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Review Article

Phytochemistry, traditional uses, and pharmacology of the genus *Ekebergia* (Meliaceae): A review

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ABSTRACT

Ekebergia (Meliaceae) is a genus of flowering shrubs and trees widely distributed in the African continent. It is represented by four species namely *E. capensis* Sparrm, *E. benguelensis* Welw. ex C.DC, *E. pterophylla* (C.DC.) Hofmeyr and *E. pumila* I.M.Johnst. The information for this review has been collected via a survey performed through several online libraries including the Plantlist, Jstor, Scifinder, PubMed, Google Scholar, Web of Science and Dictionary of Natural Products. So far, about 69 distinct compounds have been isolated during the previous phytochemical studies of *Ekebergia* genus plants. These compounds belong to diverse classes of metabolites such as limonoids, triterpenoids, coumarins, steroids, alkaloids, stilbenes and phenolic compounds. Some of these isolates displayed various bioactivities including antiplasmodial, antimicrobial, antiproliferative or uterotonic activities. This review covers the traditional uses, the phytochemical and pharmacological investigations of the genus *Ekebergia* over the last four decades (1980 to 2020).

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1. Introduction

Meliaceae is a family of about 53 plants genera and about 600 known species which are distributed throughout the tropical and subtropical zones around the world with only slight penetration into temperate zone (Christenhusz and Byng, 2016). The genus *Ekebergia* is endemic to Africa where its plant species are widely introduced in several preparations in tradition medicine for the treatment of diseases such as malaria, cancer, microbial and parasitic affections (Burkill, 1985; Ochwang'I et al., 2014; Tuasha et al., 2018). It is reported that only about 1% of the actual traditional medicines have been scientifically studied (Lambert et al., 1997). This observation supports the increasing interest in phytochemical and pharmaceutical investigations of the medicinal plants including the plants from the genus *Ekebergia* which are a good source for starting compounds in the process of new potent drug discovery. The first chemical exploration of the genus *Ekebergia* was reported earlier in 1981 by Taylor with the isolation of the limonoid ekebergin (**1**) from *E. Capensis* (Taylor, 1981). Three years later in 1984, came out the second series of limonoids from *E. pterophylla* comprising methylangolensate (**2**) and its derivatives (Taylor and Taylor, 1984). The high distribution and availability of the species *E. capensis* made it affordable for the local population and the most used in folk medicine. Several pharmacological investigations have been conducted on *E. capensis* and the results strongly supported its medicinal uses for the treatment of malaria and microbial diseases. Recently, a review has been published on ethnomedicinal uses, phytochemistry and pharmacological properties of *Ekebergia capensis* Sparrm (Maroyi, 2018). However, to the best of our knowledge, no comprehensive review has been done so far on the traditional uses, the chemistry and biology

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of the whole genus *Ekebergia*. therefore, we thought that in addition to the report of Maroyi on the species *E. capensis*, it would be useful to summarize the available information for the covered period from 1980 to 2020 for future works on the genus.

2. Methodology

A comprehensive literature survey has been done during preparation of this review. Indeed, information was searched using a number of online libraries including the Plantlist, Jstor, Scifinder, PubMed, Google Scholar, Web of Science and Dictionary of Natural Products. The research articles published were collected using the main keyword "*Ekebergia*", and without language restriction.

3. Description and distribution

Ekebergia is a genus of flowering shrubs and trees which are distributed throughout the African continent (Burrows et al., 2018). It has been revised in 1975 by Pennington and Styles and now consists into four species including *E. benguelensis* Welw. Ex C.DC, *E. capensis* Sparrm, *E. pterophylla* (C.DC.) Hofmeyr, and *E. pumila* I.M.Johnst. Especially, *E. senegalensis* was considered conspecific with *E. capensis* (Mulholland et al., 1997). However, the online library theplantlist.org revealed that except *E. pumila*, the three other plant species have a total of twenty-five synonyms in the literature (Table 1) including seven synonyms for *E. benguelensis*, seventeen for *E. capensis* and one for *E. pterophylla*. The *Ekebergia* plant species are characterized by their simple hairs, with pale green blades and their unisexual flowers containing stamens bound to the top. Their leaves are alternate or tight at the end of the branches, while their fleshy and succulent fruits are sub globular with a width between 10 and 20 mm. The height of the trees varies between 6 and 15 m with a trunk diameter of 100 cm (Troupin, 1982). Although, *E. capensis* is the sole species found in Cameroon and locally called henga by the Baya (Maroyi, 2018), it is encountered across the African continent from West to South in several countries including Senegal, Ivory Coast, Togo, Nigeria, Equatorial Guinea, Gambia, Uganda, Botswana, Kenya and South Africa (Arbonier, 2004). The species *E. benguelensis* is widely distributed in Tanzanie, Zimbabwe, Burundi Rwanda, DR Congo, Angola, Mozambique and Botswana (Drummond, 1981; Burrows et al., 2018), whereas *E. pterophylla* is present in South Africa, Botswana, Malawi, Swaziland, Zimbabwe, Mozambi, Zambi, Namibi (Schmidt et al., 2002).

Table 1
List of accepted *Ekebergia* species and their synonyms.

Accepted names	Synonyms
Ekebergia benguelensis Welw. ex C.DC	*Ekebergia arborea* Baker f.
	Ekebergia discolor O.Hoffm.
	Ekebergia fruticosa C.DC.
	Ekebergia nana Harms
	Ekebergia sclerophylla Harms
	Ekebergia velutina Dunkley
	Ekebergia welwitschii Hiern ex C.DC.
Ekebergia capensis Sparrm.	*Charia chevalieri* C.DC.
	Charia indeniensis A.Chev.
	Ekebergia buchananii Harms
	Ekebergia chevalieri (C.DC.) Harms
	Ekebergia complanata Baker f.
	Ekebergia holtzii Harms
	Ekebergia indeniensis (A.Chev.) Harms ex Engl.
	Ekebergia meyeri C.Presl ex C.DC.
	Ekebergia mildbraedii Harms
	Ekebergia petitiana A.Rich.
	Ekebergia ruppeliana (Fresen.) A.Rich.
	Ekebergia senegalensis Fuss
	Ekebergia senegalensis var. coriacea C.DC.
	Ekebergia senegalensis var. parvifoliola C.DC.
	Polyscias lepidota Chiov.
	Trichilia capensis (Sparrm.) Pers.
	Trichilia ekebergia E. Mey. ex Sond.

Table 1 (continued)

Accepted names	Synonyms
Ekebergia pterophylla (C.DC.) Hofmeyr	*Trichilia pterophylla* C. DC.
Ekebergia pumila I.M.Johnst.	Not indicated

4. Traditional uses

The literature reports *E. capensis* as the most used plant species in African traditional medicine for the treatment of several illnesses. Its preparations are prescribed in case of fever and malaria (Aladesanmi et al., 2007; Muregi at al., 2004; Opio et al., 2017; Suleman et al., 2018), cancer (breast, skin, and throat) (Ochwang'I et al., 2014; Williams et al., 2013), respiratory problems (chest pains, cold, cough, respiratory complaints, and runny nose) (Sewram et al., 2000; York et al., 2011; Zerabruk and Yirga, 2012; Meragiaw et al., 2016), heart problems (heartburn and heart problems), parasitic worms (intestinal worms) (Schmidt et al., 2002; Van Wyk et al., 2013), anthrax infection, blood purifier and pressure, liver complaints (Duncan et al., 1999), gastrointestinal problems (diarrhea, dysentery, gastritis, and stomach ache) (Mulaudzi et al., 2013; Meragiaw et al., 2016; Opio et al., 2017; Tuasha et al, 2018), reproductive problems (induce labor, infertility, menstrual problems, and ovarian cyst) (Sewram et al., 2000; Jiofack et al., 2010), skin diseases (abscesses, acne, boils, scabies, and skin rash) (Rabe and Van Staden, 1997; Schmidt et al., 2002; Getaneh and Girma, 2014), venereal diseases (Gachatchi, 2007; Mulaudzi et al., 2013). The bark maceration of *E. capensis* and Diospyros lycioides is taken in case of blood in feces (Arnold and Gulumian, 1984), while infusion of *E. capensis* bark and *Euclea natalensis* root are drunken for cough, heartburn and respiratory problems (chest pains, cold, cough, respiratory complaints, and runny nose) (Maroyi, 2018). Additionally, *E. benguelensis* is reported to be used for the management of malaria, painful menstruation, abdominal pain and pneumonia (Chavez et al., 2001). The potency of these plants in treatment of several diseases is related to their active constituents presented in their extracts and which possess a large structural diversity.

