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Review

Anti-trypanosomal activity of African medicinal plants: A review update

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ABSTRACT

Ethnopharmacological relevance: African trypanosomiasis is one of the neglected tropical diseases caused by different species of trypanosomes that affect both human and livestock with devastating consequences in the continent. Most of the affected populations commonly use traditional medicinal plants for the treatment of the disease. Consequently, this prompted ethnopharmacological research activities on the anti-trypanosomal activity of a number of these African medicinal plants in order to validate their ethnomedicinal use. Furthermore, such studies could lead to the identification of chemical leads for the development of newer anti-trypanosomal agents from those plants. This review aims to provide updated information on the ethnopharmacological evidence of African medicinal plants with anti-trypanosomal activity.

Methods: Literature was collected via electronic search (PubMed, Sciencedirect, Medline and Google Scholar) from published articles that report on the *in vitro* or *in vivo* anti-trypanosomal activity of plants that were collected from different parts of Africa.

Results: African medicinal plants investigated for *in vitro* and *in vivo* anti-trypanosomal activity from January 1993 to October 2013 are systematically compiled and all the *in vivo* studies are critically discussed. A total of 264 plant species belonging to 79 families were investigated for anti-trypanosomal activity. However, only 48 bioactive anti-trypanosomal compounds were successfully isolated in pure forms. Furthermore, some of the plants were investigated for possible ameliorative effects on the trypanosome-induced pathological changes out of which 18 plants were reported to be effective while a few others were not. In spite of interesting preclinical ethnopharmacological evidence for anti-trypanosomal activity, not a single African medicinal plant was investigated in a clinical study.

Conclusion: Several African medicinal plants have demonstrated promising anti-trypanosomal effects but the studies on the anti-trypanosomal potentials of these plants are not taken beyond proof of concept stage. It is hoped that the article would stimulate future clinical studies because of the paucity of knowledge in this area.

Contents

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1. Introduction

Plants have been a source of medication to human and livestock diseases since ancient times (Odhiambo et al., 2011). This is a result of ancestral observations that plant parts possess healing abilities. With advancement in pharmaceutical and allied sciences, phytochemicals were later confirmed to be responsible for the therapeutic properties of plants. Currently, modern scientific techniques have led to the isolation and identification of thousands of these phytochemicals. Many of which had served as chemical leads for the development of chemotherapeutic drugs against several diseases (infectious and non-infectious) (Kasilo et al., 2010). Indeed, 75% of the anti-infectious disease drugs approved from 1981 to 2002, could be traced to natural origins (Newman et al., 2003) whereas 61% of all new chemical entities introduced worldwide as drugs during the same period could be traced to natural products (Gupta et al., 2005).

Apart from this impressive role of medicinal plants in drug discovery, the use of local preparations of these medicinal plants still provide the only option to large number of the African population for therapeutic purposes. This is mainly due to the lack of good health care systems in many parts of the continent which makes the population highly vulnerable to many infections (Elujoba et al., 2005). Indeed, 80% of the population in African countries depend almost entirely on herbal medicine for their primary health care needs (Kasilo et al., 2010).

An important infection that greatly affects humans and livestock in Africa is African trypanosomiasis also known as "sleeping sickness" in humans or "nagana" in animals (Atawodi, 2005; Welburn et al., 2009). It is one of the neglected parasitic diseases that affects human health and also largely accounts for the low livestock productivity of the African continent (Welburn et al., 2006). It is estimated that about 70 million people distributed over 1.55 million km^2 in Africa are at risk of the disease (Simarro et al., 2012). On the other hand, animal trypanosomiasis is distributed over approximately 25 million km^2 in Africa, where it reduces livestock productivity by up to 50%. The disease is caused by extracellular parasites called trypanosomes and the important species include *Trypanosoma brucei*, *Trypanosoma evansi*, *Tryponosoma congolense* and *Tryponosoma vivax* (Mbaya et al., 2009). At present, the chemotherapy of African trypanosomiasis remains far from satisfactory because the clinically available drugs have limitations such as toxicity, parasite resistance, high cost and poor availability as well as the need for parenteral administration of treatments (Welburn et al., 2009). Fortunately, the continent is endowed with tremendous medicinal plant resources that are traditionally utilized for the treatment of the disease.This is evident by the propensity of the ethnobotanical utilization of the medicinal plants for the management of the disease from different African sub-regions (Atawodi et al., 2002; Ntie-Kang et al., 2013). Interestingly, scientific investigations have confirmed the efficacy of many of these African medicinal plants as anti-trypanosomal agents under *in vitro* and/or *in vivo* conditions. Therefore, a critical review of these investigated (anti-trypanosomal) African medicinal plants is needed to provide a focus on the achievement so far recorded in the investigations of different African plants as well as to identify gaps in knowledge which might provide basis for strategies to address such gaps.

At present, the only available review on anti-trypanosomal medicinal plants from Africa is limited to the Nigerian flora (Mbaya and Ibrahim, 2011) and even within the Nigerian medicinal plants, majority of the investigated Nigerian plants were missing in that review. Other authors attempted to review all natural products with anti-trypanosomal activity reported between mid-1980s and 2003 and the data was not limited to Africa in addition to being too skewed on the chemistry aspect with little or no information on the plants (Hoet et al., 2004b).

In this article, available data on scientifically investigated African medicinal plants with anti-trypanosomal potentials was reviewed from January 1993 to October 2013. This could be used as an updated source of the progress or success achieved so far in the scientific investigations of anti-trypanosomal activity of different African medicinal plants. Furthermore, the article could also be relevant for other areas of biomedical interest such as identification of bioactive anti-trypanosomal compounds from African plants. In addition, this review may motivate researchers to undertake comparative *in vivo* studies using the bioactive extracts against the best anti-trypanosomal medicine *vis-à-vis* toxicity and efficacy profiles.

2. Methods

Relevant literature was collected by searching the major scientific databases including PubMed, Sciencedirect, Medline and Google scholar for medicinal plants of African origin that have been studied and investigated *vis-a-vis* their anti-trypanosomal therapeutic potentials. Some articles were found through tracking citations from other publications or by directly accessing the journals' web-site. They were considered on the basis of the geographical region of their origin. The literature considered is the one available covering the period, January 1993–October 2013. The keywords combinations for the search were: anti-trypanosomal, trypanocidal, medicinal plant and Africa. All the research articles obtained on the *in vitro* and *in vivo* antitrypanosomal activities are presented in this review. The plants were also categorized and presented based on their regional origins.

3. Results and discussion

A map of Africa indicating the sub-regions of the continent as used in this review is presented in Fig. 1. Approximately, 63% of the total investigated plants originated from West African countries. The plants from this region were predominantly from Nigeria, Burkina Faso, Mali, Cote d'Ivoire and to a lesser extent, Benin. East Africa accounts for 31.62% of the plants majority coming from Tanzania, Ethiopia and Uganda. Central, North and Southern Africa contribute to the remaining $<6\%$ of the total investigated plants (Fig. 2).

Data on scientific and common names, part and fraction investigated, possible active components and the regional origin of African medicinal plants with anti-trypanosomal activity were compiled for West (Table 1), East (Table 2), Central (Table 3), North (Table 4) and Southern (Table 5) Africa. Furthermore, all *in vivo* studies with relevant pharmacological data have been collectively compiled (Table 7). A total of 264 plant species from 79 families were found (Tables 1–5). Plants from Leguminosae (7.95%), Asteraceae (6.43%) and Euphoraceae (5.68%) families have received more scientific attention than others. Moreover, the most frequently implicated phytochemicals in the plants are flavonoids, triterpenes, alkaloids, tannins and saponins. Detailed phytochemistry studies of the plants led to the isolation of 48 specific anti-trypanosomal compounds from different parts of the plants. The structures of the compounds are provided in Fig. 3.

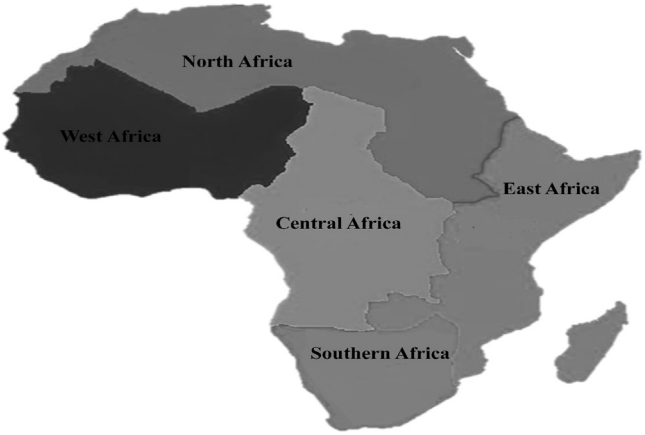

Fig. 1. Map of Africa showing the different sub-regions.

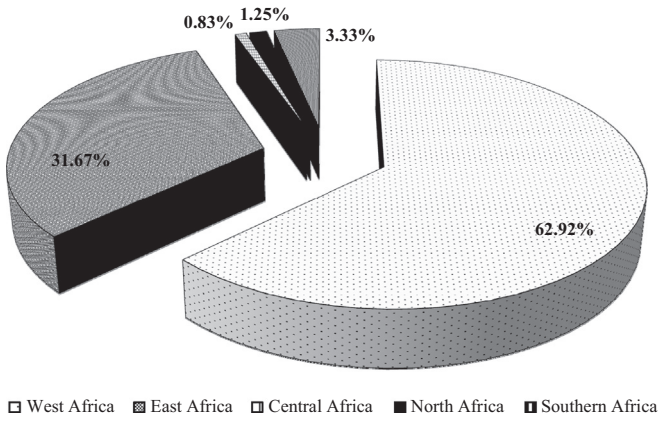

Fig. 2. Sub-regional distributions of investigated African medicinal plants with anti-trypanosomal activity.

In order to provide a more thorough view of the potentials of the plants, the scientifically investigated plants are grouped into sub-regions. All the plants that were investigated in *in vivo* studies are discussed below. However, in the case of Central and Southern African sub-regions where no *in vivo* investigation was reported on any of the plants, all the data obtained were briefly discussed.

3.1. *in vivo* anti-trypanosomal activity of West African plants

Due to the volume of investigated plants from West Africa, we intend to give more attention to plants that were investigated in *in vivo* models. All plants with multiple sources of *in vivo* anti-trypanosomal activity were discussed under specific sub-headings below. However, other plants with single source of *in vivo* anti-trypanosomal activity were discussed based on potency and the ability to ameliorate the trypanosome-induced pathological changes.

3.1.1. *Khaya senegalensis A. Juss*

Khaya senegalensis A. Juss is perhaps the most investigated African plant for anti-trypanosomal activity as manifested by the numerous studies on the plant. Atawodi et al. (2003) reported the *in vitro* anti-trypanosomal activity of extracts of different parts of the plant and found that the methanolic extract of the bark was strongly active against both *Trypanosoma congolense* and *Trypanosoma brucei gambiense* at a dose of 4 mg/mL. This was further confirmed by the findings of Wurochekke and Nok (2004) and Mikail (2009) which demonstrated that stem bark methanolic extract of the plant inhibited *Trypanosoma brucei brucei* motility within 30 min at ineffective doses of 2 and 4 mg/mL. Furthermore, dichloromethane (Aderbauer et al., 2008) and ethanolic (Umar et al., 2010) extracts of the bark showed *in vitro* anti-trypanosomal activity against *Trypanosoma brucei brucei* (MIC = 0.1 mg/mL) and *Trypanosoma evansi* (parasites eliminated at 0.5 mg/mL) respectively. Adeiza et al. (2010) also reported an *in vitro* anti-*Trypanosoma evansi* activity of the stem bark aqueous and methanolic extracts at a relatively high concentration of 20 mg/mL. The first study on the *in vivo* activity of the stem bark of the plant was reported by Ibrahim et al. (2008). The authors reported that stem bark aqueous extract at a daily oral dose of 60 mg/kg body weight (bw) was active against *Trypanosoma brucei brucei* in rats but did not prevent the parasite-induced liver damage. In a follow up study, oral administration of phenolic-rich fraction of the bark at doses of 100 and 200 mg/kg bw maintained a low level of *Trypanosoma brucei brucei* (approximately 90% inhibition) in rats and completely cleared the parasites at a higher dose of 300 mg/kg bw without relapse (Ibrahim et al., 2013a). Moreover, the 300 mg/kg bw treatment ameliorated the parasite-induced anemia and organ damage. These studies signify the anti-trypanosomal effectiveness of the stem bark extracts of the plant. In a similar study, though with *Trypanosoma evansi*, the stem bark ethanolic extract caused a significant reduction (64–71%) in the parasite count at an oral dose of 20–80 mg/kg bw but also, could not ameliorate the parasite-induced anemia (Umar et al., 2010). However, the *in vivo* anti-trypanosomal activity of crude stem bark extracts of the plant was not significant at a dose of 10 and 15 mg/animal in mice and rats respectively (Antia et al., 2009). The treatment actually led to a toxic effect and death especially in mice. This could be attributed to a rather higher dose used by the authors compared to the effective doses of 20–80 mg/kg bw (equivalent to approximately 1–4 mg/animal) of extracts used by Ibrahim et al. (2008) and Umar et al. (2010). On the other hand, acute toxicity study of the stem bark methanol extract of the plant revealed an LD_{50} of 3807 mg/kg bw in rats (Suleiman et al., 2013). Phytochemical analysis of the bark showed the presence of alkaloids, carbohydrates, tannins, saponins, flavonoids, terpenes, sugars, cardiac glycosides and phlobotannins

Table 1
List of anti-trypanosomal investigated medicinal plants from West Africa.

Scientific name	Common name	Family	Part (s) used	Extract/fraction	Possible active component (s)	Model	Parasite	IC_{50} or MIC (μg/mL)	Country	References
Acacia ataxacantha DC.	Flame thorn	Leguminosae	Stem bark/ root	n-Hexane/ethanol extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma congolense*	NI	Nigeria	Adewunmi et al. (2001)
Acacia nilotica (L.) Delile	Gum Arabic tree	Mimosaceae	Stem bark/ root bark	Dichloromethane/ aqueous/methanolic extracts	Alkaloids/ flavonoids/ terpenes/ triterpenes	*In vitro/ in vivo*	*Trypanosoma brucei brucei*	50/50/5[a]	Burkina Faso/ Mali/Nigeria	Aderbauer et al. (2008), Bizimana et al. (2006), Ogbadoyi et al. (2011a), Mann et al. (2011)
Acacia polyacantha Wild. Subsp	White-stem thorn	Mimosaceae	Leaf	Ethanol extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Coted'Ivoire	Atindehou et al. (2004)
Acalypha wilkesiana Müll.Arg.	Copper leaf	Euphorbiaceae	Leaf	Aqueous extract	–	*in vivo*	*Trypanosoma brucei brucei*	NI	Nigeria	Olukunle et al. (2010)
Acanthospermum hispidum (DC.) Kuntze	Bristly Starbur	Asteraceae	Aerial part	Dichloromethane/ methanolic/aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei*	14.52 ± 5.5/ 47.5 ± 0.6/ 54.8 ± 0.4	Benin	Bero et al. (2011), Atindehou et al. (2004)
Adansonia digitata L.	Baobab	Bombacaceae	Leaf/ root/ bark	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma congolense*	NI	Nigeria	Atawodi (2005), Atawodi et al. (2003)
Adenia cissampeloides Planch. ex Hook.) Harms	Monkey rope	Passifloraceae	Stem bark/ root	n-Hexane/ethanol extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma congolense*	NI	Nigeria	Adewunmi et al. (2001)
Adenium obesum (Forssk.) Roem. & Schult.	Desert rose	Apocynaceae	Root/ bark	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei*	NI	Nigeria	Atawodi (2005)
Afrormosia laxiflora (Baker) Harms	Satin wood	Leguminosae	Leaf/ Stem bark/ root	Petroleum ether/ Chloroform/Methanol/ Aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	NI	Nigeria	Atawodi (2005)
Afzelia africana Pers.	Afzelia	Leguminosae	Leaf/ Stem bark/ root/ whole plant	Petroleum etherdichloromethane/ chloroform/methanol/ aqueous extracts	–	*in vitro/ in vivo*	*Trypanosoma brucei brucei/ Trypanosoma congolense*	500/1[a]	Nigeria /Burkina Faso/ Mali	Atawodi (2005), Atawodi et al. (2003), Antia et al. (2009); Aderbauer et al. (2008), Bizimana et al. (2006)
Albizia lebbeck (Retz.) P.Beauv.	Siris tree	Mimosaceae	Leaf/ seed	Aqueous/methanol extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	NI	Nigeria	Wurochekke and Nok (2004), Atindehou et al. (2004)
Albuca spp. Jacq.	Slime	Asparagaceae	Bulb	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	NI	Nigeria	Atawodi (2005)
Alchornea cordifolia (Schumach. & Thonn.) Müll.Arg.	Christmas bush	Euphorbiaceae	Leaf	n-Hexane/ethanol extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma congolense*	NI	Nigeria	Adewunmi et al. (2001)
Allium sativum L.	Garlic	Alliaceae	Pulp	Acetic acid/methanolic fractions	–	*in vivo*	*Trypanosoma brucei brucei/ Trypanosoma congolense/ Trypanosoma vivax*	NI	Nigeria	Nok et al. (1996)
Aloe vera (L.) Burm.f.	True Aloe	Aloaceae	Pulp	Extract	–	*in vivo*	*Trypanosoma brucei brucei*	NI	Nigeria	Abubakar et al. (2005)

