

AFRICAN NATURAL PRODUCTS WITH POTENTIAL ANTITRYPANOSOMA PROPERTIES. A REVIEW

ABSTRACTS

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 represent 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. This review presents the profiles of natural product (plants and insect) with antitrypanosoma properties, reported in the literature. The profiles presented include information about the scientific name, family, methodology used, the degree of antitrypanosoma activity and the active agents. 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. It is clear that these review 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

Nature has presented to humanity the gift of biological and cultural diversity of natural product for healing practices. African traditional healing practices, is 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 on this planet (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).

Human African trypanosomiasis (HAT) also known as sleeping sickness is a fatal, fly-borne neuro-inflammatory disease caused by two germs (protozoa), *Trypanosoma brucei gambiense* which is responsible for chronic form of HAT in West and Central Africa, and *Trypanosoma brucei rhodesiense*, the etiological factor for the acute form of the disease in East Africa. 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 *Trypanosoma brucei*, *Trypanosoma evansi*, *Trypanosoma congolense* and *Trypanosoma vivax* (Mbaya *et al.*, 2009). The disease distributed over approximately 25million km² 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; *Trypanosoma brucei rhodesiense* and *Trypanosoma brucei gambiense* therefore new epidemics of this disease could appear (Seke and Mahomoodally, 2012).

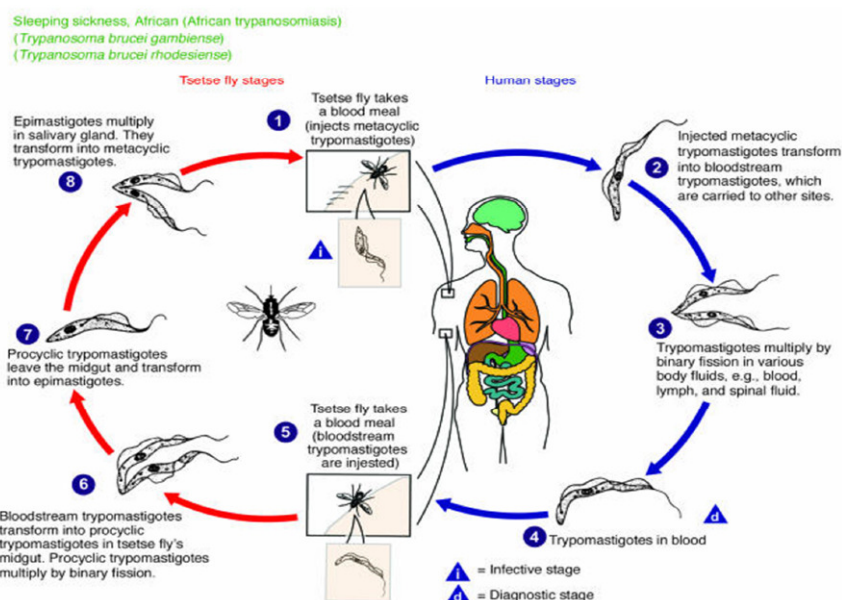
In this regards, the last few decades have witnessed a surfeit of investigations which have been geared to investigate the effect of common traditionally-used medicinal plants in alleviating the cellular changes *in vivo* produced during the *T. b. brucei* infections of animals. In Nigeria, a number of medicinal plants used in the traditional management of trypanosomiasis have been screened and showed both significant *in vitro* /*in vivo* antitrypanosomal activity. In addition to herbal plant, researchers (Ekanem and Yusuf, 2005, 2007; Shittu and Elekwuchi, 2014; Shittu and Bashir, 2014) targeted finding new antitrypanosomal agents to combat the trypanosomiasis by screening extracts from insect and their products.

At present, the available review on anti-trypanosomal agents focus only on medicinal plants (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/and *in vitro* antitrypanosomal 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 antitrypanosomal 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 these disease.

1.1 Life cycle of trypanosome

There are two stages in the life cycle of trypanosome is the tsetse fly stage and the human stage. The trypomastigote is the only form to be observed in the mammalian host, whereas the epimastigote form occurs during the development phase in the tsetsefly. During the entire life cycle, *T. brucei* cells multiply by binary fission and are considered to be exclusively extracellular (Yusuf, 2010).

99 Tsetse fly becomes infected by ingesting a blood meal that contains the trypanosome
100 form the infected host. In the gut of the fly the trypanosome transformed into procyclic
101 trypomastigote that divide for 10 days and then migrate to the salivary Gland and
102 transformed into epimastigote which later transformed into metacyclic trypanosome that
103 can infect a new host(Bashir, 2014). Infection of human host occur when a tsetse fly bite
104 human and transmit from it salivary gland the metacyclic stage (infection state) of the
105 trypanosome (metacyclic trypomastigote). These metacyclic stage quickly give way to a
106 blood borne stage that begin a series of binary fission division at the site of inoculation
107 and these process lead to the formation of primary chancre. The trypanosome enter the
108 bloodstream through the lymphatic and continue to multiply they also enter the C.N.S
109 (Bashir, 2014) details of the life cycle are shown in Figure 1 below.



110
111
112

Figure 1: The life cycle of *Trypanosoma brucei*
Source: Alexander and Melanie (2008)

113
114
115
116
117

2. Natural Product with Antitrypanosoma Properties

2.1 *Adamsonia digitata* (Baobab)

118 *Adamsonia digitata* (Baobab) is a deciduous long-lived tree belonging to the Malvaceae
119 family. It is native to arid central Africa distribution in most of sub-Sahara Africa's
120 semi-arid and sub-humid regions as well as in Western Madagascar. The different parts
121 of Baobab are widely used as foods, medicines and the bark fibres are also used (Sibibe
122 and Williams, 2002). The seed extract of *Adansonia digitata*(50-500mg/kg) was
123 investigated for in-vivo antitrypanosomal activity against *Trypanosoma brucei brucei*.
124 The seed extract at dose of 400mg/kg administered to the infected rats for 14 days
125 produce showed significant antitrypanosomal activity ($P<0.05$) compared with the
126 untreated control. 67% of the experimental animals survived for over 18 days with
127 300mg/kg up to 38 days. The authors concluded that *Adansonia digitata* has great
128 potential as anti-trypanosomal agent, which could be developed into an alternative drug
129 to complement treatment options for African trypanosomiasis (Hassan *et al.*, 2012).

2.2 *Acacia nilotica*

130

Among the Four medicinal plants (*Acacia nilotica*, *Bombax buonopozense*, *Terminalia avicennioides* and *Zanthoxylum zanthoxyloides*) traditionally used for treatment of sleeping sickness in Nupeland area of niger state that were investigated for *in vivo* antitrypanosomal activity. *Acacia nilotica* exhibited the most significant *invivo* antitrypanosomal effects at 200mg/kg the extract was able to clear the parasites from circulation within 6 days of treatment and prolong the survival period of up to 30 days. The authors suggested that methanol extracts of *Acacia nilotica* contain metabolites that are associated with antitrypanosomal effects and therefore, may be sources of new compounds that may be active against *T. b. brucei* (Mann *et al.*, *et al.*, 2011)

2.3 African Herbal Formula (AFH)

A herbal mixture of herbs code named African Herbal Formula (AFH) has been applied by members of the family and close-associates for all kinds of health problems and it is very popular among the low socio-economic class. The influence of these Herbal Formula on the haematological parameters of trypanosome infected rats were investigated. Observations showed that the formula has an effect on the haemopoietic system manifested by a positive increase in the levels of haemoglobin, packed cell volume and red blood cell while the white blood cell and lymphocyte levels were decreased. AHF also delayed the proliferation of the parasites and improved the level of the characteristic weight loss associated with trypanosomiasis (Okpuzor *et al.*, 2003).

2.4 *Allium sativum*

Recently the bulb of *Allium sativum* has been demonstrated to possess some trypanocidal activity both *invitro* and *invivo* in rabbits infected with trypanosome *brucei* (Ajagbonna *et al.*, 2002). Antitrypanosoma activities of methanolic extract of garlic (*Allium sativum*) against *T.brucei* infected rat were evaluated (Yusuf, 2010). The garlic (*Allium sativum*) extract was able to reduced parasitaemia and extension of life span from 8 days in the infected untreated (control) group to 17days. The extract also produce 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. While there were significant increase in serum and liver SOD of infected garlic treated when compared with infected untreated groups.

Effects of *Allium sativum* bulb extract in combination with diminazene aceturate on parasitemia and biochemical indices in *trypanosome brucei brucei* infection was evaluated. Sub therapeutic dose of *Allium sativum* at 20mg/kg/bw in combination with 1.7mg/kg/bw of diminazene aceturate caused a significant reduction ($P<0.05$) in parasitaemia count of *trypanosome brucei* infected rat. The treated mice also had their liver function enzymes towards normal, compare with control (untreated) (Peni *et al.*, 2012).