5. Chemical constituents

The chemical investigations of *E. capensis* seeds by David Taylor (1981) was the beginning of a long journey of exploration of the genus *Ekebergia* for its constituents. Four decades later, an important number of compounds belonging to different classes of natural products have been reported from seeds, leaves, barks and roots of *Ekebergia* plant species. As expected in the Meliaceae family, limonoids were the most important class of metabolites consisting to 30.98% of total reported metabolites from the genus, followed by triterpenoids and coumarins accounting for 26.76% and 16.90%, respectively (Fig. 1). Collectively, these three classes of compounds might be considered as chemotaxonomic markers of the genus. Furthermore, 7 steroids (9.9%), 2 alkaloids (2.8%), 4 stilbenes (5.6%) and 5 other phenolic compounds (7.0%) were previously reported from *Ekebergia* species (Table 2). A similar study was also carried out to identify the rate of chemical investigations of each plant species in terms of the number of reported specialized compounds. The results revealed that *E. capensis* (also known as *E. senegalensis*) was the most investigated plant species with a total of 54 compounds (68.3%), followed by 18 compounds counting for 22.8% reported from *E. pterophylla*. The less investigated species was *E. benguelensis* with 7 reported compounds counting for 8.9%. However, no compounds have been reported from the species *E. pumila*, which may indicate that the species is not yet investigated so far. Furthermore, the chemical investigations reported on *Ekebergia* genus indicated that the different organs of plant material (leaves, bark, root, seeds) have been extracted with organic solvents either by maceration at room temperature or with heating in a Soxhlet apparatus to afford the crude extracts which were further purified using the common

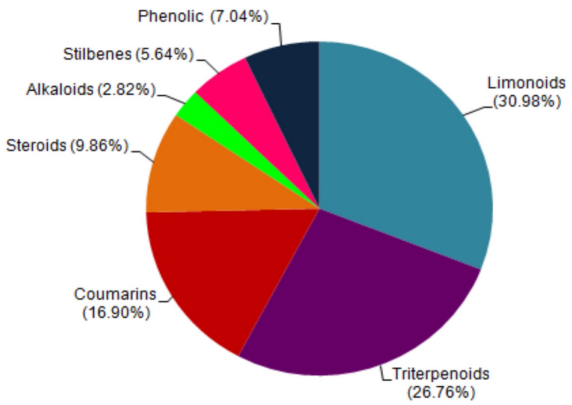

Fig. 1. The distribution by classes of compounds isolated from the genus *Ekebergia*.

Table 2
Chemical constituents isolated from the genus *Ekebergia*.

Class of compounds	N°	Name	Organ	Source	Reference
Limonoids	1	Ekebergin	S	*E. capensis*	Kehrli et al., 1990; Mullholand and Iourine 1998; Taylor, 1981; Taylor and Taylor 1984
				E. pterophylla	
	1a	3-Ketoekebergin*			Taylor, 1981
	1b	Ekebergin acetate*			Taylor, 1981
	2	Methylangolensate	S	*E. capensis*	Kehrli et al., 1990; Mullholand and Iourine, 1998; Taylor, 1981; Taylor and Taylor 1984
				E. pterophylla	
	3	Methyl-3a-hydrox-3-deoxyangolensate	S	*E. capensis*	Mullholand and Iourine, 1998
	4	2-Acetyl-15-deacetylekebergin	S	*E. pterophylla*	Taylor and Taylor, 1984
	5	EP2	S	*E. pterophylla*	Kehrli et al., 1990
	6	2-Aacetylekebergin	S	*E. pterophylla*	Taylor and Taylor, 1984
	7	3a,15b-diacetoxy-3-dihydromethyl angolensate	S	*E. pterophylla*	Taylor and Taylor, 1984
	8	15-deacetylekergin-2-tiglate	S	*E. pterophylla*	Kehrli et al., 1990
	9	15-deacetylekebergin	S	*E. pterophylla*	Kehrli et al., 1990
	10	EP4	S	*E. pterophylla*	Kehrli et al., 1990
	11a	Capensolactone 3	S	*E. capensis*	Mullholand and Iourine, 1998
	11b				
	12a	Capensolactone 2	S	*E. capensis*	Mullholand and Iourine, 1998
	12b				
	13	Capensolactone 1	S	*E. capensis*	Mullholand and Iourine, 1998
	14	EP5	S	*E. pterophylla*	Murata et al., 2008
	15	Ekeberin C1	SB	*E. capensis*	Murata et al., 2008
	16	7-Deacetoxy-7-oxogedunin	SB	*E. capensis*	Murata et al., 2008
	17	7-Acetylneotrichilenone	SB	*E. capensis*	Murata et al., 2008
	18	Ekeberin C2	SB	*E. capensis*	Murata et al., 2008
	19	Ekeberin C3	SB	*E. capensis*	Murata et al., 2008
	20	Proceranolide	L	*E. capensis*	Irungu et al., 2014
	21	Mexicanolide	SB	*E. capensis*	Murata et al., 2008
	22	Swietenolide	SB	*E. capensis*	Murata et al., 2008
Acyclic triterpenoids	23	2,3,22,23-Tetrahydroxy-2,6,10,15,19,23-hexamethyl-6,10,14,18-tetracosatetraene (3R,22R)	SB	*E. capensis*	Jonker et al. 1997; Nishiyama et al., 1996, 1999; Sewram et al., 2000; Murata et al., 2008; Kemayou et al., 2020;
				E. senegalensis	
	24	2-Hydroxymethyl-2,3,22,23-tetrahydroxy-2,6,10,15,19,23-hexamethyl-6,10,14,18-tetracosatetraene (2R,3R,22R)	SB	*E. capensis*	Jonker et al., 1997; Kemayou et al., 2020; Murata et al., 2008; Nishiyama et al., 1996, 1999
				E. senegalensis	
	25	Ekeberin D1	SB	*E. capensis*	Murata et al., 2008
	26	Ekeberin D5	SB	*E. capensis*	Murata et al., 2008
	27	Ekeberin D2	SB	*E. capensis*	Murata et al., 2008
	28	Ekeberin D3	SB	*E. capensis*	Murata et al., 2008
	29	Ekeberin D4	SB	*E. capensis*	Murata et al., 2008
Cyclic triterpenoids	30	β-Amyrin	SB	*E. pterophylla*	Mulholland et al., 1998
	31	β-Amyrone	SB	*E. pterophylla*	Mulholland et al., 1998
	32	3-*epi*-Oleanolic acid	SB	*E. capensis*	Sewram et al., 2000

Table 2 (continued)

