

African Natural Products with Potential Anti-trypanosomal Properties: A Review

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Authors' contributions

This work was carried out in collaboration between all authors. Authors LB and author OKS designed the study, wrote the protocol and final editing of the manuscript. Author LB did the literature search and wrote the first draft of the manuscript. Author OKS supervised the work. Author SS, MBB and KAA took part in the literature search, undertook the initial editing and took part in final editing of the paper. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJBcRR/2015/16039

Editor(s):

(1) Chunying Li, Department of Biochemistry and Molecular Biology, Wayne State University, School of Medicine, Detroit, USA.

Reviewers:

(1) Anonymous, Brazil.

(2) Anonymous, Brazil.

(3) Anonymous, Nigeria.

Complete Peer review History: <http://www.sciencedomain.org/review-history.php?id=1037&id=3&aid=8778>

Review Article

Received 1st January 2015

Accepted 14th March 2015

Published 13th April 2015

ABSTRACT

Ethnopharmacological Relevance: Africa is considered to be the cradle of mankind with a rich biological and cultural diversity marked regional difference in healing practices. Natural product of Africa represents a constant interest as sources of health remedies, nutrition and cosmetic formulations. African trypanosomiasis is one of the neglected tropical diseases caused by fly-borne protozoa known as trypanosomes that affect both human and livestock with devastating consequences. Chemotherapy of African trypanosomiasis is unsatisfactory for various reasons including unacceptable toxicity, poor efficacy, undesirable route of administration and drug

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resistance. In this regards, the last few decades have witnessed a surfeit of investigations which have been geared to investigate the effect of common traditionally-used medicinal plants/insect in alleviating the cellular changes produced during trypanosome infection.

Major Objective: This review presents the profiles of African natural product (plants and insect) with anti-trypanosomal properties, reported in the literature.

Methodology: Literature was collected from published articles (through electronic search), thesis, Proceedings as well as book of abstract that report on the in vitro or in vivo anti-trypanosomal activity of plants, insects and their products.

Results: A total of 215 plants species from 82 families were found. While two herbal formulation and three insect/there product were reviewed for invivo anti-trypanosomal activity Furthermore, some of the plants were investigated for possible ameliorative effects on the trypanosome-induced pathological changes. Phyto- chemistry studies of the anti-trypanosomal plants led to the isolation of 96 specific bioactive anti-trypanosomal compounds from different parts of the plants

Conclusion: It is clear that these reviews provide strong evidence of the potential beneficial effects of phytotherapy in the traditional management of trypanosomiasis, which could be subsequently developed into a cost effective alternative medicine to complement treatment of trypanosomiasis.

Keywords: Africa; trypanosomiasis; natural product; plants; insect.

1. INTRODUCTION

Human African trypanosomiasis (HAT) also known as sleeping sickness is a fatal, fly-borne neuro-inflammatory disease caused by two agents (protozoa), *T. brucei gambiense* which is responsible for chronic form of HAT in West and Central Africa, and *T. brucei rhodesiense*, the etiological factor for the acute form of the disease in East Africa (Fig. 1). The parasites are transmitted by the bite of infected tsetse flies (*Glossina* spp.) [1]. Over 60 million people living in 36 countries are threatened with sleeping sickness and the estimated number of cases is thought to be between 300,000 and 500,000 [2]. In Latin America, infection with *T. cruzi* is responsible for Chagas' disease, which is the leading cause of heart disease [3]. Nearly 90 million people in 19 endemic countries are at risk of contracting Chagas' disease and 16 million people are already infected [4].

Animal trypanosomiasis is caused by *T. brucei*, *T. evansi*, *T. congolense* and *T. vivax* [5]. The disease distributed over approximately 25 million 2 km in Africa. It is a major factor retarding the growth of the livestock industry in Africa [2], and it has constituted a major obstacle to the economic development and thus an important priority for biomedical and public agencies, agricultural sector and the scientific community [6].

Although, the increasing trend of HAT cases has been reversed and not more than 50 cases of HAT are diagnosed yearly outside Africa [7], effective and satisfactory chemotherapy has not

been found against the causative agents; *T. brucei rhodesiense* and *T. brucei gambiense* therefore new epidemics of this disease could appear [8].

Nature has presented to humanity the gift of biological and cultural diversity of natural product for healing practices. African traditional healing practices are holistic involving both the body and the mind. The traditional healer typically diagnoses and treats the psychological basis of an illness before prescribing medicines to treat the symptoms [9]. The vast majority of people (80% of the world's population) still rely chiefly on their traditional materia medica (medicinal plants and other materials) for their primary health care needs [9]. In sub-Saharan Africa, the ratio of traditional healers to the population is 1/500, while that for medical doctors to the population is 1/40 000 ([10]. This is as a result of the high cost of Western pharmaceuticals and health care, or because the traditional medicines are more acceptable from a cultural and spiritual perspective [11]. It is also a fact that one quarter of all medical prescriptions are formulations based on substances derived from natural origin. Natural products also benefit from containing many specific molecular principles in their natural state, which possess a variety of influences on human physiological and biochemical systems, as opposed to purified synthetic drugs which are based on a single molecular substance derived from the natural product [12].

In this regards, the last few decades have witnessed a surfeit of investigations which have been geared to investigate the effect of common

traditionally-used medicinal plants in alleviating the cellular changes in vivo produced during the *T.b. brucei* infections of animals. In Africa, a number of medicinal plants used in the traditional management of trypanosomiasis have been screened and showed both significant in vitro /in vivo anti-trypanosomal activity. In addition to herbal plant, researchers (Ekanem and Yusuf, [13;14]; Shittu and Elekwechi, [15], Shittu and Bashir, [16] targeted finding new anti-trypanosomal agents to combat the trypanosomiasis by screening extracts from insect and their products.

At present, the available review on anti-trypanosomal agents focus only on medicinal plants [17], synthetic chemicals [18], chemistry aspect with little or no information on the plants [19]. This review article has been presented to enumerate some indigenous plants/insect with potential in vivo or/and in vitro anti-trypanosomal properties. This could be used as an updated source for recent progress in the identification of promising agents with selective, trypanocidal activity that can serve as novel lead compounds for effective anti-trypanosomal chemotherapy.

Furthermore, this review may serve as a motivator and reference point for researchers who are working day and night to find a divine solution to this disease.

2. METHODS

A systematic study was carried out through a computer search of data on PubMed, Sciencedirect, Sciencedomain, Medline and Google Scholar from published articles using key words (trypanosomiasis; Africa; ethnobotany; anti-trypanosomal activity; medicinal insects and their products; medicinal plants; plant extracts; active compounds; and mode of action). Data was also obtained from thesis, proceedings as well as book of abstract that report on the in vitro or in vivo anti-trypanosomal activity of plants/insect and their product that were collected from different parts of Africa. Data presented including the scientific name, family, methodology used, the degree of activity of the plant and insect. However anti-trypanosomal plants whose levels of activity were not indicated by the authors were excluded.

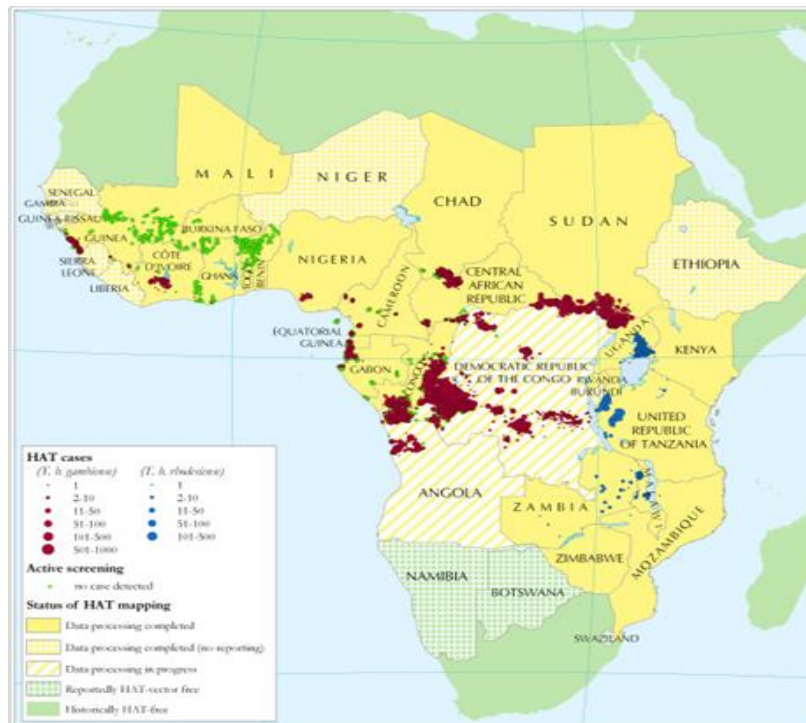


Fig. 1. The distribution and burden of trypanosomiasis in Africa; the map follows the expected lines of demarcation for the occurrence of *T. brucei gambiense* and *T. brucei rhodesiense*, and also suggest a high occurrence of disease. However the case in this map only includes those that were reported or captured and so comprise a minority of the total case

3. RESULTS

Tables 1-6 show the review datas on scientific name, Family, Part (s) used Extract/fraction, Model, Parasite IC₅₀ or MIC (µg/mL), Country, References of African natural products with anti-trypanosomal property. A total of 215 plants species from 82 families were found. Plants from Asteraceae (13.0%), Leguminosae (6.19%), Anacardaceae (4.28%), Maliceae (4.28%), Fabaceae (3.80%), Rubiaceae (3.33%) and Euphoraceae (3.33%) families have received more scientific attention than others. A total of 104 plants from 55 family (in vitro) and 36 plants from 16 family (in vivo) were found in west Africa, a total 68 plant from 14 family (in vitro) and 7 plants from 5 family (In vivo) were found in east African, a total 42 plant from 21 family (Invivo) were found in southern African, a total 5 plant from 5 family (Invivo) were found in central African, 1 plant from 1 family (in vitro) and 3 plants from 3 family (in vivo) were found in north Africa While two herbal formulation and three insect/their product were reviewed for invivo anti-trypanosomal activity. Phyto-chemistry studies of the anti-trypanosomal plants led to the isolation of 96 specific anti-trypanosomal compounds from different parts of the plants (Table 7).

4. DISCUSSION

Different techniques used in assessment of anti-trypanosomal activities present problems associated with comparing the trypanocidal potency of the plants reviewed in this study. Some authors presented there results minimum inhibitory concentration (MIC), mean lethal dose 50 (IC₅₀) and % inhibition of parasite motility in vitro. However, IC₅₀ values of 20µg/mL are considered good activity while IC₅₀ values of 21–60 and 61–100 µg/mL are considered moderate and low activities respectively. Any IC₅₀>100µg/mL are considered ineffective [20]. Furthermore, Atawodi et al. [21] and Maikai et al. [22], corroborated the report of Kaminsky et al. [23], showing that parasite motility is a reliable index for determining anti-trypanosomal activity of crude plant extracts.

4.1 Anti-trypanosomal Activity of West African Plant

A total of 35 West Africa plant shows good anti-trypanosomal activity IC₅₀ (<20 µg/mL). The most

interesting results were those of *Alcornea cordifolia*, *Maytenus laevis*, *Lantana ukambensis*, *Crataeva religiosa* and *Ocimum gratissimum* with IC₅₀ (µg/mL) 0.2, 0.62, 1.5, 1.6 and 1.66 respectively. The high activity values obtained for these plants render them candidates for the isolation of anti-trypanosomal compounds which could be developed into new lead structures for drug development. 19 West Africa plant shows moderate anti-trypanosomal activity IC₅₀ (21-60 µg/mL), while 4 plants shows low anti-trypanosomal activity IC₅₀ (61-100 µg/mL). Furthermore, 18 of the plants were reported to inhibit the parasite motility in less than 30 minute at 4mg/ml. The most interesting result is *Securidaca longepedunculata* (5 minute) while extracts from 23 West African plants inhibit the parasite motility within 31-60 minute at 4mg/ml. However, methanol extracts of *T. globiferus*, *G. latifolium* at 10 mg/ml ceases the parasite motility in less than 10 min [24], while other were reported not to be active. According to Atawodi et al. [21], statement on trypanocidal activity of a plant extract should be made in the context of the method and solvent of extraction. Different extracts from some of the plant reviewed demonstrated different degree of trypanocidal property for instance DCM extracts of *Acanthospermum hispidum*, *Byrsocarpus coccineus*, *Byrsocarpus coccineus*, *Carpolobia lutea* and *Keetia leucantha* shows good trypanocidal activity while the methanol and aqueous extracts shows moderate or low trypanocidal activity. In contrast, methanol and aqueous extracts of *Dialium guineense* shows a moderate activity while DCM extract was inactive [20]. The variation in the trypanocidal activities of these plants may be attributed to the variation in the availability and amounts of phytoconstituents in the extracts. Phytoconstituents such as flavonoids, alkaloids, terpenes, quinones, polyphenols, Triterpenoids and sterols are the most frequently implicated phytochemicals in the plants extracts. A total of about 47 specific anti-trypanosomal compounds were isolated from different parts of the West African plants (Fig. 2). The most active compounds were Citronellal (IC₅₀ 2.76 µg/mL), myrcene (IC₅₀ 2.24 µg/mL), limonene (IC₅₀ 4.24 µg/mL), isolated from *Ocimum gratissimum* seed oil [25], erythrodiol, (IC₅₀ 5.30 µg/mL), betulin (IC₅₀ 4.0 µg/mL), 24 hydroperoxy-24-vinylcholesterol (IC₅₀ 3.20 µg/mL), from *Strychnos spinosa* [26]. The DNA intercalation in combination with portion biosynthesis inhibition is reported to be the mechanism of action responsible for the observed antitypanosomal effect of most of

these compounds [27]. Extract from different part of plants also exhibit different degree of trypanocidal activity for instance methanol and aqueous extracts of *Keetia leucantha* twig show a low activity [20], while the oil extracted from the leaf show a good activity [28], this observation might be due to variations in geographical location, time or period of collection and chemical constituents [19].

4.2 Anti-trypanosomal Activity of Southern African Plants

Appreciable numbers of plant, as well as bioactive compounds were found to have been investigated for in vitro anti-trypanosomal activity in south African. Among the south Africa medicinal plants screened for trypanocidal activity against *T.b. rhodesiense*, dichloroethane leaves extract of *Abrus precatorius* was found to be the most potent with an IC₅₀ value 0.01 µg/mL. Similarly, DCM extracts of *Hypericum aethiopicum* was found to be active with an IC₅₀ value 4.47 µg/mL followed by *Vernonia oligocephala* with an IC₅₀ value 4.67 µg/mL while *Alepidea amatymbica* was the least effective with an IC₅₀ value 73.1 µg/mL [29]. Further more among 10 South African plants recently evaluated against *T. brucei rhodesiense*, DCM extract of *Psoralea pinnata* leaves was found to be the most potent with an IC₅₀ value 0.15 µg/mL [30].