2.5 *Annona senegalensis*

Annona senegalensis Pers. (Annonaceae), commonly known as wild custard apple and locally called “Gwandar daji” in Hausa language, “Abo” in Yoruba, “Uburu ocha” in Ibo, is widespread in the Savannah region of Nigeria especially near streams. The plant decoction has been reported to be used traditionally in the treatment of sleeping sickness (Igwe, and Onabanjo, 1989) The antitrypanosomal potentials of *Annona senegalensis* (leaf) was also evaluated in a combination therapy with methanol extracts of *Annona senegalensis* (leaf) and *Eucalyptus camaldulensis* (leaf) against *T. b. brucei* - infected mice. The combined therapy at equal ratio (1:1) completely had parasites cleared from circulation two weeks into the treatment period and continued to survive for more than

three months. The weight of the surviving animal increased tremendously over the period and infectivity tests using blood and cerebrospinal fluid from the animal were negative because parasites never appeared in the circulation of sub-inoculated animals. It is concluded that the methanol extracts of the two plants, acting synergistically, possess appreciable potential for the development of drug combinations to overcome the problem of parasite resistance to conventional drugs (Kabiru *et al.*, 2012)

2.6 *Anthemis tinctoria*

Anthemis tinctoria L. is a perennial herb cultivated in Mediterranean countries, and several secondary metabolites have been identified in this species, such as volatile oils, triterpenes, polyacetylenes, and flavonoids (Ubik, 2005). In 2011, Nilza de Lucas *et al.*, investigated the antitrypanosomal effect of a crude extract, fractions, and a semi-purified subfraction rich in a mixture of isomeric labdane sesquiterpenes, obtained from flowers of *Anthemis tinctoria*, against *Trypanosoma cruzi*. In epimastigote forms, the aqueous crude extract, dichloromethane fraction, and semi-purified subfraction showed a dose-dependent inhibitory activity, with IC₅₀ of 2.3 µg/ml, 1.8 µg/ml, and 0.2 µg/ml, respectively. In the interaction index, the semi-purified subfraction showed a reduction in both the percentage of infected LLCMK2 cells and the mean number of amastigotes per infected cell. The cytotoxicity evaluation demonstrated that the cytotoxic concentrations of the semi-purified subfraction were higher for LLCMK2 cells than for the protozoans, with a selectivity index of 35.0. Epimastigote forms treated with the semi-purified subfraction showed ultrastructural and morphological alterations such as rounding of the cells and bleb formation in the flagellum and cytoplasmic membrane. These results show that the flowers from *A. tinctoria* may be a source of new drugs with antiprotozoal activity (Nilza de Lucas *et al.*, 2011)

2.7 *Artemisia absinthium*

Artemisia absinthium especially the leaf was also reported to possess promising antitrypanosomal activity. Methanolic *Artemisia absinthium* of the leaf was found to significantly reduce parasitaemia and helped improve body weight, PCV and survival of *Trypanosoma congolense* infected mice compared to the water-treated control ($P < 0.01$ in all cases). These effects were comparable to that with diminazene aceturate (Kifleyohannes *et al.*, 2014)

2.8 *Artemisia abyssinica*

The methanolic aerial parts extracts of *Artemisia abyssinica* at doses of 200 and 400 mg/kg body weight administered intraperitoneally daily for 7 days to *Trypanosoma congolense* infected mice reduced the parasitaemia ($p < 0.05$), ameliorated anaemia ($p < 0.05$), prevented body weight loss ($p < 0.05$). The study established that aerial parts of *A. abyssinica* have antitrypanosomal potential and can be considered a potential source of new drugs for the treatment of tropical diseases caused by trypanosomes (Teka *et al.*, 2014).

2.9 *Artemisia herba-alba*

Artemisia herba-alba commonly known as white wormwood or desert wormwood (Arabic name chih), is a greyish-strongly aromatic dwarf shrub native to the Northern Africa, Arabian Peninsula, South Western Europe, and Western Asia. This plant belongs to an important source of biological compounds for insecticides and fungicides, antibacterial, allelopathic products (Chauhan *et al.*, 2010). Chloroform extracts of *Artemisia herba-alba* when administered to *Trypanosoma evansi* infected rabbits causes significant reduction in parasitaemia count and significantly ameliorated the parasite induced alteration in haematological (PCV, Hb, RBCs and WBC) and biochemical values (ALT, ALP and AST) comparable to normal (uninfected) rabbits thereby confirming their antiparasitic properties (Awad *et al.*, 2013).

231 Fathy *et al.*, 2013 evaluated the antitrypanosomal efficacy of crude ethanolic extracts
232 (CEE) of the aerial parts of *Artemisia herba alba* against *Trypanosoma evansi* infection
233 The results indicated significant difference ($p<0.05$) in the context of reduction in the
234 extent of clinical signs, low levels of parasitaemia and mortality pattern in animals
235 received crude ethanolic extracts (CEE) of *Artemisia herba alba* compared to those
236 served as negative group. The extract also increases the PCV of infected animals
237 compare to untreated control. There was no statistically significant difference in almost
238 all investigated parameters between standard group (positive control) and treatment
239 group. It is concluded that CEE of *A. herba-alba* and Berenil® showed relatively
240 aparasitaemia and normal heamatologic values in the infected rabbits, thereby
241 confirming their antiparasitic properties.

242 2.10 *Artemisia maritima*

243 Ene *et al.*, (2014) evaluated the *in vitro* and *in vivo* antitrypanosomal activity of
244 petroleum ether, chloroform and methanol extracts of the whole plant of *Artemisia*
245 *maritima* against *Trypanosoma brucei brucei* in mice. There results show that all the
246 extracts showed trypanocidal activity against *T. brucei brucei* *in vitro* with the
247 petroleum ether extract showing the highest activity. The *in vivo* study revealed that
248 only the chloroform extract *A. maritima* exhibited antitrypanosomal activity. This
249 extract at a dose of 100mg/kg body weight significantly ($p<0.05$) reduced the
250 parasitemia in *T. brucei brucei* infected mice when compared with the other treatment
251 groups. The chloroform extract of *A. maritima* at this dose reduced the level of
252 parasitemia to 26% compared to the other treatment groups and the untreated control
253 group.

254 2.11 Black seed oil (*Nigella sativa* oil)

255 The effect of black seed oil (*Nigella sativa* oil) on parasitaemia, haematological and
256 biochemical parameters in *Trypanosoma brucei*-infected rats was investigated. The seed
257 oil results in low parasitaemia load and also prolong life span of the infected rats from
258 12 days of the infected untreated (control) rats to 22 days for the infected black seed oil-
259 treated rats. The seed oil also causes significant increases in haematological (Hb, PCV,
260 RBC, WBC and platelet counts) and some serum biomarker enzyme (Serum ALP, AST
261 and ALP) with decreases in the liver enzyme activities. Protein concentrations show
262 significant decreases in the serum and increases in the liver when compared with the
263 infected untreated. The authors however suggested that black seed oil has trypanocidal
264 properties and probably stimulate the host immune system to control parasite
265 proliferation thereby making it a possible agent for managing African sleeping sickness
266 despite possible gradual damage to host organs as shown by increases in some serum
267 enzymes.

268 2.12 *Bombax buonopozense*

269 Among the Four medicinal plants (*Acacia nilotica*, *Bombax buonopozense*, *Terminalia*
270 *avicennioides* and *Zanthoxylum zanthoxyloides*) traditionally used for treatment of
271 sleeping sickness in Nupeland area of niger state that were investigated for *in vivo*
272 antitrypanosomal activity. *Bombax buonopozense* exhibited the second most significant
273 *invivo* antitrypanosomal effects. At 300mg/kg the extract was able to clear the parasites
274 from circulation within 7 days of treatment and prolong the survival period of up to 30
275 days. The authors suggested that methanol extracts of *Acacia nilotica* contain
276 metabolites that are associated with antitrypanosomal effects and therefore, may be
277 sources of new compounds that may be active against *T. b. brucei* (Mann *et al.*, *et al.*,
278 2011)

279 2.13 *Boswellia diazelli*

280 Ethanolic stem bark of *Boswellia diazelli* was evaluated for its trypanocidal effect against
 281 *Trypanosoma brucei brucei* infected mice. The extract after 8 days of administration at
 282 a dose of 300 and 400 mg/kg completely cleared the parasite from circulation and
 283 extended the life span of the mice for more than 2 months. Sub-inoculation of the blood
 284 and cerebrospinal fluid drawn from the cured mice to healthy ones failed to produce any
 285 infection within 50 days post-inoculation (Garba *et al.*, 2014).

