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Traditional Uses and Anticancer Potential of the *Combretum* Genus: A Literature Review

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Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

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ABSTRACT

Background: Cancer incidence is increasing annually in all countries. So, it is nowadays a great burden for the different nations of the world. Research for new therapeutics is becoming an urgent need, particularly for intractable and chemoresistant cancer cases. The solutions can still be found by investigating natural products which are recognized as promising sources of bioactive compounds with a potential for the discovery of new preventive and therapeutic anticancer agents.
Methodology: The present work used databases such as Pubmed, Science Direct and Google scholar to investigate the ethnobotanical uses of some *Combretum* species in the literature. It also allowed us to summarize some pharmacological studies on *Combretum* species.
Results: This review gathers all available traditional uses and cytotoxicity studies of *Combretum* species in the literature. Special focus is given to pharmacological studies highlighting isolated potential anticancer molecules. These molecules present potent cytotoxic effect on various cancer cell lines and may contribute to improving the health of people suffering from various cancer diseases.

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Conclusion: The *Combretum* species are widely used in folk medicine for the treatment of several pathologies including cancers. This study is of fundamental importance in highlighting *Combretum* species as a potential source for research of new anticancer compounds.

Keywords: Anticancer potential; combretum; ethnobotanical uses; natural product; traditional medicine.

1. INTRODUCTION

The different cancer diseases continue to have a negative impact on the world. Despite advances in the search for better solutions against the scourge, its incidence is tending to increase. Indeed, statistics show that new cases of cancer increased from 12.7 million in 2008 [1] to 14.1 million in 2012 [2], then to 18.1 million in 2018 [3]. Estimates predict 28.4 million new cases of cancer in 2040 [4]. Cancer caused nearly 10 million deaths in 2020, making cancer one of the leading causes of death worldwide [4]. Cancer is also a major concern for Burkina Faso. In the year 2020, GLOBOCAN estimates revealed 12,045 new cases of cancer, including 8,695 deaths. More than 18,884 new cases are expected for the next five years. Within non-communicable diseases, cancer is the second most causing death in this country after cardiovascular diseases. The most common cancers are breast (16%), liver (10.3%), cervix uteri (9.4%), prostate (8.3%), and bladder (5.5%) [5]. To fight cancer effectively, the Ministry of Health has adopted a strategic plan for 2021 to 2025 in which strong actions against cancer in Burkina Faso have been undertaken. Among other things, there is the strengthening of cancer research, in particular the identification of new antitumor molecules contained in the country's medicinal plants. Burkina Faso has a very rich and varied traditional pharmacopeia [6,7] to which more than 80% of the population has recourse to it for their essential healthcare needs [8].

Medicinal plants have always been a credible alternative for the search for active molecules to counter major public health scourges in the interest of the survival of populations since antiquity [9]. Active molecules of natural origin have long served as a source of therapeutic agents or as a model for the synthesis of derivatives [10]. As part of the fight against cancer, many anti-cancer molecules have been identified from certain medicinal plants. This is the case of vincristine and vinblastine isolated from species of the genus *Catharanthus*; paclitaxel isolated from species of the genus *Taxus*; podophyllotoxin isolated from *Podophyllum emodi*; Colchicine isolated from species of the genus *Colchicum* and many other compounds that are currently used clinically for the treatment of patients with cancer [11]. Given the emergence of cancer resistance forms to current treatments, it is important to always look for new anticancer bioactive molecules. Ethnobotanical studies show that *Combretum* species are used in the treatment of several pathologies including cancers and their cytotoxicity effects on various cancer cell models have been pharmacologically demonstrated [12-15]. These diverse therapeutic properties of *Combretum* species are due to the wide variety of secondary metabolites contained in these plants. Indeed, phytochemical analyzes have revealed the presence of many classes of constituents, including triterpenes, flavonoids, lignans, alkaloids, and non-protein amino acids, among others in most species of the *Combretum* genus [16-18]. So, species of the *Combretum* genus which are widely used in traditional medicine can be an important source of new anticancer molecules discovery.

The objective of this review was to gather all available traditional uses and cytotoxicity studies of *Combretum* species in the literature. Pharmacological studies highlighting isolated potential anticancer molecules from *Combretum* species were reported as well. This study will contribute to highlight *Combretum* species as a potential source for research of new anticancer compounds.

2. METHODOLOGY

PubMed, Science Direct and Google Scholar databases were used to select the articles. For the search in these databases, the following keywords were used: "*Combretum*," "Traditional uses," "Cytotoxicity" and "Cancer". The articles were selected according to these inclusion criteria: made with *Combretum* species; title and summary with traditional uses of combretum species; title and summary with the assessment of cytotoxicity activity of *Combretum* extracts on cancer cell lines; title and summary with the evaluation of cytotoxicity activity of isolated compound from *Combretum* extracts. Exclusion criteria were: duplication of articles and abstracts and full texts irrelevant to the topics in question.