Different parts of the same plants, same plants of different origin as well as different solvents extracts show different anti-trypanosomal activity. For instance, *Abrus precatorius* from West Africa show trypanocidal activity with IC₅₀ value of 17.9 µg/ml [31], against *T. brucei rhodesiense* while the same plant from southern Africa had IC₅₀ value of 0.01 µg/ml [32]. Fruit extract of *Ekebergia capensis* had IC₅₀ value of 11.5 µg/ml against *T. cruzi* while the root extract of the same plants had IC₅₀ value of 1.36 µg/ml against *T.b. rhodesiense* [29]. As said earlier, the variation in the trypanocidal activities of these plants may be attributed to the variation in the availability and amounts of phytoconstituents in the extracts. Among the specific bioactive compounds isolated from south Africa plant were Abruquinone A, B, D, G, H, I, J, K, L and 7, 8, 3', 5'-tetramethoxyisoflavan-1',4'-quinone from whole plant of *Abrus precatorius* [32,33], schkuhrin I

and II from *Schkuhria pinnata*, cynaropicrin from the leaves of *Vernonia mespilifolia* [30], and putranoside A from stem of *Drypetes gerrardii* [33]. All the bioactive compounds isolated show a potent trypanocidal activity with an IC₅₀ less than 1 µg/ml against *T. b. rhodesiense*, except schkuhrin II, Abruquinones J and putranoside A with IC₅₀ of 1.5, 11.2 and 8.0 µg/ml respectively. The compounds were also found to be more effective against *T. b. rhodesiense* than *T. cruzi*, for instance schkuhrin I had IC₅₀ of 0.18 µg/ml against *T. b. rhodesiense* and 16.4 µg/ml against *T. cruzi* while schkuhrin II had IC₅₀ of 1.50 µg/ml against *T. b. rhodesiense* and 26.9 µg/ml against *T. cruzi* [30]. Although, a considerable numbers of medicinal plants from this region have been investigated and were found active against trypanosome parasite, there exist a very few researchers on the subject matter, researchers in this region of Africa are therefore encourage to intensify studies on the trypanocidal potency of their natural flora.

4.3 Anti-trypanosomal Activity of Central African Plants

A very little information on trypanocidal potency of medicinal plant from central Africa were obtained from literature. Five medicinal plants from central Africa have been reported to exhibit activities in vitro include *Garcinia lucida*, [34] *Aframomum letestuanum* [35], *Vernonia guineensis* with IC₅₀ ranged of 3–5 mg/ml [36], *Enantia chlorantha* (1.87 µg/ml), *Isolona hexaloba* (1.95 µg/ml) and *Quassia Africana* (1.88 µg/ml) [37]. The bioactive agents isolated from these region include Letestuienin A (IC₅₀ >100 µg/ml), Letestuienin B (IC₅₀ 67 µg/ml), Letestuienin C (IC₅₀ 2.6 µg/ml) and 5-hydroxy-1,7-bis (4- hydroxyphenyl) hepta-4,6- dien-3-one (IC₅₀ 2.6 µg/ml) isolated from DCM seed extract of *Aframomum letestuanum* they demonstrate activity against *T. brucei brucei* [35]. Furthermore 4 bioactive agents including, 6-acetyl dihydrochelerythrine (IC₅₀ 3.9 µg/ml), Dihydrochelerythrine (IC₅₀ 0.8 µg/ml), Lucidamine A (IC₅₀ 14.1 µg/ml), Lucidamine B (IC₅₀ 4. [34,36] isolated vernoguinoside and vernoguinosol from stem bark of *Vernonia guineensis* both compound demonstrated significant trypanocidal activity against *T. brucei rhodesiense* with an IC₅₀ range of 3–5 mg/ml.

Table 1. *In vitro* anti-trypanosomal activity of West African plant

Scientific name	Family	Part (s) used	Extract/fraction	Parasite	IC50 MIC (µg/mL)	Motility of the parasite	Country	Authors
<i>Abrus precatorius</i>	papillionaceae	Leaf	Chloroform fraction	T. b. r	17.9 ug/ml	-	Nigeria	Saganuwan et al. [31]
<i>Acacia artaxacantha</i>	Leguminosae	Stem bark/ root	n-Hexane/ethanol	T. b. b/ T. co	Btw 13 and 69 ug/ml	-	Nigeria	Adewunmi et al. [38]
<i>Acanthospermum hispidum</i>	Asteraceae	Aerial part	DCM/ Methanol / Aqueous	T. b. b	14.5/47.5/54.8	-	Benin	Bero et al. [20]
<i>Adansonia digitata</i>	Bombacaceae	Leaf	Aqueous	T. b. b	-	4mg/ml@ 40mint	Nigeria	Atawodi, [39]
<i>Adenium obesum</i>	Apocynaceae	Root	Pet. Ether	T. b. b	-	4mg/ml@ 35mint	Nigeria	Atawodi, [39]
<i>Afrormosialaxiflora</i>	Leguminosae	Leaf	Pet. Ether	T. b. b	-	4mg/ml@ 20mint	Nigeria	Atawodi, [39]
<i>Azelia africana</i>	Leguminosae	Leaf/ Stem bark	Pet. Ether	T. b. b	-	4mg/ml@ 30mint	Nigeria	Atawodi, [39]
<i>Albuca spp</i>	Asparagaceae	Bulb	Aqueous	T. b. b	-	4mg/ml@ 55mint	Nigeria	Atawodi, [39]
<i>Alcornea cordifolia</i>	Euphorbiaceae	Bark/Leaf	Methanol	T. b. b	<0.2	-	Nigeria	/Adewunmi et al. [38]
<i>Ampelocissus grantii</i>	Vitaceae	Aerial part	DCM	T. b. b	500	-	BurkinaFaso	Aderbauer et al. [40]
<i>Anchomanes difformis</i>	Araceae	Rhizome	Methanol	T. b. b/ T. co	13.87 ug/ml	45 min at 4 mg/ml	Nigeria/Benin	Atawodi et al. [41] Bero et al. [20]
<i>Anchomanes difformis</i>	Araceae	Root	DCM/ Methanol / Aqueous	T. b. b	50.7/14.7/13.8	-	Benin	Bero et al. [20]
<i>Annona senegalensis</i>	Annonaceae	Root	Pet. Ether	T. b. b	-	4mg/ml@ 35mint	Nigeria	Atawodi [39]
<i>Anthocleista vogelii</i>	Loganiaceae	Root bark	Aqueous/ Ethanol	T. b. b	-	100% activity@ 20mg/ml	Nigeria	Abu et al. [42]
<i>Baillonella toxisperma</i>		Barks	Ethanol	T. r	9.6 µg/ml	-	Bénin	Lagnika et al. [43]
<i>Balanites aegyptiaca</i>	Balanitaceae	Stem bark/ Shoot	Aqueous/ DCM	T. b. b	500/50	-	Nigeria/BurkinaFaso	Wurochekke and Nok [44]/Aderbauer et al. [40]
<i>Blighia unijugata</i>	Sapindaceae	leaf	Aqueous/ethanolic	T. b. b	-	No acivity @40mg/ml	Nigeria	Abu et al. [42].
<i>Boswellia dalzielii</i>	Burseraceae	leaves	Ethanol/Methanol	T. r	9.6 µg/ml	-	Bénin/Nigeria	Lagnika et al. [43]
<i>Brassicaoleracea</i>	Brassicaceae	Leaf	Methanol	T. e	-	1000 µg/ml	Nigeria	Shaba et al. [45]
<i>Bridelia ferruginea</i>	Euphorbiaceae	Stem bark	methano	T. b. b	-	4mg/ml@ 35mint	Nigeria	Atawodi, [39]
<i>Byrsocarpus coccineus</i>	Connaraceae	Aerial part	DCM/ Methanol / Aqueous	T. b. b	14.7/21.1/49.5	-	Benin	Bero et al. [20]
<i>Canarium schweinfurthii</i>	Burseraceae	Stem bark	Pet. Ether/Chloroform	T. b. b	-	4mg/ml@ 30/35mint	Nigeria	Atawodi, [39]
<i>Carpolobia lutea</i>	polygalaceae	Aerial part	DCM/ Methanol / Aqueous	T. b. b	18.3/>100/>100	-	Benin	Bero et al. [20]
<i>Cassia siamae</i>	Leguminosae	Leaf/ Stem bark/ Root	Aqueous/hexane/ ethylacetate	T. b. b	25.8/ 10.19/ 46.50	-	Nigeria	Abiodun et al. [46]

Scientific name	Family	Part (s) used	Extract/fraction	Parasite	IC50 MIC (µg/mL)	Motility of the parasite	Country	Authors
<i>Cassia sieberiana</i>	Caesalpiniaceae	leaf	DCM	T. b. b	> 19	-	Nigerian	Hoet et al. [47]
<i>Cassytha filiformis</i>	Lauraceae	Leaf	Pet. Ether	T. b. b	-	4mg/ml@ 20mimt	Nigeria	Atawodi, [39]
<i>Cassytha sp.</i>	Lauraceae	Leaves	Methanol	T. b. b	-	25min at 4mg/ml	Nigeria	Atawodi et al. [41]
<i>Ceiba pentandra</i>	Bombacaceae		DCM	T. b. b	200	-	BurkinaFaso	Aderbauer et al. [40]
<i>Clerodendrom capitatum</i>	Stem bark	Root	n-Hexane/ethanol	T. b. b/ T. co	Btw 13 and 69 ug/ml	--	Nigeria	Adewunmi et al. [38]
<i>Cochlospermum planchonii</i>	Cochlospermaceae	Root/leaf	Pet. Ether	T. b. b	-	4mg/ml@ 20/40mint	Nigeria	Atawodi, [41]
<i>Crataevareligiosa</i>	Capparaceae	Leaves	cyclohexane	T. r	1.6 µg/ml		Bénin	Lagnika et al. [43]
<i>Cratva adansonii</i>	Capparaceae	Leaves	crude hexane	T. b. b	12.5 µg/ml		Nigeria	John et al. [48]
<i>Cussonia arborea</i>	Araliaceae	Root /stem	Aqueous/ Ethanolic	T. b. b	-	No activity @ 40mg/ml	Nigeria	Abu et al. [42]
<i>Cymbopogon nardus</i>	Poaceae		Methanol	T. b. b	0.31 µg/mL		Nigeria	John et al., [52]
<i>Dialium guineense</i>	Leguminosae	Aerial part	Dcm/ Methanol / Aqueous	T. b. b	>100/42.3/52.0	-	Benin	Bero et al. [20]
<i>Diospyros mespiliformis</i>	Ebenaceae	Leaf	chloroform	T. b. b	-	4mg/ml@ mint45	Nigeria	Atawodi, [41]
<i>Dissotis rotundifolia</i>	Melastomataceae	Leaf	Ethanol	T. b. b	-	100% activity@ 800mg/kg	Nigeria	Mann et al. [49]
<i>Erythrophleum suaveolens</i>	Leguminosae	Stem bark	Pet. Ether	T. b. b	-	4mg/ml @40mimt	Nigeria	Atawodi, [41].
<i>Eucalyptus citriodora</i>	Myrtaceae	Leaf	aqueous	T. b. b	-	0.4 g/mL@2mimt	Nigeria	Habila et al. [50]
<i>Eugenia uniflora</i>	Myrtaceae	Leaf	n-Hexane/ethanol	T. b. b/ T.co	-	Btw 13 and 69 ug/ml	Nigeria	Adewunmi et al. [38]
<i>Euphorbia hirta</i>	Euphorbiaceae	Leaf	ethylacetate	T. b. r	8.70	-	Nigeria	Abiodun et al. [46]
<i>Ficus platyphylla</i>	Moraceae		Methanol	T. b. b	25	-	BurkinaFaso	Sawadogo et al. [51]
<i>Ficus sycomorus</i>		Stem	Methanol	T. b. b	-	4mg/ml @60mimt	Nigeria	Atawodi, [41]
<i>Gardenia erubescens</i>	Rubiaceae	Leef/stem bback	Aqueous/ Ethanolic	T. b. b	-	100% activity@ 20mg/ml	Nigeria	Abu et al. [42]
<i>Gongronema latifolium</i>	Asclepiadaceae.	Stem bark	Methanol	T. b. b	-	15 min at 10 mg/ml	Nigeria	Josephine et al. [24]
<i>Haematostaphis barteri</i>	Anacardiaceae.	Leaves	aqueous	T.co	-	40 minutes @ 0.25 mg	Nigeria	Wurochekke et al. [53]
<i>Heliotropium indicum</i>	Boraginaceae	Aerial part	Dcm/ Methanol / Aqueous	T. b. b	58.3/80.2/>100	-	Benin	Bero et al. [20]
<i>Hymenocardia acida</i>	Hymenocardiaceae	Root bark /stem bback	Aqueous/ Ethanolic	T. b. b	-	100% activity@ 2.5mg/ml	Nigeria	Abu et al. [42]
<i>Hymenocardia acida</i>	Hymenocardiaceae	Twig and leaf	DCM	T. b. b	≤19 µg/ml	-	Nigerian	Hoet et al. [47]
<i>Keetia leucantha</i>	Rubiaceae	Leaf	essential oil	Bloodstream/procyclic	20.90/>100 ug/ml	-	Nigerian	Bero et al. [28]