Table 1 (*continued*)

Scientific name	Common name	Family	Part (s) used	Extract/fraction	Possible active component (s)	Model	Parasite	IC_{50} or MIC (μg/mL)	Country	References
Ampelocissus grantii (Baker) Planch.	–	Vitaceae	Aerial part	Dichloromethane/ Methanolic/Aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei*	500/10[a]	Burkina Faso/ Mali	Aderbauer et al. (2008), Bizimana et al. (2006)
Anchomanes difformis (Blume) Engl.	Anchomanes	Araceae	Root/ Rhizome	Petroleum ether/ chloroform/ dichloromethane/ methanol/aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma congolense*	50.7 ± 7.3/ 14.7 ± 3.8/ 13.8 ± 2.3	Nigeria/Benin	Atawodi (2005); Atawodi et al. (2003); Bero et al. (2011)
Annona senegalensis Pers.	African custard-apple	Annonaceae	Leaf/ stem/ Root	Hexane/ethyl acetate/ acetone/ dichloromethane/ methanol/aqueous extract	Saponins/Tannins/ Phlobatannin	*in vivo*	*Trypanosoma brucei brucei/ Trypanosoma brucei gambiense*	–	Nigeria/ Cote d'Ivoire/ Burkina Faso/ Mali	Abubakar et al. (2005); Ogbadoyi et al. (2007); Youan et al. (1997); Atawodi et al. (2003); Atawodi (2005); Aderbauer et al. (2008)
Anogeissus leiocarpus (DC.) Guill. & Perr.	Axle- wood tree	Combretaceae	Leaf/ stem bark	Aqueous/methanol/ dichloromethane extracts/compounds	Ellagic acid/ flavogallonic acid bislactone/ punicalagin/ terchebulin/ castalagin	*in vivo/ in vitro*	*Trypanosoma brucei gambiense/ Trypanosoma evansi/ Trypanosoma brucei brucei*	200[a]	Cote d'Ivoire/ Nigeria/ Burkina Faso/ Mali	Youan et al. (1997); Shuaibu et al. (2008); Aderbauer et al. (2008); Atawodi et al. (2003)
Anthocleista vogelii Planch.	Cabbage tree	Loganiaceae	Stem bark/ root bark	Aqueous/ethanolic extracts	–	*in vitro*	*Trypanosoma brucei brucei*	NI	Nigeria	Abu et al. (2009)
Artemisia maciverae Hutch. & Dalziel	–	Asteraceae	Whole plant	Petroleum ether/ chloroform/methanol/ aqueous extracts	Alkaloids/ flavonoids/ terrpenes/ triterpenes	*in vitro/ in vivo*	Trypanosoma brucei brucei	NI	Nigeria	Ene et al. (2009)
Azadirachta indica A.Juss.	Neem	Meliaceae	Stem bark/ Leaf	Ethanol	–	*in vitro/ in vivo*	Trypanosoma brucei	NI	Nigeria	Mbaya et al. (2010)
Balanites aegyptiaca (L.) Delile	Desert date	Balanitaceae	Stem bark/ Shoot/ Root	Aqueous/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	500/50/200[a]	Nigeria/ Burkina Faso/ Mali	Wurochekke and Nok (2004); Aderbauer et al. (2008)
Bauhinia reticulata DC.	Mountain ebony	Leguminosae	Twig/ Leaf	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei brucei*	200[a]	Burkina Faso/ Mali	Aderbauer et al. (2008)
Blighia unijugata Baker		Sapindaceae	Leaf	Aqueous/ethanolic extracts	–	*in vitro*	*Trypanosoma brucei brucei*	NI	Nigeria	Abu et al. (2009)
Brassica oleracea L.	Cabbage	Cruciferae	Leaf	Aqueous extract	–	*in vitro*	*Trypanosoma brucei brucei*	NI	Nigeria	Igweh et al. (2002)
Bridelia ferruginea Benth.	–	Euphorbiaceae	Stem bark	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*In vitro/ In vivo*	*Trypanosoma brucei brucei/Trypanosoma brucei gambiense*	NI	Nigeria/ Cote d'Ivoire	Atawodi (2005); Youan et al. (1997)
Bridelia grandis Pierre ex Hutch.	Bruin stink out	Euphorbiaceae	Stem/ root barks	Ethanol extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. 2004
Bombax buonopozense P.Beauv.	Red-flowered Silk	Bombacaceae	Stem bark	Methanolic extract	–	*in vivo*	*Trypanosoma brucei brucei.*	NI	Nigeria	Mann et al. (2011)
Boscia angustifolia A.Rich.	Rough-leaved Shepherd Tree	Capparaceae	Stem bark	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei brucei*	200[a]	Burkina Faso/ Mali	Aderbauer et al. (2008)
	Frankincense	Burseraceae			–	*in vitro*		NI	Nigeria	Atawodi (2005)

Boswellia dalzieli Hutch.			Leaf/ Stem bark/ Root	Petroleum ether/ chloroform/methanol/ Aqueous extracts			*Trypanosoma brucei brucei.*			
Bussea occidentalis Hutch	Long purple-flag	Leguminosae	Stem bark	Ethanol extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. 2004
*Byrsocarpus coccineus*Schu-mach. & Thonn.	Rourea coccinea	Connaraceae	Aerial part	Dichloromethane/ methanolic/aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei*	14.7 ± 1.2/ 21.1 ± 1.9/ 49.5 ± 4.9	Benin	Bero et al. (2011)
Calotropis procera (Aiton) Dryand.	Milkweed	Asclepiadaceae	Leaf	Methanolic extract/n-butanolic fraction	Saponins	*in vitro*	*Trypanosoma evansi*	NI	Nigeria	Ibrahim et al. (2013c)
Canarium schweinfurthii Engl.	White mahogany	Burseraceae	Stem bark	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	NI	Nigeria	Atawodi (2005); Atindehou et al. (2004)
Carpolobia lutea G.Don	Cattle stick	Polygalaceae	Aerial part	Dichloromethane/ methanolic/aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei*	18.3 ± 2.5/ > 100/ > 100	Benin	Bero et al. (2011)
Cassia alata L. (Syn: *Senna alata*)	Candle brush	Leguminosae	Root	Ethanol extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Cassia siamae Lam. (Syn: *Senna siamae*)	Thailand shower	Leguminosae	Leaf/ Stem bark/ Root	Aqueous/hexane/ ethylacetate/ methanolic extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	25.88 ± 4.17/ 10.19 ± 1.74/ 46.50 ± 4.11	Nigeria	Abiodun et al. (2012)
Cassia sieberiana DC. (Syn: *Senna sieberiana*)	African laburnum	Leguminosae	Leaf/ Stem bark/ root/ twig	Aqueous/methanol/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma brucei gambiense/ Trypanosoma brucei rhodesiense*	20.0 ± 11.3/ 25.8 ± 4.5	Nigeria/ Burkina Faso/ Mali /Cote d'Ivoire/ Benin	Wurochekke and Nok (2004); Aderbauer et al. (2008); Youan et al. (1997); Hoet et al. (2004a)
Cassytha filiformis L.	Seashore dodder	Lauraceae	Leaf/ stem bark	Petroleum etherchloroform/ Methanol/Aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	NI	Nigeria	Atawodi (2005)
Cassytha sp.	laurel dodder	Lauraceae	Leaf	Methanolic extract	–	*in vitro*	*Trypanosoma congolense*	NI	Nigeria	Atawodi et al. (2003)
Ceiba pentandra (L.) Gaertn.	Silk-cotton tree	Bombacaceae	Leaf/ stem bark/ root	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei brucei*	200/ > 500/500[a]	Burkina Faso/ Mali	Aderbauer et al. (2008)
Celtis integrifolia Lam	African nettle tree	Ulmaceae	Twig/ Leaf	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei brucei*	> 500[a]	Burkina Faso/ Mali	Aderbauer et al. (2008)
Cissus multistriata		Vitaceae	Leaf	Hydromethanolic extract	–	*in vivo*	*Trypanosoma brucei brucei.*	NI	Nigeria	James and Emmanuel (2011)
Citrus sinensis (L.) Osbeck	Sweet orange	Rutaceae	Peels	Aqueous extract	Cyclobutane/6-octenal/ Eucalyptol/Citral	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma evansi*	NI	Nigeria	Habila et al. (2010)
Clerodendrom capitatum (Wild) Schumach & Thonn.	Glory-Bower	Verbenaceae	Stem bark/ Root	n-Hexane/ethanol extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma congolense*	NI	Nigeria	Adewunmi et al. (2001)
Cochlospermum planchonii Hook.f. ex Planch.	False cotton	Cochlospermaceae	Leaf/ Root	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	NI	Nigeria	Atawodi (2005)
Cochlospermum tinctorium Perrier ex A.Rich.		Cochlospermaceae	Root	Dichloromethane \ethanolic extracts	–	*in vitro*	*Trypanosoma brucei brucei\ Trypanosoma brucei rhodesiense*	500[a]	Burkina Faso/ Mali	Aderbauer et al. (2008); Atindehou et al. (2004)
	Caper-bush	Combretaceae	Stem bark	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei brucei*	100[a]	Burkina Faso/ Mali	Aderbauer et al. (2008)

Table 1 (*continued*)

Scientific name	Common name	Family	Part (s) used	Extract/fraction	Possible active component (s)	Model	Parasite	IC_{50} or MIC (μg/mL)	Country	References
Combretum glutinosum Perr. ex DC.										
Combretum micranthum G.Don	African Bushwillow	Combretaceae	Leaf	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei brucei*	500[a]	Burkina Faso/ Mali	Aderbauer et al. (2008)
Combretum molle R. Br. ex G. Don.	Velvet brush	Combretaceae	Leaf/ Stem/ Root	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Combretum smeathmannii G. Don.	–	Combretaceae	Leaf	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Commiphora kerstingii Engl.		Burseraceae	Stem bark	Methanolic extract	–	*in vitro*	*Trypanosoma brucei brucei*	NI	Nigeria	Mikail (2009)
Cucumis metuliferus E.Mey. ex Schrad	African horned cucumber	Cucurbitaceae	Pulp	–	Glycosides/resins/ flavonoids/ saponins/	*in vivo*	*Trypanosoma brucei brucei*	NI	Nigeria	Abubakar et al. (2011)
Cussonia arborea Hochst. ex A.Rich.	Octopus cabbage tree	Araliaceae	Stem bark/ Root bark	Aqueous/Ethanolic extracts		*in vitro*	*Trypanosoma brucei brucei*	NI	Nigeria	Abu et al. (2009)
Cymbopogon citratus (DC.) Stapf	–	Poaceae	Leaf	Aqueous extract	Cyclobutane/6-octenal/ Eucalyptol/Citral	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma evansi*	NI	Nigeria	Habila et al. (2010)
Dacryodes klaineana (Pierre) H. J. Lam.	Monkey plum	Burseraceae	Stem bark	Ethanolic extract	-	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Detarium microcarpum Guill. & Perr.	Tallow tree	Leguminosae	Roots	Aqueous extract	–	*in vivo*	*Trypanosoma brucei gambiense*	NI	Cote d'Ivoire	Youan et al. (1997)
Dichrostachys cinerea (L.) Wight & Arn.	Sickle bush	Leguminosae	Leaf	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Dialium guineense Willd.	Velvet tamarind	Leguminosae	Aerial part	Dichloromethane/ Methanolic/aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei*	$>100/42.3 \pm 3.1/$ 52.0 ± 5.0	Benin	Bero et al. (2011)
Diospyros mespiliformis Hochst. ex A.DC.	African Ebony	Ebenaceae	Leaf	Petroleum etherchloroform/ methanol/aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei*	500[a]	Nigeria/ Burkina Faso/ Mali	Atawodi (2005); Aderbauer et al. (2008)
Dioscorea minutiflora Engl.	–	Dioscoreaceae	Tuber	Ethanol extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Dissotis rotundifolia (Sm.) Triana	Pink lady	Melastomataceae	Leaf	Ethanolic extrac	–	*in vitro/ in vivo*	*Trypanosoma brucei brucei*	NI	Nigeria	Mann et al. (2009)
Enantia polycarpa Engl. & Diels	African yellow wood	Annonaceae	Stem bark	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Entada africana Guill. & Perr.	Iron wood	Leguminosae	Stem bark/ root	Dichloromethane extract	–	*in vitro/*	*Trypanosoma brucei brucei*	200[a]	Burkina Faso/ Mali	Aderbauer et al. (2008)
Entada abyssinica Steud. ex Rich.	Splinter bean	Leguminosae	Stem bark	Ethanolic extract		*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Erythrina senegalensis DC.	Coral tree	Leguminosae	Stem bark	Ethanol extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Erythrophleum ivorense A. Chev.	Odeal tree	Leguminosae	Root bark	Ethanol extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
	Saucy bark	Leguminosae	Leaf		–	*in vitro*		500[a]		Aderbauer et al. (2008)

Erythrophleum guineense G.Don				Dichloromethane extract			*Trypanosoma brucei brucei*		Burkina Faso/ Mali	
Erythrophleum suaveolens (Guill. & Perr.) Brenan	Sasswood	Leguminosae	Stem bark	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	NI	Nigeria	Atawodi (2005)
Eucalyptus camaldulensis Dehnh.	Red river gum	Myrtaceae	Leaf	Aqueous extract	Cyclobutane/6-octenal/ Eucalyptol/Citral	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma evansi*	NI	Nigeria	Habila et al. (2010)
Eucalyptus citriodora Hook.	Lemon Scented Gum	Myrtaceae	Leaf	Aqueous extract	Cyclobutane/6-octenal/ Eucalyptol/Citral	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma evansi*	NI	Nigeria	Habila et al. (2010)
Eugenia uniflora L.	Surinam Cherry	Myrtaceae	Leaf	n-hexane/ chloroform/ ethylacetate/ methanolic extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma congolense*	NI	Nigeria	Adewunmi et al., 2001
Euphorbia hirta L.	Asthma plant	Euphorbiaceae	Leaf	Hexane/ethylacetate/ methanolic extracts	–	*in vitro*	*Trypanosoma brucei rhodesiense*	9.91 ± 2.13/ 8.70 ± 2.94/ 54.24 ± 3.39	Nigeria	Abiodun et al. (2012)
Evolvulus alsinoides L.	Dwarf morning-glory	Convolvulaceae	Whole plant	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Fagara zanthoxyloides Lam.	Senegal Prickly-ash	Rutaceae	Roots	Aqueous extract	–	*in vivo*	*Trypanosoma brucei gambiense*	NI	Cote d'Ivoire	Youan et al. (1997)
Ficus iteophylla Miq.	Ficustree	Moraceae	Leaf	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei brucei*	100	Burkina Faso/ Mali	Aderbauer et al. (2008)
Ficus sycomorus L.	Bush fig	Moraceae	Stem bark	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	NI	Nigeria	Atawodi (2005)
Ficus thonningii Blume	Bark-cloth fig	Moraceae	Roots	Aqueous extract	–	*in vivo*	*Trypanosoma brucei gambiense*	NI	Cote d'Ivoire	Youan et al. (1997)
Garcinia kola Heckel	Bitter kola	Clusiaceae	Nut	Methanolic extract	–	*in vivo*	*Trypanosoma brucei brucei*	NI	Nigeria	Ogbadoyi et al. (2011b)
Gardenia aqualla Stapf & Hutch.		Rubiaceae	Roots	Aqueous extract	–	*in vivo*	*Trypanosoma brucei gambiense*	NI	Cote d'Ivoire	Youan et al. (1997)
Gardenia erubescens Stapf & Hutch.		Rubiaceae	Leaf/ stem bark	Aqueous/ethanolic extracts	–	*in vitro*	*Trypanosoma brucei brucei*	NI	Nigeria	Abu et al. (2009)
Gardenia triacantha DC.	cape jessamine	Rubiaceae	Root	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei brucei*	200[a]	Burkina Faso/ Mali	Aderbauer et al. (2008)
Gongronema latifolium Benth.		Asclepiadaceae	Stem bark	Methanolic extract	–	*In vitro/ In vivo*	*Trypanosoma congolense*	NI	Nigeria	Abedo et al. (2013)
Guiera senegalensis J.F.Gmel.	Moshi medicine	Combretaceae	Leaf/ stem bark/ root	Aqueous/methanol extracts	–	*in vitro/ in vivo*	*Trypanosoma brucei brucei/ Trypanosoma brucei gambiense*	50/200	Nigeria/ Burkina Faso/ Mali	Wurochekke and Nok (2004); Youan et al. (1997); Atawodi et al. (2003); Atawodi (2005); Aderbauer et al. (2008)
Harrisonia abyssinica Oliv.	–	Simaroubaceae	Leaf	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Harungana madagascariensis Lam ex Poir.	Dragon's blood tree	Clusaceae	Root bark	Ethanol extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Heliotropium indicum L.	Indian heliotrope	Boraginaceae	Aerial part	Dichloromethane/ methanolic/aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei*	58.3 ± 1.5/ 80.2 ± 8.0/ > 100	Benin	Bero et al. (2011)
Hibiscus sabdariffa L.	Red sorrel	Malvaceae	Calyces	Aqueous extract	–	*in vivo*	*Trypanosoma congolense*	NI	Nigeria	Umar et al. (2009)

