anta DIOP University of Dakar, Senegal. The plant samples were dried, reduced to powder by a cryo-grinder, packed in dark plastic bags, and kept at room temperature.

### 2.7. Ultrasonic-assisted extraction

The powder of leaves (4 kg) was mixed with 20 L of 70% ethanol and sonicated for 15 min in a Fisher 15051 ultrasonic bath (Fisher Scientific, Loughborough, UK, 37 kHz, 280 W). After centrifugation at 5000 rpm for 10 min, the supernatant was recovered. The residue was reextracted under the same conditions two times. The supernatants were combined. After elimination of ethanol by rotary evaporation, the sample was freeze-dried.

### 2.8. Evaluation of the antioxidant activity

#### 2.8.1. Trolox equivalent antioxidant capacity (TEAC)

This method is based on electron transfer and uses $ABTS^{\cdot+}$, a chromophore radical which is a blue-green cation formed when ABTS reacts with potassium persulfate. $ABTS^{\cdot+}$ has absorption maxima at wavelengths of 412, 645, 734 and 815 nm. In the presence of antioxidant compounds, the $ABTS^{\cdot+}$ free radical is captured, leading to a loss of color and therefore a reduction in the measured absorbance quantitatively related to the antioxidant concentration [9]. Trolox is used as a reference for quantitative assessment and calibration. A stock solution of 1 mmol/L was prepared in a water/methanol mixture (50/50) of trolox. Diluted solutions at concentrations of 50, 60, 300 and 400 µmol/L were used to obtain the calibration curve, which were prepared using Milli-Q water. Each concentration was carried out in triplicate. DMSO, which was used to dissolve the extracts, served as a negative control. Before testing, the extract stock solutions were diluted in Milli-Q water with 3% DMSO (*v*:*v*). Each diluted extract (10 µL) were then deposited in a microplate well followed by 200 µL of $ABTS^{\cdot+}$ at 7 mmol/L in PBS. After 10 minutes of incubation at 37 °C, the absorbance at 734 nm was read using a VarioSkan spectrophotometer (ThermoFisher Scientific). The experiments were carried out in triplicate [10].

#### 2.8.2. Oxygen radical absorbance capacity (ORAC)

The ORAC test is based on the oxidation of a fluorescent probe (fluorescein) by free radicals, which are often peroxylic radicals but may also be hydroxyl radicals. These free radicals are produced by a radical generator (AAPH) [11]. During the experiment, free radicals damage the probe and thus reduce the intensity of the fluorescence. The degree of intensity change reflects the amount of damage caused by free radicals. To quantify the protection conferred by an antioxidant, a measurement of the area under the curve of the sample was made and compared to the area under the curve [12] of trolox as a reference antioxidant [9,10]. A calibration curve was constructed using different concentrations of trolox in Milli-Q Water (10, 50, 100; 200 and 500 µmol/L). Before testing, the extract stock solutions were diluted in Milli-Q water with 3% DMSO (v: v). Each diluted extract (10 µL) were then deposited in a microplate well followed by 150 µL of fluorescein $8.5\times10^{-8}$ mol/L in Milli-Q water. After a 10-minute incubation at 37 °C, AAPH at $153\times10^{-3}$ mol/L in PBS was automatically distributed in the microplate wells. The fluorescence kinetics was then monitored every 5 min for 120 min using a VarioSkan spectrophotometer with excitation and emission wavelengths of 485 and 530 nm, respectively. The experiment was carried out in triplicate. The ORAC results were expressed in µmol of equivalent trolox per gram of dry extract.

