

## AFRICAN NATURAL PRODUCTS WITH POTENTIAL ANTI-TRYPANOSOMAL PROPERTIES: A REVIEW

## ABSTRACTS

**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 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 there products.

**Results:** A total of 215 plants pecies 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 (figure 1). The parasites are transmitted by the bite of infected tsetse flies (*Glossina* spp.). (Dietmar and Kevin, 2005) 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 (WHO, 2001) In Latin America, infection with *T. cruzi* is responsible for Chagas' disease, which is the leading cause of heart disease (Williams-Blangero *et al.*, 2003). Nearly 90 million people in 19 endemic countries are at risk of contracting Chagas' disease and 16 million people are already infected (Molyneux, 2003)

Animal trypanosomiasis is caused by *T. brucei*, *T. evansi*, *T. congolense* and *T. vivax* (Mbaya *et al.*, 2009). The disease distributed over approximately 25millionkm<sup>2</sup> in Africa. It is a major factor retarding the growth of the livestock industry in Africa (WHO, 2001) 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 (Aksoy, 2003).

Although, the increasing trend of HAT cases has been reversed and not more than 50 cases of HAT are diagnosed yearly outside Africa (Lejon *et al.*, 2003), 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 (Seke and Mahomoodally, 2012).

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 (Gurib-Fakim, 2006). 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 (Gurib-Fakim, 2006). 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 (Abdool-Karim *et al.*, 1994). 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 (Cunningham, 1988). 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 (Taylor *et al.*, 2001).

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, 2005, 2007; Shittu and Elekwechi, 2014; Shittu and Bashir, 2014) targeted finding new anti-trypanosomal agents to combat the trypanosomomiasis by screening extracts from insect and their products.

At present, the available review on anti-trypanosomal agents focus only on medicinal plants (Mohammed *et al.*, 2014), synthetic chemicals (Dietmar and Kevin, 2005), chemistry aspect with little or no information on the plants (Hoet *et al.*, 2004b). This review article has been presented to enumerate some indigenous plants/insect with potential *in vivo* or *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.

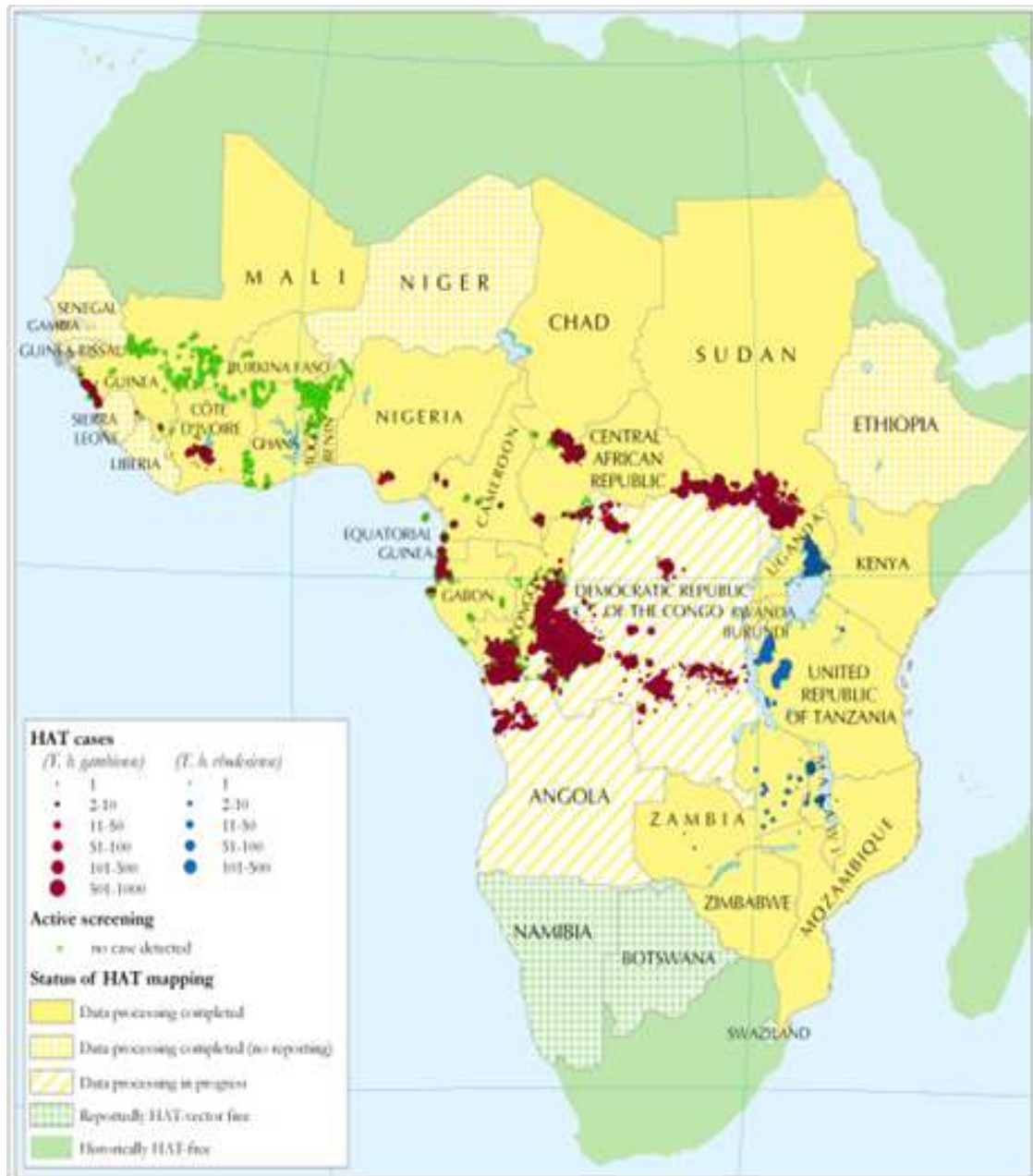


**Figure 1;** the distribution and burden of trypanosomiasis in Africa; the map follows the expected lines of demarcation for the occurrence of *T.brucei gambiense* and *T.brucei rhodesiense*, and also suggest a high occurrence of disease. However the case in this map only includes those that were reported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

## 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

114 plants/insect and there product that were collected from different parts of Africa. Data  
115 presented including the scientific name, family, methodology used, the degree of  
116 activity of the plant and insect. However anti-trypanosomal plants whose levels of  
117 activity were not indicated by the authors were excluded.

### 118 3. Results

119 Table 1-6; show the review data on scientific name, Family, Part (s) used  
120 Extract/fraction, Model, Parasite IC<sub>50</sub> or MIC (µg/mL), Country, References of African  
121 natural products with anti-trypanosomal property. A total of 215 plants species from 82  
122 families were found. Plants from Asteraceae (13.0%), Leguminosae (6.19%),  
123 Anacardaceae (4.28%), Malvaceae (4.28%), Fabaceae (3.80%), Rubiaceae (3.33%) and  
124 Euphoraceae (3.33%) families have received more scientific attention than others. A total  
125 of 104 plants from 55 family (in vitro) and 36 plants from 16 family (in vivo) were  
126 found in west Africa, a total 68 plant from 14 family (in vitro) and 7 plants from 5  
127 family (In vivo) were found in east African, a total 42 plant from 21 family (In vivo)  
128 were found in southern African, a total 5 plant from 5 family (In vivo) were found in  
129 central African, 1 plant from 1 family (in vitro) and 3 plants from 3 family (in vivo)  
130 were found in north Africa. While two herbal formulation and three insect/there  
131 product were reviewed for in vivo anti-trypanosomal activity. Phyto- chemistry studies  
132 of the anti-trypanosomal plants led to the isolation of 96 specific anti-trypanosomal  
133 compounds from different parts of the plants (Table 7).

### 134 4. Discussion

135 Different techniques used in assessment of anti-trypanosomal activities present  
136 problems associated with comparing the trypanocidal potency of the plants reviewed in  
137 this study. Some authors presented their results minimum inhibitory concentration  
138 (MIC), mean lethal dose 50 (IC<sub>50</sub>) and % inhibition of parasite motility in vitro.  
139 However, IC<sub>50</sub> values of 20 µg/mL are considered good activity while IC<sub>50</sub> values of 21–  
140 60 and 61–100 µg/mL are considered moderate and low activities respectively. Any IC<sub>50</sub>  
141 >100 µg/mL are considered ineffective (Bero et al., 2011). Furthermore, Atawodi et al.,  
142 (2003) and Maikai et al., (2008) corroborated the report of Kaminsky et al., (1996)  
143 showing that parasite motility is a reliable index for determining anti-trypanosomal  
144 activity of crude plant extracts.

#### 145 Anti-trypanosomal activity of West African plant

146 A total of 35 West African plant shows good anti-trypanosomal activity IC<sub>50</sub> (<20  
147 µg/mL). The most interesting results were those of *Alcornea cordifolia*, *Maytenus*  
148 *laevis*, *Lantana ukambensis*, *Crataeva religiosa* and *Ocimum gratissimum* with IC<sub>50</sub>  
149 (µg/mL) 0.2, 0.62, 1.5, 1.6 and 1.66 respectively. The high activity values obtained for  
150 these plants render them candidates for the isolation of anti-trypanosomal compounds  
151 which could be developed into new lead structures for drug development. 19 West  
152 Africa plant shows moderate anti-trypanosomal activity IC<sub>50</sub> (21-60 µg/mL), while 4  
153 plants shows low anti-trypanosomal activity IC<sub>50</sub> (61-100 µg/mL). Furthermore, 18 of  
154 the plants were reported to inhibit the parasite motility in less than 30 minute at  
155 4mg/ml. The most interesting result is *Securidaca longepedunculata* (5 minute) while  
156 extracts from 23 west African plants inhibit the parasite motility within 31-60 minute at  
157 4mg/ml. However, methanol extracts of *T. globiferus*, *G. latifolium* at 10mg/ml ceases  
158 the parasite motility in less than 10min (Josephine et al., 2013), while others were  
159 reported not to be active. According to Atawodi et al., (2003) statement on trypanocidal  
160 activity of a plant extract should be made in the context of the method and solvent of  
161 extraction. Different extracts from some of the plant reviewed demonstrated different  
162 degree of trypanocidal property for instance DCM extracts of *Acanthospermum*  
163 *hispidum*, *Byrsocarpus coccineus*, *Byrsocarpus coccineus*, *Carpolobia lutea* and

164 *Keetialeucantha* shows good trypanocidal activity while the methanol and aqueous  
 165 extracts shows moderate or low trypanocidal activity. In contrast, methanol and aqueous  
 166 extracts of *Dialium guineense* shows a moderate activity while DCM extract was  
 167 inactive (Bero et al., 2011). The variation in the trypanocidal activities of these plants  
 168 may be attributed to the variation in the availability and amounts of phytoconstituents in  
 169 the extracts. Phytoconstituents such as flavonoids, alkaloids, terpenes, quinones,  
 170 polyphenols, Triterpenoids and sterols are the most frequently implicated  
 171 phytochemicals in the plants extracts. A total of about 47 specific anti-trypanosomal  
 172 compounds were isolated from different parts of the West African plants. The most  
 173 active compounds were Citronellal (IC<sub>50</sub> 2.76 µg/mL), myrcene (IC<sub>50</sub> 2.24 µg/mL),  
 174 limonene (IC<sub>50</sub> 4.24 µg/mL), isolated from *Ocimum gratissimum* seed oil (Bénédicta et  
 175 al., 2014), erythrodil, (IC<sub>50</sub> 5.30 µg/mL), betulin (IC<sub>50</sub> 4.0 µg/mL), 24 hydroperoxy-24-  
 176 vinylcholesterol (IC<sub>50</sub> 3.20 µg/mL), from *Strychnos spinosa* (Hoet et al., 2007). The  
 177 DNA intercalation in combination with portion biosynthesis inhibition is reported to be  
 178 the mechanism of action responsible for the observed antitrypanosomal effect of most  
 179 of these compounds (Sülsen et al., 2007). Extract from different part of plants also  
 180 exhibit different degree of trypanocidal activity for instance methanolic  
 181 and aqueous extracts of *Keetia leucantha* twig show a low activity (Bero et al., 2011)  
 182 while the oil extracted from the leaf show a good activity (Bero et al., 2013), this  
 183 observation might be due to variations in geographical location, time or period of  
 184 collection and chemical constituents (Hoet et al., 2004)

#### 185 **Anti-trypanosomal activity of Southern African plants**

186 Appreciable numbers of plant, as well as bioactive compounds were found to have been  
 187 investigated for *in vitro* anti-trypanosomal activity in south African. Among the south  
 188 Africa medicinal plants screened for trypanocidal activity against *T.b. rhodesiense*,  
 189 dichloroethane leaves extract of *Abrus precatorius* was found to be the most potent with  
 190 an IC<sub>50</sub> value 0.01 µg/mL (Hata et al., 2013). Similarly, DCM extracts of *Hypericum*  
 191 *aethiopicum* was found to be active with an IC<sub>50</sub> value 4.47 µg/mL followed by *Vernonia*  
 192 *oligocephala* with an IC<sub>50</sub> value 4.67 µg/mL while *Alepidea amatymbica* was the least  
 193 effective with an IC<sub>50</sub> value 73.1 µg/mL (Mokoka et al., 2011). Further more among 10  
 194 south African plants recently evaluated against *T. brucei rhodesiense*, DCM extract of  
 195 *Psoralea pinnata* leaves was found to be the most potent with an IC<sub>50</sub> value 0.15  
 196 µg/mL (Mokoka et al., 2013).

197 Different part of the same plants, same plants of different origin as well as different  
 198 solvents extracts show different anti-trypanosomal activity. For instance, *Abrus*  
 199 *precatorius* from west Africa show trypanocidal activity with IC<sub>50</sub> value of 17.9 µg/mL  
 200 (Saganuwan et al., 2015), against *T. brucei rhodesiense* while the same plant from  
 201 southern Africa had IC<sub>50</sub> value of 0.01 µg/mL (Hata et al., 2013). Fruit extract of  
 202 *Ekebergia capensis* had IC<sub>50</sub> value of 11.5 µg/mL against *T. cruzi* (Mokoka et al., 2011)  
 203 while the root extract of the same plants had IC<sub>50</sub> value of 1.36 µg/mL against  
 204 *T.b. rhodesiense* (Mokoka et al., 2011). As said earlier, the variation in the trypanocidal  
 205 activities of these plants may be attributed to the variation in the availability and  
 206 amounts of phytoconstituents in the extracts. Among the specific bioactive compounds  
 207 isolated from south Africa plant were Abruquinone A, B, D, G, H, I, J, K, L and  
 208 7,8,3',5'-tetramethoxyisoflavan-1',4'-quinone from whole plant of *Abrus*  
 209 *precatorius* (Matthias et al., 2014a, Hata et al., 2013), schkuhrin I and II from *Schkuhria*  
 210 *pinnata*, cynaropicrin from the leaves of *Vernonia mespilifolia* (Mokoka et al., 2013)  
 211 and putranoside A from stem of *Drypetes gerrardii* (Matthias et al., 2014b). All the

212 bioactive compounds isolated show a potent trypanocidal activity with an  $IC_{50}$  less than  
 213 1 $\mu$ g/ml against *T. b. rhodesiense*, except schkuhrin II, Abruquinones and putranoside A  
 214 with  $IC_{50}$  of 1.5, 11.2 and 8.0  $\mu$ g/ml respectively. The compounds were also found to be  
 215 more effective against *T. b. rhodesiense* than *T. cruzi*, for instance schkuhrin I had  $IC_{50}$   
 216 of 0.18  $\mu$ g/ml against *T. b. rhodesiense* and 16.4  $\mu$ g/ml against *T. cruzi* while schkuhrin II  
 217 had  $IC_{50}$  of 1.50  $\mu$ g/ml against *T. b. rhodesiense* and 26.9  $\mu$ g/ml against *T. cruzi* (Mokoka  
 218 et al., 2013). Although, a considerable number of medicinal plants from this region  
 219 have been investigated and were found active against trypanosome parasite, there exist a  
 220 very few researchers on the subject matter, researchers in this region of Africa are  
 221 therefore encouraged to intensify studies on the trypanocidal potency of their natural  
 222 flora.