Table 1 (*continued*)

Scientific name	Common name	Family	Part (s) used	Extract/fraction	Possible active component (s)	Model	Parasite	IC_{50} or MIC (μg/mL)	Country	References
Holarrhena africana A.DC.	Conessi-bark	Apocynaceae	Leaf	Methanol/chloroform fractions	Alkaloids/ Flavonoids	*in vitro*/ *in vivo*	*Trypanosoma brucei brucei*/ *Trypanosoma brucei rhodesiense*	NI	Nigeria	Nwodo et al. (2007)
Holarrhena floribunda (G.Don) T.Durand & Schinz	False rubber tree	Apocynaceae	Twigs/ leaf	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei brucei*	200[a]	Burkina Faso/ Mali	Aderbauer et al. (2008)
Hymenocardia acida Tul.	Large red-hear	Phyllanthaceae	Stem bark/ root bark	Hydroethanolic/ dichloromethane/ methanolic\ethanolic extracts	Alkaloids/ Saponins/ Flavonids	*in vivo*/ *in vitro*	*Trypanosoma brucei brucei*/ *Trypanosoma brucei rhodesiense1*	5.0 ± 1.4/9.1 ± 4.9	Nigeria/Benin	Abu and Uchendu (2011); Abu et al. (2009); Hoet et al. (2004a); Atindehou et al. (2004)
Irvingia gabonensis Baill.	Wild mango	Irvingiaceae	Stem bark	Ethanol extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Imperata cylindrical Raeusch.	–	Poaceae	Leaf	Hexane/ethylacetate/ methanolic extracts	–	*in vitro*	*Trypanosoma brucei rhodesiense*	12.56 ± 0.09/ 42.49 ± 0.99/ 30.37 ± 4.40	Nigeria	Abiodun et al. (2012)
Jatropha curcas L.	Barbados nut	Euphorbiaceae	Leaf	Hexane/ethylacetate/ methanolic extracts	–	*in vitro*	*Trypanosoma brucei rhodesiense*	9.67 ± 1.20/ 4.72 ± 0.06/ 26.35 ± 1.86	Nigeria	Abiodun et al. (2012)
Keetia leucantha (K.Krause) Bridson	Raisin-fruit keetia	Rubiaceae	Leaf/ twig	Dichloromethane/ methanolic/aqueous extracts/essential oils	Oleanolic acid /ursolic acid /betulinic acid/ phytol, α-ionone and β-ionone.	*in vitro*	*Trypanosoma brucei brucei*	24.4 ± 1.8/ 47.6 ± 5.2/ 70.2 ± 10.8 5.8 ± 1.3/ 86.9 ± 5.3/ 52.0 ± 2.8	Benin	Bero et al. (2011); Bero et al. (2013)
Khaya ivorensis A. Chev.	Gold coast mahogany	Meliaceae	Stem bark	Ethanolic extract	-	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Khaya senegalensis (Desv.) A.Juss.	African mahogany	Meliaceae	Leaf/ Stem bark/ Root	Petroleum ether/ chloroform/methanol/ ethanolic/aqueous extracts/phenolic fraction	Alkaloids/ Terpenes/ Saponins/ Flavonids	*in vitro*/ *in vivo*	*Trypanosoma evansi*/ *Trypanosoma brucei gambiense*/ *Trypanosoma brucei brucei*	1.6/6300/100[a]	Nigeria/ Cote d'Ivoire/ Burkina Faso/ Mali	Adeiza et al. (2010); Umar et al. (2010); Mikail (2009); Youan et al. (1997); Antia et al. (2009); Atawodi (2005); Atawodi et al. (2003); Ibrahim et al. (2008); Ibrahim et al. (2013a); Wurochekke and Nok (2004); Aderbauer et al. (2008)
Kigelia africana (Lam.) Benth.	Sausage tree	Bignoniaceae	Root bark	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Landolphia uniflora (Stapf) Pichon	Rubber	Apocynaceae	Leaf/ stem bark/ root	Petroleum ether/ chloroform/methanol/ aqueous extracts	Tannins	*in vitro*/ *in vivo*	*Trypanosoma brucei brucei.*	NI	Nigeria	Atawodi and Alafiatayo (2007)
Lannea kerstingii Engl. & K.Krause		Anacardiaceae	Leaf/ stem bark/ root	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei*/ *Trypanosoma congolense*	NI	Nigeria	Atawodi (2005); Atawodi et al. (2003)
Lannea microcarpa Engl. & K.Krause	African locust	Apocynaceae	Leaf/ stem bark	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei brucei*	> 200/200[a]	Burkina Faso/ Mali	Aderbauer et al. (2008)
Lannea welwistchii (Hiern) Engl.	Indian ash tree	Anacardiaceae	Leaf	Methanol extract	–	*in vitro*/ *in vivo*	*Trypanosoma brucei brucei*	6.3[a]	Nigeria	Antia et al. (2009)
Lawsonia alba Lam.	Amharic	Lythraceae	Twigs/ leaf	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei brucei*	200[a]	Burkina Faso/ Mali	Aderbauer et al. (2008)
Lawsonia inermis L.	Henna	Lythraceae	Leaf/ Root	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*/ *in vivo*	*Trypanosoma brucei brucei*/ *Trypanosoma congolense*	NI	Nigeria	Wurochekke and Nok (2004); Wurochekke et al. (2004); Atawodi et al. (2003); Atawodi (2005)

*Leea guineensis*G. Don	Broadleaf	Leeaceae	Leaf/ stem bark/ root bark	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Leptadenia hastata Vatke	Shea butter	Asclepiadaceae	Aerial parts	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei brucei*	> 500[a]	Burkina Faso/ Mali	Aderbauer et al. (2008)
Lippia multiflora Moldenke		Verbenaceae	Leaf	Aqueous extract	–	*in vivo*	*Trypanosoma brucei brucei*	NI	Nigeria	Olukunle et al. (2010)
Lonchocarpus laxiflorus Guill. & Perr.		Leguminosae	Stem bark	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	NI	Nigeria	Atawodi (2005)
Lophira lanceolata Tiegh. ex Keay	Dwarf red	Ochnaceae	Leaf/ stem bark	Aqueous/ethanolic extracts	–	*in vitro*	*Trypanosoma brucei brucei*	NI	Nigeria	Abu et al. (2009)
Loranthus pentagonia DC.	Summer mistletoe	Loranthaceae	Whole plant	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei brucei*	500[a]	Burkina Faso/ Mali	Aderbauer et al. (2008)
Mallotus oppositifolius Muell. Arg.	Mallotus	Euphorbiaceae	Leaf	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Mangifera indica L.	Mango	Anacardiaceae	Root	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma congolense*	NI	Nigeria	Atawodi (2005); Atawodi et al. (2003)
Maranthes floribunda (Bak.) F. White	Sea bean	Chrysobalanaceae	Stem bark	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Maytenus senegalensis (Lam.) Exell	Confetti tree	Celastraceae	Twig/ Leaf/ Root	Aqueous/methanol/ Ethanolic extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma brucei rhodensiense*	200[a]	Nigeria/ Burkina Faso/ Mali/Cote d'Ivoire	Wurochekke and Nok (2004); Aderbauer et al. (2008) Atindehou et al. (2004)
Mitracarpus scaber Zucc. ex Schult. & Schult.f	Button grass	Rubiaceae	Leaf	Ethanolic extract/ azaanthraquinone isolate	Azaanthraquinone	*in vitro/ in vivo*	*Trypanosoma congolense*	NI	Nigeria	Nok (2002)
Mitragyna ciliata Aubrev. & Pellegra.		Rubiaceae	Root	Petroleum ether/ chloroform/ ethylacetate/butanol/ aqueous extracts	-	*in vivo*	*Trypanosoma brucei brucei*	NI	Nigeria	Ogbunugafor et al. (2007); Ogbunugafor et al. (2008)
Mitragyna inermis (Wild.) Kuntze	False abura	Rubiaceae	Leaf/ stem bark	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei brucei*	100/200[a]	Burkina Faso/ Mali	Aderbauer et al. (2008)
Momordica balsamina L.	Balsam pear	Cucurbitaceae	Whole plant/ Pulp	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro/ in vivo*	*Trypanosoma brucei brucei/ Trypanosoma congolense*	NI	Nigeria	Abubakar et al. (2005); Atawodi (2005); Atawodi et al. (2003)
Morinda morindiodes (Baker) Milne-Redh.	Brimstone tree	Rubiaceae	Root bark/ leaf	Aqueous\ethanolic extract	–	*in vivo*	*Trypanosoma brucei brucei| Trypanosoma brucei rhodesiense*	NI	Nigeria	Olukunle et al. (2010); Atindehou et al. (2004)
Moringa oleifera Lam.	Horseradish tree	Moringaceae	Leaf/ stem bark/ root	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	NI	Nigeria	Atawodi (2005)
Murraya koenigii (L.) Spreng.	Curry leaf	Rutaceae	Leaf	n-Hexane/chloroform/ ethylacetate/ methanolic extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma congolense*	NI	Nigeria	Adewunmi et al., 2001

Table 1 (*continued*)

Scientific name	Common name	Family	Part (s) used	Extract/fraction	Possible active component (s)	Model	Parasite	IC_{50} or MIC (μg/mL)	Country	References
Nauclea latifolia Sm.	African peach	Rubiaceae	Leaf/ Stem bark/ Root	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*/ *in vivo*	*Trypanosoma brucei brucei*/ *Trypanosoma brucei gambiense*	NI	Nigeria/ Cote d'Ivoire	Atawodi (2005); Youan et al. (1997)
Ocimum grattissimum L.	African basil	Lamiaceae	Leaf	Hexane/ethylacetate/ methanolic/aqueous extracts	–	*in vitro*/ *in vivo*	*Trypanosoma brucei brucei*/ *Trypanosoma brucei rhodesiense*	2.38 ± 0.13/ 2.08 ± 0.01/ 5.45 ± 1.14	Nigeria	Olukunle et al. (2010); Abiodun et al. (2012); Adamu et al. (2009)
Opilia celtidifolia (Guill. & Perr.) Endl. ex Walp.	–	Opiliaceae	Twigs/ leaves	Dichloromethane/ aqueous extracts	–	*in vitro*/ *in vivo*	*Trypanosoma brucei brucei*/ *Trypanosoma brucei gambiense*	500[a]	Burkina Faso/ Mali/ Cote d'Ivoire	Aderbauer et al. (2008); Youan et al. (1997)
Parkia biglobosa (Jacq.) R. Br. ex. G.Don	African locust bean	Leguminosae	Bark	Aqueous extract	–	*in vivo*	*Trypanosoma brucei gambiense*	NI	Cote d'Ivoire	Youan et al. (1997)
Parkia clappertoniana Keay	Clapperton's parkia	Leguminosae	Stem bark/ root	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei*/ *Trypanosoma congolense*	NI	Nigeria	Atawodi (2005); Atawodi et al. (2003)
Pericopsis laxiflora (Baker) Meeuwen	Satin wood	Leguminosae	Leaf/ twig	Dichloromethane/ methanolic/aqueous/ hexane/ethylacetate extracts	–	*in vitro*	*Trypanosoma brucei brucei*/ *Trypanosoma brucei rhodesiense*	39.2 ± 1.6/ 11.8 ± 0.8; IC_{50} = 10.71 ± 3.97/ 7.36 ± 0.50/ 23.07 ± 7.55	Benin/Nigeria	Hoet et al. (2004a); Abiodun et al. (2012)
Peristrophe bicalyculata (Retz.) Nees	–	Acanthaceae	Whole plant	Aqueous/butanol/ methanolic extract/ aceton:methanol fractions	–	*in vitro*/ *in vivo*	*Trypanosoma brucei brucei*	NI	Nigeria	Abdulazeez et al. (2013)
Phyllantus amarus Schumach. & Thonn.	Gulf leafflower	Euphorbiaceae	Leaf	Hexane/ethylacetate/ methanolic extracts	–	*in vitro*	*Trypanosoma brucei rhodesiense*	17.48 ± 0.05/ 10.56 ± 0.78/ 22.57 ± 0.47	Nigeria	Abiodun et al. (2012)
Piliostigma reticulatum (DC.) Hochst. (syn:	Camel's foot	Leguminosae	Leaf/ Stem bark/ root	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei*/ *Trypanosoma congolense*	NI	Nigeria	Atawodi (2005); Atawodi et al. (2003)
Piliostigma thonningii (Schum.) Milne-Redh. (Syn: *Bauhinia thonningii*)	Monkey bread	Leguminosae	Bark	Aqueous extract	–	*in vivo*	*Trypanosoma brucei gambiense*	NI	Cote d'Ivoire	Youan et al. (1997)
Pothomorphe umbellata (L.) Miq.	Monkey's hand	Piperaceae	Leaf	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Prosopis africana (Guill. & Perr.) Taub.	African mesquite	Leguminosae	Leaf/ stem bark/ root	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei*/ *Trypanosoma congolense*	NI	Nigeria	Atawodi (2005), Atawodi and Ogunbusola (2009), Atawodi et al. (2003)
Pterocarpus erinaceus Poir.	African rosewood	Leguminosae	Shoot	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei brucei*	200[a]	Burkina Faso/ Mali	Aderbauer et al. (2008)
Pseudocedrela kotschyi (Schweinf). Harms	Hard cedar-mahogany	Meliaceae	Stem bark	Methanolic extract	–	*in vitro*	*Trypanosoma congolense*	NI	Nigeria	Atawodi et al. (2003)

Psidium guajava L.	Guava tree	Myrtaceae	Leaf	Ethanolic extract	Alkaloids/ terpenes/ saponins/ flavonids	*in vivo*	*Trypanosoma brucei brucei*	NI	Nigeria	Adeyemi et al. (2009)
Pupalia lappacea (L.) Juss.	Creeping cock's comb	Amaranthaceae	Aerial part	Dichloromethane/ methanolic/aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei*	$52.0 \pm 2.8 / > 100 / > 100$	Benin	Bero et al. (2011)
Rauvolfia vomitoria Afzel.	Serpent wood	Apocynaceae	Roots	Aqueous extract	–	*in vivo*	*Trypanosoma brucei gambiense*	NI	Cote d'Ivoire	Youan et al. (1997)
Saba florida (Benth.) Bullock	Rubber vine	Apocynceae	Whole plant/ leaf	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro/ in vivo*	*Trypanosoma brucei brucei/ Trypanosoma congolense*	NI	Nigeria	Atawodi (2005); Atawodi et al. (2003); James and Emmanuel (2011)
Sansevieria liberica Hort. ex Gèrôme & Labroy	African bowstring hemp	Dracaenaceae	Aerial part	Dichloromethane/ methanolic/aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei*	$60.1 \pm 1.5 / > 100 / > 100$	Benin	Bero et al. (2011)
Schrankia leptocarpa DC.		Leguminosae	Leaf/ Twig	Dichloromethane/ Methanolic/aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei*	$49.2 \pm 2.9 // > 100 / > 100$; $55.9 \pm 3.5 // > 100 / > 100$	Benin	Bero et al. (2011)
Sclerocarya birrea (A.Rich.) Hochst.	Marula	Anacardiaceae	Leaf/ stem bark	Methanolic extract	–	*in vitro*	*Trypanosoma brucei brucei*	NI	Nigeria	Mikail (2009)
Securidaca longipenduculata Fresen.	Violet tree	Polygalaceae	Stem bark/ root	Methanolic extract	–	*in vitro/ in vivo*	*Trypanosoma brucei brucei/ Trypanosoma brucei gambiense*	50[a]	Nigeria/ Cote d'Ivoire/ Burkina Faso/ Mali	Abubakar et al. (2005), Atawodi et al. (2003), Atawodi (2005), Youan et al. (1997), Aderbauer et al. (2008)
Senna occidentalis (L.) Link (Syn: *Cassia occidentalis*)	Coffee senna	Leguminosae	Leaf	Ethanolic extract	–	*in vitro/ in vivo*	*Trypanosoma brucei brucei*	NI	Nigeria	Ibrahim et al. (2010)
Spilanthes oleracea var. *fusca* (Lam.) DC.	Eyeball plant	Asteraceae	Flowers	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei brucei*	500[a]	Burkina Faso/ Mali	Aderbauer et al. (2008)
Sterculia setigera Delile	Karaya gum tree	Sterculiaceae	Root bark	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	NI	Nigeria	Atawodi (2005)
Sterculia tomentosa Guill & Perr	False plane	Sterculiaceae	Root	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei brucei*	500[a]	Burkina Faso/ Mali	Aderbauer et al. (2008)
Stereospermum Kunthianum Cham.		Bignonianceae	Leaf/ stem bark	Aqueous/ethanolic extracts	–	*in vitro*	*Trypanosoma brucei brucei*	NI	Nigeria	Abu et al. (2009)
Striga spp (Spreng.) Parodi	Asiatic witchweed	Orobanchaceae	Leaf	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma congolense*	NI	Nigeria	Atawodi (2005), Atawodi et al. (2003)
Strychnos spinosa Lam.	Spiny monkey-orange	Loganiaceae	Leaf/ twig/ root	Aqueous/ Dichloromethane extracts	Triterpenoids and sterols	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma brucei rhodesiense*	$1.5 \pm 0.9 / 16.4 \pm 8.8$	Burkina Faso/ Mali/Benin	Aderbauer et al. (2008), Hoet et al. (2007)
Swartzia Madagascariensis Desv.	Snake bean	Caesalpiniaceae	Leaf/ stem bark/ root/ Pulb	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	NI	Nigeria	Atawodi (2005)
Syzygium guineense (Willd.) DC.	Water pear	Myrtaceae	Stem bark	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	NI	Nigeria	Atawodi (2005)