Class of compounds	N°	Name	Organ	Source	Reference
	33	Oleanonic acid	SB	*E. capensis*	Kemayou et al., 2020; Mulholland et al., 1997; Murata et al., 2008; Nishiyama et al., 1996; Sewram et al., 2000
Cyclic triterpenoids	30	β-Amyrin	SB	*E. pterophylla*	Mulholland et al., 1998
	31	β-Amyrone	SB	*E. pterophylla*	Mulholland et al., 1998
	32	3-*epi*-Oleanolic acid	SB	*E. capensis*	Sewram et al., 2000
	33	Oleanonic acid	SB	*E. capensis*	Kemayou et al., 2020; Mulholland et al., 1997; Murata et al., 2008; Nishiyama et al., 1996; Sewram et al., 2000
			W	*E. pterophylla*	
	34	Oleanolic acid	SB	*E. capensis*	Kemayou et al., 2020; Mulholland et al., 1997; Murata et al., 2008; Nishiyama et al., 1996; Sewram et al., 2000
	35	Melliferone	SB	*E. capensis*	Murata et al., 2008
	36	3-oxo-12β-Hydroxy-oleanan-28,13β-olide	SB	*E. capensis*	Irungu et al., 2014
	37	3,11-Dioxo-olean-12-en-28-oic acid	SB	*E. capensis*	Murata et al., 2008
	38	3-oxo-11,13(18)-Oleandien-28-oic acid	SB	*E. capensis*	Murata et al., 2008
	39	Ekeberin A	SB	*E. capensis*	Murata et al., 2008; Irungu et al., 2014
	40	Lupeol	SB	*E. pterophylla*	Kemayou et al., 2020; Mulholland et al., 1997, 1998
				E. capensis	
				E. senegalensis	
	41	Betulinic acid	RB	*E. benguelensis*	Chavez et al., 2001
Coumarins	42	Pterophyllin 1	SB	*E. pterophylla*	Mulholland et al., 1998
	43	Pterophyllin 2	SB	*E. pterophylla*	Mulholland et al., 1998
	44	Pterophyllin 3	W	*E. pterophylla*	Mulholland et al., 1998
	45	Pterophyllin 4	W	*E. pterophylla*	Mulholland et al., 1998
	46	Pterophyllin 5	W	*E. pterophylla*	Mulholland et al., 1998
	47	Xanthoxyletin	SB	*E. senegalensis*	Lontsi et al., 1985
	48	7-Hydroxy-6-methoxycoumarin	SB	*E. senegalensis*	Kemayou et al., 2020
	49	5-Hydroxymethyl-4-methoxycoumarin	SB	*E. benguelensis*	Jonker et al., 1997
	50	4,6-Dimethoxy-5-methylcoumarin	SB	*E. senegalensis*	Kemayou et al., 2020; Murata et al., 2008
				E. capensis	
	51	Ekersenin (pereflorin)	SB	*E. capensis*	Bevan et al., 1965; Lontsi et al., 1985; Murata et al., 2008; Mulholland et al., 1997
				E. senegalensis	
	52	6-Hydroxy-4-methoxy-5-methylcoumarin	SB	*E. senegalensis*	Kemayou et al., 2020
	53	5-(4-Hydroxyphenethenyl)-4,7-dimethoxycoumarin	RB	*E. benguelensis*	Chavez et al., 2001
Steroids	54	β-Sitosterol	W	*E. pterophylla*	Kemayou et al., 2020; Mulholland et al., 1997, 1998;
			SB	*E. capensis*	
			SB	*E. senegalensis*	
	55	β-Sitosterol acetate	W	*E. pterophylla*	Mulholland et al., 1997, 1998
			SB	*E. capensis*	

Table 2 (continued)

Class of compounds	N°	Name	Organ	Source	Reference
	56	β-Sitosterol palmitate	SB	*E. capensis*	Mulholland et al., 1997
	57	β-Sitosterol oleate	SB	*E. capensis*	Mulholland et al., 1997
	58	Stigmasterol	SB	*E. capensis* *E. senegalensis*	Kemayou et al., 2020; Mulholland et al., 1997
	59	(Z)-Volkendousin	SB	*E. capensis*	Murata et al., 2008
	60	Ekeberin B	SB	*E. capensis*	Murata et al., 2008
Alkaloids	61	Ekeberginine	SB	*E. senegalensis*	Lontsi et al., 1985
	62	N-Methylekeberginine	SB	*E. senegalensis*	Lontsi et al., 1985
Stilbenes	63	5-[(1*E*)-2-(4-Hydroxyphenyl) ethenyl]-4,7-dimethoxy-3-methyl-2*H*-1-benzopyran-2-one	RB	*E. benguelensis*	Chavez et al., 2001
	64	5-[(1*E*)-2-(4β-D-Lucopyranosyloxyphenyl)]-4,7-dimethoxy-3-methyl-2*H*-1-benzopyran-2-one	RB	*E. benguelensis*	Chavez et al., 2001
	65	1-{2-Hydroxy-6-[(1*E*)-2-(4-hydroxyphenyl)ethenyl]-4-methoxyphenyl}-2-methyl-1-propanone	RB	*E. benguelensis*	Chavez et al., 2001
	66	1-{2,4-Dihydroxy-6-[(1*E*)-2-(4-hydroxyphenyl) ethenyl]-phenyl}-2-methyl-1-propanone	RB	*E. benguelensis*	Chavez et al., 2001
Phenolic compounds	67	Kaempferol-3-*O*-β-D-glucopyranoside	L	*E. capensis*	Irungu et al., 2014
	68	Quercetin-3-*O*-β-D-glucopyranoside	L	*E. capensis*	Irungu et al., 2014
	69	Methyl-2,4-dihydroxy-3,6-dimethylbenzoate (atraric acid)	SB	*E. pterophylla*	Mulholland et al., 1998
	70	4-Hydroxy-3,5-dimethylbenzoic acid	SB	*E. senegalensis*	Kemayou et al., 2020
	71	Senegalin	SB	*E. senegalensis*	Kemayou et al., 2020

(*): Hemisynthetic derivatives, S: seed, SB: stem bark, L: leaves, W: wood, RB: root bark.

techniques of isolation including, liquid-liquid partition, column chromatography on silica gel, sephadex LH20 (both monitored by TLC or LCMS), prep-TLC, prep-HPLC and recrystallization to obtained the pure compounds. The structures of these isolated compounds were determined by exploring their spectroscopic and spectrometric data including 1D and 2D NMR, mass spectrometry, IR, UV, CD, melting point, optical rotation, X-ray crystallography, chemical transformations like oxidation (Taylor, 1981), acetylation (Taylor, 1981; Nishiyama et al., 1996) or the modified Mosher's method (Nishiyama et al., 1999), as well as by the comparison of their data with those reported in the literature.

5.1. Limonoids

It is well reported that limonoids are major compounds encountered in the plants of the Meliaceae, Rutaceae and Simaroubaceae family (Happi et al., 2018). They are also called meliacins and consist in highly oxygenated C-26 tetranortriterpenes which have a β-substitued C-17 furan ring (Tan and Luo, 2011). So far, the chemical investigations of the genus *Ekebergia* led to the isolation of 22 limonoids (Fig. 2) sorted into five classes including: andirobin-class limonoids (**1**-**9**), trijugin-class limonoids (**10**-**14**), gedunin-class limonoids (**15** and **16**), azadirone-class limonoid (**17**) and mexicanolide-class limonoids (**18**-**22**). It is important to indicate that the most of the limonoids in the genus *Ekebergia* was isolated from the seeds and only some rare limonoids were found in the other parts of the plants (leaves or bark). The limonoid ekebergin (**1**) was reported from the seeds of *E. capensis* (Taylor, 1981). It belongs to the andirobin-class of limonoids identified by their rings B,D-seco (Happi et al., 2018). In order to confirm the structure of 1, its oxidation was performed using Jones reagent and gave the corresponding ketone (**1a**), while its acetylation gave compound **1b** (Taylor,

1981). Additional derivatives from ekebergin (**1**) have been reported later and their structures were characterized as 2-acetyl-15-deacetylekebergin (**4**), 2-acetylekebergin (**6**), 15-deacetylekergin 2-tiglate (**8**), and 15-deacetylekebergin (**9**) (Taylor and Taylor, 1984; Kehrli et al., 1990). The well-known limonoid methylangolensate (**2**) was isolated for the first time in the genus *Ekebergia* from the seeds of *E. capensis* by Taylor (1981). Later, during other chemical investigations, it was reported along with its derivatives methyl-3α-hydrox-3-deoxyangolensate (**3**), 3α,15β-diacetoxy-3-dihydromethylangolensate (**7**) and EP2 (**5**) (Taylor and Taylor, 1984; Kehrli et al., 1990). A series of rings B,C,D-seco group limonoids (trijugin-class limonoids) was obtained from the seeds of *E. pterophylla* and this includes EP4 (**10**), EP5 (**14**), capensolactone 1 (**13**) and the position isomers capensolactones 2 (**12a**/**12b**) and 3 (**11a**/**11b**) (Kehrli et al., 1990; Mulholland and Iourine, 1998). The chemical exploration of the methanol stem bark extract of *E. capensis* by Murata and co-workers led to the isolation of one azadirone-class limonoid 7-acetylneotrichilenone (**17**) with intact rings, as well as two gedunin-class limonoids namely ekeberin C1 (**15**), 7-deacetoxy-7-oxogedunin (**16**) identified by their ring D-seco (Murata et al., 2008). Furthermore, the literature survey indicates that ekeberin C2 (**18**), ekeberin C3 (**19**), mexicanolide (**21**) and swietenolide (**22**) are mexicanolide-class limonoids isolated from the stem bark from *E. capensis* (Murata et al., 2008), while proceranolide (**20**) has been isolated from the leaves of the same species (Irungu et al., 2014).