### 223 **Anti-trypanosomal activity of central African plants**

224 A very little information on trypanocidal potency of medicinal plant from central  
 225 Africa were obtained from literature. Five medicinal plants from central Africa have  
 226 been reported to exhibit activities *in vitro* include *Garcinia lucida*, (Fotie et al., 2007),  
 227 *Aframomum letestuanum* (Kamnaing et al., 2003), *Vernonia guineensis* with  $IC_{50}$  ranged  
 228 of 3–5 mg/ml (Joseph et al., 2002), *Enanatia chlorantha* (1.87  $\mu$ g/ml), *Isolona hexaloba*  
 229 (1.95  $\mu$ g/ml) and *Quassia Africana* (1.88  $\mu$ g/ml) (Musuyu et al., 2012). The bioactive  
 230 agents isolated from these regions include Letestuienin A ( $IC_{50}$  > 100  $\mu$ g/ml), Letestuienin  
 231 B ( $IC_{50}$  67  $\mu$ g/ml), Letestuienin C ( $IC_{50}$  2.6  $\mu$ g/ml) and 5-hydroxy-1,7-bis (4-  
 232 hydroxyphenyl) hepta-4,6-dien-3-one ( $IC_{50}$  2.6  $\mu$ g/ml) isolated from DCM seed extract  
 233 of *Aframomum letestuanum* they demonstrate activity against *T. brucei* (Kamnaing  
 234 et al., 2003). Furthermore, four bioactive agents including, 6-acetyldihydrochelerythrine  
 235 ( $IC_{50}$  3.9  $\mu$ g/ml), Dihydrochelerythrine ( $IC_{50}$  0.8  $\mu$ g/ml), Lucidamine A ( $IC_{50}$   
 236 14.1  $\mu$ g/ml), Lucidamine B ( $IC_{50}$  4.1  $\mu$ g/ml), were isolated from *Garcinia lucida* (Fotie et  
 237 al., 2007). Joseph et al., 2002 isolated vernoguinoside and vernoguinoesterol from stem  
 238 bark of *Vernonia guineensis* both compounds demonstrated significant trypanocidal  
 239 activity against *T. brucei rhodesiense* with an  $IC_{50}$  range of 3–5 mg/ml

### 240 **Anti-trypanosomal activity of North African plants**

241 A very little information on trypanocidal potency of medicinal plant from North Africa  
 242 were obtained from literature. Only one and three medicinal plants were found to be  
 243 investigated for *in vitro* and *in vivo* activity. N-Hexane and DCM extract of *Ageratum*  
 244 *conyzoides* show a significant activity against *T. b. rhodesiense* with  $IC_{50}$  values of 2.4  
 245 and 0.78  $\mu$ g/ml respectively (Nour et al., 2010). The whole plant of *Argemone Mexicana*,  
 246 *Aristolochia bracteolata* and *Tinospora bakis* when administered to  
 247 *Trypanosoma evansi* infected rats at a dose of 500 mg/kg significantly reduced the  
 248 parasitaemia count and extended the survival time compared to untreated group, with  
 249 chloroform extract of *Aristolochia* been the most active (25 survival days) (Samia et al.,  
 250 2011). However, methanol extract of *Cannabis sativa* at a dose of 125/250 mg/kg prolonged  
 251 the survival days of *Trypanosoma evansi* infected mice beyond 45 days (Samia et al.,  
 252 2012). The anti-trypanosomal compounds isolated from North African plants include 4'-  
 253 hydroxy-5,6,7,3',5'-pentamethoxyflavone ( $IC_{50}$  3.01  $\mu$ g/ml), 5,6,7,3',4',5'-  
 254 hexamethoxyflavone, ( $IC_{50}$  8.58  $\mu$ g/ml), 5,6,7,5'-tetramethoxy-3',4'-  
 255 methylenedioxyflavone ( $IC_{50}$  7.29  $\mu$ g/ml), 5,6,7,8,3',4',5'-heptamethoxyflavone  
 256 ( $IC_{50}$  4.76  $\mu$ g/ml), and 5,6,7,8,5'-pentamethoxy-3',4'-methylenedioxyflavone ( $IC_{50}$   
 257 6.67  $\mu$ g/ml) from *Ageratum conyzoides* (Nour et al., 2010).

### 258 **Anti-trypanosomal activity of East African plants**

259 An appreciable data on trypanocidal potency of medicinal plant from east African plant  
 260 were obtained from literature. The most interesting *in vitro* trypanocidal activity from  
 261 east African plant were those of seed extract of *K. anthotheca* (IC<sub>50</sub> 5.72ug/ml), and root  
 262 extract of *T. ciliate* (IC<sub>50</sub> 3.2-6.9 µg/ml). However, out of the medicinal plant from this  
 263 area with *in vivo* trypanocidal activity only *Artemisia abyssinica* (Teka et al., 2014), and  
 264 *Kigelia Africana* (Esther et al., 2010) show appreciable activity by prolonging the  
 265 survival days of the rat to 40.67 and 41.8 at 400 and 100mg/kg respectively. Detailed  
 266 phytochemical study of east African plant led to the isolation of 17 compounds with  
 267 varied degree of trypanocidal activity, the most notable one were those of 8-  
 268 hydroxyheptadeca-1-ene- 4,6-diyn-2yl acetate (IC<sub>50</sub> 0.14ug/ml) and 8-  
 269 hydroxyheptadeca-4,6-diyn- 3yl acetate (IC<sub>50</sub> 5.4ug/ml) isolated from *Cussonia*  
 270 *zimmermannii* (Senn et al., 2007)

271

272 **Table 1; *In vitro* Anti-trypanosomal activity of West African plant**

273

| Scientific name                | Family               | Part (s) used   | Extract/fraction    | Parasite                | IC <sub>50</sub> MIC (µg/mL) | Motility of the parasite | Country | Authors                       |
|--------------------------------|----------------------|-----------------|---------------------|-------------------------|------------------------------|--------------------------|---------|-------------------------------|
| <i>Abrus precatorius</i>       | <i>papilionaceae</i> | leaf            | Chloroform fraction | <i>T. b. r</i>          | 17.9 ug/ml                   | -                        | Nigeria | <i>Saganuwan et al., 2015</i> |
| <i>Acacia artaxacantha</i>     | Leguminosae          | Stem bark/ root | n-Hexane/ethanol    | <i>T. b. b/ T. co</i>   | Btw 13 and 69ug/ml           | -                        | Nigeria | Adewunmi et al., 2001         |
| <i>Acanthospermum hispidum</i> | Asteraceae           | Aerial part     | <i>T. b. b</i>      | DCM/ Methanol / Aqueous | 14.5/47.5/ 54.8              | -                        | Benin   | Bero et al., 2011             |
| <i>Adansonia digitata</i>      | Bombacaceae          | leaf            | <i>T. b. b</i>      | Aqueous                 | -                            | 4 mg/ml @ 40mint         | Nigeria | Atawodi, 2005                 |
| <i>Adenium obesum</i>          | Apocynaceae          | Root            | Pet. Ether          | <i>T. b. b</i>          | -                            | 4 mg/ml @ 35mint         | Nigeria | Atawodi, 2005                 |
| <i>Afrormosia laxiflora</i>    | Leguminosae          | Leaf            | Pet. Ether          | <i>T. b. b</i>          | -                            | 4 mg/ml @ 20mint         | Nigeria | Atawodi, 2005                 |
| <i>Azelia africana</i>         | Leguminosae          | Leaf/ Stem bark | Pet. Ether          | <i>T. b. b</i>          | -                            | 4 mg/ml @ 30mint         | Nigeria | Atawodi, 2005                 |
| <i>Albica spp</i>              | Asparagaceae         | Bulb            | aqueous             | <i>T. b. b</i>          | -                            | 4 mg/ml @ 55mint         | Nigeria | Atawodi, 2005                 |
| <i>Alcornea cordifolia</i>     | Euphorbiaceae        | Bark/Leaf       | Methanol            | <i>T. b. b</i>          | <0.2                         | -                        | Nigeria | John et al., 2011/Adewu       |

|                                |               |                  |                         |                       |                    |                         |                      |                                                  |
|--------------------------------|---------------|------------------|-------------------------|-----------------------|--------------------|-------------------------|----------------------|--------------------------------------------------|
|                                |               |                  |                         |                       |                    |                         |                      | nmiet al., 2001                                  |
| <i>Ampelocissus grantii</i>    | Vitaceae      | Aerial part      | DCM                     | <i>T. b. b</i>        | 500                | -                       | BurkinaFaso          | Aderbaueret al., 2008                            |
| <i>Anchomanes difformis</i>    | Araceae       | Rhizome          | Methanol                | <i>T. b. b/ T. co</i> | 13.87ug/ml         | 45min at 4mg/ml         | Nigeria/Benin        | Atawodi et al., Bero et al.(2011)                |
| <i>Anchomanes difformis</i>    | Araceae       | root             | DCM/ Methanol / Aqueous | <i>T. b. b</i>        | 50.7/14.7/ 13.8    |                         | Benin                | Bero et al., 2011                                |
| <i>Annona senegalensis</i>     | Annonaceae    | root             | Pet. Ether              | <i>T. b. b</i>        | -                  | 4mg/ml @ 35min t        | Nigeria              | Atawodi 2005                                     |
| <i>Anthocleista vogelii</i>    | Loganiaceae   | root bark        | Aqueous/ Ethanollic     | <i>T. b. b</i>        | -                  | 100% activity @ 20mg/ml | Nigeria              | Abu et al., 2009                                 |
| <i>Baillonella toxisperma</i>  |               | barks            | Ethanol                 | <i>T. r</i>           | 9.6 µg/ml          | -                       | Bénin                | Lagnika et al., 2013                             |
| <i>Balanites aegyptiaca</i>    | Balanitaceae  | Stem bark/ Shoot | Aqueous/ DCM            | <i>T. b. b</i>        | 500/50             | -                       | Nigeria/ BurkinaFaso | Wurochekke andNok(2004 ); Aderbauer et al., 2008 |
| <i>Blighia unijugata</i>       | Sapindaceae   | leaf             | Aqueous/ethanollic      | <i>T. b. b</i>        | -                  | No activity @40mg/ml    | Nigeria              | Abu et al., 2009                                 |
| <i>Boswellia dalzielii</i>     | Burseraceae   | leaves           | Ethanol/Methanol        | <i>T. r</i>           | 9.6 µg/ml          | -                       | Bénin/ Nigeria       | Lagnika et al., 2013                             |
| <i>Brassicaoleracea</i>        | Brassicaceae  | leaf             | Methanol                | <i>T. e</i>           | -                  | 1000 µg/ml              | Nigeria              | Shaba et al., 2012                               |
| <i>Bridelia ferruginea</i>     | Euphorbiaceae | Stem bark        | methanol                | <i>T. b. b</i>        | -                  | 4 mg/ml @ 35min t       | Nigeria              | Atawodi, 2005                                    |
| <i>Byrsocarpus coccineus</i>   | Connaraceae   | Aerial part      | DCM/ Methanol / Aqueous | <i>T. b. b</i>        | 14.7/21.1/ 49.5    |                         | Benin                | Bero et al., 2011                                |
| <i>Canarium schweinfurthii</i> | Burseraceae   | Stem bark        | Pet. Ether/ Chloroform  | <i>T. b. b</i>        | -                  | 4 mg/ml @ 30/35 mimt    | Nigeria              | Atawodi, 2005                                    |
| <i>Carpolobia lutea</i>        | polygalaceae  | Aerial part      | DCM/ Methanol / Aqueous | <i>T. b. b</i>        | 18.3/>100 />100    | -                       | Benin                | Bero et al., 2011                                |
| <i>Cassia siamae</i>           | Leguminosae   | Leaf/ Stem bark/ | Aqueous/hexane/         | <i>T. b. b</i>        | 25.8/ 10.19/ 46.50 | -                       | Nigeria              | Abiodun et al., 2012                             |

|                                 |                  |             |                         |                       |                    |                          |              |                       |
|---------------------------------|------------------|-------------|-------------------------|-----------------------|--------------------|--------------------------|--------------|-----------------------|
|                                 |                  | Root        | ethylacetate            |                       |                    |                          |              |                       |
| <i>Cassia sieberiana</i>        | Caesalpiaceae    | leaf        | DCM                     | <i>T. b. b</i>        | > 19               | -                        | Nigeria      | Hoet et al., 2004     |
| <i>Cassytha filiformis</i>      | Lauraceae        | Leaf        | Pet. Ether              | <i>T. b. b</i>        | -                  | 4 mg/ml @ 20min          | Nigeria      | Atawodi, 2005         |
| <i>Cassytha sp.</i>             | Lauraceae        | Leaves      | Methanol                | <i>T. b. b</i>        | -                  | 25min at 4mg/ml          | Nigeria      | Atawodi et al.,       |
| <i>Ceiba pentandra</i>          | Bombacaceae      |             | DCM                     | <i>T. b. b</i>        | 200                | -                        | Burkina Faso | Aderbaueretal. (2008) |
| <i>Clerodendrom capitatum</i>   | Stem bark        | Root        | n-Hexane/ethanol        | <i>T. b. b/ T. co</i> | Btw 13 and 69ug/ml | --                       | Nigeria      | Adewunmi et al., 2001 |
| <i>Cochlospermum planchonii</i> | Cochlospermaceae | Root/leaf   | Pet. Ether              | <i>T. b. b</i>        | -                  | 4mg/ml @ 20/40 mint      | Nigeria      | Atawodi, 2005         |
| <i>Crataevareligiosa</i>        | Capparaceae      | leaves      | cyclohexane             | <i>T. r</i>           | 1.6 µg/ml          |                          | Bénin        | Lagnikaet al., 2013   |
| <i>Cratva adansonii</i>         | Capparaceae      | leaves      | crude hexane            | <i>T. b. b</i>        | 12.5µg/ml          |                          | Nigeria      | John et al., 2012     |
| <i>Cussonia arborea</i>         | Araliaceae       | root /stem  | Aqueous/ Ethanol        | <i>T. b. b</i>        | -                  | No activity @ 40mg/ml    | Nigeria      | Abu et al., 2009      |
| <i>Cymbopogon nardus</i>        | Poaceae          |             | Methanol                | <i>T. b. b</i>        | 0.31µg/mL          |                          | Nigeria      | John et al., 2011     |
| <i>Dialium guineense</i>        | Leguminosae      | Aerial part | Dcm/ Methanol / Aqueous | <i>T. b. b</i>        | >100/42.3 /52.0    | -                        | Benin        | Bero et al., 2011     |
| <i>Diospyros mespiliformis</i>  | Ebenaceae        | leaf        | chloroform              | <i>T. b. b</i>        | -                  | 4mg/ml @ mint45          | Nigeria      | Atawodi, 2005         |
| <i>Dissotis rotundifolia</i>    | Melastomataceae  | Leaf        | Ethanol                 | <i>T. b. b</i>        | -                  | 100% activity @ 800mg/kg | Nigeria      | Mann et al., 2009     |
| <i>Erythrophleum suaveolens</i> | Leguminosae      | Stem bark   | Pet. Ether              | <i>T. b. b</i>        | -                  | 4mg/ml @ 40min           | Nigeria      | Atawodi, 2005.        |
| <i>Eucalyptus citriodora</i>    | Myrtaceae        | Leaf        | aqueous                 | <i>T. b. b</i>        | -                  | 0.4 g/mL @ 2min          | Nigeria      | Habila et al., 2010   |
| <i>Eugenia uniflora</i>         | Myrtaceae        | Leaf        | n-Hexane/ethanol        | <i>T. b. b/ T.co</i>  | -                  | Btw 13 and 69ug/         | Nigeria      | Adewunmi et al., 2001 |

|                               |                  |                      |                               |                                          |                     |                          |               |                                                                   |
|-------------------------------|------------------|----------------------|-------------------------------|------------------------------------------|---------------------|--------------------------|---------------|-------------------------------------------------------------------|
| <i>Euphorbia hirta</i>        | Euphorbiaceae    | Leaf                 | ethylacetate                  | T. b. r                                  | 8.70                | -                        | Nigeria       | Abiodun et al., 2012                                              |
| <i>Ficus platyphylla</i>      | Moraceae         |                      | Methanol                      | T. b. b                                  | 25                  | -                        | Burkina Faso  | Sawadogo et al., 2011                                             |
| <i>Ficus sycomorus</i>        |                  | Stem                 | Methanol                      | T. b. b                                  | -                   | 4mg/ml @60min            | Nigeria       | Atawodi, 2005                                                     |
| <i>Gardenia erubescens</i>    | Rubiaceae        | Leaf/stem bark       | Aqueous/Ethanollic            | T. b. b                                  | -                   | 100% activity @ 20mg/ml  | Nigeria       | Abu et al., 2009                                                  |
| <i>Gongronema latifolium</i>  | Asclepiadaceae.  | stem bark            | Methanol                      | T. b. b                                  | -                   | 15min at 10mg/ml         | Nigeria       | Josephine et al., 2013                                            |
| <i>Haematostaphis barteri</i> | Anacardiaceae.   | leaves               | aqueous                       | T.co                                     | -                   | 40 minutes @ 0.25 mg     | Nigeria       | Wurochekke et al., 2014                                           |
| <i>Heliotropium indicum</i>   | Boraginaceae     | Aerial part          | DCM/Methanol / Aqueous        | T. b. b                                  | 58.3/80.2/>100      | -                        | Benin         | Bero et al., 2011                                                 |
| <i>Hymenocardia acida</i>     | Hymenocardiaceae | root bark /stem bark | Aqueous/Ethanollic            | T. b. b                                  | -                   | 100% activity @ 2.5mg/ml | Nigeria       | Abu et al., 2009                                                  |
| <i>Hymenocardia acida</i>     | Hymenocardiaceae | twig and leaf        | DCM                           | T. b. b                                  | ≤19µg/ml            | -                        | Nigerian      | Hoet et al., 2004                                                 |
| <i>Keetia leucantha</i>       | Rubiaceae        | leaf                 | essential oil                 | Bloodstream/procyclic forms of T. brucei | 20.90/>100 µg/ml    | -                        | Nigerian      | Bero et al., 2013                                                 |
| <i>Keetia leucantha</i>       | Rubiaceae        | twig                 | DCM/METHANOL / AQUEOUS        | T. b. b                                  | 5.8/53.1/86.9       | -                        | Nigerian      | Bero et al., 2011                                                 |
| <i>Khaya senegalensis</i>     | Meliaceae        | Stem bark/leaves     | Ethanollic/Methanol / Ethanol | T. r                                     | 300 µg/ml/9.6 µg/ml | 35min at 4mg/ml          | Nigeria/Bénin | Bulus and Addau, 2013, Atawodi et al., 2003, Lagnika et al., 2013 |
| <i>Lannea kerstingii</i>      | Anacardiaceae    | leaf                 | Methanol                      | T. b. b                                  |                     | 4mg/ml @ 40 min          | Nigeria       | Atawodi, 2005                                                     |
| <i>Lannea welwistchii</i>     | Anacardiaceae    | leaf                 | Aqueous                       | T. b. b                                  | 6.3mg/ml(mic)       | -                        | Nigeria       | Antia et al., 2009                                                |