Some books and Ph.D. thesis on the topics were also consulted.

3. RESULTS AND DISCUSSION

3.1 Ethnobotanical Uses of *Combretum* Species

Traditional medicine has a prominent place in the world and specifically in Sub-Sahara developing countries [19]. Indeed, with the resurgence of diseases and the non-accessibility of pharmaceutical drugs, populations living in low-income regions of the world are looking to folk medicine for their healthcare needs [20]. Medicinal plants are mostly used by traditional healers for therapeutic purposes [21]. Ethnobotanical studies have been very important in highlighting some traditional medical knowledge of indigenous peoples and traditional healers, which has contributed to the establishment of a list of medicinal plants used in folk medicine as the first line of primary healthcare in the rural community. Such information is useful for researchers looking for new bioactive compounds, especially anti-cancer agents.

The *Combretum* genus belonging to the Combretaceae family includes nearly 250 plant species among which 12 species are represented in Burkina Faso [22]. Species of *Combretum* are well spread across Sub-Sahara Africa. The geographical distribution of *Combretum* species in Burkina Faso has been investigated, and results showed that these species are widespread on the territory [23]. A positive correlation has been observed by some authors between the accessibility of plants and their medicinal uses [24]. Thus, the wide distribution of *Combretum* species across Africa and particularly on the territory of Burkina Faso could explain the medicinal knowledge of these plants and consequently their wide use by populations.

Combretum species are variously used for the treatment of several pathologies. An ethnobotanical study revealed that different parts of *C. molle* are used by traditional healers in Uganda for the treatment of various cancers such as abdominal, bone, cervical, intestinal, liver, skin, throat cancers, and leukemia [25]. Another ethnobotanical investigation realized in Nigeria points out three *Combretum* species such as *C. micranthum*, *C. Camporum,* and *C. molle* that are used by traditional healers for the treatment of cancers [14]. The roots and leaves of *C. zeyheri* are used by traditional healers in Tanzania for the treatment of cancer [12]. A study reported the traditional uses of *C. fragrans* in the northern part of Cameroon for the treatment of cancers [15]. Others traditional uses of some *Combretum* species recorded in the literature are showed in Table 1.

Medicinal plants from Burkina Faso are also well used by populations for their healthcare needs. Some ethnobotanical studies allowed to highlight the traditional knowledge of traditional healers in the country. Indeed, some researchers have listed 61 species of medicinal plants used in the care of kidney diseases in Burkina Faso, among which *C. micranthum* was mentioned [26]. Another study reported nearly 134 medicinal recipes from 106 species of medicinal plants from Burkina Faso including *C. molle* for their various medicinal uses [27]. Also, an investigation showed that 94 species of medicinal plants are used to combat different pathologies in Burkina Faso of which *C. glutinosum*, *C. micranthum*, *C. nigricans,* and *C. paniculatum* are cited [28]. To the best of our knowledge, a study highlighting the ethnobotanical uses of *Combretum* species for cancer treatment in Burkina Faso is not yet reported.

These *Combretum* species could be an important resource for researchers, especially to those from Burkina Faso where the cancer healthcare system and chemotherapy are not accessible, to investigate their anticancer potential and to isolate new anticancer molecules as well.

3.2 Anticancer Potential of *Combretum* Species

Cancer is a great burden for the different nations of the world. This has led different nations to adopt strategic plans to overcome this pathology. Also, the fact that resistance to available treatments is increasingly appearing motivate researchers to look for new therapeutic molecules and even new therapeutic targets for cancer therapy. Species of the genus *Combretum* could play a key role in the discovery of new therapeutic molecules against cancer. Indeed, some species of this genus are well known for their traditional uses against cancer. Also, several pharmacological studies have been undertaken to elucidate the anticancer properties of plant species from the *Combretum* genus.