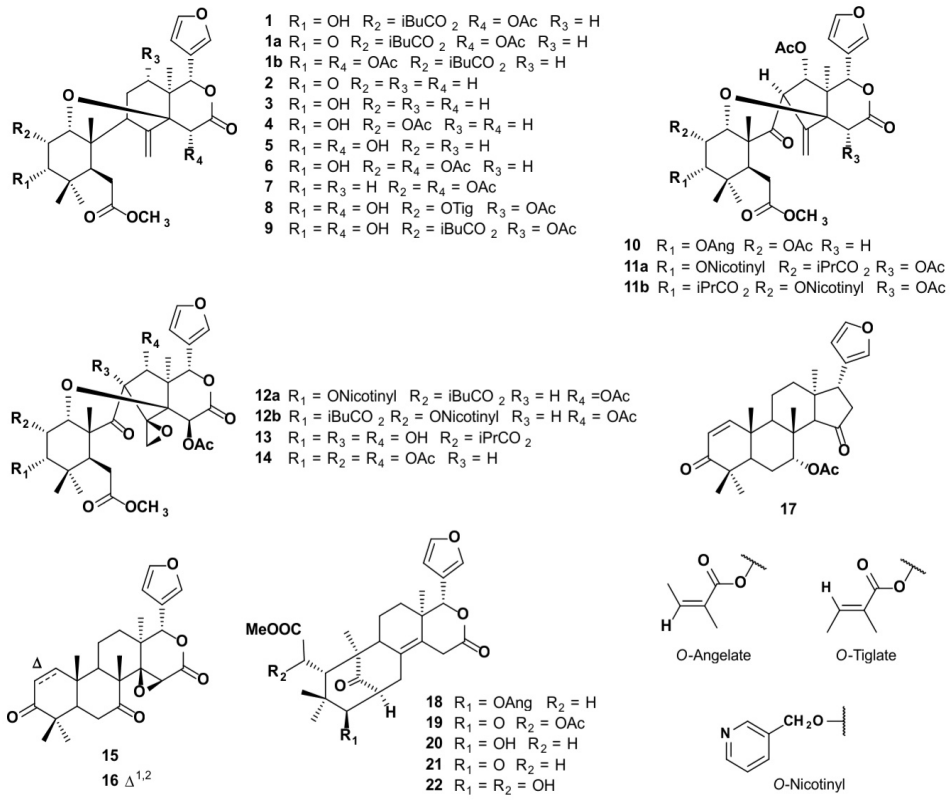

Fig. 2. Limonoids 1-22 from *Ekebergia* species.

5.2. Triterpenoids

Since 1965, studies carried out on the genus *Ekebergia* have led to isolation of 19 triterpenoids (Table 2) classified into two groups: seven acyclic triterpenes (**23**-**29**, Fig. 3) and twelve pentacyclic triterpenes (**30**-**41**, Fig. 4). Acyclic triterpenes also described as the squalene-group triterpenes are particularly characteristic of the species *E. capensis* from which they have been mostly reported and can be considered as the chemomarkers of the species. The two compounds, namely 2,3,22,23-tetrahydroxy-2,6,10,15,19,23-hexamethyl-6,10,14,18-tetracosatetraene (3R,22R) (**23**) and 2-hydroxymethyl-2,3,22,23-tetrahydroxy-2,6,10,15,19,23-hexamethyl-6,10,14,18-tetracosatetraene (2R,3R,22R) (**24**) were isolated from the dried bark of *E. capensis* (Nishiyama et al., 1996). Their conventional acetylation was carried out in order to determine the position of the hydroxyl groups through their carbon skeleton. The reaction of compound **23** gave its mono and diacetylated derivatives while compound **24** gave its three derivatives (mono, di and tri-) acetylated (Nishiyama et al., 1996). Their absolute configuration was determined later by modified Mosher's method (Nishiyama et al., 1999). Recently, Kemayou and co-workers isolated again compounds **23**

and **24** from the stem bark of *E. senegalensis* (Kemayou et al., 2020). This result was in agreement with the new classification of *E. senegalensis* as conspecific with *E. capensis* (Mulholland et al., 1997). Moreover, the acyclic triterpenes ekeberins D1-D5 (**25**-**29**) were obtained from the stem bark of *E. capensis* (Murata et al., 2008). Among the pentacyclic triterpenes isolated from the genus *Ekebergia*, β-amyrin (**30**) and β-amyrone (**31**) have been isolated from the stem bark from *E. pterophyllia* (Mulholland et al., 1998), oleanonic acid (**33**), oleanolic acid (**34**) and lupeol (**40**) were obtained during the investigations of *E. capensis* and *E. senegalensis* (Nishiyama et al., 1996; Mulholland et al., 1997; Sewram et al., 2000; Murata et al., 2008; Irungu et al., 2014; Kemayou et al., 2020), while 3-*epi*-oleanolic acid (**32**), melliferone (**35**), 3-oxo-12β-Hydroxy-oleanan-28,13β-olide (**36**), 3,11-dioxo-olean-12-en-28-oic acid (**37**), 3-oxo-11,13(18)-oleandien-28-oic acid (**38**) and ekeberin A (**39**) were also reported from the stem bark of *E. capensis* (Murata et al., 2008; Irungu et al., 2014). Finally, betulinic acid (**41**) was obtained from the root bark of *E. benguelensis* (Chavez et al., 2001).

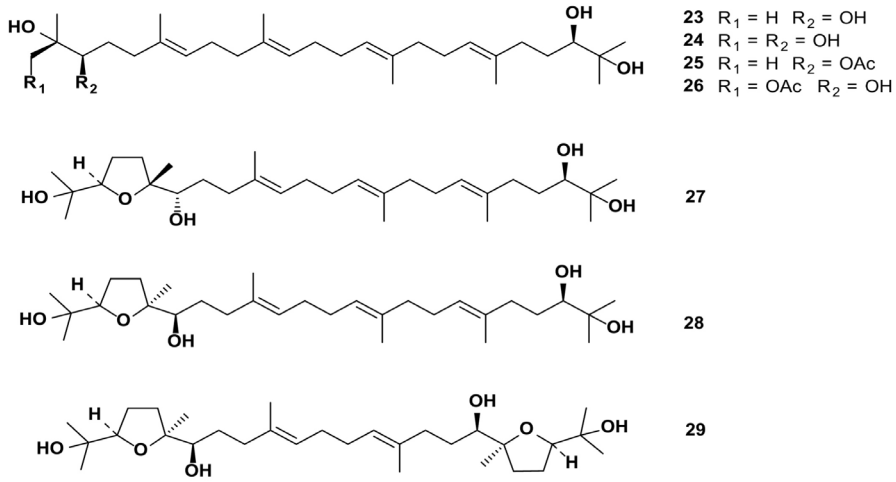

Fig. 3. Acyclic triterpenoids **23**-**29** from *Ekebergia* species.