|                                 |                  |                |                        |                |                 |                                               |              |                         |
|---------------------------------|------------------|----------------|------------------------|----------------|-----------------|-----------------------------------------------|--------------|-------------------------|
| <i>Lantana ukambensis</i>       | Verbenaceae      |                | Methanol               | <i>T. b. b</i> | 1.5             | -                                             | Burkina Faso | Sawadogo et al., 2011   |
| <i>Lawsonia inermis</i>         |                  | root           | Methanol               | <i>T. b. b</i> | -               | 4mg/ml@45 min                                 | Nigeria      | Atawodi, 2005           |
| <i>Lonchocarpus laxiflorus</i>  |                  | stem           | Methanol               | <i>T. b. b</i> | -               | 4mg/ml@30 min                                 | Nigeria      | Atawodi, 2005           |
| <i>Lophira lanceolata</i>       | Ochnaceae        | Leaf/stem bark | Aqueous/Ethanollic     | <i>T. b. b</i> | -               | 100% activity@20mg/ml                         | Nigeria      | Abu et al., 2009        |
| <i>Magnifera indica</i>         | Anacardiaceae    | root           | Pet. Ether             | <i>T. b. b</i> | -               | 4mg/ml@30 min                                 | Nigeria      | Atawodi, 2005           |
| <i>Maytenus laevis</i>          | Celastraceae     | root           | hexane + ethyl acetate | <i>T. b. b</i> | 0.625           |                                               | Nigeria      | John et al., 2001       |
| <i>Momordica balsamina</i>      | Cucurbitaceae    | Whole plant    | Pet. Ether             | <i>T. b. b</i> | -               | 4mg/ml@35 min                                 | Nigeria      | Atawodi, 2005           |
| <i>Monodora myristica</i>       | Annonaceae       | Seed           | Ethyl acetate          |                | 3.12            | -                                             | Nigeria      | John et al.             |
| <i>Morinda lucida</i>           | Rubiaceae        |                | Methanol fraction      | <i>T. b. b</i> | 6.25-12.5 µg/m  | -                                             | Nigeria      | Nwakaego, 2012          |
| <i>Moringa oleifera</i>         | Moringaceae      | Leaf           | chloroform             | <i>T. b. b</i> | -               | 4mg/ml@35 min                                 | Nigeria      | Atawodi, 2005           |
| <i>Nauclea latifolia</i>        | Rubiaceae        | Leaf           | Methanol               | <i>T. b. b</i> | -               | 4mg/ml@30 min                                 | Nigeria      | Atawodi, 2005           |
| <i>Nauclea pobeguini</i>        | Rubiaceae        | Bark           | ethyl acetate          | <i>T. b. b</i> | 6.25            | -                                             | Nigeria      | John et al., 2011       |
| <i>Ocimum gratissimum</i>       | Lamiaceae        | Leaves         | ethanol                | <i>T. b. b</i> | 1.66/1.29 µg/mL | -                                             | Benin        | Bénédicta et al., 2014  |
| <i>Ozoroa insignis</i>          | Anacardiaceae    |                | Methanol               | <i>T. b. b</i> | 6.2             | -                                             | Burkina Faso | Sawadogo et al., 2011   |
| <i>Parinari curatellifolia</i>  | Chrysobalanaceae |                | Methanol               | <i>T. b. b</i> | 25              | -                                             | Burkina Faso | Sawadogo et al., 2011   |
| <i>Parkia clappertoniana</i>    | Leguminosae      | Stem bark      | Pet. ether             | <i>T. b. b</i> | -               | 50min at 4mg/ml                               | Nigeria      | Atawodi, 2005           |
| <i>Pericopsis laxiflora</i>     | Loganiaceae      | Leaf           | DCM                    | <i>T. b. b</i> | >19 µg/ml       |                                               | Nigeria      | Hoet et al., 2004       |
| <i>Peristrophe bicalyculata</i> | Acanthaceae      | Whole plant    | aqueous                | <i>T. b. b</i> | -               | immobilized 90% of the parasites, @ 100 mg/kg | Nigeria      | Abdulazeez et al., 2013 |
| <i>Picralima nitida</i>         | Apocynaceae      | root           | Methanol               | <i>T. b. b</i> | -               | 10min at 4mg/m                                | Nigeria      | Ene et al., 2014.       |

|                                    |               |                |                         |                |                 |                       |          |                      |
|------------------------------------|---------------|----------------|-------------------------|----------------|-----------------|-----------------------|----------|----------------------|
| <i>Piliostigma reticulatum</i>     | Leguminosae   | Leaves         | aqueous                 | <i>T. b. b</i> | -               | 25min at 4mg/ml       | Nigeria  | Atawodi et al.       |
| <i>Prosopis africana</i>           | Leguminosae   | leaf           | Pet.ether               | <i>T. b. b</i> | -               | 35min at 4mg/ml       | Nigeria  | Atawodi, 2005        |
| <i>Prosopis Africana</i>           | leguminaceae  | Bark           | Methanol                | <i>T. b. b</i> | 12.5            |                       | Nigeria  | John et al., 2011    |
| <i>Psidium guajava</i>             | Myrtaceae     |                | ethanol                 | <i>T. b. b</i> | 6.3 µg/mL       | -                     | Nigeria  | Oluyomi et al., 2011 |
| <i>Pupalia lappacea</i>            | Amaranthaceae | Aerial part    | Dcm/ Methanol / Aqueous | <i>T. b. b</i> | 52.0/>100 />100 | -                     | Benin    | Bero et al., 2011    |
| <i>Saba florida</i>                | Apocynaceae   | Whole plant    | Pet.Ether               | <i>T. b. b</i> | -               | 25min at 4mg/ml       | Nigeria  | Atawodi, 2005        |
| <i>Sansevieria liberica</i>        | Dracaenaceae  | Aerial part    | Dcm/ Methanol / Aqueous | <i>T. b. b</i> | 60.1/>100 />100 | -                     | Benin    | Bero et al., 2011    |
| <i>Schranksia leptocarpa</i>       | Leguminosae   | Leaf           | Dcm/ Methanol / Aqueous | <i>T. b. b</i> | 49.2/>100 />100 | -                     | Benin    | Bero et al., 2011    |
| <i>Securidaca longepedunculata</i> | Polygalaceae  | Root           | Methanol                | <i>T. b. b</i> | -               | 5min at 4mg/ml        | Nigeria  | Atawodi et al.,      |
| <i>Spondias mombim</i>             | Anacardiaceae | root           | hexane + ethyl acetate  | <i>T. b. b</i> | 25              | -                     | Nigeria  | John et al., 2011    |
| <i>Sterculia setigera</i>          | Sterculiaceae | Root bark      | Pet.ether               | <i>T. b. b</i> | -               | 25min at 4mg/ml       | Nigeria  | Atawodi, 2005        |
| <i>Stereospermum kunthianum</i>    | Bignoniaceae  | Leaf/stem bark | Aqueous/ Ethanol        | <i>T. b. b</i> | -               | No activity @ 40mg/ml | Nigeria  | Abu et al., 2009     |
| <i>Striga spp.</i>                 | Orobanchaceae | Leaves         | Methanol                | <i>T. b. b</i> | -               | 40min at 4mg/ml       | Nigeria  | Atawodi et al.       |
| <i>Strychnos spinosa</i>           | Loganiaceae   | leaf           | DCM                     | <i>T. b. b</i> | ≤19µg/ml        | -                     | Nigerian | Hoet et al., 2004    |
| <i>Syzygium guinense</i>           | Myrtaceae     | Stem bark      | Pet.ether               | <i>T. b. b</i> | -               | 25min at 4mg/ml       | Nigeria  | Atawodi, 2005        |
| <i>Tapinanthus</i>                 |               | Leaves         | Methanol                | <i>T. b. b</i> | -               | 10min                 | Nigeria  |                      |

|                                 |                  |                       |                                   |                                  |                    |                       |              |                                     |
|---------------------------------|------------------|-----------------------|-----------------------------------|----------------------------------|--------------------|-----------------------|--------------|-------------------------------------|
| <i>globiferus</i>               | mistletoe        |                       | nol                               |                                  |                    | at 10mg/ml            | a            | Josephine et al., 2013              |
| <i>Terminalia avicennioides</i> | Combretaceae     | Stem bark             | hexane + ethyl acetate / Methanol | <i>T. b. b</i>                   | 2.5                | 40min at 4mg/ml       | Nigeria      | John et al., 2011<br>Atawodi et al. |
| <i>Terminalia catapa</i>        | Combretaceae     | leaf                  | hexane + ethyl acetate / Methanol | <i>T. b. b</i>                   | 17.24/7.80/1321.   | -                     | Nigeria      | Abiodun et al., 2012                |
| <i>Terminalia ivorensis</i>     | Combretaceae     |                       | n-Hexane/ethanol                  | <i>T. b. b</i> /<br><i>T. co</i> | Btw 13 and 69ug/ml | -                     | Nigeria      | Adewunmi et al., 2001               |
| <i>Terminalia superba</i>       | Combretaceae     | stem                  | Aqueous                           | <i>T. b. b</i>                   | 0.8mg/ml(mic)      | -                     | Nigeria      | Antia et al., 2009                  |
| <i>Trichilia emetica</i>        | Meliaceae        | leaf                  | DCM                               | <i>T. b. b</i>                   | ≤19µg/ml           | -                     | Nigeria      | Hoet et al., 2004                   |
| <i>Uapaca togoensis</i>         | Euphorbiaceae    | root bark /stem bback | Aqueous/ Ethanol                  | <i>T. b. b</i>                   | -                  | No activity @ 40mg/ml | Nigeria      | Abu et al., 2009                    |
| <i>Verbascum sinaiticum</i>     | Scrophulariaceae | leaf                  | Aqueous                           | <i>T. co</i>                     | -                  | 60min at 4mg/ml       | Nigeria      | Mergia et al., 2014                 |
| <i>Vitex doniana</i>            | Lamiaceae        | Stem bark             | Pet.ether                         | <i>T. b. b</i>                   | -                  | 45min at 4mg/ml       | Nigeria      | Atawodi, 2005                       |
| <i>Waltheria indica</i>         | Sterculiaceae    | stem bark             | aqueous                           | <i>T. b. b</i>                   | -                  | 1mg/ml @ 25minute     | Nigeria      | Bala et al., 2009.                  |
| <i>Withania somnifera</i>       | Solanaceae       | Whole plant           | Ethyl acetate                     | <i>T. b. b</i>                   | 50.0ug/ml          | -                     | Nigeria      | John et al., 2011                   |
| <i>Xeoderris sthulmannii</i>    | Fabaceae         | Stems, leaves         | Methanol                          | <i>T. b. b</i>                   | 25                 |                       | Burkina Faso | Sawadogo et al., 2011               |
| <i>Ximenia americana</i>        | Olcaceae         | stem bark             | aqueous                           | <i>T. b. b</i>                   | -                  | 2mg/ml @ 55minute     | Nigeria      | Bala et al., 2009.                  |

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

275

276 **Table 2: Invitro Anti-trypanosomal activity of Southern African plants**

| Scientific name | Family | Part (s) | Extract/ fraction | Parasite | IC <sub>50</sub> MIC (µg/mL) | Concentration | References |
|-----------------|--------|----------|-------------------|----------|------------------------------|---------------|------------|
|-----------------|--------|----------|-------------------|----------|------------------------------|---------------|------------|

|                              |               | used         |                                               |                  |                    |              |                                             |
|------------------------------|---------------|--------------|-----------------------------------------------|------------------|--------------------|--------------|---------------------------------------------|
| <i>Abrus precatorius</i>     | Leguminosae   | leaves       | CH <sub>2</sub> Cl <sub>2</sub> /MeOH (1 : 1) | T. b. r          | 0.01-17            | South Africa | Hata et al., 2013/<br>Matthias et al., 2014 |
| <i>Acacia erioloba</i>       | Fabaceae      | Roots        | DCM/MeOH (1 : 1)                              | T. b. r          | 18.50              | South Africa | Mokoka et al., 2013                         |
| <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., 2011                         |
| <i>Alepidea amatymbica</i>   | Apiaceae      | whole plant  | DCM/MeOH (1 : 1)                              | T. cruzi         | 20.3/73.1          | South Africa | Mokoka et al., 2011                         |
| <i>Artabotrys monteiroae</i> | Annonaceae    | leaves       | DCM/MeOH (1 : 1)                              | T. b. r / T. c   | 10.3/41.3          | South Africa | Mokoka et al., 2011                         |
| <i>Artemisia afra</i>        | Asteraceae    | leaves       | DCM                                           | T. b. r / T. c   | 9.6/27.6           | South Africa | Mokoka et al., 2011                         |
| <i>Asystasia gangetica</i>   | acanthaceae   | leaves       | DCM/MeOH (1 : 1)                              | T. b. r / T. c   | 13.2/74.7          | South Africa | Mokoka et al., 2011                         |
| <i>Catha edulis</i>          | Celastraceae  | Root         | DCM                                           | T. b. r / T. c   | 14.2/19.1          | South Africa | Mokoka et al., 2011                         |
| <i>Clausena anisata</i>      | Rutaceae      | Roots        | T.b. rhodesiense                              | DCM/MeOH (1 : 1) | 7.19               | South Africa | Mokoka et al., 2013                         |
| <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., 2011                         |
| <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., 2011                         |
| <i>Conyza scabrida</i>       | Asteraceae    | leaves       | DCM/MeOH (1 : 1)                              | T. b. r / T. c   | 30.0/49.4          | South Africa | Mokoka et al., 2011                         |
| <i>Croton menyhartii</i>     | Euphorbiaceae | leaves       | DCM/MeOH (1 : 1)                              | T. b. r / T. c   | 11.7/33.3          | South Africa | Mokoka et al., 2011                         |
| <i>Cymbopogon validus</i>    | Poaceae       | leave        | DCM/MeOH (1 : 1)                              | T. b. r / T. c   | 11.9/47.1          | South Africa | Mokoka et al., 2011                         |
| <i>Drypetes gerrardii</i>    | Meliaceae     | Stems/leaves | T.b. rhodesiense                              | DCM/MeOH (1 : 1) | 7.31/12.1          | South Africa | Mokoka et al., 2013/<br>hota et al., 2014   |
| <i>Ekebergia capensis</i>    | Meliaceae     | Fruit/root   | DCM/MeOH (1 : 1)                              | T. b. r / T. c   | 11.5/24.4/<br>1.36 | South Africa | Mokoka et al., 2011,<br>Mokoka et al., 2013 |
| <i>Euclea natalensis</i>     | Ebenaceae     | roots        | DCM/MeOH (1 : 1)                              | T. b. r / T. c   | 28.1/43.7          | South Africa | Mokoka et al., 2011                         |
| <i>Eucomis autumnalis</i>    | Asparagaceae  | flowers/buds | DCM                                           | T.b. rhodesi     | 37.1/29.7          | South Africa | Mokoka et al., 2011                         |