Table 1. Traditional uses of some *Combretum* species reported in the literature

Species	Used parts	Traditional uses	References
C. aculeatum Vent.	Leafy stems, roots	Diarrhea, gonorrhea, intestinal parasites, colic, dysentery, jaundice, malaria, hypertension, fevers, constipation, fractures, weight delays, hypocalcemia, remineralizing, spasmodic, mental disorders, leprosy, wounds, female sterility, etc.	[29,30]
C. adenogonium Stend. Ex A. Rich.	Leaves	Liver and gallbladder diseases, colds, bronchitis, malaria, anemia, migraine, wounds, amoebic dysentery, diarrhea, urinary disorders, bilious and hematuric fevers, edema, albuminuria, anorexia, cough, severe jaundice, Hypertension, hepatitis, epilepsy, snakebites, asthenia.	[29]
	Bark	Epigastralgia, intestinal parasites, sexual weakness, vomiting, analgesic, aphrodisiac, anthelmintic.	
	Roots	Diseases of the stomach, cough, intestinal parasites, syncope, snake bite, pregnancy bleeding.	
C. apiculatum Sond.	Bark	Aphrodisiac	[31]
C. camporum Engl.	Bark, roots	Cancer	[14]
C. coccineum (Sonn.) Lam.	Leaves	Herbal tea cholagogue	[32]
	Roots and fruits	Anthelmintic	
C. collinum Fresen	Roots	Painful legs, cramps, and joint pains.	[33]
C. crotonoides Hutch et Dalz	Leafy stems	Pneumonia, bronchitis, liver disorders, cholagogue, general fatigue, rheumatism	[29]
C. erythrophyllum (Burch.) Sond.	Leaves, roots, bark	Abdominal pain, sexually transmitted diseases, diarrhea, dysentery, coughs, colds, infertility, sores, and wounds.	[34,35]
C. fragrans F. Hoffm.	Whole plant	Leprosy, coughs, diarrhea, pain and inflammation, jaundice, ulcers, wounds, and cancers.	[12,15,32,36]
	Leaves	Dysentery, burns, and wounds	
	Leafy twigs	Diarrhea,	
	Fruits	Wounds	
	Roots	Diarrhea, pain	
C. glutinosum Perr. ex DC	Leaves	Cholagogues, depurative, diuretic, pectoral, malaria.	[32]
	Leafy twigs	Cholagogues, anemia, childhood gastritis, jaundice, edema, malaria, and various eye conditions.	
	Powdered fruit	Wounds, syphilis.	
C. hartmannianum (Schweinf)	Wood, bark	Febrile, jaundice, bacterial infections, cough, tuberculosis, neoplasia	[37-39]
C. hereroense Schinz	Leaves	Abdominal pain, sexually transmitted diseases	[40]
C. imberbe Engl. & Diels	Roots, stem, leaves	Menstruation, stomachache	[31,33]
C. krausii Hochst.	Leaves	Wounds, antiseptic.	[40]

Species	Used parts	Traditional uses	References
C. leprosum Mart.	Leaves and flowers	Inflammation, pain, treatment of wounds, sedative, diarrhea, expectorant, and antitussive.	[41,42]
C. micranthum G. Don	Leaves	Diarrhea, dysentery, colic, stomach disorder, digestion disorder, malaria, beriberi, intestinal parasites, asthenia, cough, bronchitis, fevers, lumbago, gallbladder disease, anemia, gonorrhea, hypertension, mastitis, bilious and hematuric fevers, cancer.	[14,29,32,43]
	Roots	Female sterility, intestinal parasites, syphilis, enuresis, stimulant, constipation, fever gastritis, jaundice, trichocephalosis, cancer.	
	Bark	Contusions, sprains, massage before and after muscular effort, lumbago, cancer.	
	Fruits	Hypertension, stomatitis, hypotension	
	Seeds	Candidiasis, thrush, boils abscess, leucorrhea.	
C. molle G. Don	Leaves, roots, bark	Gonorrhoea, syphilis, influenza, edema, skin diseases and wounds, diarrhea, stomachache, measles, cough, eye pain, asthma, and cancer.	[14,35,40]
C. mucronatum Schumach. & Thonn.	Stem bark	Anthelmintic	[32]
	Leaves	Wounds and injuries.	
C. nigricans Lepr. ex Guill. et Perr.	Leafy stems	Hematuria, gastric diseases, malaria, fever, strengthening babies, cancer	[22,28]
	Bark	Headache, intestinal disorders, rheumatism	[30]
	Roots	Mental illness	
C. nioroense Aubrev. ex keay	Leafy stems	Malaria, dysentery, diarrhea, strengthening babies	[44]
	Leaves	Metastasis, neck, head, face and breast cancers	[43]
C. paniculatum Vent.	Gall	Vomit	[28]
	Leaves	Gastric colic, hernial pain, strengthening, rickets, cough, injuries, hemorrhoids, wounds	
	Roots	Diarrhea, malaria with inflammation of the spleen, wounds	
C. psidioides Welw.	Roots, leaves	Diarrhea, muscle pain, edema.	[12]
C. racemosum P. Beauv.	Whole plant	Anthelmintic, gastrointestinal and genito-urinary infections, hemorrhoid, convulsive coughing, tuberculosis, toothache, and male sterility	[32,45,46]
	Leaves, rootbark	Hypertension	
C. sericeum G. Don	Leafy stems	Malaria, weight delay, open fractures, stomach ache, conjunctivitis, fevers.	[28,47]
	Roots	Diarrhea, pneumonia, wounds.	
C. tomentosum G. Don	Bark, leaves	Breast, neck, throat and head Cancers	[43]
C. zeyheri Sond.	Roots, leaves	Diarrhea, cancer	[12]