Scientific name	Family	Part (s) used	Extract/fraction	Parasite forms of <i>T. brucei</i>	IC50 MIC (µg/mL)	Motility of the parasite	Country	Authors
<i>Keetia leucantha</i>	Rubiaceae	Twig	DCM/ METHANOL / AQUEOUS	T. b. b	5.8/53.1/86.9	-	Nigerian	Bero et al. [20]
<i>Khaya senegalensis</i>	Meliaceae	Stem bark/leaves	Ethanolic/Methanol / Ethanol	T. r	300 µg/ml/9.6 µg/ml	35 min at 4 mg/ml	Nigeria/ Bénin	Bulus and Addau, [54], Atawodi et al. [21], Lagnika et al. [43]
<i>Lannea kerstingii</i>	Anacardiaceae	Leaf	Methanol	T. b. b		4mg/ml@40min	Nigeria	Atawodi, [41]
<i>Lannea welwistchii</i>	Anacardiaceae	Leaf	Aqueous	T. b. b	6.3 mg/ml(mic)	-	Nigeria	Antia et al. [55]
<i>Lantana ukambensis</i>	Verbenaceae		Methanol	T. b. b	1.5	-	Burkina Faso	Sawadogo et al. [51]
<i>Lawsonia inermis</i>		Root	Methanol	T. b. b	-	4mg/ml@45min	Nigeria	Atawodi, [41]
<i>Lonchocarpus laxiflorus</i>		Stem	Methanol	T. b. b	-	4mg/ml@30min	Nigeria	Atawodi, [41]
<i>Lophira lanceolata</i>	Ochnaceae	Leaf/stem bark	Aqueous/ Ethanolic	T. b. b	-	100% activity@ 20mg/ml	Nigeria	Abu et al. [42]
<i>Magnifera indica</i>	Anacardiaceae	Root	Pet. Ether	T. b. b	-	4mg/ml@30min	Nigeria	Atawodi, [41]
<i>Maytenus laevis</i>	Celastraceae	Root	hexane + ethyl acetate	T. b. b	0.625		Nigeria	John et al. [52]
<i>Momordica balsamina</i>	Cucurbitaceae	Whole plant	Pet. Ether	T. b. b	-	4mg/ml@35min	Nigeria	Atawodi, [41]
<i>Monodora myristica</i>	Annonaceae	Seed	Ethyl acetate		3.12	-	Nigeria	John et al. [52]
<i>Morinda lucida</i>	Rubiaceae		Methanol fractio	T. b. b	6.25-12.5 µg/m	-	Nigeria	Nwakaego, [56]
<i>Moringa oleifera</i>	Moringaceae	Leaf	chloroform	T. b. b	-	4mg/ml@35min	Nigeria	Atawodi, [41]
<i>Nauclea latifolia</i>	Rubiaceae	Leaf	Methanol	T. b. b	-	4mg/ml@30min	Nigeria	Atawodi, [41]
<i>Nauclea pobeguinii</i>	Rubiaceae	Bark	ethyl acetate	T. b. b	6.25	-	Nigeria	John et al. [52]
<i>Ocimum gratissimum</i>	Lamiaceae	Leaves	ethanol	T. b. b	1.66/1.29 µg/mL	-	bennin	Bénédicta et al. [25]
<i>Ozoroa insignis</i>	Anacardiaceae		Methanol	T. b. b	6.2	-	Burkina Faso	Sawadogo et al. [51]
<i>Parinari curatellifolia</i>	Chrysobalanaceae		Methanol	T. b. b	25	-	Burkina Faso	Sawadogo et al. [51]
<i>Parkia clappertoniana</i>	Leguminosae	Stem bark	Pet.ether	T. b. b	-	50 min at 4 mg/ml	Nigeria	Atawodi, [41]
<i>Pericopsis laxiflora</i>	Loganiaceae	Leaf	DCM	T. b. b	>19 µg/ml		Nigeria	Hoet et al. [47]
<i>Peristrophe bicalyculata</i>	Acanthaceae	Whole plant	aqueous	T. b. b	-	immobilized 90% of the parasites,@ 100mg/kg	Nigeria	Abdulazeez et al. [57]
<i>Picralima nitida</i>	Apocynaceae	Root	Methanol	T. b. b	-	10 min at 4 mg/ml	Nigeria	Ene et al. [58]

Scientific name	Family	Part (s) used	Extract/fraction	Parasite	IC50 MIC (µg/mL)	Motility of the parasite	Country	Authors
<i>Piliostigma reticulatum</i>	Leguminosae	Leaves	aqueous	T. b. b	-	25 min at 4 mg/ml	Nigeria	Atawodi et al. [59]
<i>Prosopis africana</i>	Leguminosae	Leaf	Pet.ether	T. b. b	-	35 min at 4 mg/ml	Nigeria	Atawodi, [41]
<i>Prosopis Africana</i>	leguminaceae	Bark	Methanol	T. b. b	12.5		Nigeria	John et al. [52]
<i>Psidium guajava</i>	Myrtaceae		ethanolic	T. b. b	6.3 µg/mL	-	Nigeria	Oluyomi et al. [60]
<i>Pupalia lappacea</i>	Amaranthaceae	Aerial part	Dcm/ Methanol / Aqueous	T. b. b	52.0/>100/>100	-	Benin	Bero et al. [20]
<i>Saba florida</i>	Apocynceae	Whole plant	Pet.Ether	T. b. b	-	25 min at 4 mg/ml	Nigeria	Atawodi, [41]
<i>Sansevieria liberica</i>	Dracaenaceae	Aerial part	Dcm/ Methanol / Aqueous	T. b. b	60.1/>100/>100	-	Benin	Bero et al. [20]
<i>Schrankia leptocarpa</i>	Leguminosae	Leaf	Dcm/ Methanol / Aqueous	T. b. b	49.2/>100/>100	-	Benin	Bero et al. [20]
<i>Securidaca longepedunculata</i>	Polygalaceae	Root	Methanol	T. b. b	-	5 min at 4 mg/ml	Nigeria	Atawodi et al. [21]
<i>Spondias mombim</i>	Anacardiaceae	Root	hexane + ethyl acetate	T. b. b	25	-	Nigeria	John et al. [52]
<i>Sterculia setigera</i>	Sterculiaceae	Root bark	Pet.ether	T. b. b	-	25 min at 4 mg/ml	Nigeria	Atawodi, [41]
<i>Stereospermum kunthianum</i>	Bignoniaceae	Leaf/stem	Aqueous/ Ethanolic	T. b. b	-	No activity @ 40mg/ml	Nigeria	Abu et al. [42]
<i>Striga spp.</i>	Orobanchaceae	Leaves	Methanol	T. b. b	-	40 min at 4 mg/ml	Nigeria	Atawodi et al. [21]
<i>Strychnos spinosa</i>	Loganiaceae	Leaf	DCM	T.b. b	≤19 µg/ml	-	Nigerian	Hoet et al. [47]
<i>Syzygium guinense</i>	Myrtaceae	Stem bark	Pet.ether	T. b. b	-	25 min at 4 mg/ml	Nigeria	Atawodi, [41]
<i>Tapinanthus globiferus</i>		Leaveva	Methanol	T. b. b	-	10 min at 10 mg/ml	Nigeria	Josephine et al. [24]
	mistletoe							
<i>Terminalia avicennioides</i>	Combretaceae	Stem bark	hexane + ethyl acetate/ Methanol	T. b. b	2.5	40 min at 4 mg/ml	Nigeria	John et al. [52] Atawodi et al. [211]
<i>Terminalia catapa</i>	Combretaceae	Leaf	hexane + ethyl acetate/ Methanol	T. b. b	17.24/ 7.80/ 1321.	-	Nigeria	Abiodun et al.[46]
<i>Terminalia ivorensis</i>	Combretaceae		n-Hexane/ethanol	T. b. b/ T. co	Btw 13 and 69 ug/ml	-	Nigeria	Adewunmi et al. [38]
<i>Terminalia superba</i>	Combretaceae	Stem	Aqueous	T.b. b	0.8 mg/ml(mic)	-	Nigerian	Antia et al. [55]
<i>Trichilia emetica</i>	Meliaceae	Leaf	DCM	T.b. b	≤19 µg/ml	-	Nigerian	Hoet et al. [47]
<i>Uapaca togoensis</i>	Euphorbiaceae	Root bark /stem	Aqueous/ Ethanolic	T.b. b	-	No activity @ 40mg/ml	Nigeria	Abu et al. [42]
<i>Verbascum sinaiticum</i>	Scrophulariaceae	Leaf	Aqueous	T.co	-	60 min at 4 mg/ml	Nigeria	Mergia et al. [61]
<i>Vitex doniana</i>	Lamiaceae	Stem bark	Pet.ether	T. b. b	-	45 min at 4 mg/ml	Nigeria	Atawodi, [41]
<i>Waltheria indica</i>	Sterculiaceae	stem bark	aqueous	. T. b. b	-	1mg/ml @ 25minute	Nigeria	Bala et al. [62]
<i>Withania somnifera</i>	Solanaceae	Whole plant	Ethyl acetate	T. b. b	50.0 ug/ml	-	Nigeria	John et al. [52]
<i>Xeoderris sthulmannii</i>	Fabaceae	Stems, leaves	Methanol	T. b. b	25		Burkina	Sawadogo et al. [51]

Scientific name	Family	Part (s) used	Extract/fraction	Parasite	IC50 MIC (µg/mL)	Motility of the parasite	Country	Authors
<i>Ximения americana</i>	Olacaceae	Stem bark	aqueous	T. b. b	-	2mg/ml @ 55minute	Faso Nigeria	Bala et al. [62]

T.b. b = *Trypanosoma brucei brucei*, T.e = *Trypanosoma evansi*, T.co = *Trypanosoma congolense*

Table 2. In vitro anti-trypanosomal activity of Southern African plants

Scientific name	Family	Part (s) used	Extract/fraction	Parasite	IC ₅₀ MIC (µg/mL)	Country	References
<i>Abrus precatorius</i>	Leguminosae	Leaves	CH ₂ Cl ₂ /MeOH (1 : 1)	T. b. r	0.01-17	South Africa	Hata et al. [32]/ Matthias et al. [33]
<i>Acacia erioloba</i>	Fabaceae	Roots	DCM/MeOH (1 : 1)	T. b. r	18.50	South Africa	Mokoka et al. [30]
<i>Agathosma apiculata</i>	Rutaceae	Whole plant	DCM/MeOH (1 : 1)	T. b. r/T. c	11.1/41.5	South Africa	Mokoka et al. [29]
<i>Alepidea amatymbica</i>	Apiaceae	Whole plant	DCM/MeOH (1 : 1)	T. cruzi	20.3/73.1	South Africa	Mokoka et al. [29]
<i>Artabotrys monteiroae</i>	Annonaceae	Leaves	DCM/MeOH (1 : 1)	T. b. r/T. c	10.3/41.3	South Africa	Mokoka et al. [29]
<i>Artemisia afra</i>	Asteraceae	Leaves	DCM	T. b. r/T. c	9.6/27.6	South Africa	Mokoka et al. [29]
<i>Asystasia gangetica</i>	acanthaceae	Leaves	DCM/MeOH (1 : 1)	T. b. r/T. c	13.2/74.7	South Africa	Mokoka et al. [29]
<i>Catha edulis</i>	Celastraceae	Root	DCM	T. b. r/T. c	14.2/19.1	South Africa	Mokoka et al. [29]
<i>Clausena anisata</i>	Rutaceae	Roots	DCM/MeOH (1 : 1)	T. b. r	7.19	South Africa	Mokoka et al. [30]
<i>Conyza albida</i>	Asteraceae	Whole plant	DCM/MeOH (1 : 1)	T. b. r/T. c	18.8/38.3	South Africa	Mokoka et al. [29]
<i>Conyza podocephala</i>	Asteraceae	Whole plant	DCM/MeOH (1 : 1)	T. b. r/T. c	13.9/47.2	South Africa	Mokoka et al. [29]
<i>Conyza scabrada</i>	Asteraceae	Leaves	DCM/MeOH (1 : 1)	T. b. r/T. c	30.0/49.4	South Africa	Mokoka et al. [29]
<i>Croton menyhartii</i>	Euphorbiaceae	Leaves	DCM/MeOH (1 : 1)	T. b. r/T. c	11.7/33.3	South Africa	Mokoka et al. [29]
<i>Cymbopogon validus</i>	Poaceae	Leaf	DCM/MeOH (1 : 1)	T. b. r/T. c	11.9/47.1	South Africa	Mokoka et al. [29]
<i>Drypetes gerrardii</i>	Meliaceae	Stems/leaves	DCM/MeOH(1 : 1)	T. b. r	7.31/12.1	South Africa	Mokoka et al. [30]
<i>Ekebergia capensis</i>	Meliaceae	Fruit/root	DCM/MeOH (1 : 1)	T. b. r/T. c	11.5/24.4/1.36	South Africa	Mokoka et al. [29], Mokoka et al. [30]
<i>Euclea natalensis</i>	Ebenaceae	Roots	DCM/MeOH (1 : 1)	T. b. r/T. c	28.1/43.7	South Africa	Mokoka et al. [29]
<i>Eucomis autumnalis</i>	Asparagaceae	Flowers/buds	DCM	T. b. r/T. c	37.1/29.7	South Africa	Mokoka et al. [29]
<i>Helichrysum nudifolium</i>	Asteraceae	Whole plant	DCM/MeOH (1 : 1)	T. b. r/T. c	33.1/43.9	South Africa	Mokoka et al. [29]
<i>Hypericum aethiopicum</i>	Hypericaceae	Leaves	DCM/MeOH (1 : 1)	T. b. r/T. c	4.47/18.1	South Africa	Mokoka et al. [29]
<i>Leonotis leonurus</i>	Lamiaceae	Leaves	DCM/MeOH (1 : 1)	T. b. r/T. c	14.7/50.1	South Africa	Mokoka et al. [29]
<i>Leonotis ocymifolia</i>	Lamiaceae	Leaves	DCM	T. b. r/T. c	9.1/63.5	South Africa	Mokoka et al. [29]
<i>Maytenus undata</i>	Celastraceae	Roots	DCM	T. b. r/T. c	35.2/28.4	South Africa	Mokoka et al. [29]
<i>Oedera genistifolia</i>	Asteraceae	Whole plant	DCM/MeOH(1 : 1)	T. b. r	4.38	South Africa	Mokoka et al. [30]
<i>Ozoroa sphaerocarpa</i>	Anacardiaceae	Whole plant	DCM	T. b. r/T. c	10.90	South Africa	Mokoka et al. [30]
<i>Pappea capensis</i>	Sapindaceae	Roots / leaves	DCM/ DCM/MeOH (1 : 1)	T. b. r/T. c	15.4/14.10	South Africa	Mokoka et al. [30]
<i>Pentzia globosa</i>	Asteraceae	Roots	DCM	T. b. r/T. c	5.76/31.3	South Africa	Mokoka et al. [29]
<i>Plumbago zeylanica</i>	Plumbaginaceae	Leaves	DCM/MeOH (1 : 1)	T. b. r/T. c	13.0/54.5	South Africa	Mokoka et al. [29]
<i>Psoralea pinnata</i>	Fabaceae	Leaves	DCM/MeOH(1 : 1)/DCM	T. b. r	0.15/0.31	South Africa	Mokoka et al. [30]
<i>Ptaeroxylon obliquum</i>	Rutaceae	Leaves	DCM	T. b. r/T. c	11.3/41.5	South Africa	Mokoka et al. [29]