### 2.9. In vitro assay for cytotoxic activity

#### 2.9.1. Human cancer cell lines

All human cell lines were purchased from ATCC (LGC Standards, Molsheim, France). Human mammary (MCF-7, ATCC® HTB-22), human skin malignant melanoma (A-375, ATCC® CRL-CRL-1619) and human carcinoma colorectal (HTC-116, ATCC® CCL-247™) cell lines were maintained in DMEM high glucose medium (Dominique Dutscher, 67172 Brumath, France, Cat No L0102-500), while the human acute monocytic leukemia cell line (THP-1, ATCC® TIB-202) was maintained in RPMI-1640 Medium (ATCC® 30-2001™, LGC Standards, Molsheim, France), supplemented with 10 % (v/v) heat inactivated fetal bovine serum (FBS, Life Technologies, Paisley, UK, Cat No 10270-106) and 1 % (v/v) penicillin-streptomycin (10000 units/mL and 10000 µg/mL, Life Technologies, Paisley, UK, Cat No 15140-122). Cells were kept at 37 °C in a humidified atmosphere containing 5 % (v/v) $CO_2$ during their exponential growth phase and during the course of incubation with the investigated compounds. Before confluence, adherent cells were trypsinized and subcultured twice a week. The investigated extracts were initially dissolved in dimethyl sulfoxide (DMSO) in a concentrated stock solution. Further dilutions of the experimental concentrations applied to the cells

were made in RPMI-1640 or DMEM media prior to each experiment; thus, the final concentration of DMSO in treated cells was 0.5 % (*v*:*v*) for the highest concentrations applied.

#### *2.9.2. Apoptosis assay and microcapillary flow cytometry analysis*

For the assay, cells were washed with phosphate buffer saline (PBS) free of magnesium and calcium. The PBS was decanted and cells were detached with 0.025% trypsin-EDTA (Sigma) and PBS was added to a volume of 50 mL. The cell pellet, obtained by centrifugation (1000 × g, 5 min) was resuspended in 10 mL of DMEM for MCF-7, A-375, and HTC-116 and 10 mL of RPMI for THP-1. The viable cell density was counted by the Guava easy Check Kit 4500-0025 (Guava/ Luminex CA, USA) and the suspensions were diluted with medium to obtain the previously determined optimal plating densities for, MCF-7, A-375, HTC116, and THP-1, respectively. 100 µL/well of these cell suspensions were seeded in 96-well microtiter plates and incubated at 37 ° C to allow cell attachment. A minimum of 5000 cells was acquired per sample. The final concentration of DMSO applied to cells during incubation with the tested samples was always 0.5 %, which had no adverse effects on cell viability or cell morphology. To discriminate between negative and positive events in the analysis, a non-stained control sample for each culture condition always accompanied acquisition of the stained cells to define their cut-off. Negative control samples containing cells and 0.5 % of DMSO without samples, as well as a positive control containing 50 µM Celastrol, a natural pentacyclic triterpenoid (Enzo Life Sciences, Farmingdale, USA), were included in each experiment. After 24 h, the cells were treated with 100 µg/mL of each crude hydroalcoholic leaves extract and apoptotic rates were assessed by using annexin V-FITC (ImmunoTools GmbH, Friesoythe, Germany, Cat No 31490013) and propidium iodide in a volume of 3 µL. Gates were drawn around the appropriate cell population using the forward scatter (FSC) versus side scatter (SSC) acquisition dot plot to exclude any debris. The cells were classified according to Annexin V-FITC (green fluorescence) and PI (red fluorescence) on viable (double negative), pre-apoptotic cells (Annexin V-FITC single-stained cells) and necrotic cells (PI single-stained cells). Each extract was tested against all cancer cell lines and the percentages of pre-apoptotic cells were calculated at exposure time 24 h.

## 3. Results and discussion

### *3.1. Plant identification and frequency of citation for medicinal plants*

Traditional healers cited a total of 63 medicinal species belonging to 35 families (Table 1). Their scientific and local names were established using the African Pharmacopoeia. The most represented families were the Fabaceae, with 7 species, followed by the Euphorbiaceae, with 5 species. The other families contributed with less than 4 species.

The data analysis revealed that *A. Africana* Engler was the plant most cited with 6.78% of the frequency of citation, followed by *H. Acida* with 3.93% and *H. Halal* with 3.57%.