286 2.14 Brassica Oleracea (Cabbage)

287 Methanolic plant extracts (MPES) of *Brassica oleracea* (Brassicaceae) fruits and leaves
 288 at different concentrations (250-1000 µg/ml) were tested against *Trypanosoma evansi*
 289 on Vero cell line grown in Dulbecco's Modified Eagle Medium (DMEM) with foetal
 290 calf serum (FCS) (20-40%) at appropriate conditions. Both MPES of *B. oleracea* fruits
 291 and leaves demonstrated trypanocidal activity, which ranged from immobilization,
 292 reduction and to the killing of trypanosomes. At 500 µg/ml of MPES of *B. oleracea*
 293 fruits and leaves with trypanosomes undergoing incubation, there were marked
 294 reductions of trypanosomes (19.33±0.33) (15.33±0.33) in the corresponding ELISA
 295 plate wells. But at 1000 µg/ml of MPE of *B. oleracea* fruits, there was no complete
 296 killing of the trypanosomes (5.33±0.33) as to that of MPE of leaves where
 297 trypanosomes could not be detected at 7 h of incubation, which was statistically
 298 comparable to the standard drug, diminazine aceturate at concentration of 50 µg/ml at 4
 299 h of incubation (Shaba *et al.*, 2012)

300 2.15 Butyrospermum paradoxum

301 *Butyrospermum paradoxum*, is one of the plants whose extracts have been found useful
 302 in the traditional treatment of various diseases including animal and human
 303 trypanosomiasis in north-eastern Nigeria. The stem bark of *Butyrospermum paradoxum*
 304 when administered to *Trypanosoma congolense* and *Trypanosoma brucei* infected rat
 305 produced anti-trypanosomal effect through the complete suppression or delay in parasite
 306 establishment with reduction in the level of parasitaemia and the severity of the
 307 attendant disease as well as enhanced survival of the rats (Chukwunyeri *et al.*, 2007)

308 2.16 Camellia sinensis

309 Green tea, the dried leaf of *Camellia sinensis*, contains a variety of biologically active
 310 compounds such as polyphenols, methylxanthines, essential oils, proteins, vitamins, and
 311 amino acids (Yamamoto 1997). The purified compounds from ethyl acetate fraction of
 312 *Camellia sinensis* green tea leaves, lysed more than 50% of the parasites present in the
 313 blood of infected BALB/c mice at concentrations as low as 0.12 to 85 pM. The most
 314 active compounds were gallic acid, gallic acid gallate and epigallocatechin gallate. The number
 315 of amastigotes in infected Vero cells decreased by 50% in the presence of each of these
 316 compounds at 100 nM. The activity of recombinant arginine kinase, a key enzyme in the
 317 energy metabolism of the parasite was inhibited by about 50% by nanomolar
 318 concentrations of catechin gallate or gallic acid gallate (Cristina *et al.*, 2004).

319 2.17 Cissus multistriata

320 *Cissus multistriata* belongs to the family of plant known as Vitaceae. It is a climber
 321 found around the rivers especially the Niger basin. It is used in the management of
 322 protein deficiency disease in children. Methanolic leaf extracts, of *Saba florida* (Benth)
 323 when administered to *T. brucei* infected rat at a dose of 200 and 400 mg/kg b.w produce
 324 significant improvements of packed cell volume (PCV), red blood cell counts (RBC)
 325 and increase in total serum protein when compared to untreated group (Omole and
 326 Joseph, 2011)

327 2.18 Citrullus lanatus

328 *Citrullus lanatus* leaf aqueous extract shows a dose dependent decrease in parasitaemia
 329 count when administered to *Trypanosoma brucei* infected albino rats (BIU *et al.*, 2013)

330 2.19 *Citrus sinensis*

331 Essential oils (EOs) from *Citrus sinensis* (CS) were evaluated in vitro for activity
332 against *Trypanosoma brucei brucei* (Tbb) and *Trypanosoma evansi* (*T. evansi*). The
333 EOs were found to possess antitrypanosomal activity in vitro in a dose-dependent
334 pattern in a short period of time. The drop in number of parasite over time was achieved
335 doses of 0.4 g/ml, 0.2 g/mL, and 0.1 g/mL. The concentration of 0.4 g/mL *Citrus*
336 *sinensis* was more potent at 3 minutes and 2 minutes for Tbb and *T. evansi*, respectively
337 (Habila *et al.*, 2010).

338 2.20 *Crateva adansonii*

339 *Crateva adansonii* also known as sacred garlic pear, belongs to family Capparaceae is
340 widely use in traditional medicines for the treatment of ear infections, stomach troubles,
341 syphilis, jaundice and yellow fevers . According to John *et al.*,2012, crude hexane and
342 ethyl acetate extracts of *Crateva adansonii* exhibited moderate anti-trypanosomal
343 activity against *Trypanosoma brucei brucei* at Minimum Inhibitory Concentration
344 (MIC) of 12.5µg/ml).

345 2.21 *Cucumis metuliferus*

346 The antitrypanosomal efficacy of different doses of *Cucumis metuliferus* pulp was
347 investigated in rabbits. Parasitaemia level fluctuated and was kept low in all the treated
348 groups. The extract also significant increase PCV and body weight ($P < 0.05$), prolonge
349 the survival period to 47 days and alleviated hepatomegaly and splenomegaly that
350 were observed in untreated group. the authors suggested the use of *Cucumis*
351 *metuliferus* pulp for the management of *T. b. brucei* induced anaemia, weight loss,
352 hepatomegaly and splenomegaly (Abubakar *et al.*, 2011).

353 2.22 *Cymbopogon nardus*

354 *Cymbopogon nardus* belonging to the family Poaceae is known for its rich essential oil.
355 The bioactive constituents and bioactivity of *C. nardus* have been reported, including
356 antimicrobial insect repellent, anticancer, antiplasmodial and antioxidant (Cheel *et al.*
357 2005) activities. Out of a total of 119 plant species collected from different localities in
358 Malaysia that screened for *in vitro* antitrypanosomal activity against *Trypanosoma*
359 *brucei brucei* strain BS221. *Cymbopogon nardus* exhibited the most significant
360 antitrypanosomal activity with IC50 values $0.31 \pm 0.03 \mu\text{g mL}^{-1}$ (SI > 323) (Norhayati
361 *et al.*, 2013)

362 2.23 *Dissotis rotundifolia*

363 *Dissotis rotundifolia* is a medicinal plant which is widely used in Nupe ethnomedicine
364 for treatment of trypanosomiasis. According to mann *et al.*, (2009) crude extract of
365 *Dissotis rotundifolia* at dose of 800 mg/kg administered to *Trypanosoma b. brucei*
366 infected rat, cause significant reduction in level of parasitemia count compare to
367 untreated group. *In vitro* exposure of blood forms to high concentration (800 mg/kg)
368 crude extract test resulted in complete paralysis or killing within 45 s of exposure. This
369 finding show that *D. rotundifolia* may contain antitrypanosomal constituents

370 2.24 *Dyera costulata*

371 *Dyera costulata* is normally found in primary evergreen lowlands or on hills and can be
372 found in Peninsular Malaysia, south of Thailand, Sumatra, Borneo and the intervening
373 islands. The bark and leaves of *D. costula* have been traditionally used for treatment of
374 fever and inflammation (Subhadhirasakul *et al.* 2003). Out of a total of 119 plant species
375 collected from different localities in Malaysia that screened for *in vitro*
376 antitrypanosomal activity against *Trypanosoma brucei brucei* strain BS221. *Dyera*
377 *costulata* exhibited the most significant antitrypanosomal activity next to *Cymbopogon*
378 *nardus* ($0.31 \pm 0.03 \mu\text{g mL}^{-1}$ (SI > 323) with IC50 values of $0.58 \pm 0.01 \mu\text{g mL}^{-1}$.

379 These plants could be attractive candidates for treatment of sleeping sickness (Norhayati
380 *et al.*, 2013)

381 2.25 *Deterium senegalensis*

382 *Deterium senegalensis* (leaf), is a plant widely used as an anti poison in some local
383 communities in Nigeria. Aqueous extract of *Deterium senegalensis* when administered
384 to *Trypanosoma brucei brucei* Infected mice exhibited some antitrypanosomal activity
385 and prolong the survival of the mice to thirty two days post infection, The weight and
386 %PCV of animals in the aqueous group appreciated by 2.5 and 1.2 % respectively two
387 weeks into treatment after an initial decrease (Kabiru *et al.*, 2010)

388 2.26 *Eucalyptus camaldulensis*

389 *Eucalyptus camaldulensis* (Myrtaceae), is a tall, evergreen and magnificent trees
390 cultivated the world over for its oil, gum, pulp, timber, medicine and aesthetic value.
391 Essential oil found in its *Eucalyptus camaldulensis* is use extensively in food,
392 perfumery and pharmaceutical industry. In addition, the oil possesses a wide spectrum
393 of biological activity including anti-microbial, fungicidal, insecticidal/insect repellent,
394 herbicidal, acaricidal and nematocidal (Batish *et al.*, 2008). Antitrypanosomal activities
395 of leaves, stem and root barks of *Eucalyptus camaldulensis* were evaluated in
396 *Trypanosoma brucei brucei* infected mice doses. The extract werw administerd at dose
397 ranging from 200-600mg/kg body weight/day for 21 consecutive days. The methanol
398 extract of *E. camaldulensis* (leaf) produced complete cure for the animals in the
399 different dose groups and survived as long as those treated with the standard drug,
400 berenil. Sub inoculation of healthy mice with the blood and Cerebrospinal Fluid (CSF)
401 of the cured mice did not result in infection, thus indicating a complete and permanent
402 cure. Bioassay-guided fractionation of the crude methanol extract of *E. camaldulensis*
403 leaf gave 10 fractions, with only fractions 8 and 9 exhibiting minimal antitrypanosomal
404 activities that were not comparable to those of the crude extract. The authors concluded
405 that the methanol extract of *E. camaldulensis* (leaf) has immense potential for the
406 development of drugs against African trypanosomiasis (Kabiru *et al.*, 2013)

407 2.27 *Eucalyptus citriodora* (EC),

408 Essential oils (EOs) from *Eucalyptus citriodora* (EC), were evaluated in vitro for
409 activity against *Trypanosoma brucei brucei* (Tbb) and *Trypanosoma evansi* (*T. evansi*).
410 The EOs were found to possess antitrypanosomal activity in vitro in a dose-dependent
411 pattern in a short period of time. The drop in number of parasite over time was achieved
412 doses of 0.4 g/ml, 0.2 g/mL, and 0.1 g/mL. The concentration of 0.4 g/mL *Eucalyptus*
413 *citriodora* was more potent at 3 minutes and 2 minutes for Tbb and *T. evansi*,
414 respectively (Habila *et al.*, 2010).