|                                  |                |              |                      |                      |            |              |                     |
|----------------------------------|----------------|--------------|----------------------|----------------------|------------|--------------|---------------------|
| <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., 2011 |
| <i>Hypericum aethiopicum</i>     | Hypericaceae   | leaves       | DCM/MeOH (1 : 1)     | T. b. r / T. c       | 4.47/18.1  | South Africa | Mokoka et al., 2011 |
| <i>Leonotis leonurus</i>         | Lamiaceae      | leaves       | DCM/MeOH (1 : 1)     | T. b. r / T. c       | 14.7/50.1  | South Africa | Mokoka et al., 2011 |
| <i>Leonotis ocymifolia</i>       | Lamiaceae      | leaves       | DCM                  | T. b. r / T. c       | 9.1/63.5   | South Africa | Mokoka et al., 2011 |
| <i>Maytenus undata</i>           | Celastraceae   | roots        | DCM                  | T. b. r / T. c       | 35.2/28.4  | South Africa | Mokoka et al., 2011 |
| <i>Oederia genistifolia</i>      | Asteraceae     | Whole plant  | T.b. rhodesiense     | DCM/MeOH (1 : 1)     | 4.38       | South Africa | Mokoka et al., 2013 |
| <i>Ozoroa sphaerocarpa</i>       | Anacardiaceae  | Whole plant  | <b>DCM</b>           | T. b. r / T. c       | 10.90      | South Africa | Mokoka et al., 2013 |
| <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., 2013 |
| <i>Pentzia globosa</i>           | Asteraceae     | roots        | DCM                  | T. b. r / T. c       | 5.76/31.3  | South Africa | Mokoka et al., 2011 |
| <i>Plumbago zeylanica</i>        | Plumbaginaceae | leaves       | DCM/MeOH (1 : 1)     | T. b. r / T. c       | 13.0/54.5  | South Africa | Mokoka et al., 2011 |
| <i>Psoralea pinnata</i>          | Fabaceae       | Leaves       | T.b. rhodesiense     | DCM/DCM/MeOH (1 : 1) | 0.15/0.31  | South Africa | Mokoka et al., 2013 |
| <i>Ptaeroxylon obliquum</i>      | Rutaceae       | leaves       | DCM                  | T. b. r / T. c       | 11.3/41.5  | South Africa | Mokoka et al., 2011 |
| <i>Rauvolfia caffra</i>          | Apocynaceae    | roots        | DCM                  | T. b. r / T. c       | 17.9 /41.1 | South Africa | Mokoka et al., 2011 |
| <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., 2011 |
| <i>Schefflera umbellifera</i>    | Araliaceae     | roots        | DCM/MeOH (1 : 1)     | T. b. r / T. c       | 20.9 /57.6 | South Africa | Mokoka et al., 2011 |
| <i>Schkuhria pinnata</i>         | Asteraceae     | Whole plant  | DCM/MeOH (1 : 1)     | T. b. r / T. c       | 2.04       | South Africa | Mokoka et al., 2013 |
| <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., 2013 |
| <i>Tarchonanthus camphorates</i> | Asteraceae     | whole plant  | DCM/MeOH (1 : 1)     | T. b. r / T. c       | 3.93 /18.6 | South Africa | Mokoka et al., 2013 |

|                              |            |                |                         |                        |                |                 |                        |
|------------------------------|------------|----------------|-------------------------|------------------------|----------------|-----------------|------------------------|
| <i>Turraea floribunda</i>    | Meliaceae  | Bark/leaves    | DCM/M<br>eOH (1 :<br>1) | T. b. r<br>/<br>T. c   | 24.4/<br>17.10 | South<br>Africa | Mokoka et<br>al., 2013 |
| <i>Vernonia hirsuta</i>      | Asteraceae | whole<br>plant | DCM/M<br>eOH (1 :<br>1) | T. b. r<br>/<br>T. c   | 18.1 /43.0     | South<br>Africa | Mokoka et<br>al., 2011 |
| <i>Vernonia mespilifolia</i> | Asteraceae | leaves         | DCM/M<br>eOH<br>(1 : 1) | T. b. r<br>/<br>T. c   | 1.01           | South<br>Africa | Mokoka et<br>al., 2013 |
| <i>Vernonia natalensis</i>   | Asteraceae | whole<br>plant | DCM/M<br>eOH (1 :<br>1) | T. b. r<br>/<br>T. c   | 12.6/ 39.3     | South<br>Africa | Mokoka et<br>al., 2011 |
| <i>Vernonia oligocephala</i> | Asteraceae | leaves         | <b>DCM</b>              | T. b. r<br>/<br>T. c / | 4.67 /14.3     | South<br>Africa | Mokoka et<br>al., 2011 |

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

278 **Table 3: Invitro Anti-trypanosomal activity of central African plants**

| Scientific name              | Family        | Part (s) used | Extract/fr action | Parasite         | IC <sub>50</sub> MIC (µg/mL) | Country           | References            |
|------------------------------|---------------|---------------|-------------------|------------------|------------------------------|-------------------|-----------------------|
| <i>Vernonia guineensis</i>   | Asteraceae    | stem bark     | Ethanol           | T. b.r           | 3–5 mg/ml                    | Cameroon          | Joseph et al., 2002   |
| <i>Aframomum letestuanum</i> | Zingiberaceae | seed          | DCM               | T.b.b./<br>T.b.r | 2.6                          | Cameroon          | Kamnaing et al., 2003 |
| <i>Enantia chlorantha</i>    | Annonaceae    | stem bark     | Methanol          | T. c             | 1.87                         | Republic of Congo | Musuyu et al., 2012   |
| <i>Isolona hexaloba</i>      | Annonaceae    | stem bark     | Methanol          | T.b.b.           | 1.95 µg /ml,                 | Republic of Congo | Musuyu et al., 2012   |
| <i>Quassia africana</i>      | simaroubaeae  | root bark     | Methanol          | T.c              | 1.88µg/ml                    | Republic of Congo | Musuyu et al., 2012   |

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

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282 **Table 4: Invitro Anti-trypanosomal activity of North African plants**

| Scientific name            | Family     | Part (s) | Extract/fr action | Parasite                                         | IC <sub>50</sub> MIC (µg/mL) | Country | References        |
|----------------------------|------------|----------|-------------------|--------------------------------------------------|------------------------------|---------|-------------------|
| <i>Ageratum conyzoides</i> | Asteraceae | leaves   | T. b. r           | n-<br>Hexane/<br>CH <sub>2</sub> Cl <sub>2</sub> | 2.4/0.78                     | sudan   | Nour et al., 2010 |

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

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287 **Table 5; *In vitro* Anti-trypanosomal activity of east African plant**  
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| Scientific name                    | Family        | Part (s) used | Extract/fr action                     | 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., 2009                    |
| <i>Albizia harveyi</i>             | Fabaceae      | Root          | Methanol / DCM                        | T.b.b    | 33.16/85.07      | Tanzania  | Nibret et al., 2009                    |
| <i>Artemisia absinthium</i>        | Asteraceae    | Aerial part   | Methanol/ DCM                         | T.b.b    | 27.90/27.05      | Ethiopian | Nibret, 2009                           |
| <i>Artemisia abyssinica</i>        | Asteraceae    | Aerial part   | Methanol/ DCM                         | T.b.b    | 41.76/19.13      | Ethiopian | Nibret, 2009                           |
| <i>Artemisia afra</i>              | Asteraceae    | leaf          | Methanol/ DCM                         | T.b.b    | 77.54/25.27      | Ethiopian | Nibret, 2009                           |
| <i>Artemisia annua</i>             | Asteraceae    | leaf          | Methanol/ DCM                         | T.b.b    | 99.44/41.05      | Ethiopian | Nibret, 2009                           |
| <i>Balanites aegyptiaca</i>        | Balanitaceae  | Bark          | Methanol / DCM                        | T.b.b    | 22.11/39.40      | Tanzania  | Nibret et al., 2009                    |
| <i>Cassia abbreviata</i>           | Fabaceae      | Leaf          | Methanol / DCM                        | T.b.b    | 54.07/22.14      | Tanzania  | Nibret et al., 2009                    |
| <i>Combretum zeyheri</i>           | Combretaceae  | bark          | Methanol / DCM                        | T.b.b    | 87.45/38.97      | Tanzania  | Nibret et al., 2009                    |
| <i>Entada abyssinica</i>           | Fabaceae      | Bark          | Methanol / DCM                        | T.b.b    | 46.39/56.21      | Tanzania  | Nibret et al., 2009                    |
| <i>Entandrophragma bussei</i>      | Malaceae      | Bark          | Methanol / DCM                        | T.b.b    | 52.92/14.48      | Tanzania  | Nibret et al., 2009                    |
| <i>Harrisonia abyssinica</i>       | Simaroubaeae  | leaf          | Methanol / DCM                        | T.b.b    | 28.92/22.93      | Tanzania  | Nibret et al., 2009                    |
| <i>Khaya anthotheca</i>            | Meliaceae     | seed          | Pet. ether                            | T.b.r    | 5.72             | Uganda    | Obbo et al.,                           |
| <i>Kigelia africana</i>            | Bignoniaceae  | leaf          | Methanol / DCM                        | T.b.b    | 53.24/23.65      | Tanzania  | Nibret et al., 2009                    |
| <i>Lannea humilis</i>              | Anacardiaceae | bark          | Methanol / DCM                        | T.b.b    | 56.16/75.41      | Tanzania  | Nibret et al., 2009                    |
| <i>Lannea stuhlmannii</i>          | Anacardiaceae | root          | Methanol / DCM                        | T.b.b    | 44.23/22.24      | Tanzania  | Nibret et al., 2009                    |
| <i>Lonchocarpus capassa</i>        | Fabaceae      | Leaf          | Methanol / DCM                        | T.b.b    | 73.80/21.68      | Tanzania  | Nibret et al., 2009                    |
| <i>Securidaca longepedunculata</i> | polygalaceae  | leaf          | Methanol / DCM                        | T.b.b    | 55.56/11.02      | Tanzania  | Nibret et al., 2009, Wink et al., 2009 |
| <i>Senna singueana</i>             | Fabaceae      | Leaf          | Methanol / DCM                        | T.b.b    | 49.09/49.37      | Tanzania  | Nibret et al., 2009                    |
| <i>Solanecio mannii</i>            | Asteraceae    | Leaf          | Methanolic / dichloromethane extracts | T.b. b   | 50.58/24.89      | Ethiopia  | Nibret et al. (2009)                   |
| <i>Strychnos panganensis</i>       | Loganiaceae   | Leaf/ stem    | ethanol                               | T.b.r    | 56/56            | Tanzania  | Freiburghaus et al. (1997)             |
| <i>Strychnos spinosa</i>           | Strychnaceae  | leaf          | aqueous                               | T.b.r    | 2500             | Tanzania  | Freiburghaus et al. (1996a)            |

|                                   |              |                 |                                 |                    |                |          |                             |
|-----------------------------------|--------------|-----------------|---------------------------------|--------------------|----------------|----------|-----------------------------|
| <i>Teclea trichocarpa</i>         | Rutaceae     | leaves          | methanol                        | <i>T.b.r/Cruzi</i> | >90 /30        | Kenya    | Mwangi et al., 2010         |
| <i>Terminalia sericea</i>         | Combretaceae | leaf            | Methanol / DCM                  | <i>T.b.b</i>       | 36.23/21.71    | Tanzania | Nibret et al., 2009         |
| <i>Toona ciliata</i>              | Meliaceae    | roots           | Methanol/chloroform extract     | <i>T.b.r</i>       | 6.95/3.2 µg/ml | kenya    | Mercy et al., 2011          |
| <i>Turraea fischeri</i>           | Malaceae     | Bark            | Methanol / DCM                  | <i>T.b.b</i>       | 66.14/37.76    | Tanzania | Nibret et al., 2009         |
| <i>Vernonia auriculifera</i>      | Asteraceae   | Root            | DCM                             | <i>T.b.r</i>       | 9.4            | Uganda   | Freiburghaus et al. (1996b) |
| <i>Vernonia subuligera</i>        | Asteraceae   | Leaf/ root bark | Dichloromethane/petroleum ether | <i>T.b.r</i>       | 0.6/0.8        | Tanzania | Freiburghaus et al. (1996a) |
| <i>Warburgia salutaris</i>        | Canellaceae  | leaf            | Methanol / DCM                  | <i>T.b.b</i>       | 45.13/10.68    | Tanzania | Nibret et al., 2009         |
| <i>Ximenia americana</i>          | Canellaceae  | Stem            | DCM/methanol                    | <i>T.b. b</i>      | 86.64/49.18    | Tanzania | Nibret et al. (2010)        |
| <i>Ximenia americana</i>          | Oleaceae     | Leaf            | Methanol / DCM                  | <i>T.b.b</i>       | 86.64/49.18    | Tanzania | Nibret et al., 2009         |
| <i>Zanha africana</i>             | Sapindaceae  | root            | Methanol / DCM                  | <i>T.b.b</i>       | 33.53/12.63    | Tanzania | Nibret et al., 2009         |
| <i>Zanthoxylum chalybeum</i>      | Rutaceae     | leaf            | Methanol / DCM                  | <i>T.b.b</i>       | 36.00/11.02    | Tanzania | Nibret et al., 2009         |
| <i>Zanthoxylum xanthoxyloides</i> | Rutaceae     | Leaf/ stem      | DCM/methanol                    | <i>T.b.b</i>       | 36.00/11.02    | Tanzania | Nibret et al. (2010)        |

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

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292 **Table 6; In vivo Anti-trypanosomal activity of African plant**

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| Scientific name            | Family        | Part (s) used | parasite       | extract               | dose      | model                | % inhibition/survival days | Country | References                                    |
|----------------------------|---------------|---------------|----------------|-----------------------|-----------|----------------------|----------------------------|---------|-----------------------------------------------|
| <i>Thymus vulgaris</i>     | Lamiaceae     | Leaf          | <i>T. b. b</i> | methanol              | 500 mg/kg | Curative/suppressive | 8 days                     | Nigeria | Shittu et al., 2013                           |
| <i>Acacia nilotica</i>     | Mimosaceae    | stem bark     | <i>T. b. b</i> | Methanol              | 200       | curative             | 30 days                    | Nigeria | Mann et al., 2011                             |
| <i>Acalypha wilkesiana</i> | Euphorbiaceae | leaves        | <i>T.bb</i>    | aqueous               | 400 Mg/Kg | curative             | 2.03/11.00±0.0             | Nigeria | Olukunle et al., 2010                         |
| <i>Adamsonia digitata</i>  | Malvaceae     | seed          | <i>T. b. b</i> | methanol              | 300 mg/kg | curative             | 38                         | Nigeria | Hassan et al., 2012                           |
| <i>Allium sativum</i>      | Alliaceae     | Bulb /Pulp    | <i>T. b. b</i> | Methanol/ Acetic acid | 20mg/kg   | curative             |                            | Nigeria | Yusuf, 2010/ Peni et al., 20/ Noket al., 1996 |
| <i>Annona</i>              | Annonaceae    | leaf          | <i>T. b. b</i> | methanol              | 200       | curative             | 20 days                    | Nigeria | Kabiru et                                     |

|                                                              |                  |              |                |                         |                |                        |                |          |                                         |
|--------------------------------------------------------------|------------------|--------------|----------------|-------------------------|----------------|------------------------|----------------|----------|-----------------------------------------|
| <i>senegalensis</i>                                          | ae               |              |                | nol                     | mg/kg          | e                      |                | eria     | al., 2012                               |
| <i>Annona senegalensis</i> + <i>Eucalyptus camaldulensis</i> |                  | leaf         | <i>T. b. b</i> | methanol                | 200 mg/kg      | Combined therapy (1:1) | >90 days       | Nigeria  | Kabiru et al., 2012                     |
| <i>Argemone mexicana</i>                                     | Papaveraceae     | Whole plant  | <i>T. e</i>    | Chloroform / methanolic | 500 mg/kg      | curative               | 15 and 16 days | Sudan    | Samia, 2011                             |
| <i>Aristolochia bracteolata</i>                              | Aristolochiaceae | Whole plant  | <i>T. e</i>    | Chloroform / methanolic | 500 mg/kg      | curative               | 25 and 19 days | Sudan    | Samia, 2011                             |
| <i>Artemisia annua</i>                                       | Asteraceae       |              | <i>T.b. r</i>  | Methanol                | 5000 mg/kg     | curative               | 15.6           | Kenya    | Esther et al., 2010                     |
| <i>Artemisia abyssinica</i>                                  | Asteraceae       | aerial parts | <i>T.co</i>    | dichloromethane         | 400 mg/kg      | curative               | 40.67 days     | Ethiopia | Teka et al., 2014                       |
| <i>Artemisia maciverae</i>                                   | Asteraceae       | Whole plant  | <i>T.b. b</i>  | chloroform              | 100 mg/kg      | curative               | 74.15%         | Nigeria  | Ene et al., 2009                        |
| <i>Artemisia maritima</i>                                    | Asteraceae       | whole plant  | <i>T.b. b</i>  | chloroform              | 100 mg/kg      | curative               | 26%            | Nigeria  | Ene et al., 2014                        |
| <i>Azadirachta indica</i>                                    | Meliaceae        |              | <i>T.b. r</i>  | dichloromethane         | 5000 mg/kg     | curative               | 27days         | Kenya    | Esther et al., 2010                     |
| <i>Bombax buonopozense</i>                                   | Bombacaceae      | stem bark    | <i>T. b. b</i> | Methanol                | 300            | curative               | 30 days        | Nigeria  | Mann et al., 2011                       |
| <i>Buchholzia Coriacea</i>                                   | Capparaceae      | seed         | <i>T.co</i>    | Methanol/aqueous        | 500/1000 mg/kg | curative               | 29days/100%    | Nigeria  | Nweze et al., 2011/ Okere et al., 2014. |
| <i>Citrullus lanatus</i>                                     | Cucurbitaceae,   | leaf         | <i>T.b</i>     | aqueous extract         | 200            | curative               | 97.18%         | Nigeria  | BIU et al., 2013                        |
| <i>Cannabis sativa</i>                                       | cannabaceae      | Whole plant  | <i>T. e</i>    | methanol                | 125/250 mg/kg  | curative               | > 45days       | sudan    | Samia et al., 2012                      |
| <i>Cucumis metuliferus</i>                                   | Cucurbitaceae    | pulp         | <i>T. b. b</i> | methanol                | 500 mg/kg      | curative               | 47days         | Nigeria  | Abubakar et al., 2011)                  |
| <i>Dissotis rotundifolia</i>                                 | melastomataceae  | leaf         | <i>T. b. b</i> | ethanol                 | 800 mg/kg      | curative               | 78.4%          | Nigeria  | Mann et al., 2009                       |
| <i>Eucalyptus camaldulensis</i>                              | myrtaceae        | leaf         | <i>T. b. b</i> | methanol                | 200 mg/kg      | curative               | 20 days        | Nigeria  | Kabiru et al., 2012                     |
| Garcinia                                                     | Clusiaceae       | Nut          | <i>T. b. b</i> | Meth                    |                | curative               |                | Nig      | Ogbadoyi et                             |