According to the Angiosperm Phylogeny Group (APG III: 2009), species of the genus Antiaris belong to the Angiosperms phylum, the True Dicotyledons (Eudicotyledons) clade, the Rosales order and the Moraceae family. This later comprises nearly 1,400 species in more than 40 genera. They can be trees, shrubs, vines, or herbaceous plants. Trees and shrubs are the most common latex producers. *Antiaris Africana* Engler is a deciduous tree that can grow to more than 40 m in height. Its bark is smooth to slightly fissured, grayish-white, with numerous lenticels exuding a cream-colored aqueous latex that rapidly turns brown on contact with air. This tropical plant is widespread in West African forests, Madagascar, tropical Asia, and the western Pacific. In Senegal, this plant is commonly called 'Buffo', 'Bafor' and 'Tufu' by 'Djola', an ethnic group of the South, 'Mbayo' and 'Nget yana' by Serere, who live in the East, and 'Kan' by 'Wolof', an ethnic group of the whole country. In other African countries, especially Ivory Coast, the plant is called 'Gouho' by the 'Fon' ethnic group and, in Guinea Conakry 'Cili' by the Malinké ethnic group.

*H. acida* belongs to the genus Hymenocardia, the Euphorbiaceae family, the phylum of Angiosperms, the clade of True Dicotyledons (Eudicotyledons) and the order of Malpighiales (APG III 2009). It is a shrub of 4 to 6 m high, with an open crown, tortuous trunk, and smooth bark characterized by its more or less muddy surface. The twigs turn red when the bark is removed. The leaves are elliptical, rounded at both ends, leathery, and 4 to 9 cm long. The flowers are green with pear-shaped fruit capsules. Species of temporary pools, thickets, and forest galleries in Sudano-Guinean zone, it is found in Senegal, Cameroon, Madagascar, and tropical Asia (Thiam Khadidiatou). In Senegal, it is known as Kérenkodé among the 'Fulani', an ethnic group of the Fouladou area in the south of the country. Among the ethnic groups of 'Serere' and 'Djola', it is known as Ngenkelen and Tipéo, respectively. The 'Wolof' refers to it as Enkén.

In the case of the *Halouf Halal,* so named by the inhabitants of Basari ethnic group, the scientific name could not be determined for a number of reasons (language barriers, communication problems, and a lack of sharing of traditional knowledge). The Bassari ethnic group lives in a hilly area on the border between Senegal and Guinea in the region of Kédougou in the south of the Gambia River.

### *3.2. Parts of plants cited to be used*

This study indicated that leaves (63.89%), roots (11.11%), bark (15.28%), fruits (2.78%) and others (6.94%) were the most commonly used plant parts by traditional healers to treat cancer in Senegal. They were collected mainly fresh in their natural environment and preserved by drying in the shade. An informant explained that "after harvesting, these plant parts must be dried in the shade, not in the sun, to avoid degradation of active principles and disappearance of plant benefits". Similar plant parts, notably leaves (56.7%) were also the most commonly used, followed by roots (21.7%), bark (6.7%), stem (1.7%), seeds (1.7%) and whole plant (1.7%) by traditional healers to treat different types of disease, including cancer, in 11 districts in Ethiopia and Zimbabwe [13,14].

In Nigeria and many parts of Africa, different parts of these medicinal plants (*Allium cepa*, *Antiaris africana*, *Xylopiea aethiopica*) have been combined, resulting in a recipe that has traditionally been used in the treatment and management of cancer due to the presence of many active compounds such as antioxidants that can act synergistically [15].

### *3.3. Preparation techniques for therapeutic recipes*

The control of the dosage was a primary concern among the respondents. The therapeutic indications given are far from uniform. It is in this sense that an interviewee explained: “lack of knowledge and proper dosage, influenced by a strong desire to heal, can have harmful effects on patients”. Maceration was the most common technique for preparing remedies (55.38%), followed by decoction (18.46%), infusion (15.38%) and others (10.77%). In two Saharian regions of South-west of Algeria, decoction was the major mode of preparation (49.00%) [16].