415 2.28 *Eugenia uniflora*

416 *Eugenia uniflora* is often used as food and medicine in folk medicine due to
417 antimicrobial and other biological activities (Sharma *et al.*, 2006). Ethanolic extract
418 from *E. uniflora* was used to evaluate in vitro anti-epimastigote and cytotoxic activity.
419 the extract posses significant Antitrypanosoma activity with 50% of activity (EC50) at
420 concentration of 62.76 lg/mL. Minimum inhibitory concentration (MIC) was found to
421 be 61024 lg/ mL (Santos *et al.*, 2012)

422 2.29 *Faidherbia albida*

423 *Faidherbia albida* otherwise known as *Acacia albida* (Del) is of the family
424 Mimosoideae. It is native to Southwest Africa, through West, North Africa to Egypt and
425 East Africa. Common names include winter thorn and apple-ring acacia. The effect of
426 hydro-alcoholic extract of the stem bark of *Faidherbia albida* in rat infected with
427 *Trypanosoma brucei brucei* strain Lafia/CT/66/NITR was evaluated. There was
428 prolongation of life in the treated groups when compared to the negative control. The

administration of the extract led to a highly significant ($P<0.01$) increase in Total protein, albumin, and packed cell volume levels while the globulin and free fatty acid levels decreased significantly ($P<0.01$). It is suggested that the hydro-alcoholic extract of *F. albida* is trypanostatic and effective in the management of anaemia induced by *Trypanosoma brucei brucei* in rats (Tijani *et al.*, 2009).

2.30 *Gongronema latifolium*

Gongronema Latifolium belongs to the family of Asclepiadaceae. The plant is commonly known as Madumaro by Yoruba ethnic group in Nigeria, amaranth globe in English. The origin of the plant is traced to Nigeria in West Africa. It is a rainforest plant which has been traditionally used in the South Eastern part of Nigeria over the ages for the management of diseases such as diabetes, high blood pressure etc.

Gongronema latifolium has been reported to possess invitro activities but not invivo activities against *Trypanosoma congolense* infected mice (Abedo *et al.*, 2013). Methanolic stem bark of *Gongronema latifolium* at 10mg/ml completely ceased the motility of *Trypanosoma congolense* within 10 minutes. When administered to infected mice the extract did not produce any significant reduction in parasitaemia count and they all died by day 9th post treatment comparable with untreated control (Abedo *et al.*, 2013)

2.31 Honey

Honey is the sweet, viscous natural fluid produced by honeybees (*Apis mellifera*) using the nectar of flowers. In general, the composition of honey contains approximately 70-80% sugar, mainly from fructose and glucose. Water, minerals, vitamins, traces of protein, and other substances such as antioxidants make up the remainder. Ancient Egyptians, Assyrians, Chinese, Romans and Greeks have traditionally used honey as a medicinal remedy, for the management of wound healing, skin ailments and various gastrointestinal diseases. It has been reported as having antimicrobial properties (Adebolu, 2005) as well as therapeutic effects on internal and external ailments (Okeniyi, 2005)

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

479 haemoglobin, packed cell volume, red blood cell, white blood cell and platelets counts
480 was ameliorated when compared with the control ($p < 0.05$). There was a significant
481 decrease ($p < 0.05$) in liver gamma glutamyl transferase in infected untreated,
482 prophylactic and late stage treated group compared with the control groups. The authors
483 suggested that honey has ameliorative effects on symptoms and some biochemical
484 effects of *T. brucei* infections in rats.

485 2.32 Honey bee (*Apis mellifera*)

486 The trypanocidal potentials of honey bee (*Apis mellifera*) extract was investigated
487 against Trypanosome brucei brucei infected rat. The of honey bee extract significantly
488 reduced the parasitaemia count and extend the life span from 5 days of untreated to 10
489 and 15 days for prophylactic and early treated group. The extract also significantly
490 increase ($p < 0.05$) (HB, PCV, RBC and WBC) counts of infected treated groups when
491 compared with infected not treated group (Shittu and Elekwechi, 2014).

492 2.33 Hymenocardia acida

493 Oral administration of Hydro ethanolic extract of Hymenocardia acida stem bark at
494 doses of 100, 200 and 400 mg/kg body weight for 6 days significantly ($P > 0.05$)
495 reduced the level of parasitaemia and prolonged the life span of *T. brucei* infected rats
496 (Adakole and Chukwuka 2011).

497 2.34 Isolona hexaloba

498 Musuyu *et al.*, (2012) evaluated the antitrypanosoma and cytotoxic activity of the
499 aqueous extracts from 33 medicinal plants, used by traditional healers for the treatment
500 of various parasitic diseases in Congo. Out of the 33 medicinal plants *Isolona hexaloba*
501 stem bark exhibited the most significant inhibition on Trypanosoma b. brucei, with the
502 $IC_{50} = 1.95 \text{ } \mu\text{g/ml}$, $SI = 16.5$). The results can partly support and justify the traditional
503 use of some of these plant species for the treatment of parasitic diseases (Musuyu *et al.*,
504 2012)

505 2.35 Jobelyn®, (herbal preparation)

506 Jobelyn®, manufactured by Health Forever Products Ltd, Lagos, Nigeria, is a
507 commercial herbal preparation that recently made its way into the herbal medicine
508 market in Nigeria. It is available as a powdered preparation formulated into capsules
509 and suspension and contains iron, protein, fat, carbohydrates, tannins, saponins.,
510 *Sorghum bicolor* or Sorghum (family: Gramineae) is an important staple food crop in
511 Africa, South Asia, and Central America, and is also grown in some developed nations
512 for animal feed (ICRISAT, 1993). A study was carried out to determine the effect of
513 these herbal preparation on packed cell volume (PCV) and haemoglobin (Hb)
514 concentrations in anaemic rabbits. The PCV and Hb concentrations of healthy rabbits
515 infected with *Trypanosoma brucei brucei* were monitored for 49 days. *T. b. brucei*
516 produced a significant reduction in PCV and Hb concentrations in all infected rabbits
517 when compared with the controls ($p < 0.05$). These hematological parameters were
518 restored to normal levels in the anaemic rabbits by the herbal preparation. The anaemic
519 rabbits not treated with the herbal preparation presented with a progressive decline in
520 their PCV and Hb concentrations and majority of them died before the end of the study
521 (Patrick *et al.*, 2003).

522 2.36 Keetia leucantha

523 Keetia leucantha is a West African tree used in traditional medicine to treat parasitic
524 diseases. The dichloromethane extract of leaves of *K. leucantha* was previously shown to
525 have in vitro antitrypanosomal activity ($IC_{50} = 24.4 \text{ } \mu\text{g/ml}$ on *Trypanosoma brucei*
526 *brucei*) with a good selectivity ($SI = 2.7$) (Bero *et al.* 2011).

527 In another study, (Bero *et al.*, 2013), essential oil from Keetia leucantha and three
528 triterpenic acids were evaluated for their antitrypanosomal activity on Trypanosoma

brucei brucei bloodstream forms (Tbb BSF) and procyclic forms (Tbb PF) to identify an activity on the glycolytic process of trypanosomes. The oil showed an IC₅₀ of 20.9ug/ml on Tbb BSF and no activity was observed on Tbb PF. The best antitrypanosomal activity was observed for ursolic acid with IC₅₀ of 2.5 and 6.5 ug/ml respectively on Tbb BSF and Tbb PF. The inhibitory activity on a glycolytic enzyme of *T. brucei*, glyceraldehyde-3-phosphate dehydrogenase (GAPDH), was also evaluated for betulinic acid, oleanolic acid, ursolic acid, phytol, α -ionone and β -ionone. The three triterpenic acids and β -ionone showed inhibitory activities on GAPDH with oleanolic acid being the most active with an inhibition of 72.63% at 20ug/ml (Bero *et al.*, 2013)

2.37 *Khaya senegalensis*

Khaya senegalensis, locally known as Mahogany it is one of the most economically important forest tree species. That is widely distributed in east, central and West Africa subregions. The plant is commonly used by the Nupes of Niger State of Nigeria and some other parts of Africa in curing human trypanosomal infections. In an vitro and in vivo study conducted by (Bulus and Addau, 2013) to compare the antitrypanosoma activities of methanolic extracts stems of *Khaya senegalensis* and *Moringa oleifera* on *Trypanosoma brucei brucei*. The *Trypanosoma brucei brucei* was incubated in the presence of various extract concentrations in a 96-well microtitre plate against negative and drug controls. The stem extract of *Khaya senegalensis* and *Moringa oleifera* stem extract gave the highest and the least in vitro activities with per cent drop in parasite population of 43.76 and 29.46 respectively. The in vitro results compared well with that of Diminazine Aceturate, a standard trypanocides employed in the control well. Intraperitoneal treatment of *T. brucei brucei*-infected mice using these stem extracts at 200 mg/kg b.w. revealed complete elimination of the parasite from blood circulation in *Moringa oleifera* -treated animals and suppression of parasitaemia in *Khaya senegalensis*-treated group (Bulus and Addau, 2013). According to Atawodi *et al.*, 2003. Methanol extracts from *Khaya senegalensis* at dose of 4 mg/ml, 0.4 mg/ml and 0.04 mg/ml show a strong trypanocidal activities *in vitro* against *Trypanosoma brucei brucei* and *Trypanosoma congolense* (Atawodi *et al.*, 2003)

2.38 *Kigelia africana*

Peter *et al.*, 2009 evaluated the *in vivo* antitrypanosoma activities of *Kigelia africana*, and the results show that the dichloromethane fruits extract of *K. africana* tested at a dose of 2000 mg/kg was effective, curing 60% of the Swiss white mice that had previously been inoculated with *T. b. rhodesiense* KETRI 3798 (Peter *et al.*, 2009).