Scientific name	Family	Part (s) used	Extract/fraction	Parasite	IC ₅₀ MIC (µg/mL)	Country	References
<i>Rauvolfia caffra</i>	Apocynaceae	Roots	DCM	T. b. r /T. c	17.9 /41.1	South Africa	Mokoka et al. [29]
<i>Salvia repens</i>	Lamiaceae	Whole plant	DCM/MeOH (1 : 1)	T. b. r /T. c	10.8/ 36.2	South Africa	Mokoka et al. [29]
<i>Schefflera umbellifera</i>	Araliaceae	Roots	DCM/MeOH (1 : 1)	T. b. r /T. c	20.9 /57.6	South Africa	Mokoka et al. [29]
<i>Schkuhria pinnata</i>	Asteraceae	Whole plant	DCM/MeOH (1 : 1)	T. b. r /T. c	2.04	South Africa	Mokoka et al. [30]
<i>Setaria megaphylla</i>	Poaceae	Whole plant	DCM/MeOH (1 : 1)	T. b. r /T. c	16.8 /43.9	South Africa	Mokoka et al. [30]
<i>Tarhonanthus camphorates</i>	Asteraceae	Whole plant	DCM/MeOH (1 : 1)	T. b. r /T. c	3.93 /18.6	South Africa	Mokoka et al. [30]
<i>Turraea floribunda</i>	Meliaceae	Bark/leave	DCM/MeOH (1 : 1)	T. b. r /T. c	24.4/ 17.10	South Africa	Mokoka et al. [30]
<i>Vernonia hirsuta</i>	Asteraceae	Whole plant	DCM/MeOH (1 : 1)	T. b. r /T. c	18.1 /43.0	South Africa	Mokoka et al. [29]
<i>Vernonia mespilifolia</i>	Asteraceae	Leaves	DCM/MeOH (1 : 1)	T. b. r /T. c	1.01	South Africa	Mokoka et al. [30]
<i>Vernonia natalensis</i>	Asteraceae	Whole plant	DCM/MeOH (1 : 1)	T. b. r /T. c	12.6/ 39.3	South Africa	Mokoka et al. [29]
<i>Vernonia oligocephala</i>	Asteraceae	Leaves	DCM	T. b. r /T. c /	4.67 /14.3	South Africa	Mokoka et al. [29]

T.b. b =Trypanosoma brucei brucei; T.e =Trypanosomaevansi; T.co =Trypanosomacongolense

Table 3. In vitro anti-trypanosomal activity of central African plants

Scientific name	Family	Part (s) used	Extract/fraction	Parasite	IC ₅₀ MIC (µg/mL)	Country	References
<i>Vernonia guineensis</i>	Asteraceae	Stem bark	Ethanol	T. b.r	3–5 mg/ml	Cameroon	Joseph et al. [36]
<i>Aframomum letestuanum</i>	Zingiberaceae	Seed	DCM	T.b.b./T.b.r	2.6	Cameroon	Kamnaing et al. [35]
<i>Enanatia chlorantha</i>	Annonaceae	Stem bark	Methanol	T. c	1.87	Republic of Congo	Musuyu et al. [37]
<i>Isolona hexaloba</i>	Annonaceae	Stem bark	Methanol	T.b.b.	1.95 µg /ml,	Republic of Congo	Musuyu et al. [37]
<i>Quassia africana</i>	simaroubaceae	Root bark	Methanol	T.c	1.88µg/ml	Republic of Congo	Musuyu et al. [37]

T.b.b =Trypanosoma brucei brucei; T.e =Trypanosomaevansi; T.co =Trypanosomacongolense

Table 4. In vitro anti-trypanosomal activity of North African plants

Scientific name	Family	Part (s)	Extract/fraction	Parasite	IC ₅₀ MIC (µg/mL)	Country	References
<i>Ageratum conyzoides</i>	Asteraceae	Leaves	n-Hexane/ CH ₂ Cl ₂	T. b. r	2.4/0.78	sudan	Nour et al. [63]

T.b. b =Trypanosoma brucei brucei; T.e =Trypanosomaevansi; T.co =Trypanosomacongolense

Table 5. *In vitro* anti-trypanosomal activity of east African plant

Scientific name	Family	Part (s) used	Extract/fraction	Parasite	IC50 MIC(µg/mL)	Country	References
<i>Albizia anthelmintica</i>	Fabaceae	Root	Methanol / DCM	T.b.b	49.42/51.09	Tanzania	Nibret et al. [64]
<i>Albizia harveyi</i>	Fabaceae	Root	Methanol / DCM	T.b.b	33.16/85.07	Tanzania	Nibret et al. [64]
<i>Artemisia absinthium</i>	Asteraceae	Aerialpart	Methanol/DCM	T.b.b	27.90/27.05	Ethiopian	Nibret, [65]
<i>Artemisia abyssinica</i>	Asteraceae	Aerialpart	Methanol/DCM	T.b.b	41.76/19.13	Ethiopian	Nibret, [65]
<i>Artemisia afra</i>	Asteraceae	Leah	Methanol/DCM	T.b.b	77.54/25.27	Ethiopian	Nibret, [65]
<i>Artemisia annua</i>	Asteraceae	Leaf	Methanol/DCM	T.b.b	99.44/41.05	Ethiopian	Nibret, [65]
<i>Balanites aegyptiaca</i>	Balantiaceae	Bark	Methanol / DCM	T.b.b	22.11/39.40	Tanzania	Nibret et al. [64]
<i>Cassia abbreviata</i>	Fabaceae	Leaf	Methanol / DCM	T.b.b	54.07/22.14	Tanzania	Nibret et al. [64]
<i>Combretum zeyheri</i>	Combretaceae	Bark	Methanol / DCM	T.b.b	87.45/38.97	Tanzania	Nibret et al. [64]
<i>Entada abyssinica</i>	Fabaceae	Bark	Methanol / DCM	T.b.b	46.39/56.21	Tanzania	Nibret et al. [64]
<i>Entandrophragma bussei</i>	Malaceae	Bark	Methanol / DCM	T.b.b	52.92/14.48	Tanzania	Nibret et al. [64]
<i>Harrisonia abyssinica</i>	Simaroubaceae	Leaf	Methanol / DCM	T.b.b	28.92/22.93	Tanzania	Nibret et al. [64]
<i>Khaya anthotheca</i>	Meliaceae	Seed	Pet. ether	T.b.r	5.72	Uganda	Obbo et al. [67]
<i>Kigelia africana</i>	Bignoniaceae	Leaf	Methanol / DCM	T.b.b	53.24/23.65	Tanzania	Nibret et al. [64]
<i>Lannea humilis</i>	Anacardiaceae	Bark	Methanol / DCM	T.b.b	56.16/75.41	Tanzania	Nibret et al. [64]
<i>Lannea stuhlmannii</i>	Anacardiaceae	Root	Methanol / DCM	T.b.b	44.23/22.24	Tanzania	Nibret et al. [64]
<i>Lonchocarpus capassa</i>	Fabaceae	Leaf	Methanol / DCM	T.b.b	73.80/21.68	Tanzania	Nibret et al. [64]
<i>Securidaca longepedunculata</i>	polygalaceae	Leaf	Methanol / DCM	T.b.b	55.56/11.02	Tanzania	Nibret et al. [64]
<i>Senna singueana</i>	Fabaceae	Leaf	Methanol / DCM	T.b.b	49.09/49.37	Tanzania	Nibret et al. [64]
<i>Solanecio mannii</i>	Asteraceae	Leaf	Methanolic/ dichloromethane extracts	T.b. b	50.58/24.89	Ethiopia	Nibret et al. [64]
<i>Strychnos panganensis</i>	Loganiaceae	Leaf/stem	ethanol	T.b.r	56/56	Tanzania	Freiburghaus et al. [68]
<i>Strychnos spinosa</i>	Strychnaceae	Leaf	aqueous	T.b.r	2500	Tanzania	Freiburghaus et al. [69]
<i>Teclea trichocarpa</i>	Rutaceae	Leaves	methanol	T.b.r/ Cruci	>90 /30	Kenya	Mwangi et al. [70]
<i>Terminalia sericea</i>	Combretaceae	Leaf	Methanol / DCM	T.b.b	36.23/21.71	Tanzania	Nibret et al. [64]
<i>Toona ciliata</i>	Meliaceae	Roots	Methanol/chloroformextract	T.b.r	6.95/3.2 µg/ml	kenya	Mercy et al. [71]
<i>Turraea fischeri</i>	Malaceae	Bark	Methanol / DCM	T.b.b	66.14/37.76	Tanzania	Nibret et al. [64]
<i>Vernonia auriculifera</i>	Asteraceae	Root	DCM	T.b.r	9.4	Uganda	Freiburghaus et al. [72]
<i>Vernonia subuligera</i>	Asteraceae	Leaf/root bark	Dichlorometh/petroleum ether	T.b.r	0.6/0.8	Tanzania	Freiburghaus et al. [69]
<i>Warburgia salutaris</i>	Canellaceae	Leaf	Methanol / DCM	T.b.b	45.13/10.68	Tanzania	Nibret et al. [64]
<i>Ximenia americana</i>	Canellaceae	Stem	DCM/methanol	T.b. b	86.64/49.18	Tanzania	Nibret et al. [66]
<i>Ximenia americana</i>	Olaceae	Leaf	Methanol / DCM	T.b.b	86.64/49.18	Tanzania	Nibret et al. [64]
<i>Zanha africana</i>	Sapindaceae	Root	Methanol / DCM	T.b.b	33.53/12.63	Tanzania	Nibret et al. [64]
<i>Zanthoxylum chalybeum</i>	Rutaceae	Leaf	Methanol / DCM	T.b.b	36.00/11.02	Tanzania	Nibret et al. [64]
<i>Zanthoxylum xanthoxyloides</i>	Rutaceae	Leaf/stem	DCM/methanol	T.b.b	36.00/11.02	Tanzania	Nibret et al. [66]

T.b.b =Trypanosoma brucei brucei; T.e =Trypanosomaevansi; T.co =Trypanosomacongolense

Table 6. *In vivo* anti-trypanosomal activity of African plant

Scientific name	Family	Part (s) used	Parasite	Extract	Dose	Model	%inhibition/survival days	Country	References
<i>Thymus vulgaris</i>	Lamiaceae	Leaf	T. b. b	methanol	500 mg/kg	Curative/ suppressive	8 days	Nigeria	Shittu et al. [73]
<i>Acacia nilotica</i>	Mimosaceae	Stem bark	T. b. b	Methanol	200	curative	30 days	Nigeria	Mann et al. [74]
<i>Acalypha wilkesiana</i>	Euphorbiaceae	Leaves	T.bb	aqueous	400 Mg/Kg	curative	2.03/11.00±0.0	Nigeria.	Olukunle et al. [75]
<i>Adamsonia digitata</i>	Malvaceae	Seed	T. b. b	methanol	300 mg/kg	curative	38	Nigeria	Hassan et al. [76]
<i>Allium sativum</i>	Alliaceae	Bulb/Pulp	T. b. b	Methanol/Aceticacid	20 mg/kg	curative	14	Nigeria	Yusuf, [77]/ Peni et al. [78]
<i>Annona senegalensis</i>	Annonaceae	Leaf	T. b. b	methanol	200 mg/kg	curative	20 days	Nigeria	Kabiru et al. [79]
<i>Annona senegalensis+Eucalyptus camaldulensi</i>		Leaf	T. b. b	methanol	200 mg/kg	Combined therapy(1:1)	>90 days	Nigeria	Kabiru et al. [80]
<i>Argemone mexicana</i>	Papaveraceae	Whole plant	T. e	Chloroform/ methanolic	500 mg/kg	curative	15 and 16 days	Sudan	Samia, [81]
<i>Aristolochia bracteolata</i>	Aristolochiaceae	Whole plant	T. e	Chloroform/ methanolic	500 mg/kg	curative	25 and 19 days	Sudan	Samia, [81]
<i>Artemisia annua</i>	Asteraceae		T.b. r	Methanol	5000 mg/kg	curative	15.6	Kenya	Esther et al. [82]
<i>Artemisia abyssinica</i>	Asteraceae	Aerial parts	T.co	dichloromethane	400 mg/kg	curative	40.67 days	Ethiopia	Teka et al. [83]
<i>Artemisia maciverae</i>	Asteraceae	Whole plant	T.b. b	chloroform	100 mg/kg	curative	74.15%	Nigeria	Ene et al. [84]
<i>Artemisia maritima</i>	Asteraceae	Whole plant	T.b. b	chloroform	100 mg/kg	curative	26%	Nigeria	Ene et al. [85]
<i>Azadirachta indica</i>	Meliaceae		T.b. r	dichloromethane	5000 mg/kg	curative	27days	Kenya	Esther et al. [82]
<i>Bombax buonopozense</i>	Bombacaceae	Stem bark	T. b. b	Methanol	300	curative	30 days	Nigeria	Mann et al. [74]
<i>Buchholzia coriacea</i>	Capparaceae	Seed	T.co	Methanol/aeous	500/ 1000 mg/kg	curative	29days/100%	Nigeria	Nweze et al. [86]/ Okere et al. [87]
<i>Citrullus lanatus</i>	Cucurbitaceae,	Leaf	T.b	aqueous extract	200	curative	97.18%	Nigeria	BIU et al. [88]
<i>Cannabis sativa</i>	Cannabinaceae	Whole plant	T. e	methanol	125/250 mg/kg	curative	> 45days	sudan	Samia et al. [89]
<i>Cucumis metuliferus</i>	Cucurbitaceae	Pulp	T. b. b	methanol	500 mg/kg	currative	47days	Nigeria	Abubakar et al. [90]
<i>Calotropis procera</i>	Asclepiadaceae	Leaf	T. e	Methanol	200 mg/kg	curative		Nigeria	Ibrahim et al. [91]
<i>Dissotis rotundifolia</i>	Melastomataceae	Leaf	T. b. b	ethanol	800 mg/kg	curative	78.4%	Nigeria	Mann et al. [92]