**Table 1.** Inventory of medicinal plants used for the treatment of cancer by traditional healers in Senegal.

| Species | Family | Local names | Citation Freq. (%) | Plant parts | Preparation | Consumption |
|---|---|---|---|---|---|---|
| *Alium cepa L.* | Amaryllidaceae | Soble (Wolof-Lébou) | 2.14 | Bulbe | Dissolved the bulbe in oil palm | Chew |
| *Annona senegalensis* Pers.subsp. Senegalensis | Annonaceae | Butotok (Djola) | 3.21 | Stem bark / Leaves / Fruit | Maceration, Remove the seed from the epicarp | Suck the epicarp(fruit) Drink a cup twice/day for a week |
| *Annona muricata L.* | Annonaceae | Bu lollof (Djola) | 1.79 | Leaves / Fruit | Maceration, Remove the seed from the epicarp (fruit) | Drink a cup /day until signs disappear |
| *Anogeissus leiocarpa* (DC.) Guill. | Combretaceae | Kodoli (Peulh-Toucouleur) | 1.07 | Bark | Maceration | Drink a liter every night until signs disappear |
| *Antiaris africana* Engler *(Antiaris toxicaria* Lesch.*)* | Moraceae | Bafor (Djola-casamançais) | 6.78 | Leaves | Maceration with liter of water | Drink a cup twice/day for a week |
| *Avicennia africana* P. Beauv. | Avicenniaceae | Buhek, Bukelek (Djola) | 0.71 | Powder | Dissolved in palm oil | Drink a liter every night until signs disappear |
| *Azadirachta indica* A.Juss. | Meliaceae | Neem (Wolof) | 1.07 | Leaves | Tea/Decoction | Drink a liter every night until signs disappear |
| *Afzelia africana* Smith ex pers | Fabaceaae | Bu léo (Djola) | 1.79 | Leaves | Dissolved in oil palm | Drink a cup every week |
| *Casia siberiana DC.* | Caesalpiniaceae | Kaseit (Djola-Casamançais) | 2.14 | Leaves | Maceration with liter of water | Drink a liter every night until signs disappear |
| *Casia siame* Lam. | Caesalpiniaceae | Sindan (Wolof) | 0.71 | Leaves | Maceration with liter of water | Drink a liter every night |
| *Combretum glutinosum* Perr.ex.DC. | Combretaceae. | Katakudum (Djola) | 0.36 | Leaves | Infusion in water | Drink a liter every night until signs disappear |
| *Coclotropis procera W.T.A.* | Apocynaceae | Pommier de sodome | 1.07 | Leaves | Decoction in water | Drink a cup every two days in the morning |
| *Cochlospermum tintorium* Perr.ex.A. Rich. | Cochlospermaceae | Fayar | 2.5 | Roots | Maceration of roots in 1 liter of water | Drink one ½cup/day |
| *Cisampelos mucronata* A. Rich. | Menispermaceae | Kagonora (Djola-Casamançais) | 0.36 | Leaves | Maceration with liter of water | Drink regularly |
| *Chrozophora senegalensis* | Euphorbiaceae | Ndamat | 2.14 | Stem bark | Maceration with liter of water | Drink a liter every night until signs disappear |
| *Daniela oliveri* (Rolfe)Hutch. | Fabaceaae | Santan (Socé) | 2.14 | Stem bark | Maceration with liter of water | Drink a cup in the morning and a cup in the evening |