2.39 *Lawsonia inermis* (Henna)

Lawsonia inermis (Henna) is a member of the family Lythraceae it is generally considered as a native of Africa and Asia and its widely cultivated in tropical regions of the world in Sudan, Egypt, China, and India. Henna has been used cosmetically and medicinally for over 9,000 years. The leaves, flowers, seeds, stem bark and roots are used in traditional medicine to treat a variety of ailments as rheumatoid arthritis, headache, ulcers, diarrhoea, leprosyfever, leucorrhoea, diabetes, cardiac disease, hepatoprotective and colouring agent (Chetty, 2008). Crude Methanolic extract of leaf of *L. inermis* showed *invitro* activity against *Trypanosoma brucei* at concentration of 8.3 mg/ml of blood in mice but not *in-vivo*. The treatment tends to ameliorate the disease condition, but did not affect the level of parasitaemia and pack cell volume (Wurochekke *et al.*, 2004)

2.40 *Mitragyna ciliata*

The trypanocidal activity of Butanol fractions of hydroethanolic root extract of *Mitragyna ciliata* in rats infected with *Trypanosoma brucei* field isolates from a cow was evaluated (Ogbunugafor *et al.*, 2007). the fraction at a dose of 100 mg/kg for 5 days (10 days post-infection) showed trypanocidal activity with inhibition percent of 68.68. The extract also cause significant changes in the activities of oxidative stress enzymes; superoxide dismutase (SOD) and catalase compared to untreated control. The author suggested that Butanol fraction of *Mitragyna ciliata* might have affected the redox equilibrium of the infected animals causing oxidative stress to the parasites. This is the basis of inhibition of growth of the parasites by the butanol fraction

2.41 *Morinda lucida*

Morinda lucida Benth. (Rubiaceae) is a medicinal plant. The Igbos of South Eastern Nigeria call it '*nfi*'. The leaves are very bitter and are used by the natives to treat malaria, induce purgation, emesis and diuresis (Anaga, 2003). Three fractions obtained from Bioassay-guided fractionation of the crude methanol extract of *Morinda lucida* was tested for anti-trypanosomal activity using *in vitro* cultures of *Trypanosoma brucei* *brucei* S427. The three fractions exhibited good Antitrypanosoma effect with minimum inhibitory concentration (MIC) values of 6.25, 25 and 12.5 µg/ml, respectively (Nwakaego *et al.* 2012).

2.42 *Morinda morindiodes*

Aqueous extracts of the root bark of *Morinda morindiodes* were investigated for antitrypanosomal activities in an established *Trypanosoma brucei brucei* infected rat. The plant extract at 400mg/kg body weight for 7 days produce significant reduction in parasitaemia ($P < 0.05$) on the 3rd day of treatment but parasitaemia later increased till survival time and increase the mean survival time (12.6 ± 0.7) days compare to (10.00 ± 0.4) untreated control. The result may probably suggest reduction in parasite virulence by *Morinda morindiodes* root bark extract (Olukunle, *et al.*, 2010).

2.43 *Mangifera indica*

Methanolic mango leaves extract produce significant dose dependent ameliorative effect on in the PCV, HB, WBC count and prolonge the survival days of *Trypanosoma congolense* infected rat when compared with the control group (Oyebanji, 2010).

2.44 *Moringa oleifera*

The effect of aqueous extract of *Moringa oleifera* leaves on the haematological parameters of *Trypanosoma brucei*-infected rats was investigated. Results show that the extract of *Moringa oleifera* leaves significantly reduced the parasite replication the extract also has an effect on the haemopoietic system manifested by a positive increase in the levels of haemoglobin, packed cell volume and red blood cell compare to untreated control (Edoga *et al.*, 2013)

2.45 *Musca domestica*

Shittu and Bashir, (2014) evaluated the invivo anti-trypanosomal potential of crude methanolic extract of *Musca domestica* against *Trypanosoma brucei brucei* infected rats. Results showed that the methanolic extract of *Musca domestica* reduced the level of parasite replication by 26% and 49% and extend the lifespan from day 5 of the infected untreated to 7 and 11 days prophylactic and early treated respectively. The extract also results in significant decrease in antioxidant enzyme (Serum superoxide dismutase) compared to infected not treated group

2.46 *Ocimum gratissimum*

Different parts of *Ocimum gratissimum* Linn are largely used in folk medicine for the treatment of many diseases, some of which related to parasitological infections. The *in vitro* antitrypanosomal activities of essential oils and crude extracts from leaves, stems and seeds of *Ocimum gratissimum* was evaluated in pre and full flowering stages. The best

growth inhibition of *Trypanosoma brucei brucei* was observed with ethanol crude extracts of leaves ($IC_{50}=1.6670.48 \mu\text{g/mL}$) and seeds ($IC_{50}=1.29\pm0.42\mu\text{g/mL}$) in full flowering stage with good selectivity (SI_{410}). The oil contained some minor compounds such as myrcene ($IC_{50}=2.24\pm0.27 \mu\text{g/mL}$), citronellal ($IC_{50}=2.76\pm1.55\mu\text{g/mL}$), limonene ($IC_{50}=4.24\pm2.27\mu\text{g/mL}$), with good antitrypanosomal activities (B  n  dicta *et al.*, 2014)

2.47 *Picralima nitida*

Picralima nitida is a member of Apocynaceae family. The plant is popularly used in West Africa as an antipyretic and ant malarial (Herbert WJ, Lumsden, 1976). In a study design by Ene *et al.*, 2014 to evaluate *in vitro* and *in vivo* activity of methanol and aqueous extracts of the leaves, fruits, seeds, stem bark and roots of *Picralima nitida* against *Trypanosoma brucei brucei* in Swiss albino mice. The methanol extracts showed appreciably high *in vitro* and *in vivo* antitrypanosomal activities compared to the aqueous extracts of the plant. The methanol extract of the root exhibited the highest *in vitro* antitrypanosomal activity followed by the methanol extract of seed of *Picralima nitida*. Motility of *Trypanosoma brucei brucei* was stopped by the methanol extract of the root after 10 min, while the methanol extract of the seed of *Picralima nitida* stopped the motility of *Trypanosoma brucei brucei* at 15 min. The methanol extract of the root of *Picralima nitida* showed the highest *in vivo* antitrypanosomal activity at 100 mg/kg body weight. The extract cleared the parasite completely from the *T. brucei brucei* infected Swiss albino mice after day 3 of treatment (Ene *et al.*, 2014).

2.48 *Piper nigrum* l (black pepper)

P. nigrum is a famous spice King. Traditionally, *P. nigrum* fruits have been used in the treatment and prevention of diarrhoea, large intestine toxins, asthma, respiratory disorder, different gastric problems, cancer, fever, common cold and stomach disorder (Scott *et al.*, 2008). Methanolic extract (250-1000 $\mu\text{g ml}^{-1}$) of dried fruits of *Piper nigrum* (Black pepper) were evaluated for its trypanocidal activities against *Trypanosoma evansi* using Vero cells grown in Dulbecco's Modified Eagle Medium (DMEM) and supplemented with foetal calf serum (FCS) 20-40% at appropriate conditions. *In vitro* cytotoxicity test of *P. nigrum* fruits extract at concentrations (1.56-100 $\mu\text{g ml}^{-1}$) was done on Vero cells but without FCS. *In vitro* trypanocidal activity varied from immobilization, reduction and to the killing of trypanosomes in corresponding ELISA plate wells. At 750 $\mu\text{g ml}^{-1}$ of MPE, there was reduction of average mean trypanosomes count in extract. At 1000 $\mu\text{g ml}^{-1}$ of the test extract of *P. Nigrum*, there was complete killing of trypanosomes at 7 h of incubation. Trypanosomes counts decreased in concentration and time –dependent manner with MPE of *P. nigrum* and diminazine aceturate, standard drug, were cytotoxic to Vero cells except at concentrations of 1.56-3.13 and 1.56-6.25 $\mu\text{g ml}^{-1}$ (Shaba *et al.*, 2012)

2.49 *Prosopis africana*

Prosopis africana also known as African mesquite, belongs to the family, *mimosaceae* (Leguminosaceae). In different Nigerian languages it called kiriya (Hausa), kofi (Fulani), sanchi lati (Nupe), kpaye (Tiv), ayan (Yoruba), ubwa (Igbo) and ukpehie (Igala). It is very popular for its seeds, which in fermented form, is used as a food condiment (Omafuvbe *et al.*, 1999)

Petroleum ether, chloroform, methanol and aqueous extracts, obtained by cold extraction from the leaves, stem bark and roots of *Prosopis africana* showed strong *in vitro* anti-trypanosomal activity at 2 and 4 mg/ml, but *in vivo* only the methanolic extract of the leaves displayed the most promising anti-trypanosomal effect at 200 mg/kg dose (Atawodi and Funmi 2009).