Scientific name	Family	Part (s) used	Parasite	Extract	Dose	Model	%inhibition/survival days	Country	References
<i>Eucalyptus camaldulensis</i>	Myrtaceae	Leaf	T. b. b	methanol	200 mg/kg	Curative	20 days	Nigeria	Kabiru et al. [80]
<i>Garcinia kola</i>	Clusiaceae	Nut	T. b. b	Methanol		Curative		Nigeria	Ogbadoyi et al. [93]
<i>Gongrenema latifolium</i>	Asclepiadaceae	Stem bark	T. co	methanolic	400 mg/kg	Curative	9 days	Nigeria	Abedo et al. [94]
<i>Guiera senegalensis</i>	Combretaceae	Leaf	T. b.	methanol	150	Curative	42%	BurkinaFaso	Aderbauer et al. [40]
<i>Securidaca longepedunculata</i>	Polygalaceae	Root	T. b.	methanol	150	Curative	48%	BurkinaFaso	Aderbauer et al. [40]
<i>Heterotis rotundifolia</i>	Melastomataceae	Whole plant	T. b.	methanol	800	Curative	30	Nigerian	Mann and Ogbadoyi, [95]
<i>Hymenocardia acida</i>	Euphorbiaceae	Root bark	T. b. b	DCM	300 mg/kg	Curative	9days	Nigeria	
<i>Khaya senegalensis</i>	Meliaceae	Stem	T. b. b	DCM	200 mg/kg	Curative	11days	Nigeria	Bulus and Addau, [54]
<i>Kigelia africana</i>	Bignoniaceae	Fruits	T.b. r	DCM	1000 mg/kg	Curative	41.8	Kenya	Esther et al. [82]
<i>Lippia multiflora</i>	Verbenaceae	Leaves	T. b. b	Aqueous	400 Mg/Kg	Curative	3.45%/11.00days	Nigeria.	Olukunle et al. [75]
<i>Morinda morindiodes</i>	Rubiaceae	Root bark	T. b. b	Aqueous	400 Mg/Kg	Curative	6.66 %	Nigeria.	Olukunle et al. [75]
<i>Moringa oleifera</i>	Moringaceae	Stems	T. b. b	Aqueous	200 mg/kg	Curative	30 days	Nigeria	Bulus and Addau, [82]
<i>Ocimum grattissimum</i>	Lamiaceae	Leaves	T.b b	Aqueous	50 Mg/Kg	Curative	11.11/22.44+3.5	Nigeria	Adamu et al. [96]
<i>Prosopis africana</i>	Leguminosae)	Leaves	T. b. b	methanol	200 mg/kg	Curative	14days	Nigerian	Atawodi and Funmi [97]
<i>Psidium guajava</i>	Myrtaceae	Leaf	T. b. b	ethanolic		Prophylactic	32 days	Nigeria	Adeyemi et al. [98]
<i>Pterocarpuserinace us,</i>	Leguminosae	Leaf	T. b.	Methanol	40	Curative	≥14days	Nigerian	Mann and Ogbadoyi, [95]
<i>Zanthoxylum zanthoxyloides</i>	Rutaceae	Stem bark	T. b.	Methanol	100	Curative	No activity	Nigerian	Mann and Ogbadoyi, [95]
<i>Tapinanthus globiferus</i>	Loranthaceae	Leaf	T. co	methanolic	400 mg/kg	Curative	24 days	Nigeria	Abedo et al. [94]
<i>Terminalia avicennioides</i>	Combretaceae	Fruit	T. b. b	Methanol	300	Curative	12 days	Nigeria	Mann et al. [74]
<i>Tinospora bakis</i>	melastomataceae	Leaf	T. e	Chloroform/ methanolic	500 mg/kg	Curative	20 days	Sudan	Samia, [81]
<i>Tithonia diversifolia</i>	Asteraceae	Leaves	T. b. b	Aqueous	400 Mg/Kg	Curative	2.03/11.6±0.40	Nigeria.	Olukunle et al. [75]
<i>Tridax procumbens</i>	Asteraceae	Leaves	T. b. b	Methanol	300 mg/kg	Curative	28	Nigeria.	Abubakar et al. [99]
<i>Vernonia amygdalina</i>	Asteraceae	Leaf	T. b. b	Methanol	300 mg/kg	Curative	24 days	Nigeria	Yusuf et al. [100]

Scientific name	Family	Part (s) used	Parasite	Extract	Dose	Model	%inhibition/survival days	Country	References
<i>Zanthoxylumzanthoxyloides</i>	Rutaceae	Stem bark	T. b.			Curative		Nigerian	Mann and Obgbadoyi, [95]

T.b. b =*Trypanosoma brucei brucei*, *T.e* =*Trypanosomaevansi*, *T.co* =*Trypanosomacongolense*

Table 7. Anti-trypanosomal compounds isolated from African plant

Compound	Plant species	Family	Part used	Trypanosome species	IC ₅₀	Solvent	Author
16-acetoxy-11-hydroxy octadeca-17-ene-12,14-diynyl acetate	<i>Cussonia zimmermannii</i>	Araliaceae	Root bark	T.b.r	0.42	Pet.ether	Senn et al. [101]
8-hydroxyheptadeca-4,6-diyn-3ylacetate	<i>Cussonia zimmermannii</i>	Araliaceae	Root bark	T.b.r	5.4	Pet.ether	Senn et al. [101]
8-hydroxyheptadeca-1-ene-4,6-diyn-2ylacetate	<i>Cussonia zimmermannii</i>	Araliaceae	Root bark	T.b.r	0.41	Pet.ether	Senn et al. [101]
24-hydroperoxy-24- vinylcholesterol	<i>Strychnos spinosa</i>	Loganiaceae	Leaves	T.b. b	3.2	lipophilic	Hoet et al. [26]
2-oxo-3-deacetyl salannin	<i>Azadirachta indica</i>	Meliaceae	Leaf	<i>T.b. r</i>	6.9	Chloroform	Githua et al. [102]
4,7-Dimethoxy-5-methyl-2H-Chromen-2-one	<i>Toona ciliata</i>	Meliaceae	Root	<i>T.b. r</i>	31.25 µg/ml	Methanol	Mercy et al. [71]
4'-hydroxy-5,6,7,3',5'-pentamethoxyflavone (ageconyflavone C).	<i>Ageratum conyzoides</i>	Asteraceae	Leaves	T.b. r	3.01	Methanol	Nour et al. [63]
41 (4Z,6E)-5-hydroxy-1,7-bis (4- hydroxyphenyl) hepta-4,6-dien-3-one	<i>Aframomum tetestuanum</i>	Zingiberaceae	Seed	<i>T.b. b</i>	2.6	DCM	Kamnaing et al. [35]
5,6,7,3',4',5'-hexamethoxyflavone	<i>Ageratum conyzoides</i>	Asteraceae	Leaves	T.b. r	8.58	Methanol	Nour et al. [63]
5,6,7,5'-tetramethoxy-3',4'-methylenedioxyflavone	<i>Ageratum conyzoides</i>	Asteraceae	Leaves	T.b. r	7.29	Methanol	Nour et al. [63]
5,6,7,8,3',4',5'-heptamethoxyflavone (5'-methoxynobiletine	<i>Ageratum conyzoides</i>	Asteraceae	Leaves	T.b. r	4.76	Methanol	Nour et al. [63]
5,6,7,8,5'-pentamethoxy-3',4'-methylenedioxyflavone (eupalestin,)	<i>Ageratum conyzoides</i>	Asteraceae	Leaves	T.b. r	6.67	Methanol	Nour et al. [63]
6- acetonyldihydrochelerythrine	<i>Garcinia lucida</i>	Clusiacea	Stem	<i>T.b. b</i>	3.9	DCM	Fotie et al. [34]
7- deacetylkhivorin	<i>Khaya anthotheca</i>	Meliaceae	Seeds	<i>T.b. r/T.cr</i>	16.88 / 31.82	Pet. Ether	Obbo et al. [67]
7,15-dihydroxy-7,15-deoxo nimbin	<i>Azadirachta indica</i>	Meliaceae	Leaf	<i>T.b. r</i>	15.6	Chloroform	Githua et al. [102]
7,8,3',5'-tetramethoxyisoflavan-1',4'-quinone	<i>Abrus precatorius</i>	Leguminosae	Whole plant	T.b. r	0.3	DCM/ Methanol (1 : 1)	Hata et al. [32]
7-acetyl-15-methoxy-29- methylene-7,15-deoxo nimbolide	<i>Azadirachta indica</i>	Meliaceae	Leaf	<i>T.b. r</i>	7.8	Chloroform	Githua et al. [102]
7-methoxyflavone	<i>Conchocarpus heterophyllus</i>	Rutaceae	Branches	<i>T.cr</i>	787 µg/mL	Hexane	Ambrozin et al. [103]
8-hydroxyheptadeca-1-ene- 4,6-diyn-2yl acetate	<i>Cussonia zimmermannii</i>	Araliaceae	Root	<i>T.b. r</i>	0.14	Pet.ether	Senn et al. [101]
8-hydroxyheptadeca-4,6-diyn- 3yl acetate	<i>Cussonia zimmermannii</i>	Araliaceae	Root	<i>T.b. r</i>	5.4	Pet.ether	Senn et al. [101]
Abruquinone B	<i>Abrus precatorius</i>	Leguminosae	Whole plant	T.b. r	0.2	DCM/	Hata et al. [32]

Compound	Plant species	Family	Part used	Trypanosome species	IC ₅₀	Solvent	Author
abruquinone G	<i>Abrus precatorius</i>	Leguminosae	Whole plant	T.b. r	17.0	Methanol (1 : 1) DCM/ Methanol (1 : 1)	Hata et al. [32]
Abruquinone H	<i>Abrus precatorius</i>	Leguminosae	Whole plant	T.b. r	12.0	DCM/ Methanol (1 : 1)	Hata et al. [32]
abruquinone I	<i>Abrus precatorius</i>	Leguminosae	Whole plant	T.b. r	0.3	DCM/ Methanol (1 : 1)	Hata et al. [32]
Abruquinones A	<i>Abrus precatorius</i>	Leguminosae	Whole plant	T.b. r	0.02	DCM/ Methanol (1:1)	Matthias et al. [33]
Abruquinones D	<i>Abrus precatorius</i>	Leguminosae	Whole plant	T.b. r	0.01	DCM/ Methanol (1:1)	Matthias et al. [33]
Abruquinones J	<i>Abrus precatorius</i>	Leguminosae	Whole plant	T.b. r	11.2	DCM/ Methanol (1:1)	Matthias et al. [33]
Abruquinones K	<i>Abrus precatorius</i>	Leguminosae	Whole plant	T.b. r	0.11	DCM/ Methanol (1:1)	Matthias et al. [33]
Abruquinones L	<i>Abrus precatorius</i>	Leguminosae	Whole plant	T.b. r	0.02	DCM/ Methanol (1:1)	Matthias et al. [33]
Arborinine	<i>Teclea trichocarpa</i>	Rutaceae	Leaves	T.b. r	23.52	Methanol	Mwangi et al. [70]
Artemisinin	<i>Artemisia annua</i>	Asteraceae	Leaf	T.b.b	35.91	DCM/ Methanol (1:1)	Nibret, 2009
Azaanthraquinone	<i>Mitracarpus scaber</i>	Rubiaceae	Leaf	T.co	50	Methanol	Nok [124]
Beta-sitosterol	<i>Buchholziacoriacea</i>	Capparaceae	Seeds	T.b. b	12.5 µg/ml	methanol	Nweze et al. [86]
betulin	<i>Strychnos spinosa</i>	Loganiaceae	Leaves	T.b. b	54.0	lipophilic	Hoet et al. [26]
Betulinic acid	<i>Keetia leucantha</i>	Rubiaceae	Leaf	Bloodstream/procyclic forms of T.b	11.2/40. 90 µg /ml	Oil	Bero et al. [28]
Caryophyllene	<i>Keetia leucantha</i>	Rubiaceae	Leaf	Bloodstream/procyclic forms of T.b	41.2/>10 0 µg /ml	Oil	Bero et al. [28]

Compound	Plant species	Family	Part used	Trypanosome species	IC ₅₀	Solvent	Author
cedrelone	<i>Toona ciliata</i>	Meliaceae	Root	<i>T.b. r</i>	7.85 µg/ml	Methanol	Mercy et al. [71]
Cedrelone	<i>Toona ciliata</i>	Meliaceae	Root	<i>T.b. r</i>	31.25	Chloroform	Githua et al. [102]
cinerin II	<i>Chrysanthemum cinerariifolium</i>	Asteraceae	Flowers	<i>T.b. r</i>	12.2	n-hexane	Michael et al. [104]
cipadesin	<i>Cipadessa fruticosa</i>	Meliaceae	Fruits	<i>T.cr.</i>	189.0 µmol/L	DCM	Ana et al. [105]
cipadesin A	<i>Cipadessa fruticosa</i>	Meliaceae	Fruits	<i>T.cr.</i>	136.1 µmol/L	DCM	Ana et al. [105]
citronellal	<i>Ocimum gratissimum</i>	lamilaceae	Seed oil	<i>T.b. b</i>	2.76±1.55 µg/mL	Oil	Bénédicta et al. [25]
clerosterol	<i>Strychnos spinosa</i>	Loganiaceae	Leaves	<i>T.b. b</i>	53.6	lipophilic	Hoet et al. [26]
cynaropicrin	<i>Vernonia mespilifolia</i>	Asteraceae	Leaf	<i>T.b. r/ T.cr</i>	0.23/5.14	DCM/ Methanol	Mokoka et al. [30]
Dihydrochelerythrine	<i>Garcinia lucida</i>	Clusiacea	Stem	<i>T.b. b</i>	0.8	DCM	Fotie et al. [34]
drypetenone D	<i>Drypetes gerrardii</i>	Putranjivaceae	Stem	<i>T.b. r</i>	6.0	DCM/ Methanol (1:1)	Matthias et al. [33]
drypetenone E	<i>Drypetes gerrardii</i>	Putranjivaceae	Stem	<i>T.b. r</i>	-	DCM/Methanol (1:1)	Matthias et al. [33]
encecalol methyl ether 6	<i>Ageratum conyzoides</i>	Asteraceae	Leaves	<i>T.b. r</i>	78.4	Methanol	Nour et al. [63]
erythrodiol	<i>Strychnos spinosa</i>	Loganiaceae	Leaves	<i>T.b. b</i>	5.3	lipophilic	Hoet et al. [26]
Espintanol	<i>Oxandra espintana</i>	Anonaceae	Leaf	<i>T.cr</i>	25 µg/ml	methanol	Hocquemiller, [106]
febrifugin	<i>Cipadessa fruticosa</i>	Meliaceae	Fruits	<i>T.cr.</i>	168.0 µmol/L	DCM	Ana et al., [105]
flavone	<i>Conchocarpus heterophyllus</i>	Rutaceae	Branches	<i>T.cr</i>	2116 µg/mL	Hexane	Ambrozin et al.[103]
Geranylacetone	<i>Keetia leucantha</i>	Rubiaceae	Leaf	Bloodstream/procyclic forms of <i>T.b</i>	16.2/>10 0 µg g/ml	Oil	Bero et al. [28]
Grandifolione	<i>Khaya anthotheca</i>	Meliaceae	Seeds	<i>T.b.r/T.cr</i>	10.66/20 .9	Pet. Ether	Obbo et al. [67]
jasmolin I	<i>Chrysanthemum cinerariifolium</i>	Asteraceae	Flowers	<i>T.b. r</i>	30.9	n-hexane	Michael et al. [104]
jasmolin II	<i>Chrysanthemum cinerariifolium</i>	Asteraceae	Flowers	<i>T.b. r</i>	12.0	n-hexane	Michael et al., [104]
Kolavenol	<i>Entada abyssinica</i>	Leguminosae	Stem	<i>T.b. r</i>	2.5	Ethanol	Freiburghaus et al. [107]