| *Erythrina senegalensis A.DC.* | Fabaceaae | Fusentefarak (Djola-Casamançais) Dlimba (Peulh-Fouladou) | 1.79 | Stem bark / Roots / Seeds / Leaves | Maceration with liter of water | Drink a cup in the morning and a cup in the evening |
| *Crataeva religosia* G.F. | Capparaceae | Ngorel (Peulh-Toucouleur) | 1.79 | Leaves | Maceration with liter of water | Drink a cup in the morning and a cup in the evening |
| *Euphorbia hirta* L. | Euphorbiaceae | Mbal mbal (Wolof) Dabadadlé (Mandingue-Mandé) | 1.07 | Leaves | Maceration with liter of water | Drink in the morning until signs disappear |
| *Ficus ingens* (Miq.) Miq.Var. ingens | Moraceae | Bu pok baale (Djola) | 1.43 | Leaves / Bark / Roots | Infusion with water | Drink in the morning until signs disappear |
| *Ficus lecardii. Ward.* | Moraceae | Bu pok baine (Djola) | 0.71 | Leaves | Infusion with water | Drink regularly |
| *Gardenia triancantha* DC. | Rubiaceae | Dinali (Peulh) | 1.43 | Leaves | Maceration with liter of water | Drink in the morning until signs disappear |
| *Gardenia ternifolia* Schumach. | Rubiaceae | Bossede | 1.43 | Leaves | Maceration/decoction with liter of water | Drink in the morning and evening |
| *Guiera senegalensis* J.F. Gmel. | Combretaceae | Ngeer (Wolof) | 2.14 | Roots | Decoction or Tea | Drink in the morning and evening |
| - | - | *Halouf halal (Bassaris)* | 3.57 | Leaves | Maceration with liter of water | Drink regularly |
| *Hymenocardia acida* Tul.var.acida | Phyllanthaceae | Koren kode (Peulh-Fouladou) | 3.93 | Leaves | Maceration with liter of water | Drink a cup in the morning and a cup in the evening |
| *Icacina oliviformis* (Poir.) J. Raynal Var oliviformis | Icacinaceae | Makansé (Wolof) | 1.07 | Leaves | Decoction in water | Drink in the morning and evening |
| *Jatropha chevaleri* Beille | Euphorbiacea | Wetenubot (Wolof) | 2.86 | Latex | Maceration with liter of water | Drink twice a day |
| *Jatropha curcas* L. | Euphorbiacea | Duladukad (Peulh-Fouladou) | 1.07 | Stem bark, branches | Maceration with liter of water | Drink a cup in the morning and a cup in the evening |
| *Physostigma venenosum Balf* | Fabaceae | Isho (Yorouba-Nago) | 1.07 | Rhizome / Leaves | Maceration with liter of water | Drink one ½cup/day |
| *Khaya senegalensis* (Desr.) A. Juss. | Meliaceae | Khay (Wolof) | 1.43 | Leaves | Maceration with liter of water | Drink regularly |
| *Lannea velutina* A. Rich | Anacardiaceae | Tinolipoley (Peulh-Toucouleur) | 2.14 | Leaves | Decoction in water or turn leaves in to powder | Drink a cup in the morning and a cup in the evening |
| *Lannea acida* A. Rich | Anacardiaceae | Bubuka (Djola-casamançais) | 1.79 | Bark | Maceration with liter of water | Drink regularly |
| *Leptadania hastata* (Pers.) Decne. | Apocynaceae | Savato (Peulh-Firdou-Fouladou) Ngazu (Serer) | 2.14 | Leaves | Maceration with liter of water | Drink regularly |