|                                    |                 |             |                |            |            |              |                |         |                          |
|------------------------------------|-----------------|-------------|----------------|------------|------------|--------------|----------------|---------|--------------------------|
| kola                               | e               |             |                | anol       |            | e            |                | eria    | al., 2011                |
| <i>Gongrene ma latifolium</i>      | Asclepiadaceae  | stem bark   | <i>T. co</i>   | methanol   | 400 mg/kg  | curative     | 9 days         | Nigeria | Abedo et al., 2013       |
| <i>Guiera senegalensis</i>         | combretaceae    | leaf        | <i>T. b.</i>   | methanol   | 150        | curative     | 42%            | Nigeria | Aderbauer et al., 2008   |
| <i>Securidaca longepedunculata</i> | polygalaceae    | root        | <i>T. b.</i>   | methanol   | 150        | curative     | 48%            | Nigeria | Aderbauer et al., 2008   |
| <i>Heterotis rotundifolia</i>      | Melastomataceae | whole plant | <i>T. b.</i>   | methanol   | 800        | curative     | 30             | Nigeria | Mann and Obgbadoyi, 2012 |
| <i>Hymenocardia acida</i>          | Euphorbiaceae   | Root bark   | <i>T. b. b</i> | DCM        | 300 mg/kg  | curative     | 9days          | Nigeria |                          |
| <i>Khaya senegalensis</i>          | Meliaceae       | stem        | <i>T. b. b</i> | DCM        | 200 mg/kg  | curative     | 11days         | Nigeria | Bulus and Addau, 2013    |
| <i>Kigelia africana</i>            | Bignoniaceae    | fruits      | <i>T.b. r</i>  | DCM        | 1000 mg/kg | curative     | 41.8           | Kenya   | Esther et al.            |
| <i>Lippia multiflora</i>           | Verbenaceae     | leaves      | <i>T. b. b</i> | Aqueous    | 400 Mg/Kg  | curative     | 3.45%/1.00days | Nigeria | Olukunle et al., 2010    |
| <i>Morinda morindoides</i>         | Rubiaceae       | root bark   | <i>T. b. b</i> | Aqueous    | 400 Mg/Kg  | curative     | 6.66 %         | Nigeria | Olukunle et al., 2010    |
| <i>Moringa oleifera</i>            | moringaceae     | stems       | <i>T. b. b</i> | Aqueous    | 200 mg/kg  | curative     | 30 days        | Nigeria | Bulus and Addau, 2013    |
| <i>Ocimum grattissimum</i>         | Lamiaceae       | leaves      | <i>T.b b</i>   | Aqueous    | 50Mg/Kg    | curative     | 11.11/2.44+3.5 | Nigeria | Adamu et al., 2009       |
| <i>Prosopis africana</i>           | Leguminosae)    | leaves      | <i>T. b. b</i> | methanol   | 200 mg/kg  | curative     | 14days         | Nigeria | Atawodiand Funmi 2009    |
| <i>Psidium guajava</i>             | Myrtaceae       | leaf        | <i>T. b. b</i> | ethanol    |            | prophylactic | 32 days        | Nigeria | Adeyemi et al., 2009     |
| <i>Pterocarpuserinaceus</i> ,      | Leguminosae     | Leaf        | <i>T. b.</i>   | Methanol   | 40         | curative     | ≥14days        | Nigeria | Mann and Obgbadoyi, 2012 |
| <i>Zanthoxylum zanthoxyloides</i>  | Rutaceae        | stem bark   | <i>T. b.</i>   | Methanol   | 100        | curative     | No activity    | Nigeria | Mann and Obgbadoyi, 2012 |
| <i>Tapinanthus globiferus</i>      | Loranthaceae    | leaf        | <i>T. co</i>   | methanol   | 400 mg/kg  | curative     | 24th day       | Nigeria | Abedo et al., 2013       |
| <i>Terminalia avicennioides</i>    | Combretaceae    | fruit       | <i>T. b. b</i> | Methanol   | 300        | curative     | 12 days        | Nigeria | Mann et al., 2011        |
| <i>Tinospora bakis</i>             | melastomataceae | leaf        | <i>T. e</i>    | Chloroform | 500 mg/kg  | curative     | 20 days        | Sudan   | Samia, 2011              |

|                                            |                    |              |                |                |                  |              |                    |                  |                                |
|--------------------------------------------|--------------------|--------------|----------------|----------------|------------------|--------------|--------------------|------------------|--------------------------------|
|                                            |                    |              |                | metha<br>nolic |                  |              |                    |                  |                                |
| <i>Tithonia<br/>diversifoli<br/>a</i>      | Asteracea<br>e     | leav<br>es   | <i>T. b. b</i> | Aque<br>ous    | 400<br>Mg/<br>Kg | curativ<br>e | 2.03/11.<br>6±0.40 | Nig<br>eria<br>. | Olukunle et<br>al., 2010       |
| <i>Tridax<br/>procumbe<br/>ns</i>          | Asteracea<br>e     | leav<br>es   | <i>T. b. b</i> | Meth<br>anol   | 300<br>mg/k<br>g | curativ<br>e | 28                 | Nig<br>eria<br>. | Abubakar<br>et al.,2010        |
| <i>Vernonia<br/>amygdalin<br/>a</i>        | Asteracea<br>e     | leaf         | <i>T. b. b</i> | Meth<br>anol   | 300<br>mg/k<br>g | curativ<br>e | 24 days            | Nig<br>eria      | Yusuf, et<br>al., 2012         |
| <i>Zanthoxyl<br/>umzanthox<br/>yloides</i> | Rutaceae           | stem<br>bark | <i>T. b.</i>   |                |                  | curativ<br>e |                    | Nig<br>eria<br>n | Mann and<br>Obgbadoyi,<br>2012 |
| <i>Calotropis<br/>procera</i>              | Asclepiad<br>aceae | Leaf         | <i>T. e</i>    | Meth<br>anol   | 200<br>mg/k<br>g | curativ<br>e |                    | Nig<br>eria      | Ibrahim<br>etal., 2013         |

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

295 **Table 7: Anti-trypanosomal compounds isolated from African plant**

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| Compound                                                             | Plant species                    | Family            | Part<br>used | Trypa<br>nosom<br>e<br>species | IC <sub>50</sub> | Solvent    | Author                   |
|----------------------------------------------------------------------|----------------------------------|-------------------|--------------|--------------------------------|------------------|------------|--------------------------|
| 16-acetoxy-11-hydroxy octadeca-17-ene-12,14-diynyl acetate           | <i>Cussonia<br/>zimmermannii</i> | Araliaceae        | Root<br>bark | T.b.r                          | 0.42             | Pet.ether  | Senn et al.,<br>2007     |
| 8-hydroxyheptadeca-4,6-diyn-3ylacetate                               | <i>Cussonia<br/>zimmermannii</i> | Araliaceae        | Root<br>bark | T.b.r                          | 5.4              | Pet.ether  | Senn et al.,<br>2007     |
| 8-hydroxyheptadeca-1-ene-4,6-diyn-2ylacetate                         | <i>Cussonia<br/>zimmermannii</i> | Araliaceae        | Root<br>bark | T.b.r                          | 0.41             | Pet.ether  | Senn et al.,<br>2007     |
| 24-hydroperoxy-24-vinylcholesterol                                   | <i>Strychnos<br/>spinosa</i>     | Loganiace<br>ae   | leaves       | T.b. b                         | 3.2              | lipophilic | Hoet et al.,<br>2007     |
| 2-oxo-3-deacetyl salannin                                            | <i>Azadirachta<br/>indica</i>    | Meliaceae         | leaf         | <i>T.b. r</i>                  | 6.9              | Chloroform | Githua et<br>al., 2010   |
| 4,7-Dimethoxy-5-methyl-2H-Chromen-2-one                              | <i>Toona ciliata</i>             | Meliaceae         | root         | <i>T.b. r</i>                  | 31.25<br>µg/ml   | Methanol   | Mercy et<br>al., 2011    |
| 4'-hydroxy-5,6,7,3',5'-pentamethoxyflavone (ageconyflavone C).       | <i>Ageratum<br/>conyzoides</i>   | Asteracea<br>e    | leaves       | T.b. r                         | 3.01             | Methanol   | Nour et al.,<br>2010     |
| 41 (4Z,6E)-5-hydroxy-1,7-bis (4-hydroxyphenyl) hepta-4,6- dien-3-one | <i>Aframomum<br/>letestuanum</i> | Zingibera<br>ceae | seed         | <i>T.b. b</i>                  | 2.6              | DCM        | Kamnaing<br>et al., 2003 |
| 5,6,7,3',4',5'-                                                      | <i>Ageratum</i>                  | Asteracea         | leaves       | T.b. r                         | 8.58             | Methanol   | Nour et al.,             |

|                                                                    |                                   |             |             |             |               |                      |                        |
|--------------------------------------------------------------------|-----------------------------------|-------------|-------------|-------------|---------------|----------------------|------------------------|
| hexamethoxyflavone                                                 | <i>conyzoides</i>                 | e           |             |             |               |                      | 2010                   |
| 5,6,7,5'-tetramethoxy-3',4'-methylenedioxyflavone                  | <i>Ageratum conyzoides</i>        | Asteraceae  | leaves      | T.b. r      | 7.29          | Methanol             | Nour et al., 2010      |
| 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., 2010      |
| 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., 2010      |
| 6-acetonyldihydrocherythrine                                       | <i>Garcinia lucida</i>            | Clusiaceae  | Stem        | T.b. b      | 3.9           | DCM                  | Fotie et al., 2007     |
| 7-deacetylkhivorin                                                 | <i>Khaya anthotheca</i>           | Meliaceae   | seeds       | T.b. r/T.cr | 16.88 / 31.82 | Pet. Ether           | Obbo et al., 2013      |
| 7,15-dihydroxy-7,15-deoxo nimbin                                   | <i>Azadirachta indica</i>         | Meliaceae   | leaf        | T.b. r      | 15.6          | Chloroform           | Githua et al., 2010    |
| 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., 2013      |
| 7-acetyl-15-methoxy-29-methylene-7,15-deoxo nimbolide              | <i>Azadirachta indica</i>         | Meliaceae   | leaf        | T.b. r      | 7.8           | Chloroform           | Githua et al., 2010    |
| 7-methoxyflavone                                                   | <i>Conchocarpus heterophyllus</i> | Rutaceae    | branches    | T.cr        | 787 µg/mL     | hexane               | Ambrozin et al., 2004  |
| 8-hydroxyheptadecan-1-ene-4,6-diyn-2-yl acetate                    | <i>Cussonia zimmermannii</i>      | Araliaceae  | root        | T.b. r      | 0.14          | Pet.ether            | Senn et al., 2007      |
| 8-hydroxyheptadecan-4,6-diyn-3-yl acetate                          | <i>Cussonia zimmermannii</i>      | Araliaceae  | Root        | T.b. r      | 5.4           | Pet.ether            | Senn et al., 2007      |
| abruquinone B                                                      | <i>Abrus precatorius</i>          | Leguminosae | whole plant | T.b. r      | 0.2           | DCM/Methanol (1 : 1) | Hata et al., 2013      |
| abruquinone G                                                      | <i>Abrus precatorius</i>          | Leguminosae | whole plant | T.b. r      | 17.0          | DCM/Methanol (1 : 1) | Hata et al., 2013      |
| Abuquinone H                                                       | <i>Abrus precatorius</i>          | Leguminosae | whole plant | T.b. r      | 12.0          | DCM/Methanol (1 : 1) | Hata et al., 2013      |
| abruquinone I                                                      | <i>Abrus precatorius</i>          | Leguminosae | whole plant | T.b. r      | 0.3           | DCM/Methanol (1 : 1) | Hata et al., 2013      |
| Abuquinones A                                                      | <i>Abrus precatorius</i>          | Leguminosae | whole plant | T.b. r      | 0.02          | DCM/Methanol(1:1)    | Matthias et al., 2014  |
| Abuquinones D                                                      | <i>Abrus precatorius</i>          | Leguminosae | whole plant | T.b. r      | 0.01          | DCM/Methanol(1:1)    | Matthias et al., 2014  |
| Abuquinones J                                                      | <i>Abrus precatorius</i>          | Leguminosae | whole plant | T.b. r      | 11.2          | DCM/Methanol(1:1)    | Matthias et al., 2014a |

|                      |                                      |                    |                |                                                      |                             |                        |                           |
|----------------------|--------------------------------------|--------------------|----------------|------------------------------------------------------|-----------------------------|------------------------|---------------------------|
| Abruquinones K       | <i>Abrus precatorius</i>             | Legumino<br>sae    | whole<br>plant | T.b. r                                               | 0.11                        | DCM/Meth<br>anol(1:1)  | Matthias et<br>al., 2014  |
| Abruquinones L       | <i>Abrus precatorius</i>             | Legumino<br>sae    | whole<br>plant | T.b. r                                               | 0.02                        | DCM/Meth<br>anol(1:1)  | Matthias et<br>al., 2014  |
| Arborinine           | <i>Teclea trichocarpa</i>            | Rutaceae           | leaves         | T.b. r                                               | 23.52                       | Methanol               | Mwangi et<br>al., 2010    |
| Artemisinin          | <i>Artemisia annua</i>               | Asteracea<br>e     | leaf           | T.b.b                                                | 35.91                       | DCM/Meth<br>anol(1:1)  | Nibret,<br>2009           |
| Azaanthraquinone     | <i>Mitracarpus scaber</i>            | Rubiaceae          | leaf           | T.co                                                 | 50                          | methanol               | Nok (2002                 |
| Beta-sitosterol      | <i>Buchholziaceae</i>                | Capparace<br>ae    | seeds          | T.b. b                                               | 12.5<br>µg/ml               | methanol               | Nweze et<br>al.           |
| betulin              | <i>Strychnos spinosa</i>             | Loganiace<br>ae    | leaves         | T.b. b                                               | 54.0                        | lipophilic             | Hoet et al.,<br>2007      |
| Betulinic acid       | <i>Keetia leucantha</i>              | Rubiaceae          | Leaf           | Bloods<br>tream/<br>procyc<br>lic<br>forms<br>of T.b | 11.2/4<br>0.90<br>µg<br>/ml | oil                    | Bero et al.,<br>2013      |
| Caryophyllene        | <i>Keetia leucantha</i>              | Rubiaceae          | Leaf           | Bloods<br>tream/<br>procyc<br>lic<br>forms<br>of T.b | 41.2/><br>100<br>µg<br>/ml  | oil                    | Bero et al.,<br>2013      |
| cedrelone            | <i>Toona ciliata</i>                 | Meliaceae          | root           | T.b. r                                               | 7.85<br>µg/ml               | Methanol               | Mercy et<br>al., 2011     |
| Cedrelone            | <i>Toona ciliata</i>                 | Meliaceae          | Root           | T.b. r                                               | 31.25                       | Chloroform             | Githua et<br>al., 2010    |
| cinerin II           | <i>Chrysanthemum cinerariifolium</i> | Asteracea<br>e     | Flowe<br>rs    | T.b. r                                               | 12.2                        | n-hexane               | Michael et<br>al., 2011   |
| cipadesin            | <i>Cipadessa fruticosa</i>           | Meliaceae          | Fruits         | T.cr.                                                | 189.0<br>µmol/<br>L         | DCM                    | Ana et al.,<br>2010       |
| cipadesin A          | <i>Cipadessa fruticosa</i>           | Meliaceae          | fruits         | T.cr.                                                | 136.1<br>µmol/<br>L         | DCM                    | Ana et al.,<br>2010       |
| citronellal          | <i>Ocimum gratissimum</i>            | lamilaceae         | Seed<br>oil    | T.b. b                                               | 2.76±<br>1.55<br>µg/m<br>L  | oil                    | Bénédicte<br>et al., 2014 |
| clerosterol          | <i>Strychnos spinosa</i>             | Loganiace<br>ae    | leaves         | T.b. b                                               | 53.6                        | lipophilic             | Hoet et al.,<br>2007      |
| cynaropicrin         | <i>Vernonia mespilifolia</i>         | Asteracea<br>e     | Leaf           | T.b. r/<br>T.cr                                      | 0.23/5<br>.14               | DCM/Meth<br>anol       | Mokoka et<br>al., 2013    |
| Dihydrochelerythrine | <i>Garcinia lucida</i>               | Clusiaceae         | stem           | T.b. b                                               | 0.8                         | DCM                    | Fotie et al.,<br>2007     |
| drypetenone D        | <i>Drypetes gerrardii</i>            | Putranjiva<br>ceae | Stem           | T.b. r                                               | 6.0                         | DCM/Meth<br>anol (1:1) | Matthias et<br>al., 2014b |
| drypetenone E        | <i>Drypetes gerrardii</i>            | Putranjiva<br>ceae | Stem           | T.b. r                                               | -                           | DCM/Meth<br>anol (1:1) | Matthias et<br>al., 2014b |