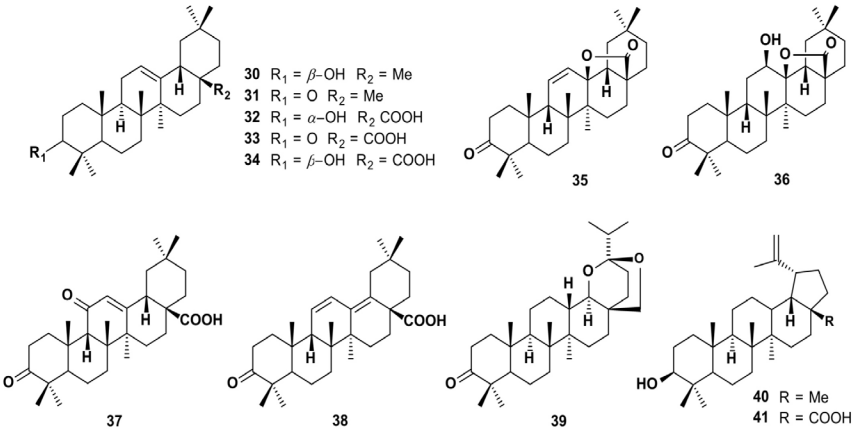

Fig. 4. Pentacyclic triterpenoids **30**-**41** from *Ekebergia* species.

5.3. Coumarins

These are natural organic aromatic substances known in the international nomenclature as 2H-1-benzopyrane-2-one. They can be considered as lactones of 2-hydroxy-Z-cinnamic acid (George and Clark, 1995; Bruneton, 1999). Twelve coumarins (**42**-**53**, Fig. 5) were isolated from *Ekebergia* species, mostly from the stem bark as compared to the other parts of the plant. Ekersenin also called pereflorin or 4-methoxy-5-methylcoumarin (**51**) is the first coumarin isolated from this genus earlier in 1965 by Bevan et al. from *E. senegalensis* (Bevan et al., 1965). Later, from the same species, a second coumarin xanthoxyletin (**47**) was obtained by Lontsi and co-workers (Lontsi et al., 1985). Pterophyllins 1-3 (**42**-**44**) were isolated from the stem bark of *E. pterophylla* while pterophyllins 4 and 5 (**45** and **46**) from the wood of same species (Mulholland et al., 1998). Three coumarins namely 7-hydroxy-6-methoxycoumarin (**48**), 4,6-dimethoxy-5-methylcoumarin (**50**) and 6-hydroxy-4-methoxy-5-methylcoumarin (**52**) have also been isolated and characterized during various phytochemical investigations on *E. senegalensis* (Murata et al., 2008; Kemayou et al., 2020).

Finally, the two coumarins 5-hydroxymethyl-4-methoxycoumarin (**49**) and 5-(4-hydroxyphenethenyl)-4,7-dimethoxycoumarin (**53**) were isolated from *E. benguelensis* (Jonker et al., 1997; Chavez et al., 2001).

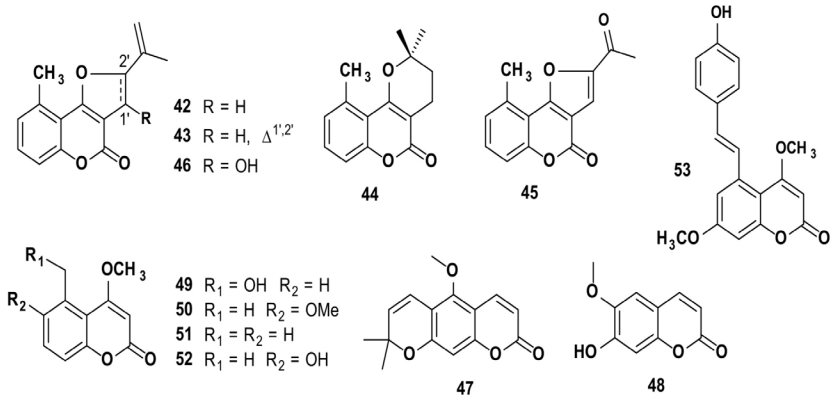

Fig. 5. Coumarins **42**-**53** from *Ekebergia* species.

5.4. Steroids

The steroids are one of the most distributed classes of specialized compounds in the higher plants. They are biosynthetically formed from the same precursor as triterpenes and are considered as tetracyclic triterpenes which have lost at least three or four methyl groups (Bruneton, 1999). During the chemical examinations of the *Ekebergia* plant species, a total of seven steroids (**54**-**60**, Fig. 6) have been isolated and consisted into five stigmastane-type steroids viz β-sitosterol (**54**), β-sitosterol acetate (**55**), β-sitosterol palmitate (**56**), β-sitosterol oleate (**57**) and stigmasterol (**58**) (Mulholland et al., 1997; Kemayou et al., 2020), as well as two pregnane-type steroids including (Z)-volkendousin (**59**) and ekeberin B (**60**) (Murata et al., 2008).

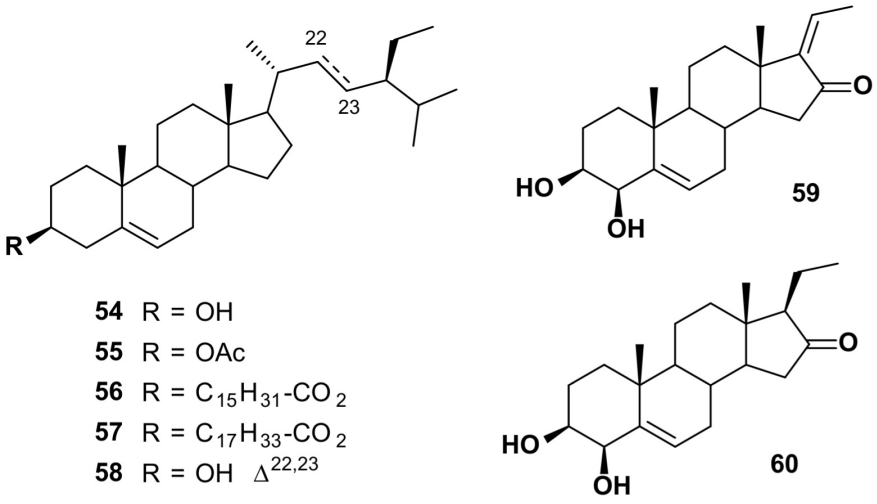

Fig. 6. Steroids **54**-**60** from *Ekebergia* species.

5.5. Alkaloids and stilbenes

Two alkaloids including one carbazole alkaloid ekeberginine (**61**) and its derivative N-methylekeberginine (**62**) (Fig. 7) have been isolated and characterized from *E. senegalensis* by Lontsi et al. (Lontsi et al., 1985). Furthermore, four stilbenes (**63**-**66**, Fig. 8) were isolated of the stem bark of *E. benguelensis* and identified as 5-[(1E)-2-(4-hydroxyphenyl)ethenyl]-4,7-dimethoxy-3-methyl-2H-1-benzopyran-2-one (**63**), 5-[(1E)-2-(4β-D-glucopyranosyloxyphenyl)ethenyl]-4,7-dimethoxy-3-methyl-2H-1-benzopyran-2-one (**64**), 1-{2-hydroxy-6-[(1E)-2-(4-hydroxyphenyl)ethenyl]-4-methoxyphenyl}-2-methyl-1-propanone (**65**) and 1-{2,4-dihydroxy-6-[(1E)-2-(4-hydroxyphenyl)ethenyl]-phenyl}-2-methyl-1-propanone (**66**) (Chavez et al., 2001).

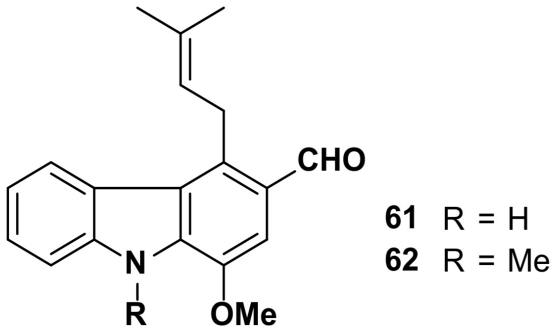

Fig. 7. Alkaloids **61**-**62** from *Ekebergia* species.