**Table 1.** Continued.

| Species | Family | Local names | Citation Freq. (%) | Plant parts | Preparation | Consumption |
|---|---|---|---|---|---|---|
| *Lippia chevalieri* Moldenke | Verbenaceae | Busag (Djola) | 2.5 | Bark | Decoction with water | Drink a cup in the morning and a cup in the evening |
| *Maytenus senegalensis* (Lam.) | Celastraceae | Giaggu (Peulh) | 1.43 | Leaves | Maceration with liter of water | Drink a cup in the morning and a cup in the evening |
| *Mitracarpus scaber* (Zucc) | Rubiaceae | Faroute | 1.07 | Aerial part | Decoction with water | Drink twice a day |
| *Momordica charantia L.* | Cucurbitaceae | Burubof (Wolof) | 1.07 | Leaves / Roots | Infusion in water | Drink a cup in the morning and a cup in the evening |
| *Molothria maderaspatana* (L.) cogn. | Cucurbitaceae | Pomey | 1.79 | Leaves | Maceration with liter of water | Drink a cup in the morning and a cup in the evening |
| *Newboldia laevis (*P. Beauty.) Seem.ex Bureau | Bignonaceae | Pasal, Fugompafu (Diola-casamançais) | 0.71 | Bark | Decoction in water | Drink a cup in the morning and a cup in the evening |
| *Opilia amentacea* Roxb. | Opiliaceae | Talel walu (Peulh), Bidana (Djola-casamançais) | 0.71 | Leaves | Maceration with liter of water | Drink a cup in the morning and a cup in the evening |
| *Parkia biblobosa* (Jacg.) R.Br. ex G. Don | Mimosaceae | Bu songay, Buyel, Nina (Djola-casamançais) | 1.79 | Leaves | Infusion in water | Drink regularly |
| *Parkinsonia aculaeta* L. | Fabaceae | Barkasoné (Mindingue-Mandé) | 0.71 | Aerial parts | Infusion in water | Drink a cup in the morning and a cup in the evening |
| *Pterocarpus erinaceus* Poir. | Fabaceae | Tikon, Bukon, Kanonaku (Djola-casamançais) | 1.43 | Leaves / Stem bark | Infusion in water | Drink a cup in the morning and a cup in the evening |
| *Psorospermun senegalensis* Spach. | Hypericaceae | Katidakuma (Mindingue-Mandé) | 1.79 | Leaves | Maceration with liter of water | Drink a cup in the morning and a cup in the evening |
| *Rhizophora racemosa* G. Mey. | Rhizophoraceae | Magli, Fusol (Diola-casamançais) | 0.71 | Aerial roots | Infusion in water | Drink one ½ cup/day |
| *Salacia senegalensis* (*Lam.) DC.* | Celastraceae | Epumbey, Bulil (Djola-casamançais) | 2.14 | Leaves | Maceration with liter of water | Drink in the morning and evening for 48 days |
| *Salvadora* persicaL.Var. persica | Salvadoraceae | Gudi | 0.36 | Leaves | Decoction in water | Drink a cup in the morning and a cup in the evening |
| *Sclerocarya birrea* (A. Rich) Hochst.Subsp. Caffra (Sond.) | Anacardiaceae | Beer (Wolof-Lébou) | 2.14 | Leaves | Maceration with liter of water | Drink a cup in the morning and a cup in the evening |
| *Sarcocephalus latifolus* (Sm.) E.A. Bruce | Rubiaceae | Fumunduluk (Diola-casamançais) | 0.71 | Leaves | Tea from leaves | Drink a cup in the morning and a cup in the evening |
| *Securidaca longipedunculata* Fresen. | Polygonaceae | Alalé (Peulh-Toucouleur) | 1.79 | Leaves | Infusion | Drink a cup in the morning and a cup in the evening |
| *Securinega virosa Flueggea virosa* (Roxb.ex. Willd.) Voigt subsp. Virosa | Euphorbiaceae | Tembelgorey (Peulh-Toucouleur) Fusabel, Funéné (Djola-casamançais) | 1.43 | Roots | Maceration in water | Drink a cup in the morning and a cup in the evening |
| *Solanum incanum L.* | Solanaceae | Gitegari (Peulh-Toucouleur) | 1.07 | Leaves | Tea from 7 leaves | Drink in the morning and evening for 48 days |
| *Swartzia madagascariensis* Desv. | Fabaceae | Gukiriki (Djola-casamançais) | 1.43 | Leaves | Decoction in water | Drink in the morning and evening for 48 days |
| *Terminalia avicennioides* Guill. | Combretaceae | Pulemi (Peulh-Toucouleur) | 1.43 | Leaves | Decoction in water | Drink in the evening for 2 weeks |
| *Treculia africana* Decne | Moraceae | Buhiteuk (Djola-casamançais) | 1.43 | Leaves | Tea from 7 leaves | Drink in the morning and evening for 48 days |
| *Trichilia roka* Vahl subsp. Emetica | Meliaceae | Kerendusa (Peulh) | 0.71 | Bark | Maceration in water | Drink regularly |
| *Trichilia emetica* Vahl | Meliaceae | Enabunuk (Djola-casamançais) | 0.36 | Leaves | Maceration with liter of water | Drink in the morning and evening for 48 days |
| *Tapinanthus bagwensis* Engler | Loranthaceae | Tonawi (Djola-casamançais) | 1.79 | Leaves | Maceration in water | Drink one ½ cup/day |
| *Uvaria chamae* P. Beauv. | Annonaceae | Furay, Boguna (Djola-casamançais) | 1.43 | Leaves | Maceration with liter of water | Drink regularly |
| *Vitex doniana* Sweet | Verbenaceae | Kukek (Djola-casamançais) | 0.71 | Roots | Maceration with liter of water | Drink in the morning and evening for 48 days |
| *Waltheria indica L.* | Sterculaliaceae | Niananisousareng (Socé) | 0.71 | Leaves | Maceration with liter of water | Drink regularly |
| *Xylopiea aethiopica* (Dunal) A. Rich. | Annonaceae | Buhelo (Djola-casamançais) | 1.79 | Leaves | Maceration in water | Drink regularly |

The most common plant preparation methods used by traditional medicine practitioners in Zimbabwe to treat cancer were infusion (72.20%) and decoction (66.70%) and the oral route of administration, such as extracts and powder put in tea and porridge, was the most used [13].