The cytotoxic effect of methanol (80%) extract from the root of *Combretum adenogonium* has been investigated, and authors found that the extract inhibits human prostate cancer cell lines (PC-3) with an IC_{50} of 24 µg/mL [48]. The methanol extract from leaves of *Combretum fragrans* inhibited several human cancer cell lines such as T24 (Bladder cancer), Hela (Cervical cancer), and MCF-7 (Breast cancer) with IC_{50} around 4.3 µg/mL for both T24 and Hela cells and 14.6 µg/mL for MCF-7 cells [13]. A study has highlighted the cytotoxicity of dichloromethane extract from leaves of *Combretum fruticosum* on human cancer cells such as adenocarcinoma human alveolar basal epithelial cells (A549), glioblastoma cells (U373; Hs683), human prostate cancer cells (PC3) and Brain primary metastases cells (Kaka) with IC_{50} of 9 µg/mL, 7 µg/mL, 8.5 µg/mL, 10 µg/mL and 8.3 µg/mL respectively [49]. The trachelogenin compound isolated from the talks of this plant has demonstrated cytotoxic properties on human brain cancer cells (SF-295) and human leukemia cells (HL-60). This compound also presented antiproliferative activity on human colon cancer cells (HCT-116) with an IC_{50} value of 4.8 µM [50]. It has been showed that *Combretum microphyllum* has potential antimutagenic activity and protective effects against cancer. Indeed, the crude extract of this plant inhibits the genotoxic end-points induced by 4-nitroquinoline 1-oxide (4NQO), mitomycin-C (MMC), and ethyl methanesulfonate (EMS) in vitro. Isolated compounds n-tetracosanol, eicosanoic acid, and arjunolic acid, presented an antimutagenicity of 42 ± 9.6%, 36 ± 1.5%, and 44 ± 0.18% in *S. typhimurium* TA98 [51]. Ethanol (80%) extract of *Combretum paniculatum* has presented a potent cytotoxic effect on Hela cancer cells at 500 µg/mL. The extract inhibited almost 70% of the growth of this cancer cell line [52]. Jurkat cells exposed to *Combretum platypetalum* extract at 31,25 µg/ml during 72 hours showed a significant reduction of cell viability of this cell line [53]. Ethanol extract from leaves of *Combretum quadrangulare* presented a cytotoxic effect on A549 cancer cells after 48 hours of treatment with an IC_{50} of 136.1 µg/mL [54]. The ethyl acetate extract from leaves of *Combretum rupicola* showed significant anticancer activities against four cell lines and the most significant activity was observed against MCF-7 cells with an IC_{50} of 65.9 µg/mL [55]. All these results contribute to highlighting the anticancer potential of *Combretum* species and in the same way justify their uses in traditional medicine for cancer treatment.

3.3 Potential Anticancer Compounds Isolated from *Combretum* Species

Many potential anticancer compounds have been isolated from *combretum* species. The cytotoxicity of some important isolated compounds is presented in Table 2 and their structures are shown in Fig. 1. Few of these compounds have been investigated in deep for preclinical studies. The myricitrin isolated from *C. lanceolatum* proved to be most effective in inhibiting the growth of leukemic HL-60 cells. The mechanism of this inhibition is through the inhibition of the topoisomerase IIα [56]. The trachelogenin compound isolated from *C. fruticosum* induced autophagy cell death in human colon cancer cells (HCT-116) with LC3 activation and altered the expression levels of Beclin-1 [50]. The triterpenoid (1-O-[α-L-(rhamnopyranosyl]-23-acetoxy-3β-acetyl-imberbic acid) isolated from *C. Sundaicum* inhibited KB, MCF7, and HCT-116 cells growth by binding to Bcl-xL protein [57]. The pentacyclic triterpene (3β, 6β, 16β-trihydroxylup-20(29)-ene) isolated from *C. leprosum* induced apoptosis in MCF7 cells by increasing levels of both cleaved caspase-9 and intracellular ROS [58].