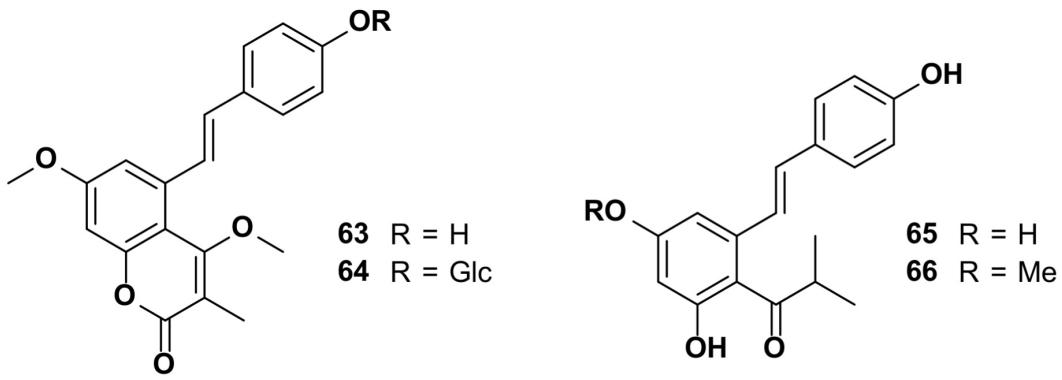

Fig. 8. Stilbenes **63**-**66** from *Ekebergia* species.

5.6. Other phenolic compounds

Two flavonoids (Fig. 9) called kaempferol-3-*O*-β-D-glucopyranoside (**67**) and quercetin-3-*O*-β-D-glucopyranoside (**68**) were isolated from the leaves from *E. capensis* (Irungu et al., 2014). Atraric acid also called methyl 2,4-dihydroxy-3,6-dimethylbenzoate (**69**) and 4-hydroxy-3,5-dimethylbenzoic acid (**70**) were isolated from the stem bark of *E. pterophylla* (Mulholland et al., 1997, 1998) and *E. senegalensis*, respectively (Mulholland et al., 1997; Kemayou et al., 2020). Recently, we reported for the first time, one phenylpropanoid named senegalin (**71**) from the stem bark of *E. senegalensis* (Kemayou et al., 2020).

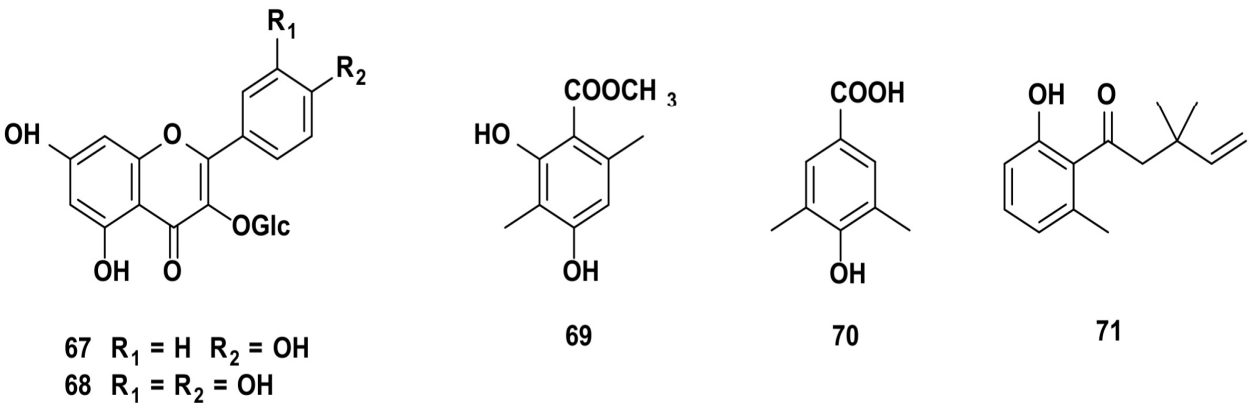

Fig. 9. Other phenolic compounds **67**-**71** from Ekebergia species.

6. Biological activities

Besides the phytochemical investigations of the genus *Ekebergia*, an important number of pharmacological works have been carried out on the crude extracts, fractions and some pure compounds isolated from *Ekebergia* plant species. As general observation, although a great part of biological investigations have been performed on plant extracts, it is important to notice that only eleven constituents of *Ekebergia* sp. (roughly 16% of all isolated compounds) have been evaluated for their biological potency.

6.1. Toxicity

The hexane seed extract of *E. capensis* as well as its limonoids capensolactones 2 and 1 (**12a**/**12b** and **13**) have been evaluated for their toxicity using the brine shrimp lethality test at the concentrations of 10 µg/mL, 100 µg/mL, and 1000 µg/mL. The authors reported that the extract and the tested compounds demonstrated moderate activities of 10% at the lowest concentration and 61-80% at the highest concentration (Mulholland and Iourine, 1998).

6.2. Antiprotozoal

Ekeberin C1 (**15**) and 2-hydroxymethyl-2,3,22,23-tetrahydroxy-2,6,10,15,19,23-hexamethyl-6,10,14,18-tetracosatetraene (**24**) isolated from the stem bark of *E. capensis* showed good antiplasmodial activities with IC_{50} values of 6 µM and 7 µM, respectively, against the chloroquine-sensitive strain of Plasmodium falciparum FCR-3, while ekeberin D4 (**29**) showed moderate activities with IC_{50} values of 40 µM against the same strain. Additionally, the acyclic triterpenoid 2-hydroxymethyl-2,3,22,23-tetrahydroxy-2,6,10,15,19,23-hexamethyl-6,10,14,18-tetracosatetraene (**24**) was evaluated for its *in vivo* antimalarial activity in mice using the chloroquine-sensitive *P. berghei* NK 65. Each mouse received the test compound **24** at a dose of 100, 250, and 500 mg/kg body weight, once a day for 4 days using a metal catheter. The compound **24** at a dose of 500 mg/kg showed moderate parasitemia suppression of 52.9% against artificially induced chloroquine-sensitive *P. berghei* NK 65 (Murata et al. 2008). The dichloromethane/methanol (DCM/MeOH) (1:1) leaf and root extracts of *E. capensis*, as well as proceranolide (**20**), oleanonic acid (**33**), oleanolic acid (**34**) and quercetin-3-*O*-β-D-glucopyranoside (**68**) exhibited moderate antiplasmodial activity against the chloroquine sensitive *P. falciparum* D6 and the chloroquine-resistant *P. falciparum* W2 with IC_{50} values ranging from 18.2 µM to 84.7 µM (Irungu et al., 2014). Koch et al. (2005) evaluated antimalarial activities of inner bark extracts of *E. capensis* against a chloroquine-sensitive *P. falciparum* D6 using a semi-automated microdilution technique. The extract showed good activity with an IC_{50} value of 3.97 µg/mL (Koch et al, 2005). Furthermore, the aqueous, dichloromethane and DCM/MeOH (1:1) fruit and twigs extracts of *E. capensis* were assessed for their antiplasmodial activity against the chloroquine-sensitive strain *P. falciparum* D10 using the parasite lactate dehydrogenase assay. The DCM/MeOH (1:1) fruit extract showed moderate activity, while DCM/MeOH (1:1) twigs extract showed weak activity with IC_{50} values of 10µg/mL and 18 µg/mL, respectively (Koch et al., 2005). The antiplasmodial activities of hexane, chloroform, ethyl acetate and methanol leaves extracts of *E. capensis* were evaluated using the [^{3}H] hypoxanthine incorporation assay using the chloroquine sensitive strain *P. falciparum* K39 and resistant strain *P. falciparum* ENT30 as the test organisms. The hexane extract exhibited no antiplasmodial activity, but the chloroform, ethyl acetate, methanol and water extracts gave good IC_{50} values (< 5 µg/mL) suggesting semi-polar and polar fractions of *E. capensis* possess a high *in vitro* antiplasmodial activities (Muregi et al., 2004). Mokaka and co-workers conducted a series of antiprotozoal tests with different extracts of *E. capensis*. Thus, in antitrypanosomal activity, the dichloromethane/methanol (1:1) root extracts of *E. capensis* showed a good potency of IC_{50} value of (1.36 ± 0.85) µg/mL against Trypanosoma brucei rhodesiense (STIB900), as well as a moderate and weak potency against *Leishmania donovani* (MHOM/ET/67/L82) and *Trypanosoma cruzi* (Tulahuen) with IC_{50} values of (6.42 ± 2.59) µg/mL and (17.40 ± 2.78) µg/mL, respectively (Mokaka et al., 2013).