### *3.4. Antioxidant activities of plant extracts*

Figure 2 shows the results of the measurement of the efficiency of the crude hydroalcoholic leaves extract in trapping free radicals compared with that of trolox using the TEAC and ORAC methods. Antioxidants protect cells against the damaging effects of reactive oxygen species otherwise called free radicals such as singlet oxygen, super oxide, peroxyl radicals, hydroxyl radicals, and peroxynite which results in oxidative stress leading to cellular damage. Natural antioxidants play a key role in the maintenance and prevention of chronic and degenerative diseases, such as atherosclerosis, cardiac and cerebral ischema, carcinogenesis, neurodegenerative disorders, diabetic pregnancy, rheumatic disorders, DNA damage, and aging [17].

The results of this study revealed that the highest antioxidant potential for radical scavenging was obtained with the crude hydroalcoholic leaves extract of *A. Africana* by TEAC with a value of 6533.64±504.08 µmol ET/g dry plant that was

**Table 2.** Percentages of pre-apoptotic cells of different phenotypes of human cancer cell lines after treatment with 100 µg/mL of hydroalcoholic leaves extracts of medicinal plants.

| Plant species | Cells | | | |
|---|---|---|---|---|
| | MFC-7 | THP-1 | HTC-116 | A-375 |
| *A. Africana* | 68.85±6.22 | 58.10±1.90 | 18.85±1.50 | 48.58±1.40 |
| *H. Acida* | 8.56±0.59 | 19.07±1.21 | 21.07±1.24 | 19.67±1.40 |
| *H. Halal* | 9.18±0.82 | 16.54±3.20 | 24.83±4.06 | 17.70±1.05 |

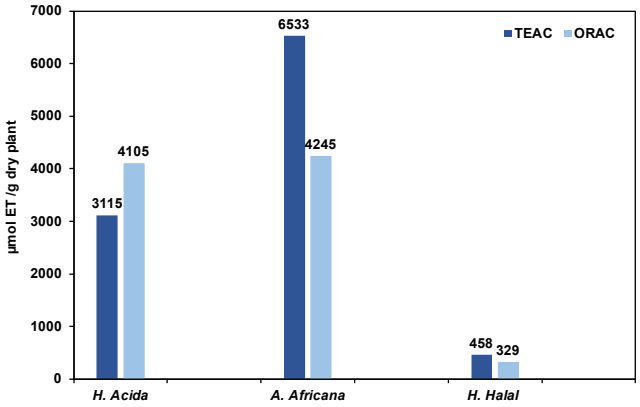


**Figure 2.** Antioxidant capacity (mean±standard deviation) of plant leaves extracts according to TEAC and ORAC.

twice higher than that of *H. Acida* (3115.5±145 µmol ET/g dry plant). Close values with the ORAC method were obtained for *H. Acida* (4105.29±872.12 µmol ET/g dry plant) and *A. Africana* (4245.18±180.48 µmol ET/g dry plant). The lowest antioxidant potential for radical scavenging was obtained with the crude hydroalcoholic leaves extract of *H. halal* in TEAC (458.32±26.84 µmol ET/g dry plant) and ORAC (329±14 µmol ET/g dry plant). Aqueous and methanol leaf extracts of *H. Acida* have been evaluated for their antioxidant activity and registered lower values than those of this study (75±35.36 mmol TEAC/100 g) [18]. Furthermore, Silva *et al.* [19] found antioxidant activity values of TEAC ranging from 1.0 to 347.1 µmol of trolox equiv/g and ORAC varying between 6.7 and 1396.4 µmol of trolox equiv / g for 15 species of Amazonian plants used in complementary medicine for their antiproliferative effect. These results suggest that the hydroalcoholic leaves extract of *A. Africana* Engler and *H. Acida* have significant free radical scavenging properties. The significant antioxidant activity of these plants could be the reason why the plant possesses anticancer activity.