Compound	Plant species	Family	Part used	Trypanosome species	IC ₅₀	Solvent	Author
Letestuiainin A	<i>Aframomum letestuanum</i>	Zingiberaceae	Seed	<i>T.b. b</i>	>100	DCM	Kamnaing et al.[35]
Letestuiainin B	<i>Aframomum letestuanum</i>	Zingiberaceae	Seed	<i>T.b. b</i>	67	DCM	Kamnaing et al.[35]
Letestuiainin C	<i>Aframomum letestuanum</i>	Zingiberaceae	Seed	<i>T.b. b</i>	2.6	DCM	Kamnaing et al. [35]
limonene	<i>Ocimum gratissimum</i>	lamilaceae	Seed oil	<i>T.b. b</i>	4.24±2.27 µg/mL	Oil	Bénédicta et al.[25]
Lucidamine A	<i>Garcinia lucida</i>	Clusiaceae	Stem	<i>T.b. b</i>	14.1	DCM	Fotie et al. [34]
Lucidamine b	<i>Garcinia lucida</i>	Clusiaceae	Stem	<i>T.b. b</i>	4.1	DCM	Fotie et al. [34]
lupeol	<i>Strychnos spinosa</i>	Loganiaceae	Leaves	<i>T.b. b</i>	19,3	lipophilic	Hoet et al. [26]
Melicopicine	<i>Teclea trichocarpa</i>	Rutaceae	Leaves	<i>T.b. r</i>	15.56	Methanol	Mwangi et al. [70]
mexicanolide	<i>Cipadessa fruticosa</i>	Meliaceae	Fruits	<i>T.cr.</i>	326.3 µmol/L	DCM	Ana et al. [105]
myrcene	<i>Ocimum gratissimum</i>	Lamiaceae	Seed oil	<i>T.b. b</i>	2.24±0.2 7 µg/mL	Oil	Bénédicta et al.[25]
n-Hexadecanoic acid	<i>Keetia leucantha</i>	Rubiaceae	Leaf	Bloodstream/procyclic forms of <i>T. b</i>	>100/>1 00 g g/ml	Oil	Bero et al. [28]
Normelicopicine	<i>Teclea trichocarpa</i>	Rutaceae	Leaves	<i>T.b. r</i>	5.24	methanol	Mwangi et al. [70]
Oleanolic acid	<i>Keetia leucantha</i>	Rubiaceae	Leaf	Bloodstream/procyclic forms of <i>T. b</i>	7.3/86.4 µg g/ml	Oil	Bero et al. [28]
Oleic acid	<i>Keetia leucantha</i>	Rubiaceae	Leaf	Bloodstream/procyclic forms of <i>T. b</i>	64.30/>1 00 µg g/ml	Oil	Bero et al. [28]
phytol	<i>Keetia leucantha</i>	Rubiaceae	Leaf	Bloodstream/procyclic forms of <i>T.b. b</i>	19.1/>100	Oil	Bero et al. [28]
putranoside A	<i>Drypetes gerrardii</i>	Putranjivaceae	Stem	<i>T.b. r</i>	18.0	DCM/ Methanol (1:1)	Matthias et al. [33]
pyrethrin I	<i>Chrysanthemum cinerariifolium</i>	Asteraceae	Flowers	<i>T.b. r</i>	6.9	n-hexane	Michael et al. [104]
pyrethrin II	<i>Chrysanthemum cinerariifolium</i>	Asteraceae	Flowers	<i>T.b. r</i>	10.6	n-hexane	Michael et al. [104]
quercetin	<i>Rapanea lancifolia</i>	Myrsinaceae	Branches	<i>T.b.b</i>	13.2 µmol/L	methanol	Camacho et al. [108]
Saringosterol	<i>Strychnos spinosa</i>	Loganiaceae	Leaves	<i>T.b. b</i>	7.8	lipophilic	Hoet et al. [26]
schkuhrin I	<i>Schkuhria pinnata</i>	Asteraceae	Whole plant	<i>T.b. r/ T.cr</i>	0.86/16.4	DCM/ Methanol	Mokoka et al. [30]
schkuhrin II	<i>Schkuhria pinnata</i>	Asteraceae	Whole plant	<i>T.b. r/ T.cr</i>	1.50/26.9	DCM/ Methanol	Mokoka et al. [30]
Siderin	<i>Toona ciliata</i>	Meliaceae	Leaf	<i>T.b. r</i>	7.18	Chloroform	Githua et al. [102]

Compound	Plant species	Family	Part used	Trypanosome species	IC ₅₀	Solvent	Author
Skimmianine	<i>Teclea trichocarpa</i>	Rutaceae	Leaves	T.b. r	15.78	Methanol	Mwangi et al. [70]
stigmastanol	<i>Strychnos spinosa</i>	Loganiaceae	Leaves	T.b. b	>100	Ipophilic	Hoet et al. [26]
stigmasterol	<i>Strychnos spinosa</i>	Loganiaceae	Leaves	T.b. b	55.5	Ipophilic	Hoet et al. [26]
Terchebulin	<i>Terminalia avicenioides</i>	Combretaceae	Leaf	T.b. b	27.5	Aqueous	Shuaibu et al. [109].
punicalagin, ,	<i>Terminalia avicenioides</i>	Combretaceae	Leaf	T.b. b	15	Aqueous	Shuaibu et al. [109]
ellagic acid	<i>Terminalia avicenioides</i>	Combretaceae	Leaf	T.b. b	25	Aqueous	Shuaibu et al. [109].
flavogallonicacid	<i>Terminalia avicenioides</i>	Combretaceae	Leaf	T.b. b	7.5	Aqueous	Shuaibu et al. [109]
ursolic acid	<i>Keetia leucantha</i>	Rubiaceae	Leaf	Bloodstream/procyclic forms of T. b	2.5/6.5 µg/ml	Oil	Bero et al. [28]
uvaol	<i>Strychnos spinosa</i>	Loganiaceae	Leaves	T.b. b	12.3	Ipophilic	Hoet et al. [26]
vernoguinoside	<i>Vernonia guineensis</i>	Asteraceae	Stem bark	T.b. r	3–5 mg/ml	Ethanol	Joseph et al. [36]
vernoguinosterol	<i>Vernonia guineensis</i>	Asteraceae	Stem bark	T.b. r	3–5 mg/ml	Ethanol	Joseph et al. [36]
α-Amyrin	<i>Teclea trichocarp</i>	Rutaceae	Leaves	T.b. r	11.21	Methanol	Mwangi et al. [70]
α-amyrin	<i>Strychnos spinosa</i>	Loganiaceae	Leaves	T.b. b	48.9	Lipophilic	Hoet et al. [26]
α-Ionone	<i>Keetia leucantha</i>	Rubiaceae	Leaf	Bloodstream/procyclic forms of T. b	13.1/81.4 µg/ml	Oil	Bero et al. [28]
α-sulphur	<i>Buchholziacoriacea</i>	Capparaceae	Seeds	T.b. b	25 µg/ml	Methanol	Nweze et al. [86]
β-amyrin	<i>Strychnos spinosa</i>	Loganiaceae	Leaves	T.b. b	54.3	Lipophilic	Hoet et al. [26]
β-Ionone	<i>Keetia leucantha</i>		Leaf	Bloodstream/procyclic forms of T. b	10.5/55.8 µg/ml	Oil	Bero et al. [28]
β-sitosterol	<i>Morinda lucida</i>	Rubiaceae	Leaves	T.b. b	12.5 µg/ml	Methanol	Nwakaeg, [56]
β-sitosterol	<i>Strychnos spinosa</i>	Loganiaceae	Leaves	T.b. b	>100	lipophilic	Hoet et al. [26]
β-Sitosterol	<i>Teclea trichocarp</i>	Rutaceae	Leaves	T.b. r	>90	Methanol	Mwangi et al. [70]

T.b. b = *Trypanosoma brucei brucei*; T.e = *Trypanosoma evansi*; T.co = *Trypanosoma congolense*

4.4 Anti-trypanosomal Activity of North African Plants

A very little information on trypanocidal potency of medicinal plant from North Africa were obtained from literature. Only one and three medicinal plant was found to have been investigated for invitro and invivo activity. N-Hexane and DCM extract of *Ageratum conyzoides* show a significant activity against *T. b. rhodesiense* with IC₅₀ values of 2.4 and 0.78 ug/ml respectively [63]. The whole plant of *Argemone Mexicana*, *Aristolochia bracteolata* and *Tinospora bakis* when administered to Trypanosoma evansi infected rats at dose of 500 mg/kg significantly reduced the parasitaemia count and extend the survival time compare to untreated group, with chloroform extract of *Aristolochia* been the most active (25 survival days) [81]. However, methanol extract of *Cannabis sativa* at dose of 125/250 mg/kg prolonge the survival days of Trypanosoma evansi infected mice beyond 45 day (Samia et al., 2012). The anti-trypanosomal compounds isolated from North african plant (Fig. 2) include 4'-hydroxy-5,6,7,3',5'-pentamethoxyflavone (IC₅₀ 3.01 ug/ml), 5,6,7,3',4',5'-hexamethoxyflavone, (IC₅₀ 8.58 ug/ml), 5,6,7,5'-tetramethoxy-3',4'-methylenedioxyflavone (IC₅₀ 7.29 ug/ml), 5,6,7,8,3',4',5'-heptamethoxyflavone (IC₅₀ 4.76 ug/ml), and 5,6,7,8,5'-pentamethoxy-3',4'-methylenedioxyflavone (IC₅₀ 6.67 ug/ml) from *Ageratum conyzoides* [63].

4.5 Anti-trypanosomal Activity of East African Plants

An appreciable data on trypanocidal potency of medicinal plant from east African plant were obtained from literature. The most interesting in vitro trypanocidal activity from east African plant were those of seed extract of *K. anthotheca* (IC₅₀ 5.72 ug/ml), and root extract of *T. ciliate* (IC₅₀ 3.2-6.9 µg/ml). However, out of the medicinal plant from this area with invivo trypanocidal activity only *Artemisia abyssinica* [83] and *Kigelia Africana* [82], show appreciable activity by prolonging the survival days of the rat to 40.67 and 41.8 at 400 and 100 mg/kg respectively. Detailed phytochemical study of east African plant led to the isolation of 17 compounds (Fig. 2) with varied degree of trypanocidal activity (Table 7), the most notable one were those of 8-hydroxyheptadeca-1-ene-4,6-diyn-2yl acetate (IC₅₀ 0.14 ug/ml) and 8-hydroxyheptadeca-4,6-diyn-3yl acetate (IC₅₀ 5.4 ug/ml) isolated from *Cussonia zimmermannii* [101].

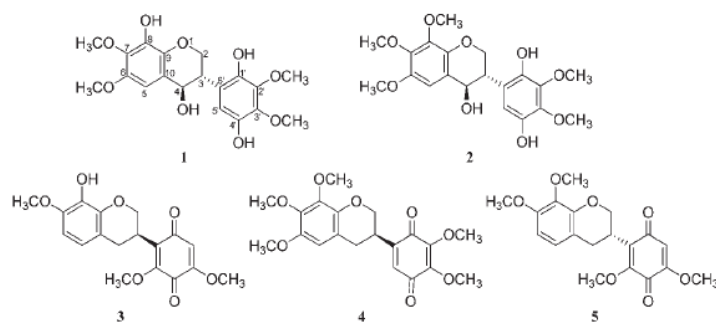
4.6 African Plants with Ameliorative Effects on the Trypanosome-induced Pathological Changes

4.6.1 African herbal formula (AFH)

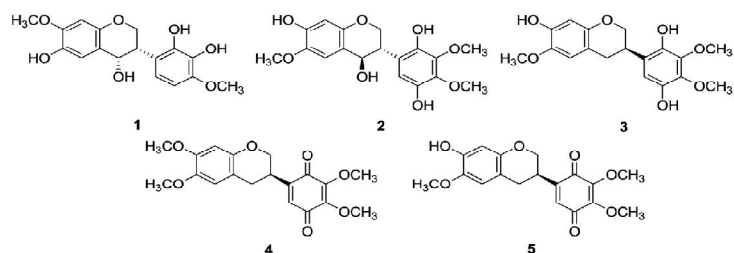
A herbal mixture of herbs code named African Herbal Formula (AFH) has been applied by members of the family and close-associates for all kinds of health problems and it is very popular among the low socio-economic class. The influence of these Herbal Formula on the haematological parameters of trypanosome infected rats were investigated. Observations showed that the formula has an effect on the haemopoietic system manifested by a positive increase in the levels of haemoglobin, packed cell volume and red blood cell while the white blood cell and lymphocyte levels were decreased. AHF also delayed the proliferation of the parasites and improved the level of the characteristic weight loss associated with trypanosomiasis [110]. This suggests that the Herbal Formula must have possibly combated the parasite directly without demanding further production of the effectors cells of the immune system.

4.6.2 Jobelyn®, (herbal preparation)

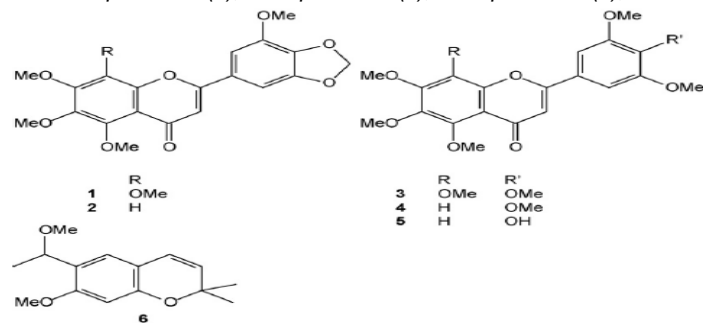
Jobelyn®, manufactured by Health Forever Products Ltd, Lagos, Nigeria, is a commercial herbal preparation that recently made its way into the herbal medicine market in Nigeria. It is available as a powdered preparation formulated into capsules and suspension and contains iron, protein, fat, carbohydrates, tannins, saponins, Sorghum b/color or Sorghum (family: Gramineae). A study was carried out to determine the effect of this herbal preparation on packed cell volume (PCV) and haemoglobin (Hb) concentrations in anaemic rabbits. The PCV and Hb concentrations of healthy rabbits infected with *T. brucei brucei* were monitored for 49 days. *T. b. brucei* produced a significant reduction in PCV and Hb concentrations in all infected rabbits when compared with the controls (p<0.05). These hematological parameters were restored to normal levels in the anaemic rabbits by the herbal preparation. The anaemic rabbits not treated with the herbal preparation presented with a progressive decline in their PCV and Hb concentrations and majority of them died before the end of the study [111].