6.3. Antimicrobial

Recently, the isolated compounds from *E. senegalensis* were evaluated for their antibacterial activity on a panel of five bacterial strains including Escherichia coli (DSMZ 1058), Bacillus subtilis (DSMZ 704), Pseudomonas agarici (DSMZ 11810) and Micrococcus luteus (DSMZ 1605). Gentamycin was used as positive control. The results showed that only the coumarin 4,6-dimethoxy-5-methylcoumarin (**50**) and the triterpene 2-hydroxymethyl-2,3,22,23-tetrahydroxy-2,6,10,15,19,23-hexamethyl-6,10,14,18-tetracosatetraene (**24**) at a concentration of 0.5 mg/mL displayed a weak inhibition on *B. subtilis* (ZOI: 8 mm for 50) and *M. luteus* (ZOI: 7 mm for 24) (Kemayou et al., 2020). Rabe and Van Staden evaluated antibacterial activities of water and methanol bark extracts of *E. capensis* against *Staphylococcus aureus*, *Staphylococcus epidermis*, *Bacillus subtilis*, *Escherichia coli*, and *Klebsiella pneumoniae* using the agar diffusion with neomycin as positive control. The extracts showed activities against *S. aureus*, *S. epidermis*, and *B. subtilis* with MIC values ranging from 2.0 mg/mL to 4.0 mg/mL (Getaneh and Girma, 2014). Moreover, the antibacterial activities of methanol leaf, root, and stem bark extracts of *E. senegalensis* were assessed against *B. subtilis*, *Es. coli*, *K. pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhi* and *S. aureus* using disc diffusion assay. The extracts showed activities with a zone of inhibition ranging from 5 mm to 23 mm and MIC value of 6.25 µg/mL (Ndukwe et al., 2006). The antibacterial properties of aqueous and DCM/MeOH (1:1) leaf extracts of *E. capensis* against

K. pneumoniae, *Moraxella catarrhalis*, *Mycobacterium smegmatis* and *S. aureus* using microdilution assay with ciprofloxacin as the positive control showed that the extracts possessed activities with MIC values ranging from 1.33 mg/mL to 16.0 mg/mL (York et al., 2012), while the antibacterial activities of the aqueous and DCM/MeOH (1:1) bark and leaf extracts of *E. capensis* using the microtiter plate dilution technique against dermatologically relevant pathogens such as *Bacillus agri*, *Propionibacterium acnes*, *Pseudomonas aeruginosa*, *S. aureus* and *S. epidermidis* with ciprofloxacin as the positive control led to the observation that the extracts showed activities with MIC values ranging from 0.38 mg/mL to >16.00 mg/mL (Mabona et al., 2013). In antimycobacterial assay, the acetone extract of *E. capensis* at the concentration of 0.5 mg/mL, against a drug-sensitive strain of *Mycobacterium tuberculosis* (H37Rv) using the agar plate method displayed potency with the MIC value of 0.1 mg/mL (Lall and Meyer, 1999). The DCM/MeOH (1:1) and methanol stem bark extracts of *E. capensis* were evaluated for their activity against one strain of *Mycoplasma mycoides* susp. capri, five strains of *Mycoplasma mycoides* susp. *mycoides* and one strain of *Mycoplasma capricolum* susp.capricolum using broth microdilution assays. All the extracts showed activities with MIC values ranging from 0.13 mg/mL to 0.15 mg/mL. These findings suggest that *E. capensis* contains phytochemical compounds that might be useful for the treatment and management of respiratory diseases in ruminants (Kama-Kama et al., 2016).

6.4. Anthelmintic

The anthelmintic activity of the crude aqueous and hydroalcoholic extracts of the seeds of *E. capensis* was evaluated on eggs and adults Haemonchus contortus. Both aqueous and hydroalcoholic extracts induced significant egg hatching inhibition with the aqueous extract requiring maximum concentration of 0.25 mg/mL to induce 100% egg hatch inhibition while the hydroalcoholic extracts did not induce complete inhibition at the highest concentration tested of 2 mg/mL. The aqueous extract induced 50% inhibition (ED_{50}) at 0.06 mg/mL while the ED_{50} value of hydroalcoholic extract was 1.03 mg/mL. After 24 h of exposure of adult *H. contortus* to different concentrations of plant extracts, hydroalcoholic extracts produced motility or mortality of adult *H. contortus* to the level of 60% at a concentration of 8 mg/mL while aqueous extract produced only 43.3% at the same concentration. These findings were comparable to the standard, albendazole which killed the parasites in a dose-dependent manner, and all the worms were dead at a concentration of 0.5 mg/mL within 24 h (Eguale et al., 2006).

6.5. Cytotoxic

The leaf and root extracts of *E. capensis* exhibited activity against vero, 4T1 and HEp2 cell lines with IC_{50} values ranging from 2.8 µg/mL to 97.8 µg/mL while among the tested compounds from the plant, oleanonic acid (**33**) showed the highest cytotoxicity with IC_{50} values of (1.4 ± 0.1) µM and (13.3 ± 0.2) µM against the HEp2 and 4T1 cells, respectively (Irungu et al., 2014). The DCM/MeOH (1:1) soluble root extract meanwhile showed an activity against myoblasts L6 cell lines with IC_{50} of (33.0 ± 23.41) µg/mL (Koch et al., 2005). In their works, Tagne and co-workers evaluated antiproliferative activity of the methanol bark extract of *E. senegalensis* on four tumor cell lines consisting of NCI-H460, MCF7, PC3, HeLa as well as the normal cell 3T3 using the sulforhodamine-B assay. The methanol bark extract showed activity with half-maximal growth inhibition (GI_{50}) values ranging from 13.5 µg/mL to 28.8 µg/mL while the positive control doxorubicin exhibited a GI_{50} value of (0.02-0.70) µg/mL (Tagne et al., 2014). Additionally, the antiproliferative activities of hexane, dichloromethane, ethyl acetate, butanol and methanol extracts of the bark of *E. senegalensis* were done against NCI-H460, MCF7 and 3T3 using the sulforhodamine-B assay. The extracts exhibited activities with GI_{50} values ranging from 10.0 µg/mL to 52.0µg/mL (Tagne et al., 2014).

6.6. Anti-inflammatory

The ethanolic extract of *E. capensis* showed a good inhibition of COX inhibitors at 82% in an in vitro assay while the positive control indomethacin showed an inhibition of 66.5% (Jäger et al., 1996). Furthermore, the anti-inflammatory activities of petroleum ether, dichloromethane, ethanol and water-soluble extracts of bark and leaves of *E. capensis* were tested against the COX (COX-1 and COX-2) enzymes. All the solvent extracts showed from moderate to high (40-90%) inhibition activity toward COX-1, and from insignificant to high (<20-85%) inhibition activity toward COX-2 at 250 µg/mL with indomethacin [(64.18 ± 3.10) and (68.50 ± 2.57) for COX-1and COX-2, respectively] as positive control (Mulaudzi et al., 2013).

6.7. Analgesic

Rats were intraperitoneally administered with doses of 100 mg/kg and 200 mg/kg of the aqueous stem bark extracts of *E. senegalensis* and a standard drug pentazocine 10 mg/kg was used. The extract showed dose-dependent activities, which were comparable to that of pentazocine in the hot plate method but higher than pentazocine in the tail immersion method. The result of extract on tail immersion test response showed that there were no significant changes in the time for tail withdrawal at all dosages of extract administered except at 100 mg/kg body weight and 200 mg/kg body weight where the time for tail withdrawal was significantly shorter than that of the pre-treatment (Williams et al., 2013).