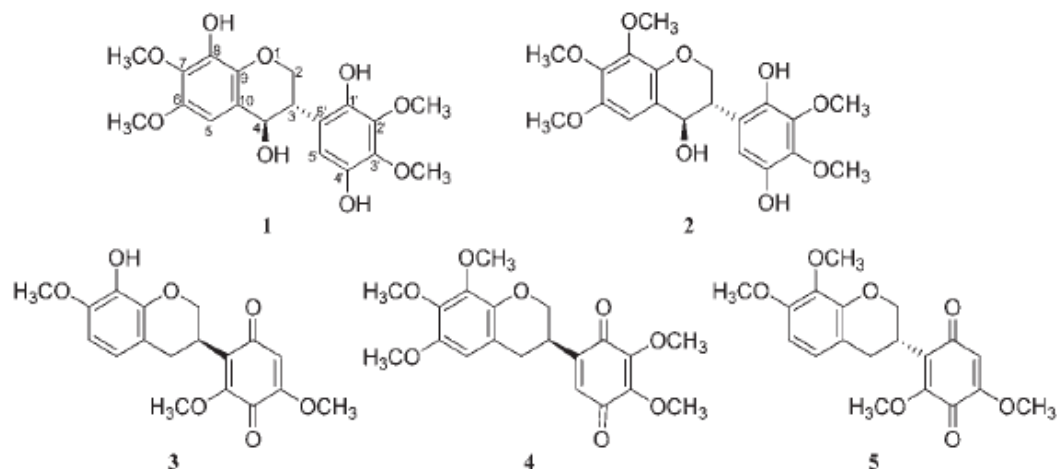
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|--------------------------|--------------------------------------|---------------|----------|------------------------------------|-----------------|------------|---------------------------|
| encecalol methyl ether 6 | <i>Ageratum conyzoides</i>           | Asteraceae    | leaves   | T.b. r                             | 78.4            | Methanol   | Nour et al., 2010         |
| erythrodil               | <i>Strychnos spinosa</i>             | Loganiaceae   | leaves   | T.b. b                             | 5.3             | lipophilic | Hoet et al., 2007         |
| Espintanol               | <i>Oxandra espintana</i>             | Anonaceae     | Leaf     | T.cr                               | 25 µg/ml        | methanol   | Hocquemiller et al., 1991 |
| febrifugin               | <i>Cipadessa fruticosa</i>           | Meliaceae     | Fruits   | T.cr.                              | 168.0 µmol/L    | DCM        | Ana et al., 2010          |
| flavone                  | <i>Conchocarpus heterophyllus</i>    | Rutaceae      | branches | T.cr                               | 2116 µg/mL      | Hexane     | Ambrozin et al., 2004     |
| Geranylacetone           | <i>Keetia leucantha</i>              | Rubiaceae     | Leaf     | Bloodstream/procyclic forms of T.b | 16.2/>100 µg/ml | oil        | Bero et al., 2013         |
| Grandifolione            | <i>Khaya anthotheca</i>              | Meliaceae     | seeds    | T.b.r/T.cr                         | 10.66/20.9      | Pet. Ether | Obbo et al.               |
| jasmolin I               | <i>Chrysanthemum cinerariifolium</i> | Asteraceae    | flowers  | T.b. r                             | 30.9            | n-hexane   | Michael et al., 2011      |
| jasmolin II              | <i>Chrysanthemum cinerariifolium</i> | Asteraceae    | flowers  | T.b. r                             | 12.0            | n-hexane   | Michael et al., 2011      |
| Kolavenol                | <i>Entada abyssinica</i>             | Leguminosae   | stem     | T.b. r                             | 2.5             | Ethanol    | Freiburghaus et al., 1998 |
| Letestuianin A           | <i>Aframomum letestuanum</i>         | Zingiberaceae | seed     | T.b. b                             | >100            | DCM        | Kamnaing et al., 2003     |
| Letestuianin B           | <i>Aframomum letestuanum</i>         | Zingiberaceae | seed     | T.b. b                             | 67              | DCM        | Kamnaing et al., 2003     |
| Letestuianin C           | <i>Aframomum letestuanum</i>         | Zingiberaceae | seed     | T.b. b                             | 2.6             | DCM        | Kamnaing et al., 2003     |
| limonene                 | <i>Ocimum gratissimum</i>            | Lamiaceae     | Seed oil | T.b. b                             | 4.24±2.27 µg/mL | oil        | Bénédicta et al., 2014    |
| Lucidamine A             | <i>Garcinia lucida</i>               | Clusiaceae    | Stem     | T.b. b                             | 14.1            | DCM        | Fotie et al., 2007        |
| Lucidamine b             | <i>Garcinia lucida</i>               | Clusiaceae    | stem     | T.b. b                             | 4.1             | DCM        | Fotie et al., 2007        |
| lupeol                   | <i>Strychnos spinosa</i>             | Loganiaceae   | leaves   | T.b. b                             | 19,3            | lipophilic | Hoet et al., 2007         |
| Melicopicine             | <i>Teclea trichocarpa</i>            | Rutaceae      | leaves   | T.b. r                             | 15.56           | methanol   | Mwangi et al., 2010       |
| mexicanolide             | <i>Cipadessa fruticosa</i>           | Meliaceae     | Fruits   | T.cr.                              | 326.3 µmol/L    | DCM        | Ana et al., 2010          |
| myrcene                  | <i>Ocimum gratissimum</i>            | Lamiaceae     | Seed oil | T.b. b                             | 2.24±0.27 µg/mL | oil        | Bénédicta et al., 2014    |
| n-Hexadecanoic acid      | <i>Keetia leucantha</i>              | Rubiaceae     | Leaf     | Bloodstream/                       | >100/>100       | oil        | Bero et al., 2013         |

|                   |                                      |                |             |                                        |                    |                    |                        |
|-------------------|--------------------------------------|----------------|-------------|----------------------------------------|--------------------|--------------------|------------------------|
|                   |                                      |                |             | procyclic forms of T. b                | g g/ml             |                    |                        |
| Normelicopicine   | <i>Teclea trichocarpa</i>            | Rutaceae       | leaves      | T.b. r                                 | 5.24               | methanol           | Mwangi et al., 2010    |
| Oleanolic acid    | <i>Keetia leucantha</i>              | Rubiaceae      | Leaf        | Bloods tream/procyclic forms of T. b   | 7.3/86.4 µg g/ml   | oil                | Bero et al., 2013      |
| Oleic acid        | <i>Keetia leucantha</i>              | Rubiaceae      | Leaf        | Bloods tream/procyclic forms of T. b   | 64.30/>100 µg g/ml | oil                | Bero et al., 2013      |
| phytol            | <i>Keetia leucantha</i>              | Rubiaceae      | Leaf        | Bloods tream/procyclic form sof T.b. b | 19.1/>100          | oil                | Bero et al., 2013      |
| putranoside A     | <i>Drypetes gerrardii</i>            | Putranjivaceae | stem        | T.b. r                                 | 18.0               | DCM/Methanol (1:1) | Matthias et al., 2014b |
| pyrethrin I       | <i>Chrysanthemum cinerariifolium</i> | Asteraceae     | Flowers     | T.b. r                                 | 6.9                | n-hexane           | Michael et al., 2011   |
| pyrethrin II      | <i>Chrysanthemum cinerariifolium</i> | Asteraceae     | flowers     | . T.b. r                               | 10.6               | n-hexane           | Michael et al., 2011   |
| quercetin         | <i>Rapanea lancifolia</i>            | Myrsinaceae    | branches    | T.b.b                                  | 13.2 µmol/L        | methanol           | Camacho et al., 2002   |
| Saringosterol     | <i>Strychnos spinosa</i>             | Loganiaceae    | leaves      | T.b. b                                 | 7.8                | ipophilic          | Hoet et al., 2007      |
| schkuhrin I       | <i>Schkuhria pinnata</i>             | Asteraceae     | Whole plant | T.b. r/ T.cr                           | 0.86/16.4          | DCM/Methanol       | Mokoka et al., 2013    |
| schkuhrin II      | <i>Schkuhria pinnata</i>             | Asteraceae     | Whole plant | T.b. r/ T.cr                           | 1.50/26.9          | DCM/Methanol       | Mokoka et al., 2013    |
| Siderin           | <i>Toona ciliata</i>                 | Meliaceae      | leaf        | T.b. r                                 | 7.18               | Chloroform         | Githua et al., 2010    |
| Skimmianine       | <i>Teclea trichocarpa</i>            | Rutaceae       | leaves      | T.b. r                                 | 15.78              | methanol           | Mwangi et al., 2010    |
| stigmastanol      | <i>Strychnos spinosa</i>             | Loganiaceae    | leaves      | T.b. b                                 | >100               | ipophilic          | Hoet et al., 2007      |
| stigmasterol      | <i>Strychnos spinosa</i>             | Loganiaceae    | leaves      | T.b. b                                 | 55.5               | ipophilic          | Hoet et al., 2007      |
| Terchebulin       | <i>Terminalia avicenioides</i>       | Combretaceae   | Leaf        | T.b. b                                 | 27.5               | Aqueous            | Shuaibu et al., 2008.  |
| punicalagin, ,    | <i>Terminalia avicenioides</i>       | Combretaceae   | Leaf        | T.b. b                                 | 15                 | Aqueous            | Shuaibu et al., 2008.  |
| ellagic acid      | <i>Terminalia avicenioides</i>       | Combretaceae   | Leaf        | T.b. b                                 | 25                 | Aqueous            | Shuaibu et al., 2008.  |
| flavogallonicacid | <i>Terminalia</i>                    | Combretaceae   | Leaf        | T.b. b                                 | 7.5                | Aqueous            | Shuaibu et             |

|                   |                            |             |           |                                      |                 |            |                     |
|-------------------|----------------------------|-------------|-----------|--------------------------------------|-----------------|------------|---------------------|
|                   | <i>avicenioides</i>        | ceae        |           |                                      |                 |            | al., 2008.          |
| ursolic acid      | <i>Keetia leucantha</i>    | Rubiaceae   | Leaf      | Bloods tream/procyclic forms of T. b | 2.5/6.5 µg/ml   | oil        | Bero et al.         |
| uvaol             | <i>Strychnos spinosa</i>   | Loganiaceae | leaves    | T.b. b                               | 12.3            | ipophilic  | Hoet et al., 2007   |
| vernoguinoside    | <i>Vernonia guineensis</i> | Asteraceae  | stem bark | T.b. r                               | 3–5 mg/ml       | Ethanol    | Joseph et al., 2002 |
| vernoguinoesterol | <i>Vernonia guineensis</i> | Asteraceae  | stem bark | T.b. r                               | 3–5 mg/ml       | Ethanol    | Joseph et al., 2002 |
| α-Amyrin          | <i>Teclea trichocarp</i>   | Rutaceae    | leaves    | T.b. r                               | 11.21           | methanol   | Mwangi et al., 2010 |
| α-amyrin          | <i>Strychnos spinosa</i>   | Loganiaceae | leaves    | T.b. b                               | 48.9            | lipophilic | Hoet et al., 2007   |
| α-Ionone          | <i>Keetia leucantha</i>    | Rubiaceae   | Leaf      | Bloods tream/procyclic forms of T. b | 13.1/81.4 µg/ml | oil        | Bero et al.         |
| α-sulphur         | <i>Buchholziaceae</i>      | Capparaceae | seeds     | T.b. b                               | 25 µg/ml        | methanol   | Nweze et al.        |
| β-amyrin          | <i>Strychnos spinosa</i>   | Loganiaceae | leaves    | T.b. b                               | 54.3            | lipophilic | Hoet et al., 2007   |
| β-Ionone          | <i>Keetia leucantha</i>    |             | Leaf      | Bloods tream/procyclic forms of T. b | 10.5/55.8 µg/ml | oil        | Bero et al.         |
| β-sitosterol      | <i>Morinda lucida</i>      | Rubiaceae   | leaves    | T.b. b                               | 12.5 µg/ml      | Methanol   | Nwakaego, 2012      |
| β-sitosterol      | <i>Strychnos spinosa</i>   | Loganiaceae | leaves    | T.b. b                               | >100            | lipophilic | Hoet et al., 2007   |
| β-Sitosterol      | <i>Teclea trichocarp</i>   | Rutaceae    | leaves    | T.b. r                               | >90             | methanol   | Mwangi et al., 2010 |

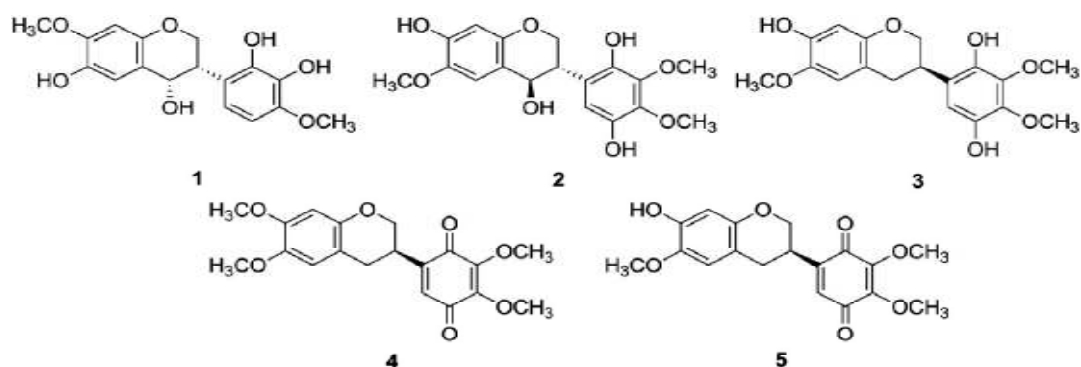
297 T.b. b =Trypanosoma brucei brucei, T.e =Trypanosoma evansi, T.co =Trypanosoma congolense,

298 **African plants with ameliorative effects on the trypanosome-induced pathological**  
299 **changes**

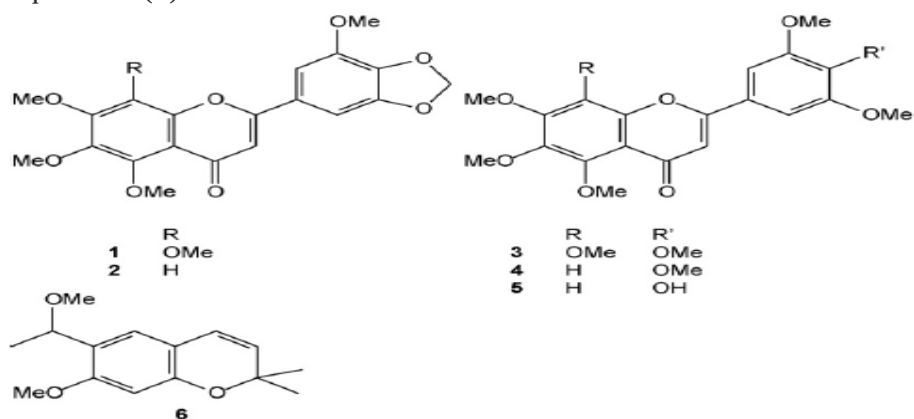


300  
 301 Abruquinone H (1) and abruquinone G (2), , abruquinone I (3), abruquinone B (4), and  
 302 7,8,3' , 5' -tetramethoxyisoflavan-1' ,4' -quinone (5).  
 303