2.50 *Psidium guajava* (guava)

Ethanollic extracts prepared from the leaves of *Psidium guajava* were evaluated for anti-trypanosoma and cytotoxicity activity in the bloodstream species of *Trypanosoma brucei brucei* (BS427) and HEK293 in 384-well Alamar Blue assays respectively. The results show that the extracts inhibited growth of *T. b. brucei* with an IC50 of 6.3 µg/mL and 48.9 µg/mL for 80% and 20% ethanollic preparations respectively, with corresponding activity of less than 50% against HEK293 at the highest screening dose of 238.10 µg/mL. The estimated selectivity index of the extracts compares favourably with pentamidine and diminazene (Adeyemi *et al et al.*, 2011).

In another study, trypanocidal activity of the ethanollic leaf extract of *Psidium guajava* (guava) was investigated in rats infected with *Trypanosoma brucei brucei*. Results showed that the extract showed that the extract produce a low to absolute zero parasitaemia and prolong the life span of mice to 32 days compared to untreated control which died on the 8th day (Adeyemi *et al.*, 2009). This result thus makes *P. guajava* leaf extract a probable agent for managing African sleeping sickness.

2.51 *Rapanea lancifolia*

Crude extracts of *Rapanea lancifolia* when evaluated for it *in vitro* activity against the trypomastigote forms of *Trypanosoma cruzi* showed significant activity (lysis % >50). The fractionation of an active extract from branches of *R. lancifolia* (99.5%) led to the isolation of two flavonoids: quercetin and taxifolin, which have weak trypanocidal activity (Ana *et al.*, 2010)

2.52 *Saba florida*

Saba florida (Benth) belongs to the family of *Apocynceae*. It grows on other trees in the riparian equatorial rain forest of Africa. The plant is very abundant in undisturbed forest coastal areas and around Great lake regions of Africa (Maundu *et al.*, 1999) hydromethanollic leaf extracts, of *Saba florida* (Benth) when administered to *T.brucei* infected rat at a dose of 200 and 400mg/kg b.w produce significant Improvements of packed cell volume (PCV), red blood cell count s (RBC) and increase in total serum protein when compared to untreated group

2.53 *Scoparia dulcis*

Scoparia dulcis was evaluated on the population of immune cells during a 28 day experimental *T. brucei* infection in rabbits. The result obtained showed that infection resulted in an initial rise in both total WBC and the absolute number of circulating lymphocytes followed by a progressive decrease in total WBC and all WBC subtypes (lymphocytes, monocytes and granulocytes), although the percentage of lymphocytes remained consistently higher than normal throughout the study period. These changes were consistent with the development of trypanosome-induced immunosuppression in their mammalian host and interestingly, treatment with *S. dulcis* at a daily oral dose of 25 mg/Kg body weight was found to significantly reduce the severity of the observed lesions when compared with untreated infected animals (Orhue *et al.*, 2009).

2.54 *Senna occidentalis*

Senna occidentalis (Linn.) (formerly *Cassia occidentalis*) is a weed of the leguminosae family, and is distributed throughout the tropical and subtropical regions of the world. The stem bark and leaf extract of *Senna occidentalis* is highly reputed for its numerous medicinal uses and is known to be used ethno-medicinally as remedy for several human and animal ailments. Ethanollic extract of leaves of *Senna occidentalis* (Fabaceae) was investigated for anti-trypanosomal activity, against *Trypanosoma brucei brucei* infected mice (Obboh *et al.*, 2013). The extracts were injected to the infected mice, at a dose 100 and 200mg/kg body weight respectively. There was a significant dose dependent reduction ($p<0.05$) in the parasite count with the mean values of 4 and 3.6 parasite per

725 microscope field observed in the dose of 100 and 200mg/kg body weight of extract
726 respectively compared with the positive control value of 8.75.

727 In another study, (Ibrahim *et al.*, 2010), the crude ethanol extract of *Senna occidentalis*
728 leaf exhibited an *in vitro* activity against *Trypanosoma brucei brucei* as it completely
729 eliminated parasites' motility within 10 minutes postincubation with 6.66 mg/ml of
730 effective extract concentration. The extract at dose 100 and 200 mg/kg body weight
731 significantly ($P < 0.05$) kept the parasitaemia lower than was recorded in the infected
732 untreated rats. The extract also significantly ($P < 0.05$) ameliorate the severity of the
733 parasite induced anemia, prevented the trypanosome-induced increase in biochemical
734 indices and significantly ($P < 0.05$) ameliorate hepatomegaly and splenomegaly
735 compare to untreated group (Ibrahim *et al.*, 2010). From all the above findings It is
736 suggested that orally administered ethanol extract of *S. occidentalis* leaf possessed anti-
737 *T. brucei brucei* activity and could ameliorate the disease-induced anemia and organ
738 damage.

739 2.55 Solanum lycocarpum

740 Martins *et al.*, (2012) investigated the possible trypanocidal activity of ethanolic extract
741 of the fruit of *S. lycocarpum*, six fractions obtained from this extract and the
742 glycoalkaloids isolated from one of these fractions.. The Citotoxicity Index (CI50) of
743 the fractions F1 (62.73 $\mu\text{g.ml}^{-1}$) and F2 (85.92 $\mu\text{g.ml}^{-1}$) demonstrated that both showed
744 tripanocidal activity. Interestingly, the isolated glycoalkaloids did not demonstrate any
745 potential trypanocidal effect as well as the other fractions. So, the fraction F1 presented
746 potential antitrypanosomal activity based on toxic effect against procyclic forms of *T.*
747 *brucei*.

748 2.56 Tapinanthus globiferus

749 *Tamianthus globeferus* (Family- Loranthaceae) known by other names as mistletoe
750 (English), Afomo onisana (Yoruba), Kauci Doruwa (Hausa) is a parasitic plant growing
751 on a large number of tree species such as Kola, Citrus, Combretum, Acacia, Aloe, Pakia
752 and Terminalia as host plants. It is wide spread and has been known to be very common
753 in North Central Namibia and the Tropical rainforest of Nigeria (Waterberg *et al.*,
754 1989).Extracts of *Tapinanthus globiferus* has been reported to possess suppressive and
755 curative effect against *Trypanosoma congolense* infected mice. The methanolic leaf
756 extracts of *Tapinanthus globiferus* administered to *Trypanosoma congolense* infected
757 mice (Abedo *et al.*, 2013) and *Trypanosoma brucei brucei* infected rats (Josephine *et al.*,
758 2013).at dose of 400mg/kg produce significant reduction in parasitaemia and extension
759 of life span up to the 24th day before they culminated in death. Result of The study also
760 showed that, the group inoculated with parasite and extract of *Tapinanthus globiferus*
761 simultaneously, did not develop parasitaemia while the experiment lasted (Abedo *et al.*,
762 2013).

763 2.57 Thymus vulgaris

764 *Thymus vulgaris* is an aromatic species of family Lamiaceae, it is highly demanded in
765 Africa for its medicinal, spice and cosmetics purposes. It is traditionally employed for the
766 treatments of cough and cold. It has been shown to have antimicrobial activity against
767 bacteria, virus, helminth, and fungi. Antitrypanosoma activities of *T. vulgaris* during
768 prophylactic and early stage of *T. brucei brucei* infection were investigated using a dose
769 of 500mg/kg body weight. There was a significant decrease in parasitaemia count of the
770 extract treated compared to untreated group. The result also shows significant increase
771 ($P < 0.05$) in packed cell volume (PCV), haemoglobin (Hb) and red blood cell (RBC)
772 count of infected prophylactic treated and infected early treated compared to infected
773 not treated rat. Therefore, this investigation showed that *T. vulgaris* has

antitrypanosomal potentials by ameliorating effect caused by *T. brucei* infection on some haematologicals parameters (Shittu *et al.*, 2013).

In another study, The extracts of the leaf parts of *Thymus vulgaris* (500mg/kg), were evaluated for antitrypanosoma properties against brucei in rat models. The extracts were found to reduce serum and liver aspartate transaminase (AST), alanine transaminase (ALT) compare to untreated group. infected early treated groups however show significant increase in the serum ALP activities while the liver ALP activity was significantly increased in prophylactic infected treated group compared to untreated group. The authors suggested that changes in the serum and liver specific activities of these biomarker enzymes may be due to interaction between infective condition and the constituents of the extracts. Hence, caution should be taken when using the extract for therapeutic purpose because it may also have some liver or tissue membrane damaging effect (Shittu *et al.*, 2013b).