6.8. Antioxidant

Sofidiya and collaborators evaluated antioxidant activities of leaf extract of *E. senegalensis* using the

DPPH free radical scavenging and reducing power assays. The extract prepared at the dose from 0.025 mg/mL to 0.2 mg/mL, showed a dose-dependent increase in activity ranging from 81.0% to 96.5% inhibition on DPPH which was comparable to the activities of the reference α-tocopherol showing 96.9% to 97.9% inhibition on DPPH (Sofidiya et al., 2006). However, in another similar assay, the methanol bark extract of *E. senegalensis* exhibited an EC_{50} value of (15.83 ± 0.40) µg/mL and (299.00 ± 3.00) µg/mL using the DPPH and nitric oxide radical scavenging assays, respectively. They also evaluated the antioxidant activities of hexane, dichloromethane, ethyl acetate, butanol and methanol bark extracts of *E. senegalensis* using DPPH radical scavenging assay. The hexane extract showed no activity, while dichloromethane revealed a weak activity with an EC_{50} value of (366.6 ± 2.90) µg/mL and ethyl acetate, butanol as well as methanol extracts were active with EC_{50} values (14.00 ± 0.20) µg/mL, (19.12 ± 0.50) µg/mL and (20.16 ± 1.30) µg/mL respectively (Tagne et al., 2014). Furthermore, the methanol leaf extract of *E. capensis* showed an antioxidant activity with an EC_{50} value of 13.3 µg/mL using the DPPH free radical scavenging assay. The standard rutin gave an EC_{50} value of 14.2 µg/mL (Aladesanmi et al., 2007).

6.9. Acetylcholinesterase inhibitory

The works of Amoo and co-workers on acetylcholinesterase inhibitory properties of *E. capensis* using colorimetric assay with galanthamine at 20 µM as a positive control, concluded that the extract exerted an inhibition 73.8%-89.7% at 1.0 mg/mL and therefore, the results suggest that *E. capensis* extract deserve further investigation as it may provide compounds which can act as natural acetylcholinesterase inhibitors required for the treatment of neurodegenerative disorders (Amoo et al., 2012).

6.10. Anti HIV

The antiviral activity of hexane, dichloromethane and methanol root extracts of *E. capensis* was carried out against CDV, CPIV-2, FHV-1 and LSDV using virucidal and attachment assays. Dichloromethane and hexane soluble extracts inhibited all viruses by at least 50% and the other extracts showed weak activities with EC_{50} values ranging from 30.9 µg/mL to 78.2 µg/mL with selectivity index values of <1 (Bagla et al., 2012). The aqueous bark and leaves extracts as well as methanol leaves extract of *E. capensis* showed good HIV-1 reverse transcriptase (RT) inhibition of 70% at 1 mg/mL based on COX-assay. The bark and leaves water extracts exhibiting dose-dependent IC_{50} values of (0.01 ± 0.00) mg/mL while leaves methanol extract exhibited IC_{50} values of (0.39 ± 0.06) mg/mL (Bagla et al., 2012).

6.11. Antihypertensive

The antihypertensive assay of ethanol and water leaves extracts of *E. capensis* was achieved using the angiotensin-converting enzyme (ACE) assay. The water and ethanol extracts exhibited ACE inhibition rate of 26% and 37%, respectively (Duncan et al., 1999). Likewise, the in vivo antihypertensive activity of the ethanolic leaves extracts of *E. capensis* was evaluated on the blood pressure of anesthetized normotensive male Wistar rats and conscious weanling Dahl salt-sensitive (DSS) rats. The authors assessed contractile or relaxant responses to extracts in the absence or presence of reference drugs in Wistar rat isolated aortic rings precontracted with methoxamine hydrochloride (10 µM). The extracts prevented the development of hypertension in weanling genetically hypertensive DSS rats and the *in vivo* reduction in blood pressure by the extract occurred without significant alterations in the heart rate, suggesting that the *in vivo* cardiovascular effects of the extract significantly contributed to the hypotensive effects. These findings showed that the hypotensive effect of the extract was in part mediated through modulation of total peripheral resistance of the vascular smooth muscles, as evidenced by the extract's elicited dose-dependent vaso-relaxations in endothelium-intact and endothelium-denuded aortic ring preparations (Kamadyaapa et al., 2009).

6.12. Uterotonic

The aqueous wood extract of *E. capensis* and the compounds 3-*epi*-oleanolic acid (**32**) and oleanonic acid (**33**) isolated from the same plant species, were subjected to evaluation of their uterotonic activity using *in vitro* both pregnant and non-pregnant guinea pig uterine smooth muscle. The extract exhibited positive uterotonic activity whereas 3-*epi*-oleanolic acid (**32**) (10 µg ACh) prepared in a DMSO solution (1%) at a concentration of 1.77 µg/µL, and oleanonic acid (**33**) (5 µg ACh) prepared in a DMSO solution (1%) at a concentration of 1.83 µg/µL, possess varying degrees of agonist activity on uterine smooth muscle with minor changes in the molecular structure affecting its intrinsic activity on uterine muscle. Especially, 3-*epi*-oleanolic acid (**32**) was observed to mediate its effect through the cholinergic receptor (Sewram et al., 2000).

7. Conclusion and future prospects

This article covers the phytochemical and pharmacological works on the genus *Ekebergia* over the last four decades. The literature survey indicates that a total of 69 distinct phytochemicals have been reported so far and limonoids (22, ~30.98%), triterpenoids (18, ~26.76%) and coumarins (11, ~16.90%) represent the most abundant classes of metabolites isolated in the genus. If the presence of limonoids as major compounds in the genus can be easily justified by the fact that *Ekebergia* belongs to the Meliaceae family, it is important to indicate that the acyclic triterpenoids and coumarins have been mostly isolated from the species *E. capensis* and it conspecific synonym *E. senegalensis*. Therefore, the acyclic triterpenoids and coumarins might be considered as chemomarkers of the species *E.*

capensis. However, further investigations will be helpful to provide significant insights to support this partial conclusion. As general observation, the limonoids have been mostly obtained from the seeds of the plant species, while *E. capensis* was found to be the most used plant species by local population to cure several diseases. In addition to be the most used in traditional medicine and chemically investigated for their constituents, *E. capensis* was extensively subjected to a large panel of biological activities. Indeed, the results obtained strongly supported the use of this plant species in folk medicine. Therefore, the genus *Ekebergia* possesses a great medicinal potential which remains unexplored due to the fact that the chemical composition of different parts (leaves, fruits, roots, flowers) of several *Ekebergia* species are still unknown and several isolated compounds are untested for their biological potency. Despite the large biological investigation realized on the species *E. capensis* and some isolated compounds, it is important to mention that to the best of our knowledge, no work has been done on the study of the action mechanisms and pharmacokinetics of isolated active compounds from the genus *Ekebergia*. It will be important to use advanced modern technique such as HPLC and LCMS to further investigate the chemistry of the other plant species and evaluate their biological activities as well as their mechanism of action, in order to found additional insights in the medicinal value and use of the genus *Ekebergia*.

Abbreviations

ACh, Acetylcholine; *B., Bacillus*, CD, Circular Dichroism; CDV, Canine Distemper Virus; COX, Cyclooxygenase; CPIV-2, Canine Para Influenza Virus-2; DPPH, 2,2-Diphenyl-1-picrylhydrazyl; DSMZ, Deutsche Sammlung von Mikroorganismen und Zellkulturen; *E., Ekebergia*; EC_{50}, Half maximal effective concentration; ED_{50}, Half maximal effective dose; *Es., Escherichia*, FHV-1, Feline Herpes Virus-1; GI_{50}, Half maximal growth inhibition; *H., Haemonchus*; HIV, Human Immunodeficiency Virus; IC_{50}, Minimum inhibition concentration for inhibiting 50% of the pathogen; IR, Infrared; *K., Klebsiella*; LCMS, Liquid Chromatography Mass Spectrum; LSDV, Lumpy Skin Disease Virus; MIC, Minimum Inhibitory Concentration; NMR, Nuclear Magnetic Resonance; *P., Plasmodium*; prep-HPLC, Preparative High Pressure Liquid Chromatography; *S., Staphylococcus*; TLC, Thin-Layer Chromatography; UV, Ultraviolet; ZOI, Zone of Inhibition.

Conflict of interest

The authors declare that there is no conflict of interest.

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