Among isolated compounds from *Combretum* species, Combretastatins were the most subject to research. They are first isolated from the South African *Combretum caffrum* specie [59]. Other *Combretum* species also contain these molecules [60,61]. Combretastatins are simple compounds formed of two phenyl rings linked by a chain of two carbon atoms. They consist of several series belonging to the stilbenoid class of compounds [62]. Several studies have been undertaken to highlight the anticancer properties of these compounds [63-65]. Combretastatins belonging to the A and B series present potent anticancer activity with the combretastatin A4 molecule being the most potent due to its broad-spectrum cytotoxicity against a variety of tumor cells [66]. It has been demonstrated that Combretastatin A4 can induce cell cycle arrest at M-phage and apoptosis in various cancer cells through a mechanism of action involving inhibition of tubulin polymerization [64,65]. It has also been revealed that combretastatin A4 can reverse daunorubicin resistance acquisition in the P-388 cell line [67]. This proves that the molecule could play an important role in the treatment of certain resistant forms of tumors. The cis isomer of this molecule is the active form while the trans isomer is inactive [63]. The cis

isomer can spontaneously isomerize into the trans isomer. This problem of isomerism added to its low solubility and its poor bioavailability has led to the development of analogs such as combretastatin A4 phosphate which is water-soluble, bioavailable, and biologically active [68]. Combretastatin A4 phosphate undergoes clinical trials as an anticancer agent for the treatment of solid cancers [69,70].

Table 2. Cytotoxicity (IC_{50}) of isolated compounds from *Combretum* species on some cancer cell models

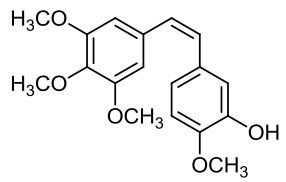
Species	Plant part	Compounds	Cell lines	Histotype	IC_{50}	References
Combretum caffrum (Eckl. and Zeyh.) Kuntze	Twigs and leaves	(1) Combretastatin A4	P-388	murine lymphocytic leukemia	0.011 µg/mL	[59]
Combretum fragrans F. Hoffm.	Leaves	(2) Combretin A	MCF-7	Breast adenocarcinoma	16.1 µg/mL	[15,36]
			U87	Glioblastoma	29.3 µM	
			PC-3	Prostate adenocarcinoma	22.57 µM	
		(3) Combretin B	MCF-7	Breast adenocarcinoma	< 1 µg/mL	[36]
		(4) Cirsilineol	U87	Glioblastoma	65.46 µM	[15]
			PC-3	Prostate adenocarcinoma	30.46 µM	
Combretum racemosum P. Beauv.	Roots	(5) 3-O-β-acetyl-ursolic acid	HL-60	Leukemia	14.5 µM	[71]
			K562	Leukemia	50.0 µM	
		(6) Betulinic acid	HL-60	Leukemia	35 µM	[71]
			K562	Leukemia	> 50 µM	
		(7) Quadranoside II	HL-60	Leukemia	13 µM	[71]
			K562	Leukemia	44.0 µM	
Combretum griffithii Heurck & Müll.	stems	(8) 1-(5-hydroxy-2,4-dimethoxyphenyl)-3-(4-hydroxy-3-methoxyphenyl)propane	KB	Cervical adenocarcinoma	24.63 µM	[72]
			MCF-7	Breast adenocarcinoma	23.12 µM	
			NCI-H18	Small cell lung cancer	34.65 µM	
		(9) (2S)-3′,4′-dihydroxy-5,7-dimethoxyflavan	KB (Hela derivative)	Cervical cancer	31.82 µM	[72]
			MCF-7	Breast adenocarcinoma	49.15 µM	
			NCI-H18	Small cell lung cancer	10.41 µM	
Combretum leprosum Mart.	Flowers	(10) 3β,6β,16β-Trihydroxylup-20(29)-ene	MCF-7	Breast adenocarcinoma	1.36 µg/mL	[58]
			HepG2	Hepatoma	6.50 µg/mL	