304

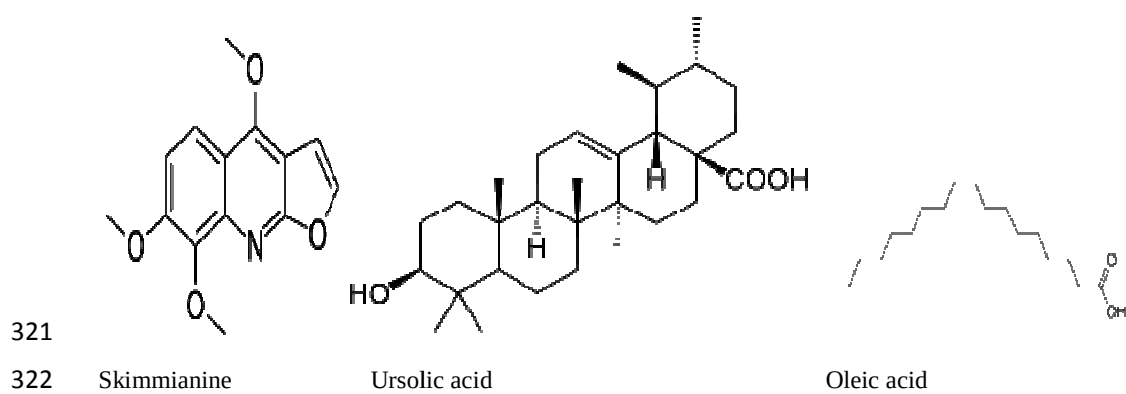
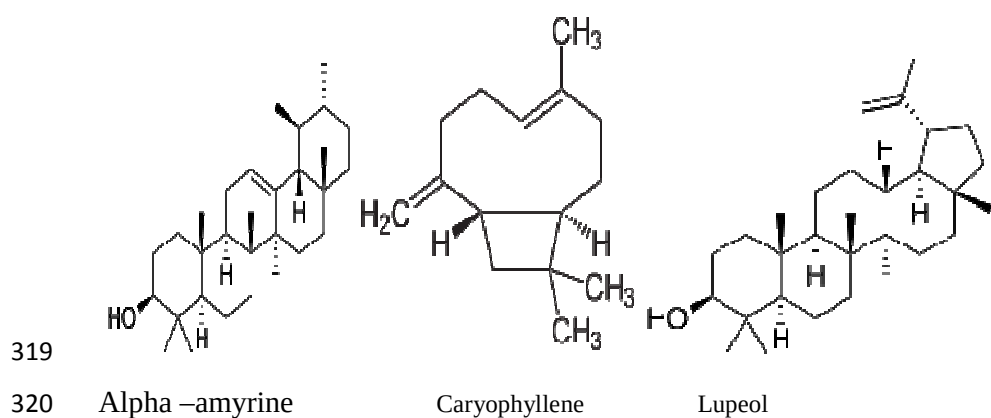
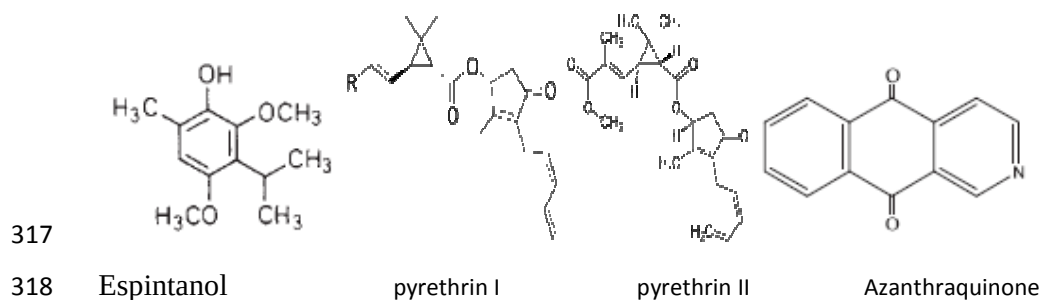
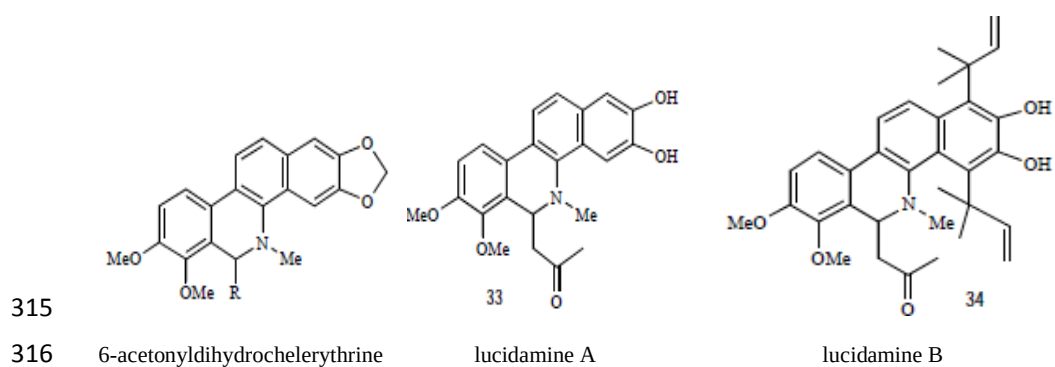


305  
 306 Abruquinone J (1) and abruquinone K (2), , abruquinone L (3), abruquinone A (4), and  
 307 abruquinoneD(5).

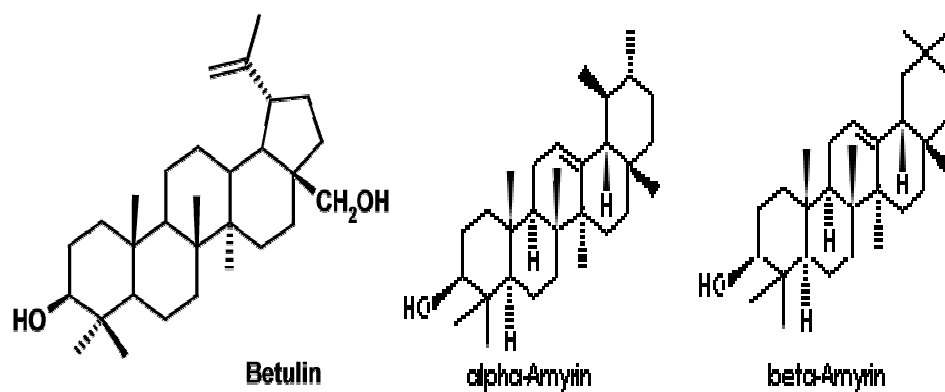


308  
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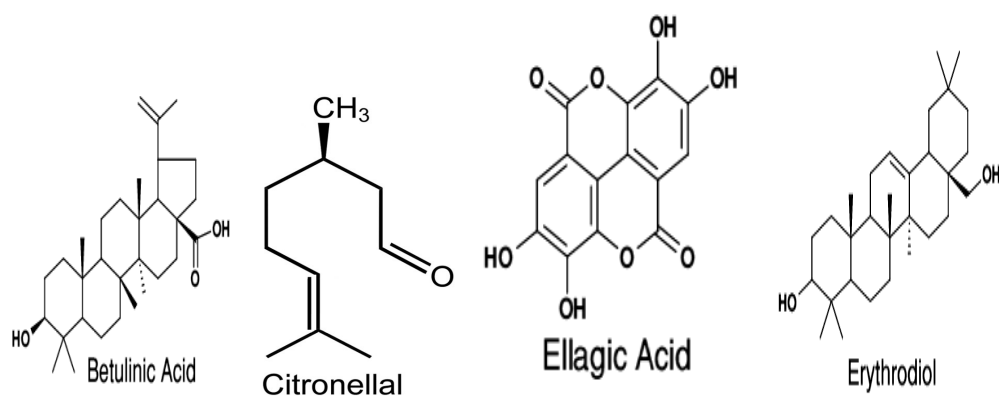
310 5,6,7,8,5'-pentamethoxy-3', 4'-methylenedioxyflavone (eupalestin, 1), 5,6,7,5'  
 311 tetramethoxy- 3',4'-methylenedioxyflavone (2), 5,6,7,8,3,4,5\_-heptamethoxyflavone  
 312 (5'-methoxynobiletine, 3), 5,6,7,3',4',5'-hexamethoxyflavone (4) and 4'-hydroxy-  
 313 5,6,7,3',5'-pentamethoxyflavone (ageconyflavone C, 5).  
 314



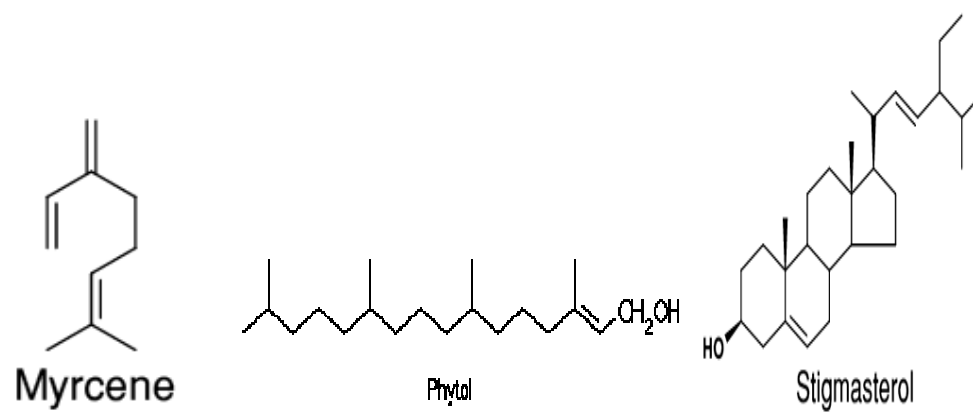
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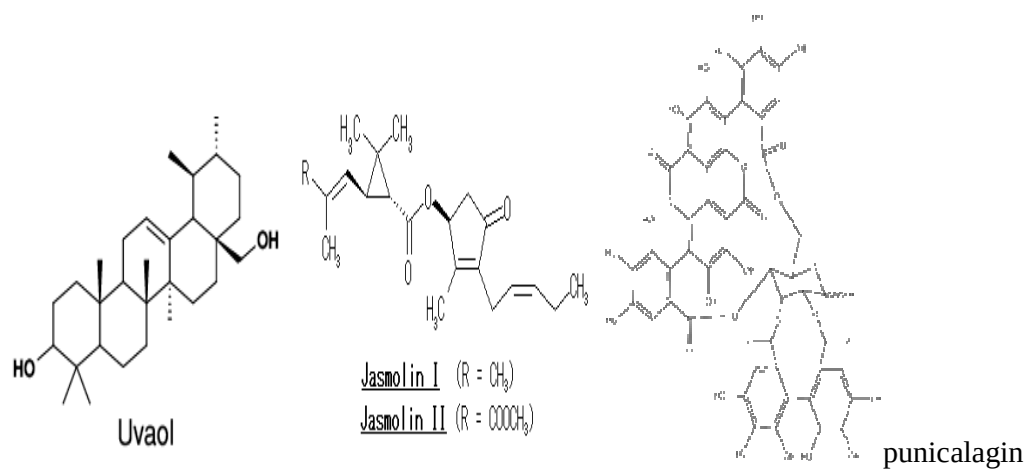
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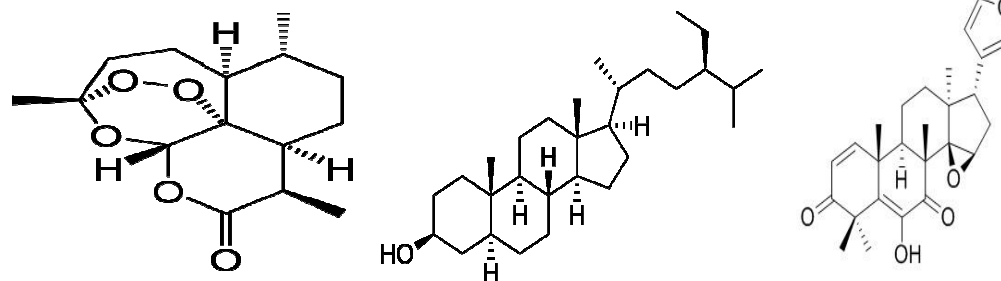


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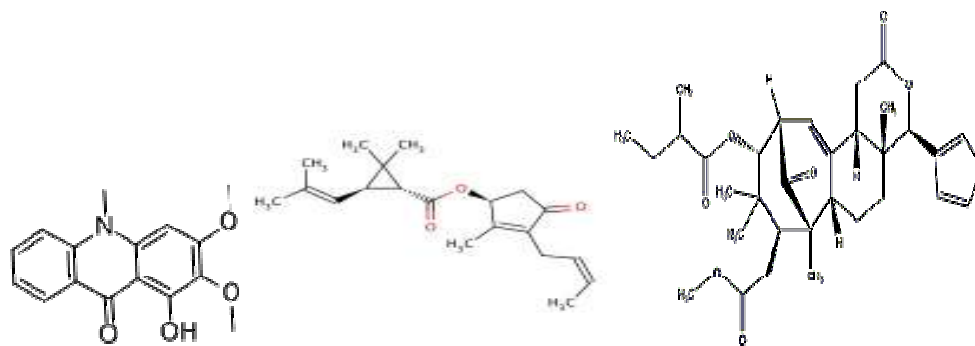
327

328 Artemisinin Stigmastanol Cedrelone



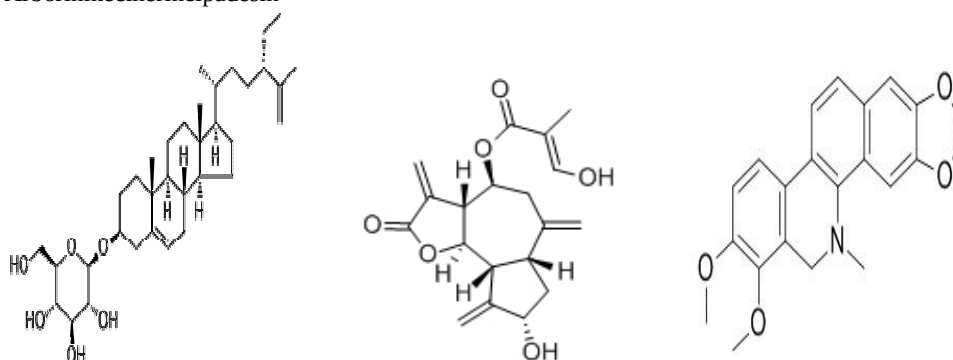
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330 Arborinine cinerincipadesin



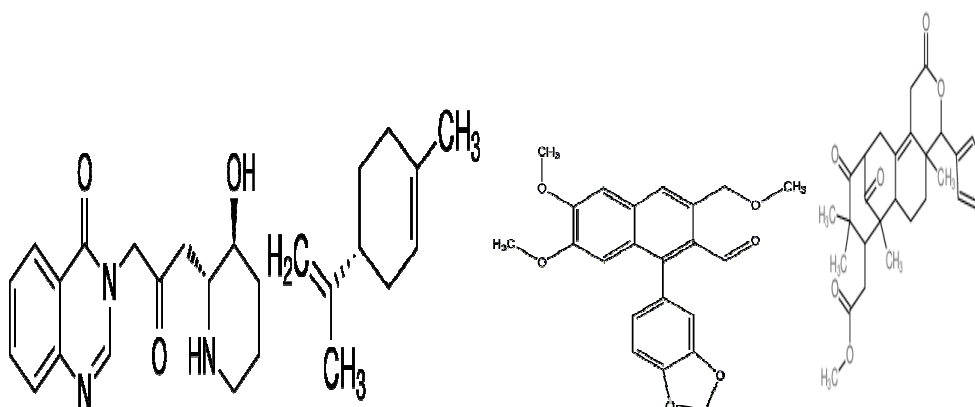
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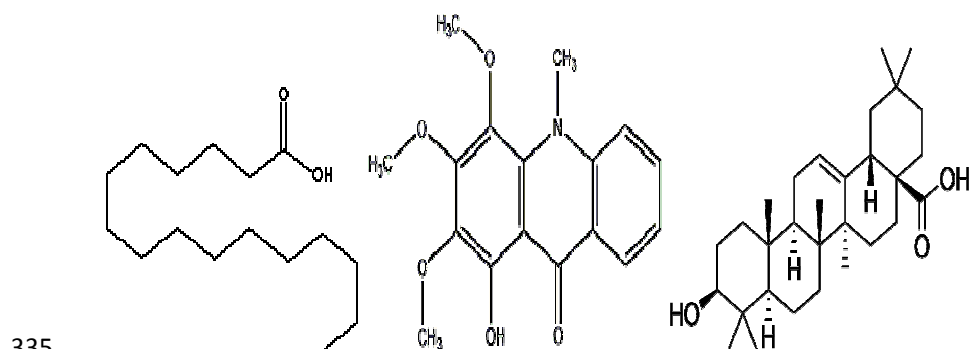
332 Clerosterol cynaropicrin Dihydrochelerythrine