2.58 *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, 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.

2.59 *Toona ciliata*

Toona ciliata is a large subtropical deciduous tree with a spreading crown, commonly attaining a height of 20-30 m and a girth of 1.8-3 m. Two antitrypanosomal terpenoids (1 and 2) were obtained from organic leaf extracts of *Toona ciliate* M. These compounds were found to exhibit strong antitrypanosomal activities against *Trypanosoma brucei rhodesiense* with MIC value ranges of 7.18 and 31.25 µg/ml. They were found to be more active than Cymerlarsan (a standard drug in the market), which had an MIC value of 187.5 µg/ml when tested against *T. b. rhodesiense*. Crude methanol extract and its chloroform fraction were found to be even more active with MIC values of 6.95 and 3.2 µg/ml respectively (Mercy *et al.*, 2011)

2.60 *Tridax procumbens*

Methanolic extract of *Tridax procumbens* when administered at dose of 100, 200, 300 and 400 mg/kg body weight for 14 days to *Trypanosoma brucei brucei* infected mice produce low parasitaemia resulting in the prolongation life of the entire extract treated animals. The group treated at 300mg/kg recorded highest prolongation of life by 28 days beyond that of untreated control. Similarly the weight loss suffered by the group treated at 300mg/kg was also minimal (6%). Thus *Tridax procumbens* has some potential which need to be exploited fully in the management of African trypanosomiasis (Abubakar *et al.*, 2010)

2.61 *Verbascum sinaiticum*

823 *Verbascum sinaiticum* belongs to the family Scrophulariaceae it is a biennial plant, 60-
824 150 cm tall commonly found in the tropical mountains. *Verbascum sinaiticum* is
825 traditional uses for wound treatment, stomachache viral infection, cancer
826 (Teklehaymanot, 2009); sun stroke fever, abdominal colic, diarrhea, hemorrhage,
827 anthrax, hepatitis (Yineger *et al.*, 2007). Moreover, powder of the leaves of *V.*
828 *sinaiticum* mixed with water is given orally (Fullas, 2010) or the filtrate is instilled into
829 left ear and nose (Weldegerim *et al.*, 2008) for treatment of animal trypanosomosis. The
830 *in vitro* antitrypanosoma activities of Aqueous and methanol leaf extracts of *V.*
831 *sinaiticum* against *Trypanosoma congolense* was carried out by monitoring test
832 concentrations of 4, 2, 1, 0.4 and 0.2 mg/ml for cessation or reduction in motility of
833 trypanosomes followed by monitoring for loss of infectivity to mice. An appreciable *in*
834 *vitro* activity was attained by the methanol extract of *V. sinaiticum* at 4 mg/ml
835 concentration. In general, the results obtained suggest ethnopharmacological usefulness
836 of the plant in managements of trypanosomiasis (Mergia *et al.*, 2014)

837 2.62 *Vernonia amygdalina*

838 *Vernonia amygdalina*, commonly known in Nigeria as “bitter leaf is a shrub or small
839 tree belonging to the family Asteraceae a very popular African vegetable which grows
840 in several parts of tropical and subtropical Africa. it has been reported to have multiple
841 health benefits such as anticancer (Sweeney *et al.*, 2005); anti-diabetic (Nwanjo, 2005),
842 antioxidant (Erasto *et al.*, 2007), antimicrobial (Ghamba *et al.*, 2014) and
843 antitrypanosomal (Wurochekke and Nok, 2004; (Yusuf *et al.*, 2012). The methanol
844 extract of *V. amygdalina* leaf at a dose of 300 mg/kg/day increased the maximum
845 survival days of *Trypanosoma brucei brucei* infected rats to 24 days compared to 8 days
846 for infected control. *V. amygdalina* leaf extract also significantly ($p < 0.05$) reduced the
847 parasitaemia and improved the packed cell volume of the infected rats. Similarly, it
848 significantly decreased ($p < 0.05$) the activities of alanine and aspartate
849 aminotransferases, urea, triglycerides and malondialdehyde levels; increased the levels
850 of reduced glutathione ($p < 0.05$), superoxide dismutase ($p < 0.05$) and catalase ($p >$
851 0.05) activities in serum, liver and kidney of *Trypanosoma brucei brucei* infected rats.
852 These suggest that the methanol extract of *V. amygdalina* leaf has ameliorative effects
853 and may therefore be useful in the management of trypanosomiasis (Yusuf *et al.*, 2012)

854 2.63 *Vernonia guineensis*

855 *Vernonia guineensis* Benth. (Asteraceae) is a small tree that grows in the savannah
856 region. The plant is used in Cameroon as an anthelmintic, an aphrodisiac, an antidote to
857 poison, and to treat malaria and jaundice (Iwu, 1993) Two bitter stigmastane
858 derivatives, vernoguinoesterol and vernoguinoside, have been isolated from the stem
859 bark of *Vernonia guineensis* these compounds exhibit trypanocidal activity when
860 tested against trypanosome isolates grown in blood forms in an HMI-18 medium
861 containing 20% fetal bovine serum (Alembert *et al.*, 2002)

862 2.64 *Waltheria indica*

863 The *in vitro* trypanocidal activity of aqueous extracts of *Waltheria indica* was evaluated
864 using *Trypanosoma brucei brucei*. The parasite were cultured using 96 well micro titer
865 plate and maintained at 37°C. About 20 – 25 parasites per microscope field were dosed
866 with 1, 2 and 4mg/ml of aqueous extract of *Waltheria indica* and a control group
867 without extracts. After 5 minutes incubation in Eppendorf tubes maintained at 37°C, the
868 parasites survived more than four (4) hours in the absence of *Waltheria indica/berenil*.
869 At 1mg/ml of the *Waltheria indica* extract complete cessation of motility of *T. brucei*
870 *brucei* within 25 minutes was observed. Berenil, the standard drug, caused cessation of
871 trypanosomal motility within 60 minutes even at 1mg/ml. From the results *Waltheria*

872 *indica* was very effective when compared with Berenil, and may be a potential source of
873 compounds with trypanocidal activity (Bala *et al.*, 2009).

874 2.65 *Ximenia Americana*

875 The *in vitro* antitrypanosomal activity of methanolic and aqueous extracts of stem bark
876 of *Ximenia americana* was evaluated. *Trypanosoma congolense* infected blood was
877 incubated with methanolic and aqueous extract at 20, 10 and 5mg/ml in a 96 well micro
878 titer plate. The results revealed that methanolic and aqueous extracts had activity at 20
879 and 10 mg/ml however, the methanolic extracts were more active than aqueous extract
880 at 10 and 5 mg/ml. The aqueous and methanolic extract appears to show some potential
881 activity against *T. congolense* (Maikai *et al.*, 2008). In another study *Trypanosoma*
882 *brucei brucei* parasite was incubated with aqueous extract at 1, 2 and 4mg/ml in a 96
883 well micro titer plate. At 2mg/ml of the *Ximenia Americana* extract complete cessation
884 of motility of *T. brucei brucei* within 55 minutes was observed. Berenil, the standard
885 drug, caused cessation of trypanosomal motility within 60 minutes at 1mg/ml (Bala *et*
886 *al.*, 2009).

887 2.66 *Zingiber officinale* (ginger)

888 *Zingiber officinale* (ginger) has been widely used around the world as food and as a
889 spice. It is considered a safe herbal medicine with only a few and insignificant
890 adverse/side-effects. It has been reported that ginger is endowed with strong *in vitro* and
891 *in vivo* anti-oxidant properties (Sepide *et al.*, 2013) *in vivo* antitrypanosomal effect of
892 methanolic extract of *Zingiber officinale* (ginger) in *Trypanosoma brucei brucei*-
893 infected mice were evaluated at dose of at 200, 400 and 800 mg/kg body weight The
894 extract of *Zingiber officinale* produce a significant dose dependent decrease in level of
895 parasitaemia compare to untreated group

897 3.0 CONCLUSION

898 This review has presented a list of natural product (plants/insect) with anti-trypanosoma
899 properties. Many new bioactive agents isolated from plants having anti-trypanosoma
900 effects showed anti-trypanosoma activity equal and sometimes even more potent than
901 known anti-trypanosoma agents such as diminazene aceturate and homidium chloride.
902 However, many other active agents obtained from plants have not been well
903 characterized. More investigations must be carried out to evaluate the mechanism of
904 action of natural product with anti-trypanosoma effect. The toxic effect of these plants
905 should also be elucidated.