Species	Plant part	Compounds	Cell lines	Histotype	IC_{50}	References
			T24	Bladder carcinoma	5.55 µg/mL	
			HCT-116	Colorectal carcinoma	7.05 µg/mL	
			HT-29	Colorectal adenocarcinoma	8.0 µg/mL	
			CACO-2	Colorectal adenocarcinoma	8.55 µg/mL	
Combretum quadrangulare Kurz	Leaves	(11) Methyl quadrangularate D	Colon 26-L5	Murine colon cancer	5.42 µM	[73]
			HT-1080	Fibrosarcoma	40.0 µM	
			HeLa	Cervical carcinoma	50.9 µM	
			A-549	Lung adenocarcinoma	63.5 µM	
		(12) Methyl quadrangularate B	Colon 26-L5	Murine colon cancer	9.54 µM	[73]
			HT-1080	Fibrosarcoma	53.3 µM	
			HeLa	Cervical carcinoma	56.0 µM	
			A-549	Lung adenocarcinoma	>100.0 µM	
		(13) Combretic acid C	K562	Leukemia	9.7 µM	[74]
		(14) Kamatakenin	Colon 26-L5	Murine colon cancer	3.0 µM	[75]
			HT-1080	Fibrosarcoma	3.2 µM	
			HeLa	Cervical carcinoma	10.6 µM	
			A-549	Lung adenocarcinoma	40.1 µM	
		(15) Isokaempferide	Colon 26-L5	Murine colon cancer	4.5 µM	[75]
			HT-1080	Fibrosarcoma	0.8 µM	
			HeLa	Cervical carcinoma	8.2 µM	
			A-549	Lung adenocarcinoma	39.2 µM	
		(16) 5,7,4'-trihydroxy-3,3'-dimethoxyflavone	Colon 26-L5	Murine colon cancer	1.8 µM	[75]
			HT-1080	Fibrosarcoma	1.5 µM	
			HeLa	Cervical cancer	6.8 µM	
			A-549	Lung adenocarcinoma	95.3 µM	
		(17) 5,4'-dihydroxy-3,7,3'-trimethoxyflavone	Colon 26-L5	Murine colon cancer	5.2 µM	[75]
			HT-1080	Fibrosarcoma	3.5 µM	
			HeLa	Cervical carcinoma	38.4 µM	

Species	Plant part	Compounds	Cell lines	Histotype	IC_{50}	References
			A-549	Lung adenocarcinoma	41.9 µM	
Combretum nigricans Lepr. ex Guill. et Perr.	Leaves	(18) 20,24-epoxy-11α,25-dihydroxy-dammar-3-one	U-373	Glioblastoma	31.6 µg/mL	[76]
			HCT-15	Colon adenocarcinoma	30.4 µg/mL	
			A-549	Lung adenocarcinoma	29.7 µg/mL	
			J82	Bladder carcinoma	29.6 µg/mL	
		(19) 11α-acetoxy-20,24-epoxy-25-hydroxy-dammar-3-one	U-373	Glioblastoma	51.7 µg/mL	[76]
			HCT-15	Colon adenocarcinoma	88.4 µg/mL	
			A549	Lung adenocarcinoma	>100 µg/mL	
			J82	Bladder carcinoma	80.6 µg/mL	
Combretum oliviforme Chao	Leaves	(20) 23-acetoxy-3β-acetylimberbic acid-29-methyl ester	SPC-A1	Lung cancer	1.09 µM	[77]
			SGC-7901	Gastric cancer	0.69 µM	
			K562	Leukemia	2.10 µM	
		(21) 23-*O*-[α-L-rhamnopyranosyl]-1,3β-diacetylimberbic acid	SPC-A1	Lung cancer	25.20 µM	[77]
			SGC-7901	Gastric carcinoma	5.44 µM	
			K562	Leukemia	2.38 µM	
Combretum fruticosum (Loefl.) Stuntz	Stalks	(22) (-)-Trachelogenin	HL-60	Leukemia	32.4 µM	[50]
			OVCAR-8	Ovarian carcinoma	3.5 µM	
			HCT-116	Colorectal carcinoma	1.9 µM	
			HCT-8	Ileocecal adenocarcinoma	5.2 µM	
			PC-3	Prostate cancer	15 µM	
			SF295	Glioblastoma	0.8 µM	
Combretum sundaicum Miq.	Leaves and flowers	(23) 1-o-[α-L-rhamnopyranosyl]-23-acetoxy-3β-acetylimberbic acid-29-methyl ester	KB	Cervical adenocarcinoma	0.9 µM	[57]