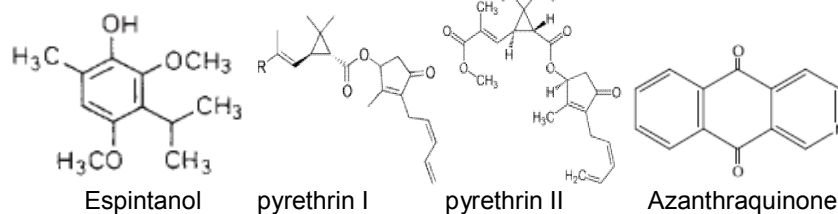
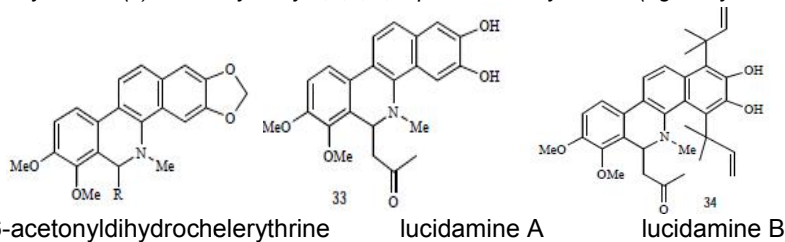
Abruquinone H (1) and abruquinone G (2); abruquinone I (3); abruquinone B (4); and 7,8,3',5'-tetramethoxyisoflavan-1',4'-quinone(5).

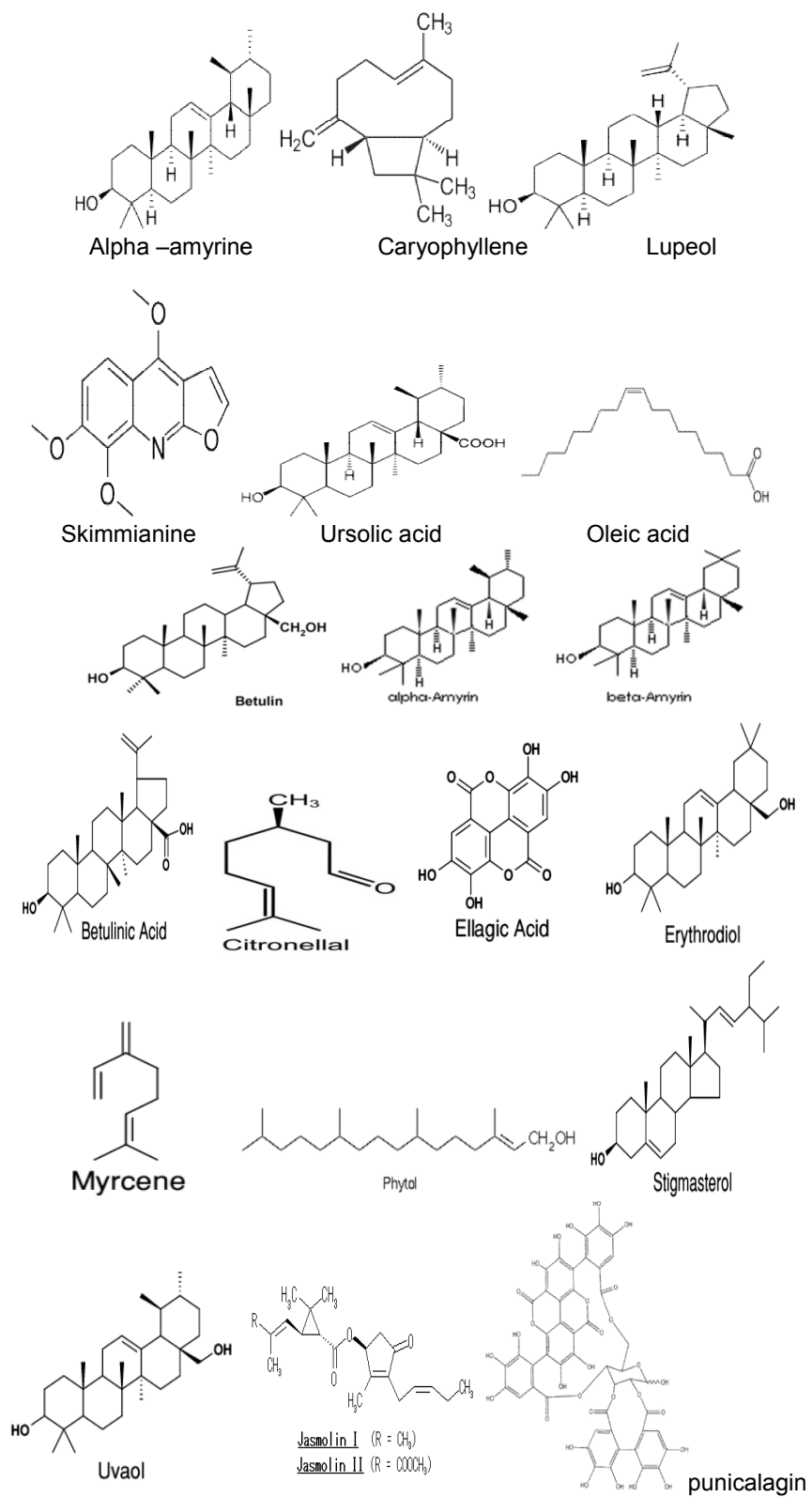


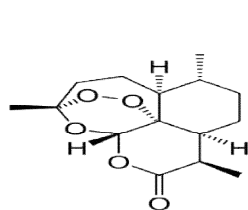
Abruquinone J (1) and abruquinone K (2); abruquinone L (3); abruquinone A (4); and abruquinone D (5).



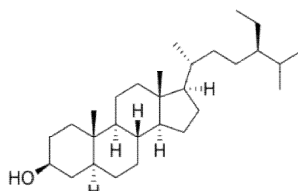
5,6,7,8,5'-pentamethoxy-3',4'-methyleneedioxyflavone (eupalestin, 1); 5,6,7,5' tetramethoxy- 3',4'-methyleneedioxyflavone (2); 5,6,7,8,3',4',5'-heptamethoxyflavone (5'-methoxynobiletine, 3), 5,6,7,3',4',5'-hexamethoxyflavone (4) and 4'-hydroxy-5,6,7,3',5'-pentamethoxyflavone (ageconyflavone C, 5).



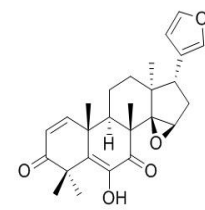




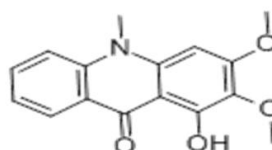
Artemisinin



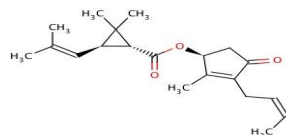
Stigmastanol



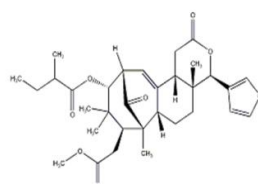
Cedrelone



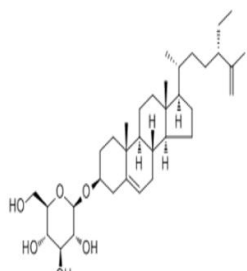
Arborinine



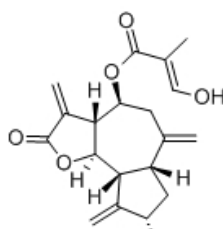
cinerin



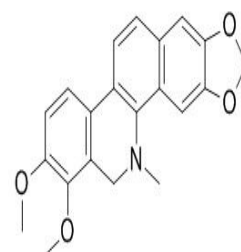
cipadesin



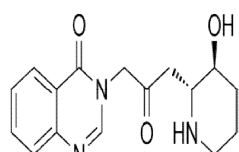
Clerosterol



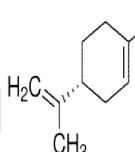
cynaropicrin



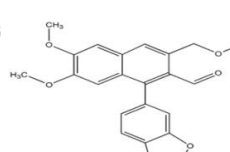
Dihydrochelerythrine



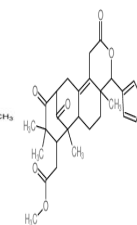
Febrifugin



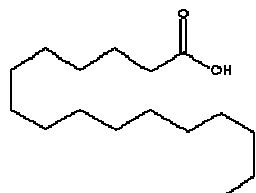
limonene



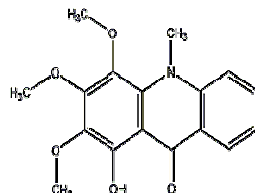
Lucidamine



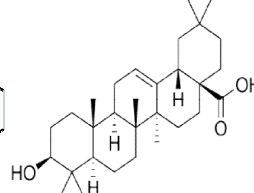
Amexicanolide



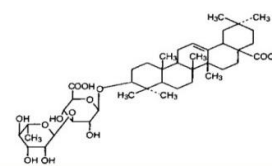
n-Hexadecanoic acid



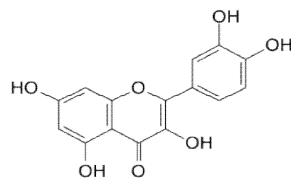
Normelicopicine



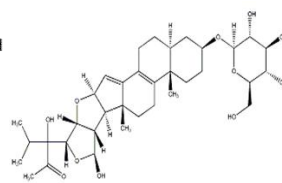
Oleanolic acid



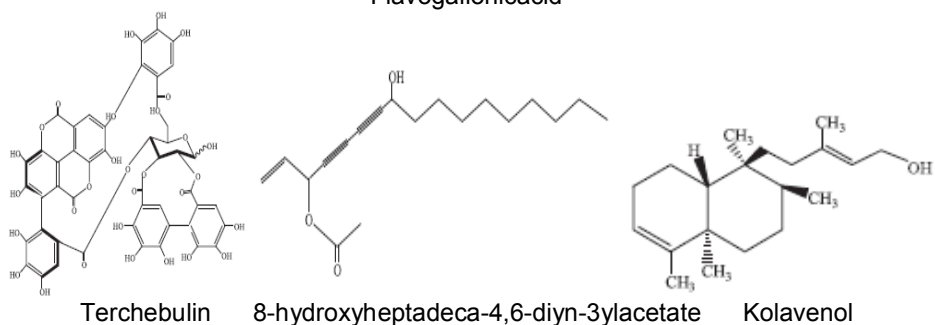
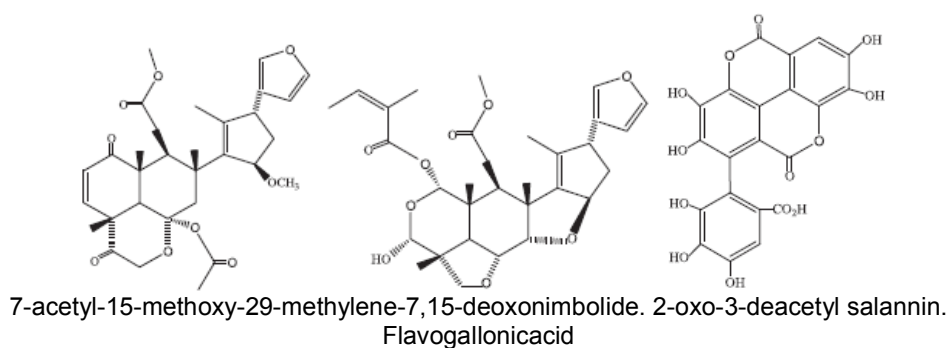
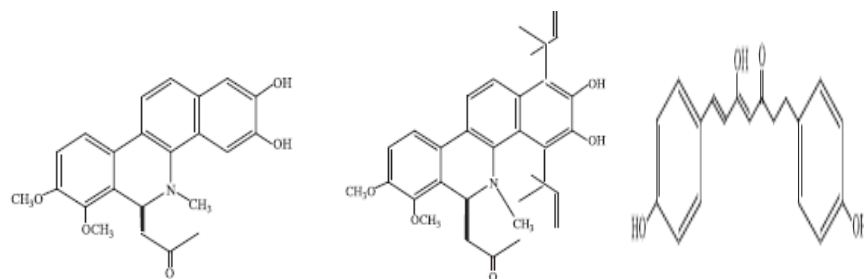
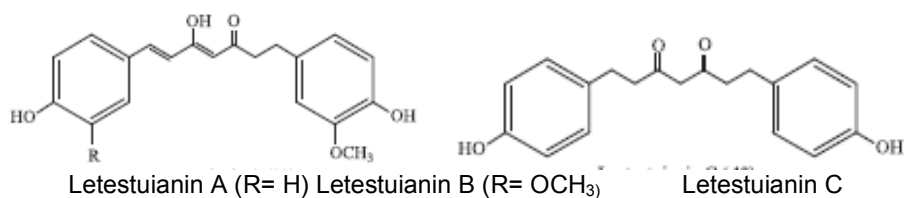
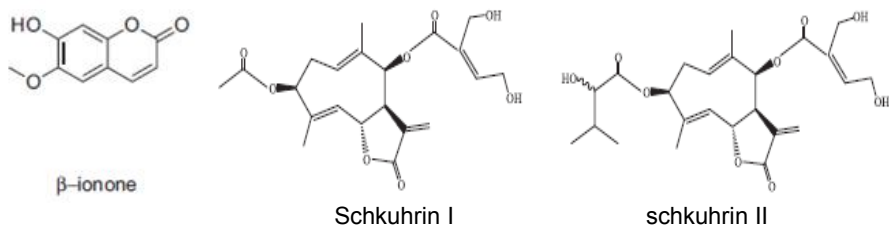
Putranoside