Table 1 (*continued*)

Scientific name	Common name	Family	Part (s) used	Extract/fraction	Possible active component (s)	Model	Parasite	IC_{50} or MIC (μg/mL)	Country	References
Tamarindus indica L.	Tamarind	Leguminosae	Leaf/ stem bark/ root	Aqueous/methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	500[a]	Nigeria/ Burkina Faso/ Mali	Wurochekke and Nok (2004), Atawodi et al. (2003), Aderbauer et al. (2008)
Tapinanthus globiferus Tiegh.	Mistletoe	Loranthaceae	Leaf	Methanolic extract	–	*in vitro/ in vivo*	*Trypanosoma congolense*		Nigeria	Abedo et al. (2013)
Terminalia avicennoides Guill. & Perr.		Combretaceae	Fruit/ Leaf/ Stem bark/ Root	Petroleum ether/ chloroform/ dichloromethane /methanol/aqueous extracts	Saponins/ellagic acid/flavogallonic acid bislactone/ punicalagin/ terchebulin/ castalagin	*in vitro/ in vivo*	*Trypanosoma brucei gambiense/ Trypanosoma evansi/ Trypanosoma brucei brucei*	100[a]	Nigeria/ Burkina Faso/ Mali	Atawodi (2005), Bizimana et al. (2006), Bulus et al. (2008); Shuaibu et al. (2008), Atawodi et al. (2003); Mann et al. (2011), Aderbauer et al. (2008), Atawodi et al. (2011)
Terminalia catappa L.	Wetland	Combretaceae	Leaf	Hexane/ethylacetate/ methanolic extracts	–	*in vitro*	*Trypanosoma brucei rhodesiense*	17.24 ± 2.79/ 7.80 ± 1.83/ 13.91 ± 2.21	Nigeria	Abiodun et al. (2012)
Terminalia ivorensis A.Chev.	Black afara	Combretaceae	Stem bark/ root	n-Hexane/ethanol extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma congolense*	NI	Nigeria	Adewunmi et al., 2001
Terminalia superba Engl. & Diels	Ofram tree	Combretaceae	Leaf/ stem bark/ root	n-Hexane/ethanol extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma congolense*	800[a]	Nigeria	Adewunmi et al., 2001), Antia et al. (2009)
Terminalia schimperiana Hochst.	–	Combretaceae	Young leaf	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Tithonia diversifolia (Hemsl.) A.Gray	Tree marigold	Asteraceae		Aqueous extract	–	*in vivo*	*Trypanosoma brucei brucei*	NI	Nigeria	Olukunle et al. (2010)
Trema orientalis (L.) Blume	Pigeon wood	Ulmaceae	Leaf/ stem bark	Hexane/ethylacetate/ methanolic extracts	–	*in vitro*	*Trypanosoma brucei rhodesiense*	10.26 ± 3.52/ 3.50 ± 0.59/ 11.70 ± 3.61; 13.46 ± 2.70/ 13.87 ± 2.57/ 20.35 ± 6.67	Nigeria	Abiodun et al. (2012)
Trichilia emetica Vahl	Banket mahogany	Meliaceae	Leaf/ twig/ stem bark \root	Aqueous/ dichloromethane \ethanolic extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma brucei rhodensiense*	8.6 ± 5.9/ 14.9 ± 10.7	Burkina Faso/ Mali/Benin/ Cote d'Ivoire	Aderbauer et al. (2008), Hoet et al. (2004a), Atindehou et al. (2004)
Trichilia monadelpha (Thonn.) J. J. De Wilde	–	Meliaceae	Stem bark	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Uapaca togoensis Pax	–	Euphorbiaceae	Stem bark/ Root bark	Aqueous/ethanolic extracts	–	*in vitro*	*Trypanosoma brucei brucei*	NI	Nigeria	Abu et al. (2009)
Vernonia amygdalina Delile	Bitter leaf	Asteraceae	Leaf	Aqueous extract	–	*in vitro*	*Trypanosoma brucei brucei.*	NI	Nigeria	Wurochekke and Nok (2004)
Vernonia blumeoides Hook.f.	Bitter leaf	Asteraceae	Leaf	Lactone-rich fraction	lactone-containing compounds	*in vitro/ in vivo*	*Trypanosoma brucei brucei*	NI	Nigeria	Ibrahim et al. (2013)b
Vernonia spp	Bitter leaf	Asteraceae	Leaf	Petroleum ether/ chloroform/methanol/ aqueous extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma congolense*	NI	Nigeria	Atawodi (2005); Atawodi et al. (2003)

Vitellaria paradoxum (C.F.Gaertn.) Hepper (Syn: *Butyrospermum paradoxum*)	Shea butter tree	Sapotaceae	Stem bark	Ethanolic extract	–	*in vivo*	*Trypanosoma brucei/ Trypanosoma congolense*	NI	Nigeria	Mbaya et al. (2007)
Vitex doniana Sweet	Black plum	Lamiaceae	Leaf/ stem bark	Petroleum ether/ chloroform/methanol/ aqueous/hexane/ ethylacetate extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma brucei rhodensiense*	10.92 ± 1.98/ 17.04 ± 1.13/ 40.98 ± 2.50; 6.58 ± 1.05/ 11.79 ± 2.05/ 58.16 ± 3.62	Nigeria	Atawodi (2005), Abiodun et al. (2012)
Waltheria indica L.	Sleepy morning	Sterculiaceae	Whole plant	Petroleum ether/ ethylacetate/n-butanol/hydroethanol extracts	Flavonoids/ Terpenes/ Alkaloids/Tannins	*in vitro*	*Trypanosoma brucei brucei.*	NI	Nigeria	Bala et al. (2011)
Waltheria lanceolata R. Br. ex Mast.	Milk weed	Steculiaceae	Root bark	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Ximenia americana L.	Yellow plum	Olacaceae	Leaf/ stem bark/ root	Methanolic/aqueous extracts/fraction	Flavonoids	*in vitro*	*Trypanosoma brucei brucei./ Trypanosoma congolense*	NI	Nigeria	Wurochekke and Nok (2004), Maikai et al. (2008), Maikai (2010)
Zanthoxylum zanthoxyloides (Lam.) Zepern. & Timler	Candlewood	Rutaceae	Stem bark	Methanolic extract	–	*in vivo*	*Trypanosoma brucei brucei*	NI	Nigeria	Mann et al. (2011)
Zanthoxylum gilletii (De Wild) Waterman	African wood	Rutaceae	–	Ethanol extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Cote d'Ivoire	Atindehou et al. (2004)
Ziziphus spina-christi (L.) Wild.	Christ's Thorn Jujube	Rhamnaceae	Leaf/ stem bark	Aqueous/methanol extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	NI	Nigeria	Wurochekke and Nok (2004)
Ziziphus abyssinica Hochst. ex A.Rich.	catch thorn	Rhamnaceae	Leaf/ stem bark	Aqueous/methanol extracts	–	*in vitro*	*Trypanosoma brucei brucei.*	NI	Nigeria	Wurochekke and Nok (2004)

IC_{50} values $\leq$ 20 μg/mL are considered good activity while IC_{50} values of 21–60 and 61–100 μg/mL are considered moderate and low activities respectively. Any $IC_{50} > 100$ μg/mL are considered ineffective (Bero et al., 2011). MIC means minimum inhibitory concentration: NI means the IC_{50} or MIC values were not indicated by the authors.

[a] Reported MIC values.

Table 2
List of anti-trypanosomal investigated medicinal plants from East Africa.

Scientific name	Common name	Family	Part(s) used	Extract/fraction	Possible active component (s)	Model	Parasite	IC_{50} or MIC (μg/mL)	Country	References
Acacia nilotica Delile	Gum Arabic tree	Leguminosae	Stem bark/ leaf	Dichloromethane/ methanolic extracts	–	*in vitro*	*Trypanosoma brucei rhodesiense*	$\leq 4400 \pm 1.0$/ 4900 ± 2.2: 4400 ± 1.7: $\leq 9300 \pm 1.5$	Tanzania	Freiburghaus et al. (1996a)
Acalypha hispida Burm.f.	Chenille plant	Euphorbiaceae	Leaf	Methanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	5.7 ± 2.5	Tanzania	Freiburghaus et al. (1996a)
Albizia anthelmintica Brongn.	Worm killer	Leguminosae	Root	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	49.42/51.09	Tanzania	Nibret et al. (2010)
Albizia gummifera (J.F.Gmel.) C.A. Sm.	Peacock flower	Leguminosae	Root bark	Dichloromethane/ methanolic/Aqueous extracts	–	*in vitro*	*Trypanosoma brucei rhodesiense*	$\leq 0.07 \pm 0.03$/ 0.2 ± 0.1/ $\leq 4.1 \pm 0.2$	Uganda	Freiburghaus et al. (1996b)
Albizia harveyi E.Fourn.	Sickle-leaved	Leguminosae	Root	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	33.16/85.07	Tanzania	Nibret et al. (2010)
Anchomanes abbreviatus Engl.	–	Araceae	Leaf/twig	Ethanolic extract		*in vitro*	*Trypanosoma brucei rhodesiense*	$> 500/19$[a]	Tanzania	Freiburghaus et al. (1997)
Anisophyllea obtusifolia Engl. & Brehmer	–	Anisophyllaceae	Root bark	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	16[a]	Tanzania	Freiburghaus et al. (1997)
Annona senegalensis Pers.	African custard-apple	Annonaceae	Stem bark	Petroleum ether/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei rhodesiense*	$\leq 5000 \pm 3.0$/ $\leq 900 \pm 0.5$[a]	Tanzania	Freiburghaus et al. (1996a)
Artemesia annua L.	Sweet wormwood	Asteraceae	Leaf	Dichloromethane extract		*in vivo*	*Trypanosoma brucei rhodesiense*	NI	Kenya	Peter et al. (2009)
Alstonia boonei De Wild.	Cheesewood	Apocynaceae	Stem bark	Petroleum ether/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei rhodesiense*	$\leq 1400 \pm 1.6$/ $\leq 1700 \pm 1.3$	Tanzania	Freiburghaus et al. (1996a)
Azadirachta indica A.Juss.	Neem	Meliaceae	Stem bark/ leaf	Dichloromethane/ aqueous extracts/fraction	Tetranotriterpenoids	*in vivo*	*Trypanosoma brucei rhodesiense*	NI	Kenya	Peter et al. (2009), Ngure et al. (2009), Githua et al. (2010)
Balanites aegyptiaca (L.) Delile	Desert date	Balantiaceae	Bark	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	22.11/39.40	Tanzania	Nibret et al. (2010)
Bidens pilosa L.	Immature stellate	Asteraceae	Leaf	Dichloromethane extract	–	*in vivo*	*Trypanosoma brucei rhodesiense*	NI	Kenya	Peter et al. (2009)
Bussea occidentalis Hutch.	Samanta	Leguminosae	Stem bark	Methanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	500 ± 0.3	Tanzania	Freiburghaus et al. (1996a)
Capparis elaeagnoides Gilg	–	Capparaceae	Root	Petroleum ether/ methanolic/ dichloromethane/aqueous extracts	–	*in vitro*	*Trypanosoma hrucei rhodesiense*	NI	Tanzania	Freiburghaus et al. (1996b)
Cassia abbreviata Oliv. (Syn: *Senna abbreviata*)	long-tail cassia	Leguminosae	Leaf	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	54.07/22.14	Tanzania	Nibret et al. (2010)
Combretum zeyheri Sond.	Large-fruited bushwillow	Combretaceae	Bark	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	87.45/38.97	Tanzania	Nibret et al. (2010)
Commiphora emenii Engl.	Umbrella thorn	Burseraceae	Stem bark/ root bark/ leaf	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	19/19/167[a]	Tanzania	Freiburghaus et al. (1997)
Cordia myxa L.	Indian cherry	Boraginaceae	Leaf	Aqueous extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	$\leq 1300 \pm 0.4$	Tanzania	Freiburghaus et al. (1996a)
	Rattle box	Leguminosae	Seed		–	*in vitro*	*Trypanosoma brucei brucei*	186.01/156.49	Ethiopia	Nibret et al. (2009)

Crotalaria agatiflora Schweinf. Ex Engl.				Methanolic/ dichloromethane extracts						
Crotalaria axillaris Aiton	Rattle pod	Leguminosae	Seed/leaf	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	126.36; 137.10/57.59	Ethiopia	Nibret et al. (2009)
Crotalaria emarginella Vatke	Desert senna	Leguminosae	Leaf	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	137.62/48.55	Ethiopia	Nibret et al. (2009)
Crotalaria fascicularis Polhill	Northern bracken	Leguminosae	Twig	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	150.01/56.89	Ethiopia	Nibret et al. (2009)
Crotalaria incana L.	Woolly rattle pod	Leguminosae	Pods/leaf/ twig/seed	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	68.35/52.67; 61.97/ 28.55; 46.29/48.27; 164.99/144.73	Ethiopia	Nibret et al. (2009)
Crotalaria gillettii Polhill	Rattle pod	Leguminosae	Aerial part/ leaf	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	111.89/104.06; 112.97	Ethiopia	Nibret et al. (2009)
Crotalaria laburnifolia L.	Bird flower	Leguminosae	Leaf/pods/ seed/twig	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	53.80/51.44; 82.68/ 93.84; 182.23/162.80; 98.62/59.05	Ethiopia	Nibret et al. (2009)
Crotalaria mildbraedii Baker f.	Rattle pod	Leguminosae	Twig/leaf	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	94.41/51.49; 106.50/ 25.32	Ethiopia	Nibret et al. (2009)
Crotalaria phillipsiae Baker	Rattle pod	Leguminosae	Twig/leaf	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	70.78/12.67; 113.63/ 49.19	Ethiopia	Nibret et al. (2009)
Crotalaria pycnostachya Benth.	Rattle pod	Leguminosae	Pods/leaf/ seed	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	70.38/67.00; 56.32/ 50.15; 165.81/164.80	Ethiopia	Nibret et al. (2009)
Crotalaria spinosa Benth.	Rattle pod	Leguminosae	Pods	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	111.64/45.58	Ethiopia	Nibret et al. (2009)
Cussonia zimmermannii Harms	Peawood	Araliaceae	Root bark	Petroleum ether extract	Polyacetylenes	*in vitro*	*Trypanosomabruceirhodesiense*/ *Trypanosomacruzi*	<5	Tanzania	Senn et al. (2007)
Cynoglossum geometricum Baker & C.H. Wright	-	Boraginaceae	Leaf/flower	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	101.36/64.01; 161.98/ 48.75	Ethiopia	Nibret et al. (2009)
Diospyros mafiensis F. White	Coromandel ebony	Ebenaceae	Leaf	Ethanolic extract		*in vitro*	*Trypanosoma brucei rhodesiense*	56[a]	Tanzania	Freiburghaus et al. (1997)
Diospyros mespililbrmis Hochst. ex A. DC.	African ebony	Ebenaceae	Stem bark/ leaf	Dichloromethane/ methanolic extracts	–	*in vitro*	*Trypanosoma brucei rhodesiense*	$\leq 9100 \pm 1.5$/ $\leq 7600 \pm 2.6$/ 1900 ± 1.0	Tanzania	Freiburghaus et al. (1996a)
Diospyros verrucosa Hiern	Mock white stinkwood	Ebenaceae	Root bark	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	6[a]	Tanzania	Freiburghaus et al. (1997)
Ehretia amoena Klotzsch	Puzzle bush	Boraginaceae	Root bark/ stem bark/ leaf	Dichloromethane/ methanolic extracts	–	*in vitro*	*Trypanosoma brucei brucei*/ *Trypanosoma brucei rhodesiense*	$\leq 4.1 \pm 2.4$; 9.6 ± 3.0; $\leq 0.9 \pm 0.2$/ $\leq 3.3 \pm 1.1$	Uganda	Freiburghaus et al. (1996b)
Entada abyssinica A.Rich.	Splinter bean	Leguminosae	Root bark	Methanolic/ dichloromethane extracts	Diastereoisomer of kolavenol	*in vitro*	*Trypanosoma brucei brucei*/ *Trypanosoma brucei rhodesiense*	46.39/56.21; 2.5	Tanzania/ Uganda	Nibret et al. (2010); Freiburghaus et al. (1996b); Freiburghaus et al. (1998)
Entandrophragma bussei Harms ex Engl.	sapelewood	Meliaceae	Bark	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	52.92/14.48	Tanzania	Nibret et al. (2010)
Foetidia africana Verdc.	Iron wood	Lecythidaceae	Leaf/stem bark	Ethanolic extrac	–	*in vitro*	*Trypanosoma brucei rhodesiense*	56/6[a]	Tanzania	Freiburghaus et al. (1997)
Garcinia huillensis Welw.	Granite mango steen	Clusiaceae	Root	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	$\leq 4.4 \pm 2.5$	Uganda	Freiburghaus et al. (1996b)
		Simaroubaceae	Leaf		–	*in vitro*	*Trypanosoma brucei brucei*	28.92/22.93	Tanzania	Nibret et al. (2010)