Species	Plant part	Compounds	Cell lines	Histotype	IC_{50}	References
			HCT-116	Colorectal carcinoma	0.3 µM	
			MCF-7	Breast adenocarcinoma	0.6 µM	
Combretum platypetalum Welw. ex M.A. Lawson	Leaves	(24) 3-o-(β-D-glucopyranosyl)-5,7,3',4',5'-pentahydroxyflavone	Jurkat T	Leukemia	3.98 µg/mL	[78]
			HL-60	Leukemia	14.18 µg/mL	
		(25) 3-o-(α-L-rhamnopyranosyl)-5,7,3',4',5'-pentahydroxyflavone	Jurkat T	Leukemia	19.33 µg/mL	[78]
			HL-60	Leukemia	28.7 µg/mL	
Combretum Lanceolatum Pohl.	Leaves and branches	(26) myricetin	MCF7	Breast adenocarcinoma	158.4 µM	[56]
			PC-3	Prostate cancer	182.8 µM	
			HT-29	Colon adenocarcinoma	95 µM	
			786-0	Kidney carcinoma	124.6 µM	
			HL-60	Leukemia	53.4 µM	
Combretum laxum Jacq.	Roots	(27) 4′-hydroxy-3,3′,4-trimethoxy-5-(3,4,5-trimethoxyphenoxy)-bibenzyl	MCF-7	Breast adenocarcinoma	72.69 µM	[79]
			NCI/ADR-RES	Ovary carcinoma, multidrug-resistant	32.09 µM	
		(28) 2,7-dihydroxy-4,6-dimethoxyphenanthrene	786-0	Kidney carcinoma	73.26 µM	[79]
			NCI/ADR-RES	Ovary carcinoma, multidrug-resistant	83.99 µM	
		(29) 2,6-dihydroxy-3,4,7-trimethoxyphenanthrene	786-0	Kidney carcinoma	64.27 µM	[79]
		(30) 6-methoxycoelonin	MCF-7	Breast adenocarcinoma	46.99 µM	[79]
			UACC-62	Human melanoma	2.59 µM	
			NCI/ADR-RES	Ovary carcinoma, multidrug-resistant	58.83 µM	
			786-0	Kidney carcinoma	56.98 µM	
		(31) 2,6-dihydroxy-3,4,7-trimethoxy-	MCF-7	Breast adenocarcinoma	42.01 µM	[79]

Species	Plant part	Compounds	Cell lines	Histotype	IC_{50}	References
		9,10-dihydrophenanthrene				
Combretum inflatum Jongkind	Leaves	(32) Combretaside G	NCI-H460	Lung carcinoma	3.9 µM	[80]
Combretum mellifluum Eichler	Roots and Leaves	(33) Tetrahydrofuran lignan	HT-29	Colon adenocarcinoma	3.9 µM	[81]
		(34) 2,3-seco-lup-20(29)-en-2,3-dioic acid	786-0	Kidney carcinoma	0.5 µM	[81]
			HT-29	Colon adenocarcinoma	2.9 µM	



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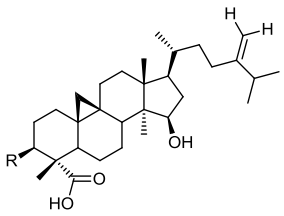
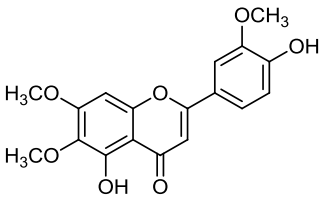


2 R = OH
3 R = O-β–D-Xylopyranoside



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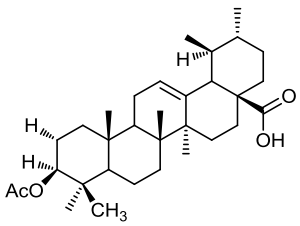

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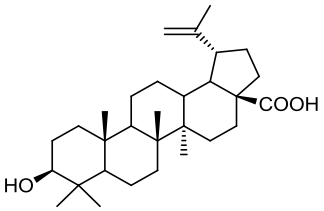

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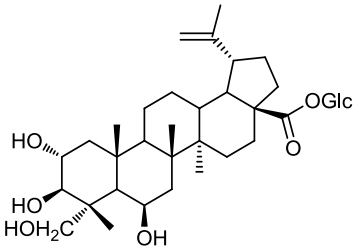

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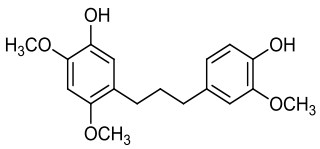

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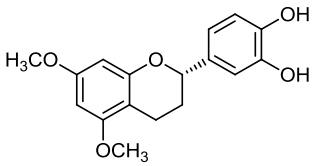

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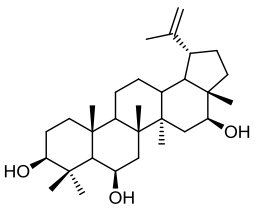

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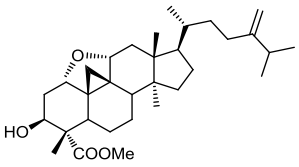

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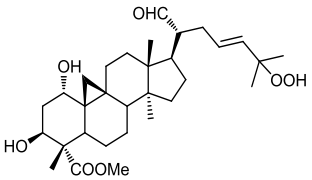

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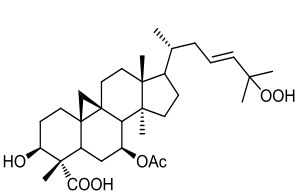