Aquercetin



vernoguinoside



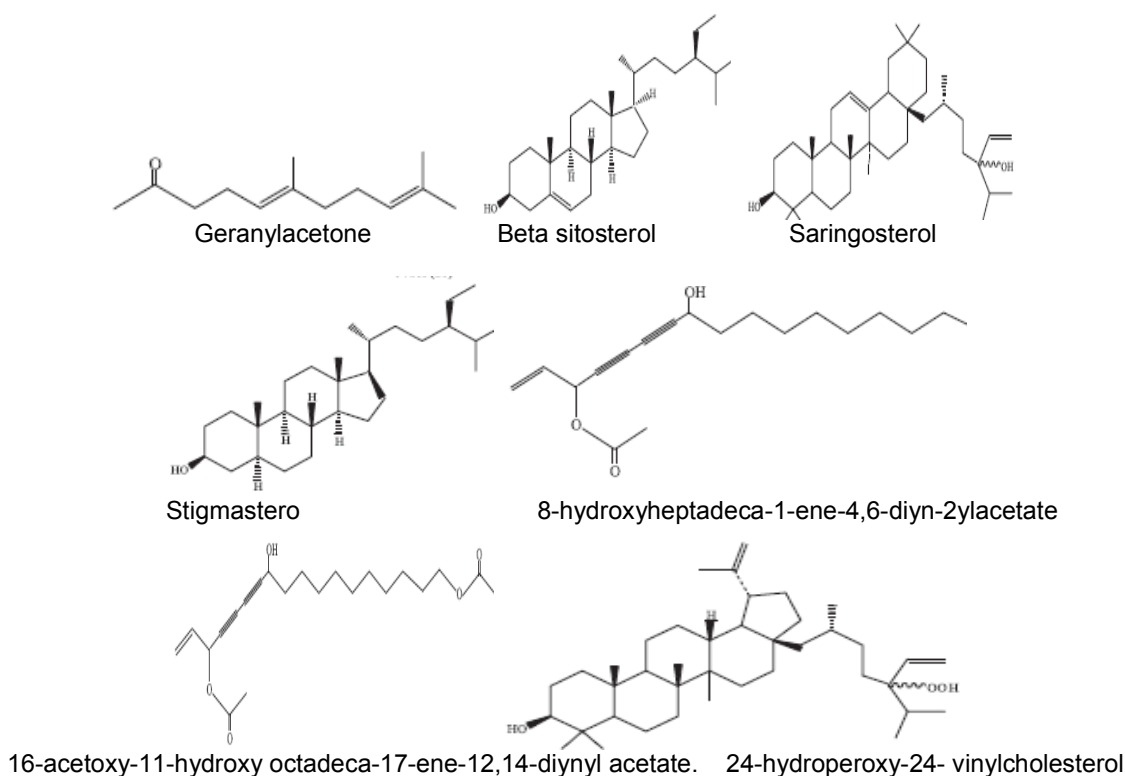


Fig. 2. Structures of isolated bioactive anti-trypanosomal compounds from African natural products

4.6.3 *Artemisia herba-alba*

Artemisia herba-alba commonly known as white wormwood or desert wormwood chloroform extracts of *Artemisia herba-alba* when administered to *Trypanosoma evansi* infected rabbits causes significant reduction in parasitaemia count and significantly ameliorated the parasite induced alteration in haematological (PCV, Hb, RBCs and WBC) and biochemical values (ALT, ALP and AST) comparable to normal (uninfected) rabbits thereby confirming their antiparasitic properties [112].

Fathy et al. [113], evaluated the anti-trypanosomal efficacy of crude ethanolic extracts (CEE) of the aerial parts of *Artemisia herba alba* against *Trypanosoma evansi* infection. The results indicated significant difference ($p < 0.05$) in the context of reduction in the extent of clinical signs, low levels of parasitaemia and mortality pattern in animals received crude ethanolic extracts (CEE) of *Artemisia herba alba* compared to those served as negative group. The extract also increases the PCV of infected animals compare to untreated control. There was no significant difference in almost all investigated

parameters between standard group (positive control) and treatment group. It is concluded that CEE of *A. herba-alba* and Berenil® showed relatively aparasitaemia and normal heamatologic values in the infected rabbits, thereby confirming their antiparasitic properties.

4.6.4 Black seed oil (*Nigella sativa* oil)

The effect of black seed oil (*Nigella sativa*) on parasitaemia, haematological and biochemical parameters in *Trypanosoma brucei*-infected rats was investigated. The seed oil results in low parasitaemia load and also prolong life span of the infected rats from 12 days of the infected untreated (control) rats to 22 days for the infected black seed oil-treated rats. The seed oil also causes significant increases in haematological (Hb, PCV, RBC, WBC and platelet counts) and some serum biomarker enzyme (Serum ALP, AST and ALP) with decreases in the liver enzyme activities. Protein concentrations show significant decreases in the serum and increases in the liver when compared with the infected untreated [114]. The black seed oil has probably stimulate the host immune system to control parasite proliferation thereby

making it a possible agent for managing African sleeping sickness despite possible gradual damage to host organs as shown by increases in some serum enzymes.

4.6.5 Camellia sinensis

Green tea, the dried leaf of *Camellia sinensis*, contains a variety of biologically active compounds such as polyphenols, methylxanthines, essential oils, proteins, vitamins, and amino acids [115]. The purified compounds from ethyl acetate fraction of *Camellia sinensis* green tea leaves lysed more than 50% of the parasites present in the blood of infected BALB/c mice at concentrations as low as 0.12 to 85 pM. The most active compounds were gallic acid, gallic acid gallate and epigallocatechin gallate, the number of amastigotes in infected Vero cells decreased by 50% in the presence of each of these compounds at 100nm. The activity of recombinant arginine kinase, a key enzyme in the energy metabolism of the parasite was inhibited by about 50% by nanomolar concentrations of catechin gallate or gallic acid [116].

4.6.6 Cissus multistriata

Cissus multistriata belongs to the family of plant known as Vitaceae. Methanolic leaf extracts, of *Saba florida* (Benth) when administered to *T. brucei* infected rat at a dose of 200 and 400mg/kg b.w produce significant improvements of packed cell volume (PCV), red blood cell counts (RBC) and increase in total serum protein when compared to untreated group [117]. The nutritional composition of this leaf extract may be responsible for this observation as it has been reported to be used in the management of protein deficiency disease in children.

4.6.7 Piper nigrum (black pepper)

P. nigrum is a famous spice King. Traditionally, *P. nigrum* fruits have been used in the treatment and prevention of diarrhoea, large intestine toxins, asthma, respiratory disorder, different gastric problems, cancer, fever, common cold and stomach disorder [118]. Methanol extract (250-1000 µg mL⁻¹) of dried fruits of *Piper nigrum* (Black pepper) were evaluated for its trypanocidal activities against *Trypanosoma evansi* using Vero cells grown in Dulbecco's Modified Eagle Medium (DMEM) and supplemented with foetal calf serum (FCS) 20-40% at appropriate conditions. In vitro cytotoxicity test of *P. nigrum* fruits extract at concentrations (1.56-100 µg ml⁻¹) was done on

Vero cells but without FCS. In vitro trypanocidal activity varied from immobilization, reduction and to the killing of trypanosomes in corresponding ELISA plate wells. At 750 µg mL⁻¹ of MPE, there was reduction of average mean trypanosomes count in extract. At 1000 µg ml⁻¹ of the test extract of *P. nigrum*, there was complete killing of trypanosomes at 7 h of incubation. Trypanosomes counts decreased in concentration and time-dependent manner with MPE of *P. nigrum* and diminazine aceturate, standard drug, were cytotoxic to Vero cells except at concentrations of 1.56-3.13 and 1.56-6.25 µg ml⁻¹ [119].

4.6.8 Triticum aestivum (wheat)

Wheat and its products are part of the regular western diet. Administration of ethyl acetate extract of wheat (*Triticum aestivum*) to *T. brucei* infected rat shows reduced parasitaemia and extension of life span from 8 days in the infected untreated (control) group to 14 days. The extract of wheat (*Triticum aestivum*) also show significant increases (p<0.05) in the haemoglobin (Hb) concentration, packed cell volume (PCV) and red blood cell (RBC) counts in infected treated groups when compared with infected untreated (control). The extract also show significant decrease in the activities of serum aspartate transaminase (AST), liver alanine transaminase (ALT) and serum alkaline phosphatase (ALP) when compared with infected untreated group. The author suggested that the crude extracts of fermented wheat could be potential agents in the management of African sleeping sickness [77]. According to Shittu and Tanimu [120], Prophylactic treatment of *T. brucei* infected rats with wheat supplemented diet extended the lifespan of infected rats by 4 extra days from the Control (infected untreated), while early stage treatments also extended the lifespan by 4 days.

4.6.9 Zingiber officinale (ginger)

Zingiber officinale (ginger) has been widely used around the world as food and as a spice. It is considered a safe herbal medicine with only a few and insignificant adverse/side-effects. It has been reported that ginger is endowed with strong in vitro and in vivo anti-oxidant properties [121], in vivo antitrypanosomal effect of methanolic extract of *Zingiber officinale* (ginger) in *Trypanosoma brucei* infected mice were evaluated at dose of 200, 400 and 800 mg/kg body weight. The extract of *Zingiber officinale* produce a dose dependent significant decrease in

level of parasitaemia compare to untreated group.

4.7 Anti-trypanosomal Activity of Insect and Their Products

4.7.1 Honey

Honey is the sweet, viscous natural fluid produced by honeybees (*Apis mellifera*). Honey administered to *T. brucei* infected rat at dose of 3 mg/Kg body weight produce an extension in the life span of infected rat from 12 days for control to 19 days for infected honey-treated rats. Parasitaemia was also effectively lowered. However the honey causes significant increase in serum ALP, AST, ALT activity but decrease in Liver ALT activities. The authors suggested that, honey could be a potential agent in the management of African trypanosomiasis. However, the Increase in serum biochemical parameters suggest possible damage to organs where these maybe abundant [13].

In another study, Ekanem et al. [122], Trypanosoma brucei-infected rats were treated with natural honey and honey supplemented diet at three days before infection (prophylaxis), early and late stages of infection. Prophylactic treatment with natural honey extended the lifespan of infected rats by 13 extra days from the control of 12 days post infection while early and late stage treatments extended the lifespan by 10 and 5 days, respectively. Prophylactic feeding with honey-supplemented diet extended the lifespan by 6 extra days while early and late stage feeding extended it for 5 and 3 days, respectively.

Still on the trypanocidal activities of honey Ekanem and Yusuf, [14], investigated whether honey has protective effect on some liver functions and blood parameters affected by trypanosome infection. The serum albumin concentration in infected untreated rats increased significantly ($p < 0.05$) compared with control whereas treatment with honey returned this effect to normal values. Anaemia which became severe by day 11 of post infection as measured by significant changes ($p < 0.05$) in the haemoglobin, packed cell volume, red blood cell, white blood cell and platelets counts was ameliorated when compared with the control ($p < 0.05$). There was a significant decrease ($p < 0.05$) in liver gamma glutamyl transferase in infected untreated, prophylactic and late stage treated group compared with the control groups.

The authors suggested that honey has ameliorative effects on symptoms and some biochemical effects of *T. brucei* infections in rats.

4.7.2 Honey bee (*Apis mellifera*)

The trypanocidal potentials of honey bee (*Apis mellifera*) extract was investigated against Trypanosome brucei brucei infected rat. The of honey bee extract significantly reduced the parasitaemia count and extend the life span from 5 days of untreated to 10 and 15 days for prophylactic and early treated group. The extract also significantly increase ($p < 0.05$) (HB, PCV, RBC and WBC) counts of infected treated groups when compared with infected not treated group [15].

4.7.3 House flies (*Musca domestica*)

Shittu and Bashir, [16], evaluated the in vivo anti-trypanosomal potential of crude methanolic extract of *Musca domestica* against *T. brucei* brucei infected rats. Results showed that the methanolic extract of *Musca domestica* reduced the level of parasite replication by 26% and 49% and extend the lifespan from day 5 of the infected untreated to 7 and 11 days prophylactic and early treated respectively. The extract also results in significant decrease in antioxidant enzyme (Serum superoxide dismutase) compared to infected not treated group.

4.8 Possible Mechanism of Natural Product against Trypanosomiasis

In many investigations conducted so far, it was found that the plant parts differ significantly in their activity. The differences observed in the anti-trypanosomal evaluation suggest the susceptibility of the test parasite to various secondary metabolites present in these medicinal plants. The possible mechanisms by which these plants extracts and phytochemicals therein carry out this role remain a subject of great speculations and debate in the scientific community [123]. The suggested mechanisms of action for the isolated anti-trypanosomal compounds from medicinal plants are (i) The DNA intercalation in combination with portion biosynthesis inhibition [27]. (ii) Interference with the redox balance of the parasites acting either on the respiratory chain or on the cellular defenses against oxidative stress [124]. For instance, the observed trypanocidal activity of *K. africana* extract was justified due to the increase of oxygen consumption and stimulation of hydrogen peroxide production in the protozoan

cell. (iii) Covalent bonds with amino groups of proteins and affect a vast number of cellular activities in parasite as in the case of drimane sesquiterpenoids (warburganal, polygodial). Isolated from *Warburgia salutaris* [64], (iv) They have also proposed that iron chelation is an effective way of killing trypanosomes and the prime target is the enzyme ribonucleotide reductase whose activity is central to DNA synthesis prior to cell division as depicted in trypanosomiasis infection.

5. CONCLUSION AND FUTURE PERSPECTIVES

This review has presented a list of natural product (plants/insect) with anti-Trypanosoma properties. Many new bioactive agents isolated from plants having anti-Trypanosoma effects showed anti-trypanosoma activity equal and sometimes even more potent than known anti-trypanosomal agents such as diminazene aceturate and homidium chloride. However, many other active agents obtained from plants have not been well characterized. However, it is of paramount importance for African scientist to embark and devise new automated bioassays with special emphasis on high through-put procedures that can screen and process data from a panoply of phytochemicals within shorter time lapse. These procedures should also attempt to rule out false positive hits and dereplication methods to remove nuisance compounds. Furthermore, despite continuous comprehensive and mechanism-orientated evaluation of medicinal plants in Africa, there is still limited information regarding procedures to be adopted for quality assurance, authentication and standardization of crude plant products. Finally, above and beyond simple in vitro and in vivo assays, randomized controlled trials using standardized products or products containing pure plant extracts must be carried out and reported for each claim.

CONSENT

It is not applicable.

ACKNOWLEDGEMENTS

We would like to express our gratitude to John Omaku, Attah Idris of Federal University of Technology minna, Nigeria and Rex Ntue of University of Calabar Nigeria for help rendered during the preparation of this manuscript.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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