Table 2 (*continued*)

Scientific name	Common name	Family	Part(s) used	Extract/fraction	Possible active component (s)	Model	Parasite	IC_{50} or MIC (μg/mL)	Country	References
Harrisonia abyssinica Oliv.				Methanolic/ dichloromethane extracts						
Heliotropium cinerascens Steud. ex DC	Indian heliotrope	Boraginaceae	Twig	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	134.19/222.92	Ethiopia	Nibret et al. (2009)
Heliotropium steudneri Vatke	White bristle bush	Boraginaceae	Leaf/twig	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	99.94/48.85; 125.61/ 98.01	Ethiopia	Nibret et al. (2009)
Heliotropium somalense Vatke	Tree heliotrope	Boraginaceae	Leaf/twig	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	135.35/49.06; 107.97/ 27.09	Ethiopia	Nibret et al. (2009)
Hymenocardia acida Tul.	Large red-heart	Euphorbiaceae	Root	Methanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	2200 ± 0.9	Tanzania	Freiburghaus et al. (1996a)
Hymenocardia ulmoides Oliv.	Small red-heart	Euphorbiaceae	Leaf/stem bark/root bark	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	167/19/19[a]	Tanzania	Freiburghaus et al. (1997)
Khaya senegalensis (Desv.) A.Juss	African mahogany	Meliaceae	Leaf	Ethanolic extract/ chloroform fractions	–	*in vitro*	*Trypanosoma brucei rhodesiense*	167[a]	Tanzania/ Kenya	Freiburghaus et al. (1997)
Kigelia africana (Lam.) Benth.	Sausage tree	Bignoniaceae	Fruit/leaf	Dichloromethane extract	–	*in vivo*	*Trypanosoma brucei rhodesiense*	53.24/23.65	Kenya/ Tanzania	Peter et al. (2009); Nibret et al. (2010)
Lannea humilis (Oliv.) Engl.	tree grap	Anacardiaceae	Bark	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	56.16/75.41	Tanzania	Nibret et al. (2010)
Lannea stuhlmannii Engl.	False marula	Anacardiaceae	Root	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	44.23/22.24	Tanzania	Nibret et al. (2010)
Lantana camara L.	Bird's brandy	Verbenaceae	Leaf	Petroleum ether extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	$\leq 1.4 \pm 0.3$	Uganda	Freiburghaus et al. (1996b)
Lonchocarpus capassa Rolfe	Apple-leaf	Leguminosae	Leaf	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	73.80/21.68	Tanzania	Nibret et al. (2010)
Morinda lucida Benth.	Brimstone tree	Rubiaceae	Root	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	$\leq 9800 \pm 0.5$	Tanzania	Freiburghaus et al. (1996a)
Moringa stenopetala (Baker f.) Cufod.	Cabbage tree	Moringaceae	Leaf/root bark/wood	Acetone/ethanolic extracts	–	*in vitro*	*Trypanosoma brucei brucei/ Trypanosoma cruzi*	10.0/9.2	Ethiopia	Mekonnen et al. 1999
Newbouldia laevis (P.Beauv.) Seem.	African border tree	Bignoniaceae	Stem bark	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	$\leq 6300 \pm 3.1$	Tanzania	Freiburghaus et al. (1996a)
Physalis angulata L.	Cut leaf ground-cherry	Solanaceae	Fruit/root/ stem/leaf	Petroleum ether/ methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei rhodesiense*	NI	Tanzania	Freiburghaus et al. (1996a)
Securidaca longipedunculata Fresen.	Violet tree	Polygalaceae	Leaf	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	55.56/11.20	Tanzania	Nibret et al. (2010)
Securinega Virosa (Roxb. Ex Wild.) Baill.	Snowberry tree	Euphorbiaceae	Root	Petroleum ether/ methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei rhodesiense*	$\leq 0.5 \pm 0.1$/ $\leq 2.1 \pm 1.4$/5.9 ± 4.6	Uganda	Freiburghaus et al. (1996b)
Senecio hadiensis Forssk.	Ragwort	Asteraceae	Leaf/flower	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	57.43/52.40; 98.21/ 104.62	Ethiopia	Nibret et al. (2009)
Senna singueana (Delile) Lock	Winter Cassia	Leguminosae	Bark	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	49.09/49.37	Ethiopia	Nibret et al. (2009)
Solanecio angulatus (Vahl) C. Jeffrey		Asteraceae	Leaf/flower	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	58.66/41.23; 12.47/ 12.17	Ethiopia	Nibret et al. (2009)
		Asteraceae	Flower	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	71.55/48.79	Ethiopia	Nibret et al. (2009)

Solanecio gigas (Vatke) C. Jeffrey										
Solanecio mannii (Hook.f.) C. Jeffrey		Asteraceae	Leaf	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	50.58/24.89	Ethiopia	Nibret et al. (2009)
Strychnos panganiensis Gilg		Loganiaceae	Leaf/stem bark	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	56/56[a]	Tanzania	Freiburghaus et al. (1997)
Strychnos spinosa Lam.	Green Monkey Orange	Strychnaceae	Leaf	Aqueous extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	$\leq 2500 \pm 1.9$	Tanzania	Freiburghaus et al. (1996a)
Terminalia sericea Burch. ex DC.	Silver cluster-leaf	Combretaceae	Leaf	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	36.23/21.71	Tanzania	Nibret et al. (2010)
Toona ciliata M. Roem.	Red cedar	Meliaceae	Root	Chloroform/methanolic extracts	Siderin and cedrolone	*in vitro*	*Trypanosoma brucei rhodesiense*	66.14/37.76	Kenya	Githua et al. 2011
Turraea fischeri Görke	Matopos honeysuckle tree	Meliaceae	Bark	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	66.14/37.76	Tanzania	Nibret et al. (2010)
Vernonia auriculifera Hiern		Asteraceae	Root	Dichloromethane extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	9.4 ± 2.8	Uganda	Freiburghaus et al. (1996b)
Vernonia subuligera O. Hoffm.	Eared vernonia	Asteraceae	Leaf/root bark	Dichlorometh/petroleum ether extracts	–	*in vitro*	*Trypanosoma brucei rhodesiense*	$\leq 0.6 \pm 0.1/0.8 \pm 0.4$	Uganda	Freiburghaus et al. (1996b)
Warburgia salutaris (G. Bertol.) Chiov.	Pepper-bark tree	Canellaceae	Bark	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	45.13/10.68	Tanzania	Nibret et al. (2010)
Warburgia ugandensis Sprague	Pepper bark tree	Canellaceae	Stem	Ethanolic extract	Sesquiterpene	*in vitro*		NI	Uganda	Olila and Opuda-Asibo (2001)
Ximenia americana L.	Sea lime	Olacaceae	Leaf	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	86.64/49.18	Tanzania	Nibret et al. (2010)
Xylopia parvifolia Hook.f. & Thomson	Bushveld bitter wood	Annonaceae	Leaf/stem bark/root bark	Ethanolic extract	–	*in vitro*	*Trypanosoma brucei rhodesiense*	56/167/167	Tanzania	Freiburghaus et al. (1997)
Zanha africana (Radlk.) Exell	Velvet-fruit zanha	Sapindaceae	Root	Methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei brucei*	33.53/12.63	Tanzania	Nibret et al. (2010)
Zanthoxylum chalybeum Engl.	betel-nut palm	Rutaceae	Leaf/stem bark/root bark/Seed	Methanolic/ dichloromethane/ ethanolic extracts	–	*in vitro*	*Trypanosoma brucei brucei*/ *Trypanosoma brucei rhodesiense*	36.00/11.02;	Tanzania/ Uganda	Nibret et al. (2010); Freiburghaus et al. (1997); Olila and Opuda-Asibo (2001)
Zanthoxylum xanthoxyloides Lam.		Rutaceae	Stem bark	Petroleum ether/ methanolic/ dichloromethane extracts	–	*in vitro*	*Trypanosoma brucei rhodesiense*	$\leq 5600 \pm 2.3$/ $\leq 8.6 \pm 3.9/7.4 \pm 1.5$	Tanzania	Freiburghaus et al. (1996a)

IC_{50} values ≤ 20 μg/mL are considered good activity while IC_{50} values of 21–60 and 61–100 μg/mL are considered moderate and low activities respectively. Any $IC_{50} > 100$ μg/mL are considered ineffective (Bero et al., 2011). MIC means minimum inhibitory concentration: NI means the IC_{50} or MIC values were not indicated by the authors.

[a] Reported MIC values.

Table 3
List of antitrypanosomal investigated medicinal plants from Central Africa.

Scientific name	Common name	Family	Part (s) used	Extract/fraction	Possible active component (s)	Model	Parasite	IC_{50} (μg/mL)	Country	References
Aframomum letestuanum Gagnep.	–	Zingiberaceae	Seed	Dichloromethane/methanol	Diarylheptanoids	*in vitro*	*Trypanosoma brucei brucei* /*Trypanosoma brucei rhodesiense*	NI	Cameroon	Kamnaing et al. (2003)
Garcinia lucida Vesque	Brunei Cherry	Clusiaceae	Stem bark	Dichloromethane/methanol	Dihydrochelerythrine derivatives	*in vitro*	*Trypanosoma brucei brucei*	NI	Cameroon	Fotie et al. (2007)

MIC means minimum inhibitory concentration: NI means the IC_{50} or MIC values were not indicated by the authors.

Table 4
List of anti-trypanosomal investigated medicinal plants from North Africa.

Scientific name	Common name	Family	Part (s) used	Extract/Fraction	Possible active component (s)	Model	Parasite	IC_{50} (μg/mL)	Country	References
Argemone mexicana L.	Mexican prickly poppy	Papaveraceae	Whole plant	Chloroform/methanolic extracts	-	*in vivo*	*Trypanosoma evansi*	NI	Sudan	Samia (2011)
Aristolochia bracteolata A Lam.	Dutchman's pipe	Aristolochiaceae	Whole plant	Chloroform/methanolic extracts	-	*in vivo*	*Trypanosoma evansi*	NI	Sudan	Samia et al. (2006); Samia (2011)
Tinospora bakis (A. Rich.) Miers	Orange grape creeper	Menispermaceae	Whole plant	Chloroform/methanolic extracts	–	*in vivo*	*Trypanosoma evansi*	NI	Sudan	Samia (2011)

MIC means minimum inhibitory concentration: NI means the IC_{50} or MIC values were not indicated by the authors.

Table 5
List of anti-trypanosomal investigated medicinal plants from Southern Africa.

Scientific name	Common name	Family	Part (s) used	Extract/Fraction	Possible active component (s)	Model	Parasite	IC_{50} (μg/mL)	Country	References
Abrus precatorius L. subsp. africanus Verdc.	Bread vine	Leguminosae	Whole plant	Dichloromethane/methanol extract	-	*in vitro*	*Trypanosoma brucei rhodesiense*	1.04	South Africa	Mokoka et al. (2013)
Clausena anisata (Wild.) Hook.f.ex Benth.var. anisata	Horse wood	Rutaceae	Root	Dichloromethane/methanol extract	-	*in vitro*	*Trypanosoma brucei rhodesiense*	7.19	South Africa	Mokoka et al. (2013)
Drypetes gerrardii Hutch.	Forest iron plum	Meliaceae	Leaf/stem	Dichloromethane/methanol extract	-	*in vitro*	*Trypanosoma brucei rhodesiense*	8.39	South Africa	Mokoka et al. (2013)
Ekebergia capensis Sparrm.	Cape ash	Meliaceae	Root	Dichloromethane/methanol extract	-	*in vitro*	*Trypanosoma brucei rhodesiense*	1.36	South Africa	Mokoka et al. (2013)
Oedera genistifolia (L.) Anderb. & K. Bremer	-	Asteraceae	Whole plant	Dichloromethane/methanol extract	-	*in vitro*	*Trypanosoma brucei rhodesiense*	4.38	South Africa	Mokoka et al. (2013)
Ozoroa sphaerocarpa R. Fern. & A. Fern.	Currant resin tree	Anacardiaceae	Whole plant	Dichloromethane extract	-	*in vitro*	*Trypanosoma brucei rhodesiense*	10.90	South Africa	Mokoka et al. (2013)
Pappea capensis Eckl. & Zeyh.	Jacket plum	Sapindaceae	Leaf/Root	Dichloromethane/methanol extract	-	*in vitro*	*Trypanosoma brucei rhodesiense*	14.10/15.4	South Africa	Mokoka et al. (2013)
Psoralea pinnata L.	African scurfpea	Leguminosae	Leaf	Dichloromethane/methanol extracts	-	*in vitro*	*Trypanosoma brucei rhodesiense*	0.15/0.31	South Africa	Mokoka et al. (2013)
Schkuhria pinnata (Lam.) Kuntze ex Thell	Curious weed	Asteraceae	Whole plant	Dichloromethane/methanol extract	Schkuhrin I & II	*in vitro*	*Trypanosoma brucei rhodesiense*	2.04	South Africa	Mokoka et al. (2013)
Turraea floribunda Hochst.	Honey suckle tree	Meliaceae	Leaf/Bark/Root	Dichloromethane/methanol extract	-	*in vitro*	*Trypanosoma brucei rhodesiense*	24.4/17.1/22.4	South Africa	Mokoka et al. (2013)
Vernonia mespilifolia Less.	Swart tree bossie	Asteraceae	Leaf	Dichloromethane/methanol extract	Cynaropicrin	*in vitro*	*Trypanosoma brucei rhodesiense*	1.01	South Africa	Mokoka et al. (2013)

IC_{50} values $\leq$ 20 μg/mL are considered good activity while IC_{50} values of 21–60 μg/mL are considered moderate activity (Bero et al., 2011). IC_{50} values $>$ 20 μg/mL are considered ineffective as suggested by Pink et al. (2005).

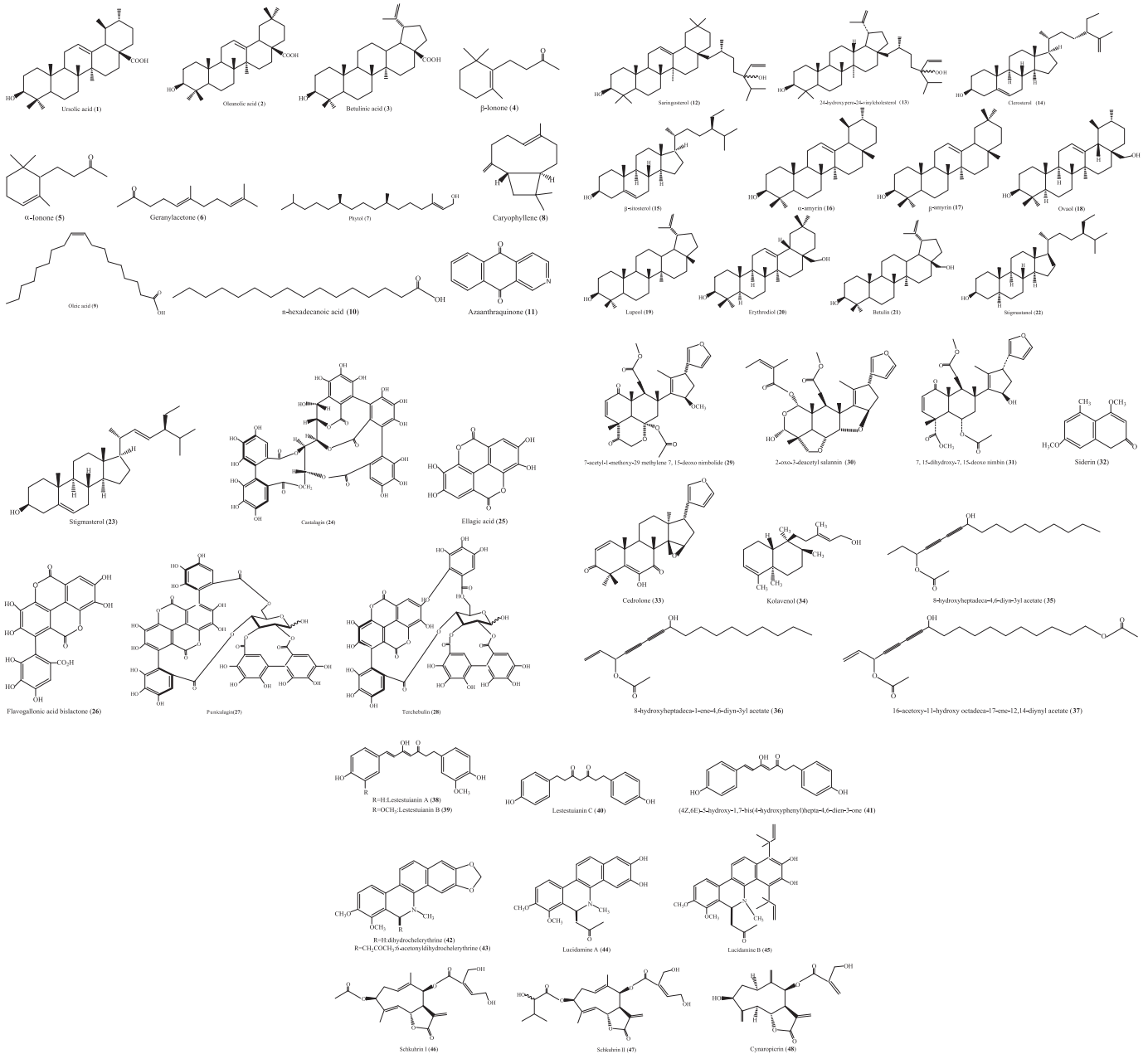

Fig. 3. Structures of isolated bioactive anti-trypanosomal compounds from African medicinal plants. Only active compounds that were isolated in pure form and tested for anti-trypanosomal activity are shown.