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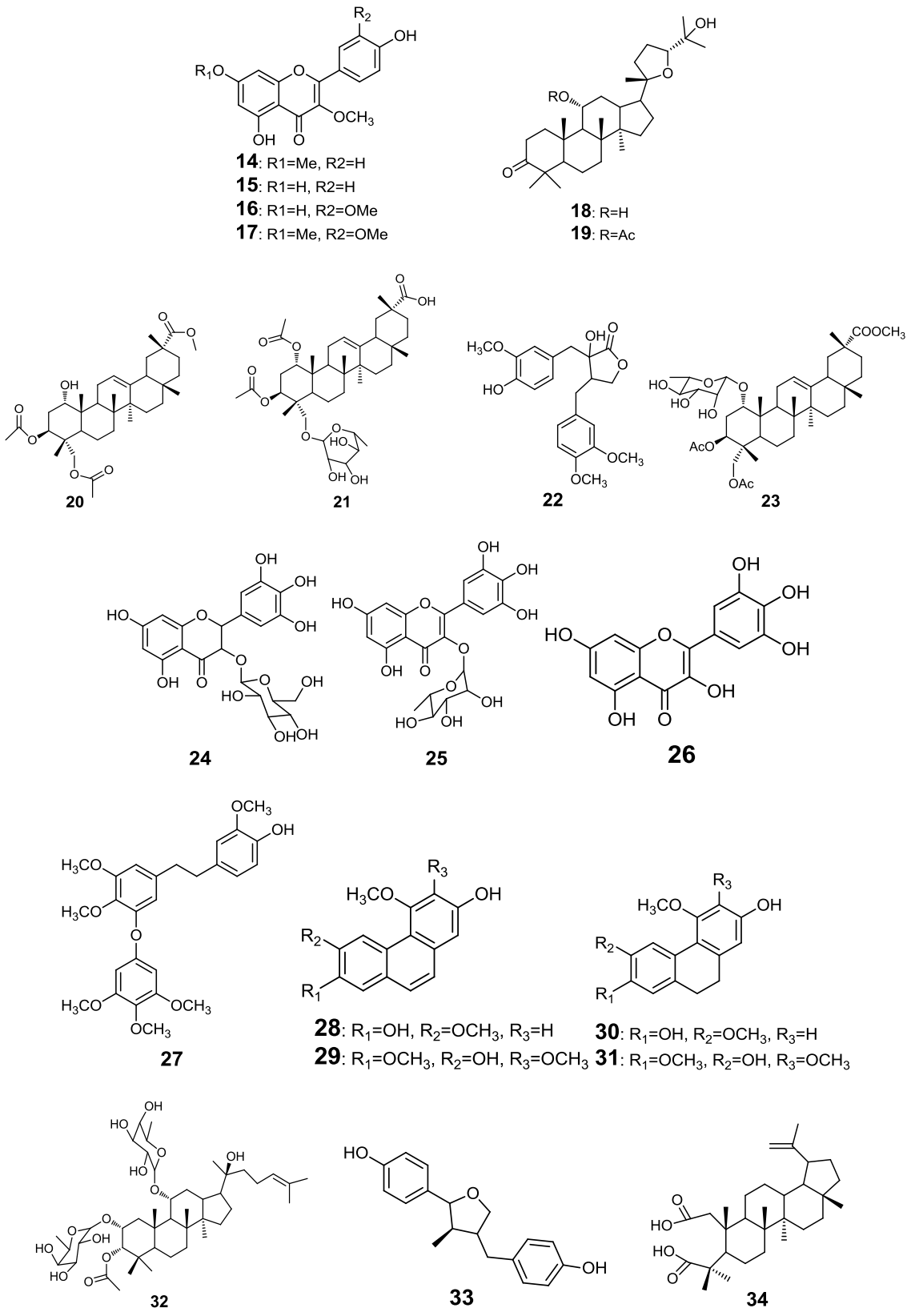

Fig. 1. Chemical structures of some important cytotoxic isolated compounds from *Combretum* species

The different numbers (1-34) correspond to the compound names in Table 2

4. CONCLUSION AND FUTURE PERSPECTIVES

In this review, we discussed the traditional uses of *Combretum* species reported in some ethnobotanical studies over the world with special emphasis on their anticancer uses. We also highlighted several pharmacological studies realized on *Combretum* species which revealed their cytotoxicity activities on various cancer cell models pointing out the anticancer potential of these plant species. Finally, some potential anticancer compounds isolated from *Combretum* species were reported as well. This proves that *Combretum* species could be an important resource for researchers to look for new anticancer molecules that may contribute to the fight against cancers. In perspectives, ethnobotanical studies must be undertaken on *Combretum* species especially the 12 *Combretum* species present in Burkina Faso to highlight their anticancer uses and correlate this finding to clinical efficacy which will be evaluated by controlled clinical studies.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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