### *3.5. Pro-apoptotic effects*

After 24 h of treatment with 100 µg/mL of crude hydro-alcoholic leaves extracts and followed by incubation with annexin V-FITC and propidium iodide, cells were analyzed by flow cytometry. The percentages of pre-apoptotic cells were then determined (Table 2).

The data in Table 2 showed the highest cytotoxic activity of the extracts of *A. Africana* leaves against human mammary (MCF-7) and human acute monocytic leukemia (THP-1) cell lines but low activity against human carcinoma colorectal (HTC-116) and skin malignant melanoma (A-375). The extract of *H. Acida* leaves was active against THP-1, HTC-116, and A-375 with percentages of pre-apoptotic cells of 19.07±1.21, 21.07±1.24 and 19.67±1.4, respectively, but was not active against the human mammary cancer cell line (MCF-7) (8.56±0.59). Similar results were also obtained from the extracts of *H. Halal* leaves; the percentages of pre-apoptotic cells were 16.54±3.20, 24.83±4.06, 17.7±1.05 and 9.18±0.82 %, respectively, for THP-1, HTC-116, A-375, and MCF-7.

The cytotoxic activity of the stem bark and latex extracts of *A. Africana* has been previously demonstrated in different human cancer cell lines, including MCF-7 (breast), OVACAR-3 (ovarian), SMMC-7721 (hepatoma), DU-145 (human prostate) and NIH-H460 (lung). The decrease in cell viability in human gastric carcinoma (SGC- 7901) and human hepatocellular carcinoma (SMMC-7721) has also been reported, with an increase in apoptosis in human lung, colon, ovary, pancreas, prostate, uterus, and stomach cancer cell lines [20]. In our previous work, we have demonstrated that the leaf extract of *A. Africana* efficiently induces apoptotic cell death in breast, colon, pancreatic, and leukemic cancer cell lines in a dose-dependent manner [20]. Cytotoxic activity of the ethanolic extract of *H. Acida* stem bark in human breast (MCF-7) and colon (HCT 116) cell lines was also reported by Adedokun *et al.* [21].

## 4. Conclusions

The survey results indicated that 65 medicinal species belonging to 35 families were cited to be used by traditional healers in Senegal to treat cancer patients. The hydro-alcoholic leaves extract of *A. Africana* exhibited the highest cytotoxic activity against the human mammary (MCF-7), the human acute monocytic leukemia cell line (THP-1), and malignant skin melanoma (A-375), but had low activity against human carcinoma colorectal (HTC-116). The hydroalcoholic extract of *H. Acida* was active against THP-1, HTC-116, and A-375, but not against the human mammary cancer cell line (MCF-7). Similar results were also obtained from the hydroalcoholic extract of *H. Halal* with percentages of cell death of 16.54±3.20, 24.83±4.06, 17.7±1.05, and 9.18±0.82, respectively, for THP-1, HTC-116 and A-375 and MCF-7. The hydro-alcoholic leaves extract of *A. Africana* had greater antioxidant activity than the hydroalcoholic extract of *H. Acida* and *H. Halal,* as well as with TEAC than with the ORAC method with radical scavenging activities depending on the method. The present work led to the identification of medicinal plants used for cancer treatment in Senegal by traditional healers and provides evidence to support the use of the most cited.

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## CRediT authorship contribution statement

Conceptualization: Thiam Khadidiatou; Methodology: Khadidiatou Thiam, Fathi Emhemmed, Diane Julien-David, Zhao Minjie; Software: Thiam Khadidiatou; Validation: Fathi Emhemmed, Diane Julien-David; Resources: Eric Marchionni, Diane Julien-David; Data Curation: Fathi Emhemmed, Thiam Khadidiatou; Writing - Original Draft: Thiam Khadidiatou, Amadou Diop; Writing - Review and Editing: Thiam Khadidiatou, Amadou Diop; Visualization: Diane Julien-David, Thiam Khadidiatou; Funding acquisition: Thiam Khadidiatou, Fathi Emhemmed, Diane Julien-David, Zhao Minjie; Supervision: Fathi Emhemmed, Diane Julien-David, Zhao Minjie; Project Administration: Yérim Mbagnick Diop, Eric Marchionni, Diane Julien-David.

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