(Adeiza et al., 2010). The presence of flavonoids in the stem bark has been implicated for the anti-*Trypanosoma evansi* activity of the plant (Umar et al., 2010). Moreover, the active phenolic rich fraction of the bark was shown to be predominated by phloroglucinol and 3,4-(dihydroxyphenyl) acetic acid (Ibrahim et al., 2013a). Overall, the data suggest potent anti-trypanosomal activity of the stem bark of the plant. Furthermore, the studies suggest a promising anti-trypanosomal activity of *K. senegalensis* stem bark on different species of the parasite although it is not very effective in ameliorating the trypanosome-associated pathological changes.

3.1.2. *Annona senegalensis Pers.*

Another highly cited plant that was tested for *in vivo* anti-trypanosomal activity is *Annona senegalensis* Pers. The *in vitro* anti -trypanosomal activities were reported for both petroleum ether and dichloromethane root extracts of the plant with an MIC value of 50 μg/mL (Aderbauer et al., 2008; Atawodi, 2005). *in vivo*, the crude preparation of the plant leaves at an oral dose of 200 mg/kg bw for 7 days did not significantly mediate parasite clearance nor improve hematological parameters (Abubakar et al., 2005). Furthermore, in a dose finding study, the root dichloromethane extract at a dose of 37.5 mg/kg bw i.p. was toxic and led to the death of mice (Aderbauer et al., 2008). These findings seem to suggest a low or no *in vivo* anti-trypanosomal activity of the plant. However, contrary to these findings, the aqueous extract of the leaves at a dose of 200 mg/kg bw i.p. per day was reported to clear both the blood and cerebrospinal fluid stages of *Trypanosoma brucei brucei* in mice and was safe at doses even as high as 5000 mg/kg bw (Ogbadoyi et al., 2007). Interestingly, Ogbadoyi et al. (2007) also reported very low activity of the root and stem bark extracts of the plants. The phytochemical screening of this extract revealed the presence of saponins, tannins and phlobotannin (Ogbadoyi et al., 2007). Hence, these findings suggest that

the aqueous leaf extract of *Annona senegalensis* has more potent anti-trypanosomal activity than other parts. Interestingly, the leaf extract is the recommended preparation used in ethnomedicine to treat trypanosomiasis (Atawodi et al., 2002).

3.1.3. *Terminalia avicennoides Guill & Perr*

The leaf and stem bark methanol, aqueous and petroleum ether extracts of *Terminalia avicennoides* Guill & Perr were strongly active against both *Trypanosoma brucei brucei* and *Trypanosoma congolense*. In an *in vitro* set up, the extracts at concentrations of 0.4–4 mg/mL inhibited the motility of the parasite in 10–30 min (Atawodi et al., 2003; Atawodi, 2005). This result was further confirmed by the work of Bizimana et al. (2006) and Bulus et al. (2008) using *Trypanosoma brucei brucei*. The stem bark methanolic extract of the plant was further shown to be effective against *Trypanosoma brucei rhodesiense*, *Trypanosoma brucei gambiense* and *Trypanosoma evansi* with MIC values ranging from 12.5 to 17.5 μg/mL and high (>100) selective indices on fibroblasts (Shuaibu et al., 2008). However, in an *in vivo* study, treatment of *Trypanosoma brucei brucei* infected mice with 100–500 mg/kg bw i.p. of the fruit methanol extract of the plant was at most trypanostatic (Mann et al., 2011). Also, administration of 100 mg/kg bw i.p. (2 times per day) of the aqueous leaves extract was able to reduce *Trypanosoma brucei brucei* load in mice after 3 days of treatment (Bizimana et al., 2006) but 200 mg/kg bw i.p. of the same extract was lethal to mice. Similarly, Atawodi et al. (2011) reported a reduction in parasitaemia (total clearance after three days with a relapse occurring after four weeks) and the associated anemia as well as extension of the life span of rats treated intramuscularly with 200 mg/kg bw of the root aqueous extract of the plant. Four anti-trypanosomal active compounds were isolated from leaves of the plant which are: punicalagin, ellagic acid, flavogallonic acid and terchebulin with MIC values of 15, 25, 7.5 and 27.5 μg/mL against *Trypanosoma brucei brucei* respectively (Shuaibu et al., 2008). From the *in vivo* studies, it seems that the different parts of *Trypanosoma avicennoides* possess the ability to retard the proliferation of the trypanosomes in the infected animals but could not completely eliminate the parasites from the bloodstream of infected animals.

3.1.4. *Acacia nilotica (L.) Delile*

Acacia nilotica (L.) Delile, especially the stem bark, was also reported to possess promising anti-trypanosomal activity. Methanolic extract of the bark was found to possess an MIC of 100 μg/mL in a long-term viability assay against *Trypanosoma brucei brucei* (Bizimana et al., 2006). On the other hand, dichloromethane stem bark extract of the plant showed anti-trypanosomal activity *in vitro* (MIC = 50 μg/mL) but did not clear the parasites in mice at a dose of 150 mg/kg bw i.p. twice daily for 3 days (Aderbauer et al., 2008). Furthermore, this extract was not toxic to mice at 75 and 150 mg/kg bw except for minor evidence of renal disorder and immunosuppressive effect (Aderbauer et al., 2008). In fact, the immunosuppressive effect was implicated for the failure of the extract to clear the *Trypanosoma brucei brucei* from the bloodstream. In a related study by Mann et al. (2011), the methanolic extract of the stem bark at a dose of 200 and 300 mg/kg bw i.p. completely cleared the parasites within 6–7 days post infection and prolonged the survival period of the mice up to 30 days. Furthermore, administration of 400 mg/kg bw i.p. of the same extract completely cured experimentally *Trypanosoma brucei brucei* infected mice (Ogbadoyi et al., 2011a). The presence of carbohydrates, saponins, tannins, cardiac glycosides (Ogbadoyi et al., 2011a), β-amyrin, betulin, β-sitosterol and D-pinitol (Aderbauer et al., 2008) was reported and implicated as the possible candidates for the observed anti-trypanosomal effects of the extracts but were not individually tested against the parasites.

3.1.5. *Securidaca longipenduculata Fresen.*

Securidaca longipenduculata Fresen. showed promising anti-trypanosomal activities against different sub-species of *Trypanosoma brucei*. The root bark of *Securidaca longipenduculata* was reported to possess *in vitro* activity with MIC ≤ 50 μg/mL (Atawodi et al., 2003; Abubakar et al., 2005; Aderbauer et al., 2008). *in vivo*, the dichloromethane extract of the bark at a dose of 150 mg/kg bw i.p. was able to reduce the level of parasitemia up to 48% in mice and was not toxic to mice at 75 and 150 mg/kg bw (Aderbauer et al., 2008). Moreover, oral administration of 100 mg/kg bw of the root bark aqueous extract improved hematological paramaters and survival period in *Trypanosoma brucei brucei* infected rats (Abubakar et al., 2005). The root of the plant was also shown to be rich in alkaloids, flavonoids and saponins (Abubakar et al., 2005).

3.1.6. *Hymenocardia acida Tul.*

The anti-trypanosomal activity of different parts of *Hymenocardia acida* Tul. was reported. The aqueous and ethanolic extracts of both root and stem bark (100% inhibition against *Trypanosoma brucei brucei*) (Abu et al., 2009) and dichloromethane extracts of the leaves and twigs ($IC_{50} < 6$ μg/mL against *Trypanosoma brucei brucei*) (Hoet et al., 2004a) of the plant were shown to be anti-trypanosomal in *in vitro* studies. At oral doses of 100–400 mg/kg bw, the stem bark hydroethanolic extract of the plant was able to reduce the level of the parasites (35–50%) and prolonged the survival period of *Trypanosoma brucei brucei* infected rats but did not significantly improve hematological parameters. This extract was shown to be rich in alkaloids, flavonoids, saponins and tannins (Abu and Uchendu, 2011).

3.1.7. *Guiera senegalensis J.F.Gmel.*

The aqueous root extract of *Guiera senegalensis* J.F.Gmel. at a concentration of 0.25 g/mL inhibited the *in vitro* motility of *Trypanosoma brucei brucei* in 45 min (Wurochekke and Nok, 2004). In a different study, the MIC of the leaf dichloromethane extract was found to be 50 μg/mL. This extract also reduced 42% of parasitemia in *Trypanosoma brucei brucei* infected mice at a dose of 150 mg/kg bw i.p. (Aderbauer et al., 2008) and was not toxic to mice at 75 and 150 mg/kg bw.

3.1.8. *Mormodica balsamina L.*

The chloroform, petroleum ether, methanol and aqueous extracts of the whole plant of *Mormodica balsamina* L. were reported to inhibit the *in vitro* motility of both *Trypanosoma brucei brucei* and *Trypanosoma congolense* at a concentration of 4 mg/mL (Atawodi et al., 2003; Atawodi, 2005). However, administration of the fresh glycosides-rich pulp of the plant at an oral dose of 150 mg/kg bw decreased parasitemia (80% inhibition against *Trypanosoma brucei brucei*) and improved hematological parameters and survival period of *Trypanosoma brucei brucei* infected rats (Abubakar et al., 2005).

3.1.9. *Terminilia superba Engl. & Diels*

Various extracts of the roots, stem and leaves of *Terminilia superba* Engl. & Diels were anti-trypanosomal in *in vitro* and *in vivo* studies (Adewunmi et al., 2001; Antia et al., 2009). Adewunmi et al. (2001) reported the anti-trypanosomal activity of the root and stem bark ethanol extracts of the plant with LC_{50} of 12.5–66.78 μg/mL. Moreover, the methanolic root extract of the plant cleared (with relapse) *Trypanosoma brucei brucei* in 3–6 days after infection at doses of 10 and 15 mg/animal i.p. (approximately 0.3 and 0.06 mg/kg bw) in mice and rats respectively (Antia et al.,

2009). However, at the same doses, the stem bark and leaf extracts of the plant were not anti-trypanosomal but were rather toxic and led to the death of the mice.

3.1.10. Other plants

Under this subheading, other West African plants that were investigated for *in vivo* anti-trypanosomal activity in a single publication with no complementary information elsewhere are discussed. The plants were further categorized based on their potency and the ability to ameliorate the disease-associated pathological alterations.

Some West African plants were reported to possess *in vivo* anti-trypanosomal activities by a single research group. Some of these plants were further investigated on their effects on the trypanosome-induced pathological changes while others were not. Among the latter is *Holarrhena africana* A.DC. which, daily treatment with 40 and 80 mg/kg bw i.p. of a fraction obtained from leaves of the plant resulted in a complete disappearance of *Trypanosoma brucei rhodesiense* in infected mice 5 days post infection (Nwodo et al., 2007). The fraction was also not cytotoxic against L-6 cells. Furthermore, intramuscular administration of the methanolic extract of *Landolphia uniflora* (Stapf) Pichon leaves, ethanolic extract of *Psidium guajava* L. leaves at 300 mg/kg bw and stem bark methanolic extract of *Bombax buonopozense* P.Beauv. at 300 mg/kg bw i.p. completely cleared *Trypanosoma brucei brucei* from the bloodstream of infected animals (Atawodi and Alafiatayo, 2007; Adeyemi et al., 2009; Mann et al., 2011). Fractions obtained from the chloroform extract of *Artemisia maciverae* Hutch. & Dalziel also cleared *Trypanosoma brucei brucei* in mice at a dose of 100 mg/kg bw i.p. administered for 7 days (Ene et al., 2009). Apart from these extracts which completely eliminated the parasites, other extracts with lesser potencies have been reported. For example, the leaf ethanolic extract of *Dissotis rotundifolia* (Sm.) Triana, at a dose of 800 mg/kg bw i.p. reduced parasitemia up to 78% in rats (Mann et al., 2009). Furthermore, oral administration of butanol extract of *Mitragyna ciliata* Aubrev. & Pellegra root (100 mg/kg bw) caused a reduction of 66.6% parasite load via a mechanism that involves modulation of Ca^{2+} concentration in the infected rats but the extract induced hepatic and renal toxicities at doses > 800 mg/kg bw (Ogbunugafor et al., 2008). Ogbadoyi et al. (2011b) also reported the trypanostatic activity of 600 mg/kg bw i.p. of 50% methanolic extract of *Garcinia kola* Heckel nut in mice. The extract consistently maintained the parasites at a very low level for up to 40 days post treatment. This finding was similar to the report by Mann et al. (2011) where administration of methanolic extracts *Zanthoxylum zanthoxyloides* (Lam.) Zepern. & Timler (stem bark) showed trypanostatic effects even at a dose of 500 mg/kg bw i.p. In another study, treatment of *Trypanosoma congolense* infected animals with 400 mg/kg bw i.p. of the methanolic extracts of *Tapinanthus globiferus* Tiegh. (leaves) and *Gongrenema latifolium* Benth. (stem bark) reduced the parasites load up to 50% in the animals (Abedo et al., 2013). Similar results were obtained in *Trypanosoma brucei brucei* infected mice given intramuscular dose of 200 mg/kg bw of the leaf methanolic extract of *Prosopis africana* (Guill. & Perr.) Taub. (Atawodi and Ogunbusola, 2009). This extract from *Prosopis Africana* was however toxic to the animals at 300 mg/kg bw i.m. leading to the death of the animals in less than a week of treatment.

3.1.10.1. Anti-trypanosomal plants from West Africa with ameliorative effects on the trypanosome-induced pathological changes. The leaf ethanol extract of *Senna occidentalis* (L.) Link was effective against the *Trypanosoma brucei brucei* because it significantly lowered parasitemia in a group of rats treated with an oral dose of 200 mg/kg bw of the extract for 6 days compared to an untreated group. Organ damage and anemia induced by *Trypanosoma brucei brucei* infection in the rats were also ameliorated by the *Senna occidentalis* leaf extract treatment (Ibrahim et al., 2010). Other plants with anti-trypanosomal activity against *Trypanosoma brucei brucei* are *Saba florida* (Benth.) Bullock and *Cissus multistriata.* Treatment of infected rats with 200 and 400 mg/kg bw of the leaf hydromethanolic extracts of the plants resulted in a reduction of the parasite load and anemia as well as improvement of body weight loss (James and Emmanuel, 2011). Similarly, oral administration of 500 and 1000 mg/kg bw of pulp extract of *Cucumis metuliferus* E.Mey. ex Schrad reduced parasitemia and ameliorated *Trypanosoma brucei brucei*-induced organ pathological changes in rabbits (Abubakar et al., 2011). Recently, the anti-trypanosomal activity of the lactone-rich fraction of *Vernonia blumeoides* Hook.f. leaves was demonstrated. Furthermore, the fraction was able to alleviate *Trypanosoma brucei brucei*-induced anemia and organ damage (approximately 90%) at an oral dose of 300 mg/kg bw (Ibrahim et al., 2013b). Improvement of organ damage and other hematological parameters was also reported in *Trypanosoma congolense* infected animals treated with aqueous extract of *Hibiscus sabdariffa* L. calyces *ad libitum* (Umar et al., 2009) which was attributed to the presence of high amount of ascorbic acid in the extract. Other West African plants extracts that were reported to increase the packed cell volume and survival period of trypanosome-infected animals are administration of 200 mg/kg bw i.p. of stem bark ethanolic extract of *Vitellaria paradoxum* (C.F.Gaertn.) Hepper (Mbaya et al., 2007), administration of 400 mg/kg bw i.p. of stem bark ethanolic extract of *Azadirachta indica* A.Juss. (Mbaya et al., 2010), oral administration of 200 mg/kg bw of acetone:methanol fraction of *Peristrophe bicalyculata* (Retz.) Nees (Abdulazeez et al., 2013) and oral treatment with 1 mL of *Aloe vera* pulp (Abubakar et al., 2005). However, treatment with high doses (> 800 mg/kg bw i.p.) of stem bark ethanolic extracts of *Vitellaria paradoxum* (LD_{50} of 820 mg/kg bw i.p.) and *Azadirachta indica* (LD_{50} of 870 mg/kg bw i.p.) was associated with morbidity and mortality in rats (Mbaya et al., 2007, 2010).