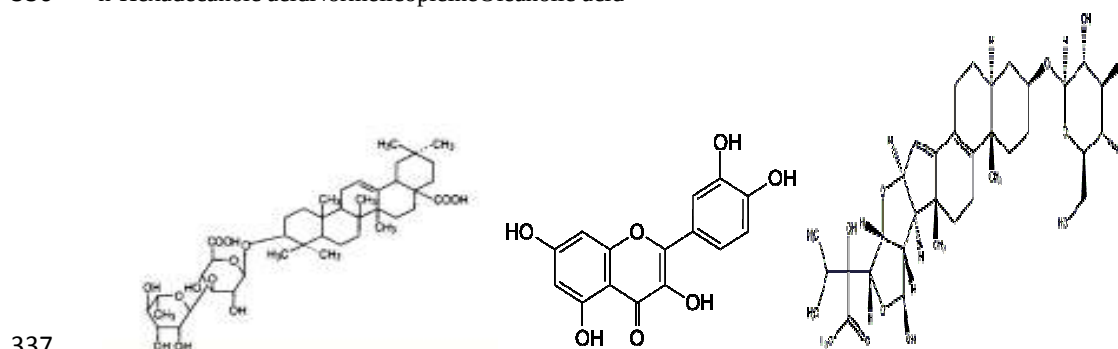
333

334 Febrifugin limonene Lucidamine Amexicanolide



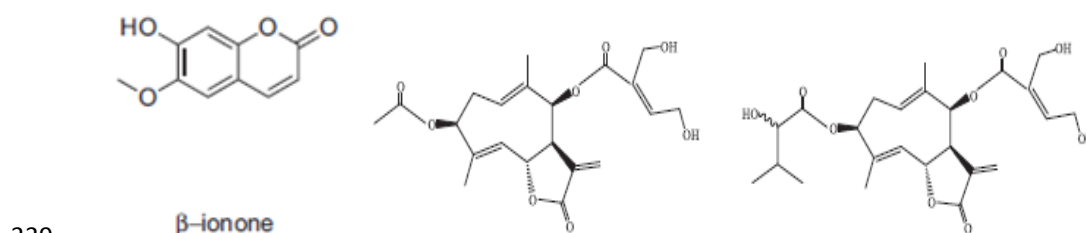


336 n-Hexadecanoic acid Normelicopicine Oleanolic acid



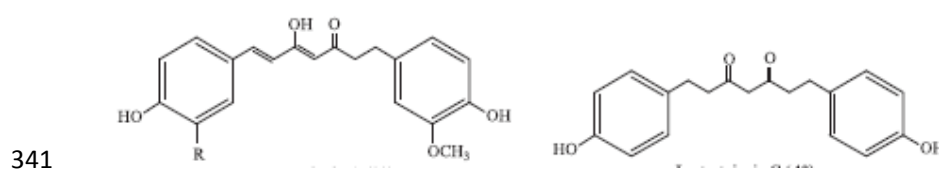
337 putranoside

338 Aquercetin vernoguinoside

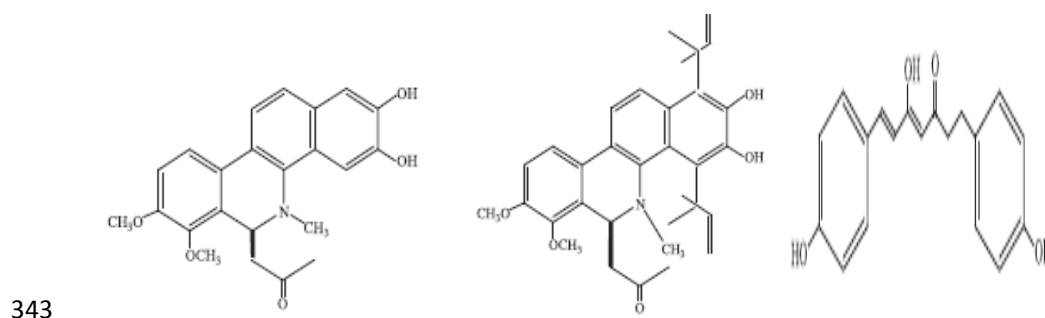


339  $\beta$ -ionone

340 schkuhrin Ischkuhrin II

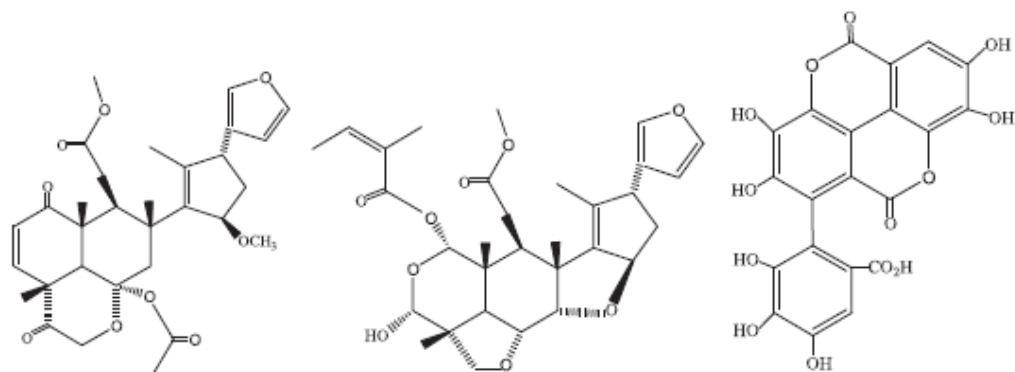


342 Letestuianin A (R= H) Letestuianin B (R= OCH<sub>3</sub>) Letestuianin C



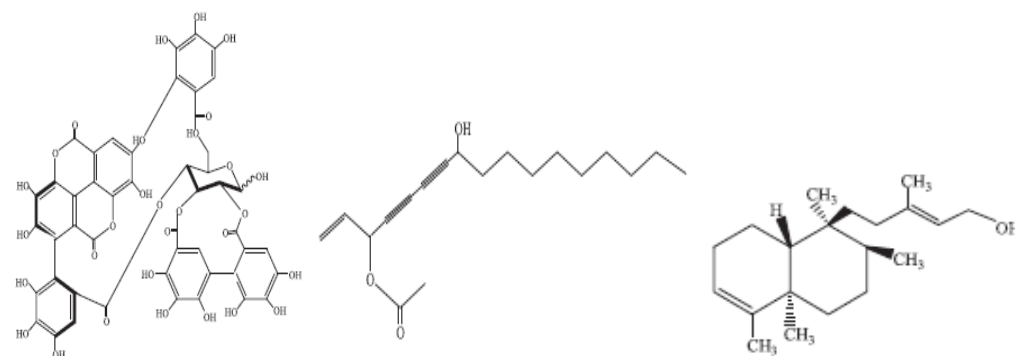
344 Lucidamine A, Lucidamine B & (4Z,6E)-5-hydroxy-1,7-bis (4- hydroxyphenyl) hepta-4,6- dien-3-one

345



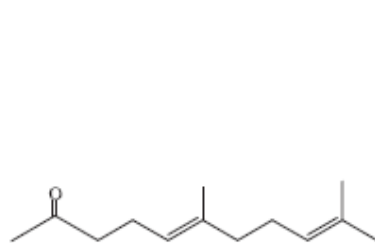
346 7-acetyl-15-methoxy-29-methylene-7,15-deoxonimbolide. 2-oxo-3-deacetyl salannin. Flavogallonic acid

347

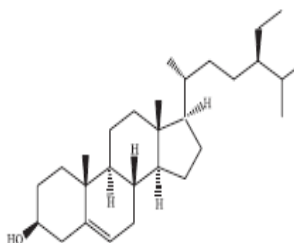


348 Terchebulin 8-hydroxyheptadeca-4,6-diyne-3ylacetate Kolavenol

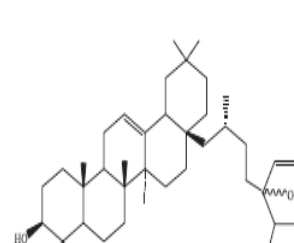
349



350 Geranylacetone

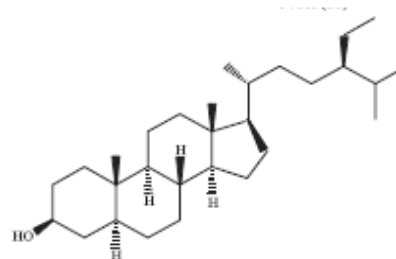


Beta sitosterol

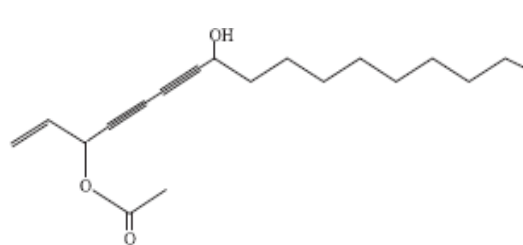


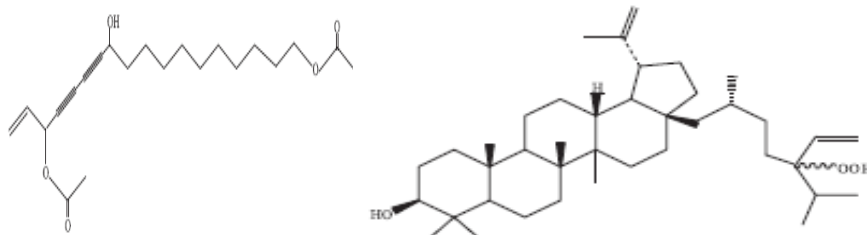
Saringosterol

351



352 Stigmasterol 8-hydroxyheptadeca-1-ene-4,6-diyne-2ylacetate





353

354 16-acetoxy-11-hydroxy octadeca-17-ene-12,14-diynyl acetate. 24-hydroperoxy-24- vinylcholesterol

355 **Figure 2:**Structures of isolated bioactive anti-trypanosomal compounds from African  
356 natural products

### 357 African Herbal Formula (AFH)

358 A herbal mixture of herbs code named African Herbal Formula (AFH) has been applied  
359 by members of the family and close-associates for all kinds of health problems and it is  
360 very popular among the low socio-economic class. The influence of these Herbal  
361 Formula on the haematological parameters of trypanosome infected rats were  
362 investigated. Observations showed that the formula has an effect on the haemopoietic  
363 system manifested by a positive increase in the levels of haemoglobin, packed cell  
364 volume and red blood cell while the white blood cell and lymphocyte levels were  
365 decreased. AHF also delayed the proliferation of the parasites and improved the level of  
366 the characteristic weight loss associated with trypanosomiasis (Okpuzor *et al.*,  
367 2003). This suggests that the Herbal Formula must have possibly combated the parasite  
368 directly without demanding further production of the effectors cells of the immune  
369 system

370

### 371 Jobelyn®, (herbal preparation)

372 Jobelyn®, manufactured by Health Forever Products Ltd, Lagos, Nigeria, is a  
373 commercial herbal preparation that recently made its way into the herbal medicine  
374 market in Nigeria. It is available as a powdered preparation formulated into capsules  
375 and suspension and contains iron, protein, fat, carbohydrates, tannins,  
376 saponins, *Sorghum bicolor* or Sorghum (family: Gramineae). A study was carried out to  
377 determine the effect of this herbal preparation on packed cell volume (PCV) and  
378 haemoglobin (Hb) concentrations in anaemic rabbits. The PCV and Hb concentrations  
379 of healthy rabbits infected with *T. brucei brucei* were monitored for 49 days. *T. b.*  
380 *brucei* produced a significant reduction in PCV and Hb concentrations in all infected  
381 rabbits when compared with the controls ( $p < 0.05$ ). These hematological parameters  
382 were restored to normal levels in the anaemic rabbits by the herbal preparation. The  
383 anaemic rabbits not treated with the herbal preparation presented with a progressive  
384 decline in their PCV and Hb concentrations and majority of them died before the end of  
385 the study (Patrick *et al.*, 2003).

### 386 *Artemisia herba-alba*

387 *Artemisia herba-alba* commonly known as white wormwood or desert wormwood  
388 chloroform extracts of *Artemisia herba-alba* when administered to  
389 *Trypanosoma evansi* infected rabbits causes significant reduction in parasitaemia count  
390 and significantly ameliorated the parasite induced alteration in haematological (PCV,  
391 Hb, RBCs and WBC) and biochemical values (ALT, ALP and AST) comparable to  
392 normal (uninfected) rabbits thereby confirming their antiparasitic properties (Awad *et*  
393 *al.*, 2013).

394 Fathy et al., 2013 evaluated the anti-trypanosomal efficacy of crude ethanolic extracts  
 395 (CEE) of the aerial parts of *Artemisia herba alba* against *Trypanosoma evansi* infection  
 396 The results indicated significant difference ( $p < 0.05$ ) in the context of reduction in the  
 397 extent of clinical signs, low levels of parasitaemia and mortality pattern in animals  
 398 received crude ethanolic extracts (CEE) of *Artemisia herba alba* compared to those  
 399 served as negative group. The extract also increases the PCV of infected animals  
 400 compare to untreated control. There was no statistically significant difference in almost  
 401 all investigated parameters between standard group (positive control) and treatment  
 402 group. It is concluded that CEE of *A. herba-alba* and Berenil® showed relatively  
 403 aparasitaemia and normal heamatologic values in the infected rabbits, thereby  
 404 confirming their antiparasitic properties.

#### 405 **Black seed oil (*Nigella sativa* oil)**

406 The effect of black seed oil (*Nigella sativa* oil) on parasitaemia, haematological and  
 407 biochemical parameters in *Trypanosoma brucei*-infected rats was investigated. The seed  
 408 oil results in low parasitaemia load and also prolong life span of the infected rats from  
 409 12 days of the infected untreated (control) rats to 22 days for the infected black seed oil-  
 410 treated rats. The seed oil also causes significant increases in haematological (Hb, PCV,  
 411 RBC, WBC and platelet counts) and some serum biomarker enzyme (Serum ALP, AST  
 412 and ALP) with decreases in the liver enzyme activities. Protein concentrations show  
 413 significant decreases in the serum and increases in the liver when compared with the  
 414 infected untreated. The black seed oil has probably stimulate the host immune system to  
 415 control parasite proliferation thereby making it a possible agent for managing African  
 416 sleeping sickness despite possible gradual damage to host organs as shown by increases  
 417 in some serum enzymes.

#### 418 ***Camellia sinensis***

419 Green tea, the dried leaf of *Camellia sinensis*, contains a variety of biologically active  
 420 compounds such as polyphenols, methylxanthines, essential oils, proteins, vitamins, and  
 421 amino acids (Yamamoto 1997). The purified compounds from ethyl acetate fraction of  
 422 *Camellia sinensis* green tea leaves, lysed more than 50% of the parasites present in  
 423 the blood of infected BALB/c mice at concentrations as low as 0.12 to 85  $\mu\text{M}$ . The most  
 424 active compounds were gallic acid, epigallocatechin gallate and epigallocatechin gallate. The number  
 425 of amastigotes in infected Vero cells decreased by 50% in the presence of each of these  
 426 compounds at 100  $\text{nM}$ . The activity of recombinant arginine kinase, a key enzyme in the  
 427 energy metabolism of the parasite was inhibited by about 50% by nanomolar  
 428 concentrations of catechin gallate or gallic acid (Cristina et al., 2004).

#### 429 ***Cissus multistriata***

430 *Cissus multistriata* belongs to the family of plant known as *Vitaceae*. Methanolic leaf  
 431 extracts, of *Saba florida* (Benth) when administered to *T. brucei* infected rat at a dose of  
 432 200 and 400  $\text{mg/kg}$  b.w produce significant improvements of packed cell volume (PCV),  
 433 red blood cell counts (RBC) and increase in total serum protein when compared to  
 434 untreated group (Omale and Joseph, 2011). The nutritional composition of this leaf  
 435 extract (Omale and Omajal, 2011) may be responsible for this observation as it has been  
 436 reported to be used in the management of protein deficiency disease in children.

#### 437 ***Piper nigrum* (black pepper)**

438 *P. nigrum* is a famous spice King. Traditionally, *P. nigrum* fruits have been used in the  
 439 treatment and prevention of diarrhoea, large intestine toxins, asthma, respiratory  
 440 disorder, different gastric problems, cancer, fever, common cold and stomach disorder  
 441 (Scott et al., 2008). Methanolic extract (250-1000  $\mu\text{g mL}^{-1}$ ) of dried fruits of *Piper*  
 442 *nigrum* (Black pepper) were evaluated for its trypanocidal activities against  
 443 *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<sup>-1</sup>) 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<sup>-1</sup> of MPE, there was reduction of average mean trypanosomes count in extract. At 1000 µg ml<sup>-1</sup> 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 acetate, standard drug, were cytotoxic to Vero cells except at concentrations of 1.56-3.13 and 1.56-6.25 µg ml<sup>-1</sup> (Shaba *et al.*, 2012)

#### ***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 (Yusuf and Ekanem, 2010). According to Shittu and Tanimu (2010), 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.

#### ***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 (Sepide *et al.*, 2013) *in vivo* antitrypanosomal effect of methanolic extract of *Zingiber officinale* (ginger) in *Trypanosoma brucei brucei*-infected mice were evaluated at dose of at 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

#### **Anti-trypanosomal activity of insect and there products**

##### **Honey**

Honey is the sweet, viscous natural fluid produced by honeybees (*Apis mellifera*). Honey administered to *T. brucei* infected rat at dose of 3mg/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 trypanosomosis. However, the Increase in serum biochemical parameters suggest possible damage to organs where these maybe abundant (Ekanem, and Yusuf 2005).

In another study, Ekanem *et al.*, (2006), *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 a 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, 2007 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.

#### **Honey bee (*Apis mellifera*)**

The trypanocidal potentials of honey bee (*Apis mellifera*) extract was investigated against Trypanosome *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 (Shittu and Elekwechi, 2014).

#### **House flies (*Musca domestica*)**

Shittu and Bashir, (2014) evaluated the invivo anti-trypanosomal potential of crude methanolic extract of *Musca domestica* against *T. 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

#### **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 (Orhue *et al.*, 2009). 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 (Sülßen *et al.*, 2007). (ii) Interference with the redox balance of the parasites acting either on the respiratory chain or on the cellular defenses against oxidative stress (Nok, 2002). 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* (Nibret *et al.*, 2010), (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

## 1. 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.

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