From the above findings, it seems that, in addition to the anti-trypanosomal activities, a number of West African plants used in ethnomedicine could reverse the trypanosome-induced pathological changes with *Senna occidentalis*, *Cucumis metuliferus* and *Vernonia blumeoides* being more promising in this respect. Furthermore, it could be deduced that the toxicity of most of the toxicologically investigated plants is manifested at a dose > 800 mg/kg bw. This is interesting because the doses proposed to be considered as effective in *in vivo* studies is < 100 mg/kg bw (Pink et al., 2005). Thus, all extracts with potent *in vivo* anti-trypanosomal activity < 100 mg/kg bw with no toxic effect below 800 mg/kg bw could be considered to possess better potentials for application as anti-trypanosomes than others.

On the other hand, some plant extracts were reported to possess no *in vivo* anti-trypanosomal activity as indicated in Table 7 but it is noteworthy that the lack of activity may not necessarily be absolute because other extracts from the same plant may give positive results. Furthermore, different trypanosome species or animal model may yield a more positive anti-trypanosomal activity.

3.1.11. Identified bioactive anti-trypanosomal agents from West African plants

The active components through which these plants exert anti-trypanosomal activities vary. Several researchers performed phytochemical analysis of the anti-antitrypanosomal plants and implicated the presence of a number of secondary metabolites to be responsible for the observed effects. Unfortunately, very few suggested a specific compound. The suggested group of secondary metabolites include alkaloids, flavonoids, saponins, tannins, glycosides, resins, steroids, anthraquinones, terpenes and phlobotannins (Abubakar et al., 2005; Atawodi and Alafiatayo, 2007; Bala et al., 2011; Bulus

et al., 2008; Adamu et al., 2009; Atawodi and Ogunbusola, 2009; Adeyemi et al., 2009; Abu and Uchendu, 2011).

Apart from the general preliminary qualitative phytochemical identification, some authors have attempted to move a step further in order to more specifically identify the active components. Diallyl-disulfide (DAD) from the pulp of *Allium sativum* L. was proved to be responsible for the *in vitro* and *in vivo* anti-trypanosomal properties of the plant possibly through disruption of membrane lipid synthesis in the parasites (Nok et al., 1996). The compound exhibited anti-trypanosomal activity in *Trypanosoma brucei brucei* infected mice at 120 mg/kg bw and also inhibited the development of procyclic forms of the parasites. In another study, bioassay guided fractionation of the chloroform extract from *Artemisia maciverae* yielded triterpenes and alkaloids as active anti-trypanosomal components against *Trypanosoma brucei brucei* (Ene et al., 2009). However, the structure of the active compound was not elucidated. In addition to bioassay guided fractionation, some authors have used GC–MS analysis to identify the possible bioactive anti-trypanosomal compounds of the plant materials. This includes the identification of 25 compounds in the lactone-rich fraction of *Vernonia blumeoides* leaves, the majority of those compounds contain lactone moiety (lactone-containing) or sesquiterpene derivatives (Ibrahim et al., 2013b). Furthermore, GC–MS analysis was used to identify phloroglucinol and 3,4-(dihydroxyphenyl) acetic acid as the possible anti-trypanosomal compounds in a phenolics-rich fraction of *Khaya senegalensis* stem bark (Ibrahim et al., 2013a). In another study, Habila et al. (2010) used GC–MS to identify cyclobutane, 6-octenal, eucalyptol and citral as the possible candidates for the observed *in vitro* anti-*Trypanosoma brucei brucei* and anti-*Trypanosoma evansi* activities of essential oils of *Citrus sinensis* (L.) Osbeck, *Eucalyptus citriodora* Hook, *Eucalyptus camaldulensis* Dehnh. and *Cymbopogon citratus* (DC.) Stapf. On the other hand, HPLC-MS was also used to implicate two triterpenes, ursolic acid (**1**) and oleanolic acid (**2**), as the main compounds responsible for the *in vitro* anti-trypanosomal activity observed with *Keetia leucantha* (K.Krause) Bridson with IC_{50} of 2.5 and 7.3 μg/mL respectively, when the pure compounds were tested against *Trypanosoma brucei brucei* (Fig. 3). Alongside these triterpenes, betulinic acid (**3**), β-lonone (**4**), α-lonone (**5**), geranylacetone (**6**), phytol (**7**), caryophyllene (**8**) oleic acid (**9**) and n-hexadecanoic acid (**10**) were also detected in *Keetia leucantha* and their pure forms were active against the bloodstream forms of *Trypanosoma brucei brucei* in an *in vitro* study (Bero et al., 2013).

Notwithstanding, other specific active anti-trypanosomal components were isolated from different plants and their structures are provided in Fig. 3 while other relevant information on the compounds are presented in Table 6. Azaanthraquinone (**11**) was isolated from the methanol fraction of *Mitracarpus scaber* Zucc. ex Schult. & Schult.f (Nok, 2002) and was found to completely clear *Trypanosoma congolense* (*in vivo*) in mice at a dose of 50 mg/kg bw for 5 days without relapse. The author proved that the compound specifically interfere with the mitochondrial electron transport system of the parasite. Other authors isolated sterols (saringosterol (**12**), 24-hydroperoxy-24-vinylcholesterol (**13**), clerosterol (**14**) and β-sitosterol (**15**)) and triterpenes (α-amyrin (**16**), β-amyrin (**17**), uvaol (**18**) and lupeol (**19**)), from the lipophilic leaf extract of *Strychnos spinosa* Lam. as the bioactive *in vitro* anti-trypanosomal compounds against *Trypanosoma brucei brucei* (Hoet et al., 2007). To assess the structure–activity relationship of these compounds, other structurally related compounds were purchased and tested for *in vitro* anti-trypanosomal activity alongside the isolated phytochemicals. The commercially obtained compounds were ursolic acid (**1**), oleanolic acid (**2**), betulinic acid (**3**), erythrodiaol (**20**), betulin (**21**), stigmastanol (**22**) and stigmasterol (**23**). A close look at the findings of the study (Table 6) revealed that the nature of the substitution at the fifth ring of the triterpenes (Fig. 3) is vital for the activity of these compounds. The presence of more polar (acidic) moieties at the fifth ring of the triterpenes mediated the best *in vitro* anti-trypanosomal activity which was reduced as the polarity decreases (Table 6 and Fig. 3). In another study, bioassay guided isolation of the methanolic extracts of barks of *Anogeissus leiocarpus* (DC.) Guill. & Perr. and *Trypanosoma avicennoides* led to the isolation of phenolics (tannins); castalagin (**24**), ellagic acid (**25**), flavogallonic acid bislactone (**26**), punicalagin (**27**) and terchebulin (**28**) as the active anti-trypanosomal compounds from the plants (Shuaibu et al., 2008). It could be deduced from above that pentacyclic triterpenes or phenolics are the most predominantly identified and/or isolated anti-trypanosomal compounds from West African plants.

3.2. Anti-trypanosomal activity of East African plants

Appreciable data on the *in vitro* anti-trypanosomal activity of East African plants exist. However, very few reported the *in vivo* action of the plants and even fewer isolated a specific compound. Peter et al. (2009) investigated the activities of *Azadirachta indica* (stem bark), *Kigelia africana* (Lam.) Benth. (fruits), *Artemesia annua* L. (leaves) and *Bidens pilosa* L. (leaves) against *Trypanosoma brucei rhodesiense* in mice. The infected mice were treated with high doses 1000–5000 mg/kg bw i.p. of the methanol, dichloromethane and aqueous extracts of the plants parts. All the infected mice treated with 5000 mg/kg bw of the preparations died 6 days before the infected control due to the toxic effects of the extracts. However, 2000 mg/kg bw of the dichloromethane extract of *Kigelia africana* cured 60% of the animals and normalized their PCV. In another study, the stem bark dichloromethane extract of *A. indica* demonstrated strong *in vivo* anti-trypanosomal activity. The extract prevented weight loss, improved anemic condition and delayed the onset of parasitemia at an oral dose of 1000 mg/kg/bw in mice (Ngure et al., 2009). Interestingly, the extract was more effective than suramin in that study. In addition to *in vivo* anti-trypanosomal activity, some authors from this region have attempted to isolate the active anti-trypanosomal compounds.

Githua et al. (2010) isolated tetranotriterpenoid derivatives of nimbolide and nimbin (7-acetyl-15-methoxy-29-methylene-7,15-deoxo nimbolide (**29**), 2-oxo-3-deacetyl salannin (**30**), 7,15-dihydroxy-7,15-deoxo nimbin (**31**) with IC_{50} values of 6.9, 15.6 and 7.8 μg/mL respectively) from the leaf chloroform and methanol extracts of the plant and showed that the compounds were potent against *Trypanosoma brucei rhodesiense in vitro* and the result was better than cymerlarsan. The same research group also reported similar results with IC_{50} of 7.18 and 31.25 μg/mL for siderin (**32**) and cedrelone (**33**) isolated from the leaf methanol extract of *Toona ciliata* M. Roem (Githua et al., 2011). In another study, kolavenol (a diterpene) was isolated from the dichloromethane extract of *Entada abyssinica* A.Rich. root bark (Freiburghaus et al., 1998). The compound demonstrated potent anti-trypanosomal activity against the *Trypanosoma brucei rhodesiense* with an IC_{50} of 2.5 μg/mL. Furthermore, Senn et al. (2007) isolated two polyacetylenes from the petroleum ether extract of *Cussonia zimmermannii* Harms root bark which were active against *Trypanosoma brucei rhodesiense in vitro* with IC_{50} of 5.4, 0.14 and 0.42 μg/mL for 8-hydroxyheptadeca-4,6-diyn-3yl acetate (**35**), 8-hydroxyheptadeca-1-ene-4,6-diyn-2yl acetate (**36**) and 16-acetoxy-11-hydroxy octadeca-17-ene-12,14-diynyl acetate (**37**) respectively.

It is evident that East Africa is also naturally blessed with anti-trypanosomal plants (Table 2) with *A. indica* and 8-hydroxyheptadeca-1-ene-4,6-diyn-2yl acetate being more potent among the investigated plants and compounds respectively.

Table 6
Isolated bioactive anti-trypanosomal compounds from African medicinal plants.

	Compound	Plant species	Parasite	IC_{50} (μg/mL) in *in vitro* studies	References
1	Ursolic acid[c]	*Keetia leucantha*	Bloodstream/procyclic forms of *Trypanosoma brucei brucei*	2.5/6.5	Bero et al. (2013)
		Strychnos spinosa	*Trypanosoma brucei brucei*	1.0	Hoet et al. (2007)
2	Oleanolic acid[c]	*Keetia leucantha*	Bloodstream/procyclic forms of *Trypanosoma brucei brucei*	7.3/86.4	Bero et al. (2013)
		Strychnos spinosa	*Trypanosoma brucei brucei*	2.9	Hoet et al. (2007)
3	Betulinic acid[c]	*Keetia leucantha*	Bloodstream/procyclic forms of *Trypanosoma brucei brucei*	11.2/40.9	Bero et al. (2013)
4	β-lonone[c]	*Keetia leucantha*	Bloodstream/procyclic forms of *Trypanosoma brucei brucei*	10.5/55.8	Bero et al. (2013)
5	α-lonone[c]	*Keetia leucantha*	Bloodstream/procyclic forms of *Trypanosoma brucei brucei*	13.1/81.4	Bero et al. (2013)
6	geranylacetone[c]	*Keetia leucantha*	Bloodstream/procyclic forms of *Trypanosoma brucei brucei*	16.2/ > 100	Bero et al. (2013)
7	phytol[c]	*Keetia leucantha*	Bloodstream/procyclic forms of *Trypanosoma brucei brucei*	19.1/ > 100	Bero et al. (2013)
8	caryophyllene[c]	*Keetia leucantha*	Bloodstream/procyclic forms of *Trypanosoma brucei brucei*	41.2/ > 100	Bero et al. (2013)
9	Oleic acid[c]	*Keetia leucantha*	Bloodstream/procyclic forms of *Trypanosoma brucei brucei*	64.3/ > 100	Bero et al. (2013)
10	n-hexadecanoic acid[c]	*Keetia leucantha*	Bloodstream/procyclic forms of *Trypanosoma brucei brucei*	> 100	Bero et al. (2013)
11	Azaanthraquinone	*Mitracarpus scaber*	*Trypanosoma congolense*	50[b]	Nok (2002)
12	Saringosterol	*Strychnos spinosa*	*Trypanosoma brucei brucei*	7.8[a]	Hoet et al. (2007)
13	24-hydroperoxy-24-vinylcholesterol	*Strychnos spinosa*	*Trypanosoma brucei brucei*	3.2[a]	Hoet et al. (2007)
14	clerosterol	*Strychnos spinosa*	*Trypanosoma brucei brucei*	53.6	Hoet et al. (2007)
15	β-sitosterol	*Strychnos spinosa*	*Trypanosoma brucei brucei*	> 100	Hoet et al. (2007)
16	α-amyrin	*Strychnos spinosa*	*Trypanosoma brucei brucei*	48.9	Hoet et al. (2007)
17	β-amyrin	*Strychnos spinosa*	*Trypanosoma brucei brucei*	54.2	Hoet et al. (2007)
18	uvaol	*Strychnos spinosa*	*Trypanosoma brucei brucei*	12.3	Hoet et al. (2007)
19	lupeol	*Strychnos spinosa*	*Trypanosoma brucei brucei*	19.3	Hoet et al. (2007)
20	erythrodiol[c]	*Strychnos spinosa*	*Trypanosoma brucei brucei*	5.3	Hoet et al. (2007)
21	betulin[c]	*Strychnos spinosa*	*Trypanosoma brucei brucei*	4.0	Hoet et al. (2007)
22	stigmastanol[c]	*Strychnos spinosa*	*Trypanosoma brucei brucei*	> 100	Hoet et al. (2007)
23	stigmasterol[c]	*Strychnos spinosa*	*Trypanosoma brucei brucei*	55.5	Hoet et al. (2007)
24	Castalagin	*Anogeissus leiocarpus*	*Trypanosoma brucei brucei, Trypanosoma brucei gambiense, Trypanosoma brucei rhodesiense, Trypanosoma evansi*	22.5, 27.5, 27.5, 31.5	Shuaibu et al. (2008)
25	Ellagic acid	*Anogeissus leiocarpus, Terminalia avicenioides*	*Trypanosoma brucei brucei, Trypanosoma brucei rhodesiense*	≥ 25, ≥ 37.5	Shuaibu et al. (2008)
26	Flavogallonic acid bislactone	*Anogeissus leiocarpus, Terminalia avicenioides*	*Trypanosoma brucei rhodesiens brucei brucei, Trypanosoma brucei rhodesiens brucei gambiense, Trypanosoma brucei rhodesiens brucei rhodesiense, Trypanosoma brucei rhodesiens evansi*	7.5, 12.5, 8.75, 15	Shuaibu et al. (2008)
27	Punicalagin	*Terminalia avicenioides*	*Trypanosoma brucei brucei, Trypanosoma brucei gambiense, Trypanosoma brucei rhodesiense, Trypanosoma evansi*	≥ 15, 18.5, 22.5, 27.5 (25)	Shuaibu et al. (2008)
28	Terchebulin	*Terminalia avicenioides*	*Trypanosoma brucei brucei, Trypanosoma brucei gambiense, Trypanosoma brucei rhodesiense, Trypanosoma evansi*	27.5, 31.5, 27.5, ≥ 25	Shuaibu et al. (2008)
29	7-acetyl-15-methoxy-29-methylene-7,15-deoxo nimbolide	*Azadirachta indica*	*Trypanosoma brucei rhodesiense*	6.9	Githua et al. (2010)
30	2-oxo-3-deacetyl salannin	*Azadirachta indica*	*Trypanosoma brucei rhodesiense*	15.6	Githua et al. (2010)
31	7,15-dihydroxy-7,15-deoxo nimbin	*Azadirachta indica*	*Trypanosoma brucei rhodesiense*	7.8	Githua et al. (2010)
32	Siderin	*Toona ciliata*	*Trypanosoma brucei rhodesiense*	7.18	Githua et al. (2011)
33	Cedrelone	*Toona ciliata*	*Trypanosoma brucei rhodesiense*	31.25	Githua et al. (2011)

Table 6 (*continued*)

34	Kolavenol	*Entada abyssinica*	*Trypanosoma brucei rhodesiense*	2.5	Freiburghaus et al. (1998)
35	8-hydroxyheptadeca-4,6-diyn-3yl acetate	*Cussonia zimmermannii*	*Trypanosoma brucei rhodesiense*	5.4	Senn et al. (2007)
36	8-hydroxyheptadeca-1-ene-4,6-diyn-2yl acetate	*Cussonia zimmermannii*	*Trypanosoma brucei rhodesiense*	0.14	Senn et al. (2007)
37	16-acetoxy-11-hydroxy octadeca-17-ene-12,14-diynyl acetate	*Cussonia zimmermannii*	*Trypanosoma brucei rhodesiense*	0.42	Senn et al. (2007)
38	Letestuianin A	*Aframomum letestuanum*	*Trypanosoma brucei brucei*	>100	Kamnaing et al. (2003)
39	Letestuianin B	*Aframomum letestuanum*	*Trypanosoma brucei brucei, Trypanosoma brucei rhodesiense*	67, >100	Kamnaing et al. (2003)
40	Letestuianin C	*Aframomum letestuanum*	*Trypanosoma brucei brucei, Trypanosoma brucei rhodesiense*	2.6, 2.8	Kamnaing et al. (2003)
41	(4Z,6E)-5-hydroxy-1,7-bis (4-hydroxyphenyl) hepta-4,6-dien-3-one	*Aframomum letestuanum*	*Trypanosoma brucei brucei, Trypanosoma brucei rhodesiense*	2.6, 2.8	Kamnaing et al. (2003)
42	Dihydrochelerythrine	*Garcinia lucida*	*Trypanosoma brucei brucei*	0.8[a]	Fotie et al. (2007)
43	6-acetonyldihydrochelerythrine	*Garcinia lucida*	*Trypanosoma brucei brucei*	3.9[a]	Fotie et al. (2007)
44	Lucidamine A	*Garcinia lucida*	*Trypanosoma brucei brucei*	14.1[a]	Fotie et al. (2007)
45	Lucidamine B	*Garcinia lucida*	*Trypanosoma brucei brucei*	4.1[a]	Fotie et al. (2007)
46	Schkuhrin I	*Schkuhria pinnata*	*Trypanosoma brucei rhodesiense*	0.86[a]	Mokoka et al. (2013)
47	Schkuhrin II	*Schkuhria pinnata*	*Trypanosoma brucei rhodesiense*	1.5[a]	Mokoka et al. (2013)
48	cynaropicrin	*Vernonia mespilifolia*	*Trypanosoma brucei rhodesiense*	0.23[a]	Mokoka et al. (2013)

Only active compounds that were isolated in pure form and tested for anti-trypanosomal activity are shown. IC_{50} values >20 μg/mL are considered ineffective as suggested by Pink et al.(2005).

[a] Unit in μM.

[b] *In-vivo* study was conducted at the specified dose (mg/kg bw).

[c] These compounds were detected in the plants but commercially purchased and tested for anti-trypanosomal activity.

3.3. Anti-trypanosomal activity of central African plants

Very little data in two studies were obtained on investigated anti-trypanosomal plants from this region (Table 3). Kamnaing et al. (2003) isolated anti-trypanosomal diarylheptanoids from 1:1 dichloromethane:methanol fraction of *Aframomum letestuianum* Gagnep. seeds. Among the diarylheptanoids, letestuianin C (**40**) and 5-hydroxy-1,7-bis(4-hydroxyphenyl)hepta-4,6-diene-3-one (**41**) were exceptionally active against the bloodstream form of *Trypanosoma brucei brucei* ($IC_{50}=2.6$ μg/mL for each of the compounds) and *Trypanosoma brucei rhodesiense* ($IC_{50}=2.6$ μg/mL for each of the compounds *in vitro*). Similarly, Fotie et al. (2007) reported the isolation of benzo[*c*]phenanthridine alkaloids; dihydrochelerythrine (**42**); 6-acetonyldihydrochelerythrine (**43**); lucidamine A (**44**); lucidamine B (**45**) from *Garcinia lucida* Vesque stem bark which are active against *Trypanosoma brucei brucei in vitro* with IC_{50} of 0.8, 3.9, 14.1 and 4.1 μg/mL respectively.

The paucity of data from Central African plants is indeed surprising considering the prevalence of trypanosomiasis in the region and the ethnomedicinal exploitation of the plants from the region in the treatment of the disease.

3.4. Anti-trypanosomal activity of North African plants

In this region, only three plants from Sudan were found to be investigated in an *in vivo* experiment (Table 4). Samia (2011) extracted the whole plants of *Argimone mexicana* L., *Aristolochia bracteolata* A Lam. and *Tinospora bakis* (A. Rich.) Miers with chloroform and methanol and orally administered the extracts at 100, 200 and 500 mg/kg bw to *Trypanosoma evansi* infected rats. The chloroform extract of *Aristolochia bracteolata* was found to be the most effective because it clears 100% of the parasite at 500 mg/kg bw. Parasite clearance from the same extracts from *Tinospora bakis* and *Argimone Mexicana* were 50% (starting from day 8) and 70% (starting from day 5) respectively, however both were accompanied by a relapse after 12–15 days. Hence, considering the activities reported in this work, more indepth studies on North African plants, especially *Aristolochia bracteolata*, may be worthwhile.

3.5. Anti-trypanosomal activity of Southern African plants

Although no much work has been done on the plants from this region on the anti-trypanosomal activities, a study reported the *in vitro* anti-*Trypanosoma brucei rhodesiense* activity of extracts from ten plant species found in South Africa (Mokoka et al., 2013). In the study, the dichloromethane extract of *Psoralea pinnata* L. leaves was found to be the most potent with an IC_{50} value 0.15 μg/mL and a high selectivity index. Moreover, dichloromethane/methanol extracts of *Abrus precatorius* L. (whole plant), *Ekebergia capensis* Sparrm. (roots), *Schkuhria pinnata* (Lam.) Kuntze ex Thell (whole plant) and *Vernonia mespilifolia* Less (leaves) were also moderately active against the parasite with IC_{50} values ranging from 0.3 to 2.04 μg/mL and low selectivity index. The authors further used HPLC-based activity profiling to identify germacranolide sesquiterpene lactones (schkuhrin I (**46**) and schkuhrin II (**47**)) and cynaropicrin (**48**) (Fig. 3) as active anti-trypanosomal compounds from *Schkuhria pinnata* and *Vernonia mespilifolia* respectively. Hence, this work as the first from the region serves as a landmark in anti-trypanosomal studies considering the number of species investigated. Detailed *in vivo* studies especially on *Psoralea pinnata* is encouraged.

Table 7
African medicinal plants investigated for *in vivo* anti-trypanosomal activity.

Plant	Part used	Extract	Mode of administration	Parasite	Effective dose (mg/kg bw)	% inhibition	Reference
Acacia nilotica (L.) Delile	Stem bark	Dicholoromethane	Intraperitoneal	*Trypanosoma brucei brucei*	37.5	–	Adebauer et al. (2008)
		Methanolic	Intraperitoneal	*Trypanosoma brucei brucei*	200, 300, 400	100	Mann et al. (2011) Ogbadoyi et al. (2011a)
Acalypha wilkesiana Müll.Arg	Leaves	Aqueous	Intraperitoneal	*Trypanosoma brucei brucei*	400	[a]	Olukunle et al. (2010)
Afzelia Africana Pers.	Leaves, stem bark, root bark	Aqueous	Intraperitoneal	*Trypanosoma brucei brucei*	10	[a]	Antia et al. (2010)
Allium sativum L.	Pulp	Acetic acid/methanolic fractions	Oral	*Trypanosoma brucei brucei*	120	100	Nok et al. (1996)
Aloe vera (L.) Burm.f.	Pulp	–	Oral	*Trypanosoma brucei brucei*	1 mL	50	Abubakar et al. (2005)
Annona senegalensis Pers.	Lleaves	Aqueous	Oral	*Trypanosoma brucei brucei*	200	28	Abubakar et al. (2005)
			Intraperitoneal	*Trypanosoma brucei brucei*	200	100	Ogbadoyi et al. (2007)
	Root, stem bark	Aqueous, methanol, ethanol, ethyl acetate, hexane	Intraperitoneal	*Trypanosoma brucei brucei*	200	–	Ogbadoyi et al. (2007)
Artemisia maciverae Hutch. & Dalziel	Whole plant	chloroform	Intraperitoneal	*Trypanosoma brucei brucei*	100	75	Ene et al. (2009)
		Petroleum ether, methanol	Intraperitoneal	*Trypanosoma brucei brucei*	100	–	Ene et al. (2009)
Azadirachta indica A.Juss.	Stem bark	Ethanolic	Intraperitoneal	*Trypanosoma brucei brucei*	400	100	Mbaya et al. (2010)
	Bark	Dichloromethane	Intraperitoneal	*Trypanosoma brucei rhodesiense*	1000	100	Ngure et al. (2009)
Bombax buonopozense P.Beauv.	Stem bark	Methanol	Intraperitoneal	*Trypanosoma brucei brucei*	300	100	Mann et al. (2011)
Calotropis procera (Aiton) Dryand.	Leaves	Saponin-rich fraction	Oral	*Trypanosoma evansi*	100, 200	–	Ibrahim et al. (2013c)
Ceiba pentandra (L.) Gaertn.	Leaves	aqueous	Intraperitoneal	*Trypanosoma brucei brucei*	150	[a]	Bizimana et al. (2006)
Cissus multistriata	Leaf	Hydromethanolic extract	–	*Trypanosoma brucei brucei*			James and Emmanuel (2011)
Cucumis metuliferus E.Mey. ex Schrad	Pulp	–	Oral	*Trypanosoma brucei brucei*	500, 1000	[a]	Abubakar et al. (2011)
Dissotis rotundifolia (Sm.) Triana	Leaves	Ethanol	Oral, intraperitoneal	*Trypanosoma brucei brucei*	800	66.7, 78.4	Mann et al. (2009)
Garcinia kola Heckel	Nut	Methanol	Intraperitoneal	*Trypanosoma brucei brucei*	600	100	Ogbadoyi et al. (2011b)
Gongronema latifolium Benth.	Stem bark	Methanol	Intraperitoneal	*Trypanosoma congolense*	400	50	Abedo et al. (2013)
Guiera senegalensis J.F.Gmel.	Leaves	Dichloromethane	Intraperitoneal	*Trypanosoma brucei brucei*	150	42	Aderbauer et al. (2008)
Hibiscus sabdariffa L.	Calyses	Aqueous	Oral	*Trypanosoma congolense*	*Ad libitum*	10	Umar et al. (2009)
Holarrhena Africana A.DC.	Leaves	Methanol/chloroform	Intraperitoneal	*Trypanosoma brucei rhodesiense*	40, 80	[a]	Nwodo et al. (2007)
Hymenocardia acida Tul.	Stem bark	Ethanol	Oral	*Trypanosoma brucei brucei*	100–400	35–50	Abu and Uchendu (2011)
Khaya senegalensis A. Juss	Stem bark	Aqueous	Oral	*Trypanosoma brucei brucei*	100–300	90–100	Ibrahim et al. (2008)
	Stem bark	Ethanol	Oral	*Trypanosoma evansi*	20–80	25–50	Umar et al. (2010)
	Leaves, stem bark, root bark	Aqueous	Intraperitoneal	*Trypanosoma brucei brucei*	10	[a]	Antia et al. (2010)
Kigelia Africana (Lam.) Benth.	Fruits	Dichloromethane	Intraperitoneal	*Trypanosoma brucei rhodesiense*	1000, 2000	40, 60	Peter et al. (2009)
Landolphia uniflora (Stapf) Pichon	Leaves	Methanolic	Intramuscular	*Trypanosoma brucei brucei*	300	100	Atawodi and Alafiatayo (2007)
Lannea welwistchii (Hiern) Engl.	Leaves, stem bark, root bark	Aqueous	Intraperitoneal	*Trypanosoma brucei brucei*	10	[a]	Antia et al. (2010)

Table 7 (*continued*)

Lawsonia inermis L.	leaves	Methanolic	Oral	*Trypanosoma brucei brucei*	800	–	Wurochekke and Nok (2004)
Lippia multiflora Moldenke	Leaves	Aqueous	Intraperitoneal	*Trypanosoma brucei brucei*	400	–	Olukunle et al. (2010)
Morinda morindiodes (Baker) Milne-Redh.	Leaves	Aqueous	Intraperitoneal	*Trypanosoma brucei brucei*	400	[a]	Olukunle et al. (2010)
Mormodica balsamina L.	Pulp	–	Oral	*Trypanosoma brucei brucei*	150	80	Abubakar et al. (2005)
Ocimum grattissimum L.	Leaves	Aqueous	Intraperitoneal	*Trypanosoma brucei brucei*	400	–	Olukunle et al. (2010)
Peristrophe bicalyculata (Retz.) Nees	Leaves	Aqueous	Intraperitoneal	*Trypanosoma brucei brucei*	50	–	Adamu et al. (2009)
	Whole plant	Acetone/methanol	Oral	*Trypanosoma brucei brucei*	200	[a]	Abdulazeez et al. (2013)
Prosopis Africana (Guill. & Perr.) Taub.	Leaves	Methanolic	Intramuscular	*Trypanosoma brucei brucei*	200	100	Atawodi and Ogunbusola (2009)
Psidium guajava L.	Leaves	ethanol	Oral	*Trypanosoma brucei brucei*	300	100	Adeyemi et al. (2009)
Saba florida (Benth.) Bullock	Leaves	Hydromethanolic	Intraperitoneal	*Trypanosoma brucei brucei*	200, 400	100	James and Emmanuel (2011)
Securidaca longipenduculata Fresen.	Root, root bark	Aqueous	Oral	*Trypanosoma brucei brucei*	100	59	Abubakar et al. (2005)
Senna occidentalis (L.) Link (Syn: *Cassia occidentalis*)	Bark	Dichloromethane	Intraperitoneal	*Trypanosoma brucei brucei*	150	48	Adebauer et al. (2008)
	Leaves	Ethanol	Oral	*Trypanosoma brucei brucei*	200	67	Ibrahim et al. (2010)
Tapinanthus globiferus Tiegh.	Leaves	Methanol	Intraperitoneal	*Trypanosoma congolense*	400	50	Abedo et al. (2013)
Terminalia avicennoides Guill. & Perr.	Leaves	aqueous	intraperitoneal	*Trypanosoma brucei brucei*	100	< 100	Bizimana et al. (2006)
Terminalia superb Engl. & Diels	Fruit	Methanol	Intraperitoneal	*Trypanosoma brucei brucei*	100, 200	[a]	Mann et al. (2011)
	Root	Aqueous	Intramuscular	*Trypanosoma brucei brucei*	200	[a]	Atawodi et al. 2011
	Leaves, stem bark	Aqueous	Intraperitoneal	*Trypanosoma brucei brucei*	10	[a]	Antia et al. (2010)
Tithonia diversifolia(Hemsl.) A.Gray	Root bark	Aqueous	Intraperitoneal	*Trypanosoma brucei brucei*	10	100	Antia et al. (2010)
	Leaves	Aqueous	Intraperitoneal	*Trypanosoma brucei brucei*	400	[a]	Olukunle et al. (2010)
Vernonia blumeoides Hook.f.	Leaves	Lactone-rich	Oral	*Trypanosoma brucei brucei*	300	68	Ibrahim et al. (2013b)
Vitellaria paradoxum (C.F.Gaertn.) Hepper (Syn: *Butyrospermum paradoxum*)	Stem bark	Ethanol	Intraperitoneal	*Trypanosoma brucei brucei, Trypanosoma congolense*	200	[a] 100	Mbaya et al. (2007)
Zanthoxylum zanthoxyloides (Lam.) Zepern. & Timler	Stem bark	Methanol	Intraperitoneal	*Trypanosoma brucei brucei*	100, 200, 300	[a]	Mann et al. (2011)

Key: – = No effect.

[a] Relapse occur after initial clearance.

4. Conclusion

Ethnopharmacological based anti-trypanosomal investigations on individual African medicinal plants are at various stages of research. Interestingly, some of the plants have been investigated in animal models and have demonstrated promising anti-trypanosomal activity that could give impetus for further studies tailored towards their development as anti-trypanosomal herbal products.

This review underscores the need to harmonize plant-based anti-trypanosomal studies so as to allow direct comparison of results obtained from different sources. For instance, the biochemistry and pathophysiology of the different trypanosome species (*Trypanosoma brucei* sub groups, *Trypanosoma evansi*, *Trypanosoma congolense*) used in the studies are distinct, the animal models (mice, rats) are also different. Furthermore, differences in the solvent systems used for extraction and the administered doses (*in vivo* studies) also makes direct comparison of the results next to impossible. In spite of these problems, the available data seem to suggest that *Khaya senegalensis*, *Anona senegalensis*, *Acacia nilotica* and *Azadirachta indica* possess better potentials for application as anti-trypanosomes.

This review also highlights that African medicinal plants have a multitude of novel chemical compounds that could provide leads for the development of newer trypanocides. The active compounds such as ursolic acid, oleonolic acid, 8-hydroxyheptadeca-1-ene-4,6-diyn-2yl acetate, 16-acetoxy-11-hydroxy octadeca-17-ene-12,14-diynyl acetate, schkuhrin I, dihydrochelerythrine and cynaropicrin with extremely low IC_{50} values deserve further *in vivo* studies. Indeed, this is an area that needs urgent attention if future trypanocides are to be developed from African plants because at present, only one pure active compound (azaanthraquinone) was investigated for *in vivo* anti-trypanosomal activity.

Another vital area of scientific weakness identified in this review is that not a single study of African anti-trypanosomal plants is taken beyond proof of concept and/or preclinical stages. Thus, there is a need to conduct clinical study on some of the active plants (earlier stated in the Section 4) as a step for their

integration into the primary healthcare system as anti-trypanosomal herbal remedies. It is hoped that relevant stakeholders will consider some of these plants for detailed future research and/or subsequent commercialization.

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