908 REFERENCES

- 910 Abdool Karim, S.S., T.T. Ziqubu-Page, R. Arendse . Bridging the gap: potential for a
911 health care partnership between African traditional healers and biomedical
912 personnel in South Africa. 1994 *South African Medical Journal* 84: 1–16.
- 913 Abubakar A, Okogun JI, Ogbadoyi EO. Screening for antitrypanosomal potential of
914 *Tridax procumbens* in infected mice. Programme Book. 3rd Stakeholders
915 Meeting of the African Network for Drugs and Diagnostics Innovation 11-13
916 October 2010 United Nations Office in Nairobi UNON, Kenya
- 917 Abubakar A.1, Iliyasu B, Ojiegbo FN, Igweh AC, Shamaki BU, Dung EC, Domtur LL,
918 Okogun JI, Gbodi TA. and Ogbadoyi EO. Evaluation of the antitrypanosomal
919 activity of *Cucumis metuliferus* pulp in rabbits. *Journal of Medicinal Plants*
920 *Research* 20115(11), pp. 2136-2142, 4

- 921 Adakole HA. and Chukwuka NU. *In Vivo* Trypanocidal activity of Hydroethanolic
922 extract of *Hymenocardia acida* stem bark in Rats. Veterinary World, 2011,
923 Vol.4(3):113-116
- 924 Adebolu TT . Effect of natural honey on local isolates of diarrheacausing bacteria in
925 southwestern Nigeria. Afr. J. Biotech. 2005, 4: 1172-1174
- 926 Adeyemi OS, Akanji MA. and Oguntoye SA.Ethanolic leaf extract of *Psidium guajava*:
927 Phytochemical and trypanocidal activity in rats infected with *Trypanosoma*
928 *brucei brucei*. Journal of Medicinal Plants Research Vol. 3(5), pp. 420-423,
929 May, 2009
- 930 Adeyemi OS, Sykes ML, Akanji MA. and Avery VM. Anti-trypanosomal and cytotoxic
931 activity of *Psidium guajava* extract. *VETERINARSKI ARHIV* 81 (5), 623-633,
932 2011
- 933 Ajagbonna, O. P., Onyeyili, P. A., and Osunkwo, U. A. Effects of dietary salt loading
934 and concurrent administration of ethanolic extract of *Rehaptopetalum coriaceum*
935 olive on water and electrolyte extraction in rats. *Bioscience research*
936 *communication* . 2002.,14(5). 487 – 493.
- 937 Alembert T. Tchindaa, Apollinaire Tsopmoa, Pierre Tanea, Johnson F. Ayafora,,
938 Joseph D. Connollyb,*, Olov SternercVernoguinoesterol and vernoguinoside,
939 trypanocidal stigmastane derivatives from Vernonia guineensis (Asteraceae),
940 Phytochemistry 59 (2002) 371–374
- 941 Alexander, J. Da silva and Melanie Moser (2008) Centre for disease control public
942 health image library.
- 943 Ana CL, Artur PN1, Alessandra RP, Ambrozini IJB, Fernandes IPC. Vieira MF. das G
944 F. da S. and Sérgio de A.Trypanocidal activity of flavonoids and limonoids
945 isolated from Myrsinaceae and Meliaceae active plant extracts. Revista
946 Brasileira de Farmacognosia Brazilian Journal of Pharmacognosy, 2010, 20(1):
947 1-6,
- 948 Anaga OA (2003). Antihyperglycaemic and glucose uptake-enhancing properties of
949 *Dennettia tripetala* G. Baker (Annonaceae). Ph.D Thesis, University of Nigeria,
950 Nsukka
- 951 Atawodi SE, Bulus T, Ibrahim S, Ameh DA, Nok AJ, Mamman M. and Galadima M. *In*
952 *vitro* trypanocidal effect of methanolic extract of some Nigerian savannah plants
953 African Journal of Biotechnology , 2003 2 (9), pp. 317-321
- 954 Atawodi SE. and Funmi O. Evaluation of Anti-trypanosomal Properties of Four Extracts
955 of Leaves, Stem and Root Barks of *Prosopis africana* in Laboratory Animals .
956 Biokemistri, 2009, 21 (No 2), 101-108
- 957 Bala AY, T. Adamu, IU. Abubakar, 2M.J. Ladan and M.G. Abubakar. Studies on the In
958 Vitro Trypanocidal Effect of the Extracts of Some Selected Medicinal Plants in
959 Sokoto State, Nigeria. Nigerian Journal of Basic and Applied Science (2009),
960 17(2):257-264
- 961 Bashir L. Effect of methanolic extract of (House fly) *Musca domestica* on total protein
962 and antioxidant enzymes of *T.brucei brucei* infected rats. A B.Tech thesis, 2014
963 Federal University of Technology Minna,
- 964 Batish DR, Singh HP, Kohli RK. and Kaur S. Eucalyptus Essential Oil as a Natural
965 Pesticide. Retrieved from: <http://www.eucalypt.oil.2008>
- 966 Bénédicta G.H.KpadonouKpoviessi a,b, SaloméD.S.Kpoviessi a,c,
967 EléonoreYayiLadekan b, FernandGbaguidi b, MichelFrédérich d,
968 MansourouMoudachirou b, Joëlle Quetin-Leclercq c, GeorgesC.Accrombessi a,
969 JoanneBero cIn vitro antitrypanosomal andantiplasmodialactivitiesofcrude

- 970 extracts and essential oil of *Ocimum gratissimum* Linn from Benin and influence
- 971 of vegetative stage *Journal of Ethnopharmacology* 155(2014)1417–1423
- 972 Bero J., C. Beaufaya, V. Hannaert, M.-F. Hérenta, P.A. Michels, J. Quetin-Leclercq
- 973 Antitrypanosomal compounds from the essential oil and extracts of *Keetia*
- 974 *leucantha* leaves with inhibitor activity on *Trypanosoma brucei* glyceraldehyde-
- 975 3-phosphate dehydrogenase. *Phytomedicine* 20 (2013) 270– 274
- 976 BIU, A.A., BURATAI, L.B., ONWUATOGWU, J., MOHAMMED, A., AGADA,
- 977 N.O. AND KONTA, M. In vivo Efficacy of Aqueous Extract of *Citrullus*
- 978 *lanatus* Leaf on *Trypanosoma brucei* Infected Albino Rats. *Journal of*
- 979 *Agriculture and Veterinary Sciences*, 2013, 5; 2, Pp. 57 – 63
- 980 Bulus T.I. and Addau F.T. Comparative Antitrypanosomal Screening Of Methanolic
- 981 Extracts Of *Khaya Senegalensis* And *Moringa Oleifera*. *Science World Journal*
- 982 *Vol 8 (No 2) 2013*
- 983 Cheel J, Theoduloz C, Rodriguez J and Schmeda-Hirschmann G. Free radical scavengers
- 984 and antioxidants from lemongrass (*Cymbopogon citratus* (DC.) Stapf.). *Journal*
- 985 *of Agricultural and Food Chemistry* 2005, 53: 2511–2517.
- 986 Chetty KM. Flowering plants of Chittoor, Edn 1, Andhra Pradesh, 2008, pp. 132
- 987 Chukwunyere O. N. Albert W. Mbaya, Patrick A. Onyeyili Toxicity and anti-
- 988 trypanosomal effects of ethanolic extract of *Butyrospermum paradoxum*
- 989 (Sapotaceae) stem bark in rats infected with *Trypanosoma brucei* and
- 990 *Trypanosoma congolense*. *Journal of Ethnopharmacology* 111 (2007) 526–530
- 991 Cristina P, María CG, Mo'nica IE, Virginia M, Jorge C, Mirtha MF, and Hector
- 992 NT. Anti-*Trypanosoma cruzi* Activity of Green Tea (*Camellia sinensis*)
- 993 Catechins. *ANTIMICROBIAL AGENTS AND CHEMOTHERAPY*, Jan. 2004,
- 994 48(1): 69–74
- 995 Cunningham, A.B. (1988). An investigation of the herbal medicine trade in
- 996 Natal/KwaZulu. Investigational Report No 29. Institute of Natural Resources.
- 997 Dietmar S and Kevin MT. Novel antitrypanosomal agents. *Expert Opin. Investig.*
- 998 *Drugs* (2005) 14(8):939-955
- 999 Edoga C.O., Njoku O.O. and Okeke J.J. The Effect of Aqueous Extracts of *Moringa*
- 1000 *Oleifera* Leaves on the Hematological Parameters of *Trypanosoma Brucei*-
- 1001 Infected Rats. *Research Journal of Animal, Veterinary and Fishery Sciences*,
- 1002 2013 1(6), 15-17,
- 1003 Ekanem JT, and Yusuf OK .Some Biochemical and Haematological effects of Black
- 1004 seed (*Nigella sativa*) oil on *T. brucei* infected rats. *Afr. J. Biotech.* 2008 7 (2):
- 1005 153 – 157.
- 1006 Ekanem JT, and Yusuf OK .Some liver function indices and blood parameters in *T.*
- 1007 *brucei*-infected rats treated with honey. *BIOKEMISTRI*, 2007 19(2):81-86
- 1008 Ekanem JT, and Yusuf OK. Activities of alkaline phosphatase, glutamate oxaloacetate
- 1009 transaminase and glutamate pyruvate transaminase in liver and serum of
- 1010 *Trypanosoma brucei*-infected rats treated with honey *Biokemistri* Vol. 17(2)
- 1011 2005: 185-191
- 1012 Ekanem JT. Majolagbe OR, Sulaiman FA, and Muhammad NO. Effects of honey-
- 1013 supplemented diet on the parasitaemia and some enzymes of *Trypanosoma*
- 1014 *brucei*-infected rats *African Journal of Biotechnology*, 2006. 5 (17), pp. 1557-
- 1015 1561, 4
- 1016 Ene AC, Edeh NG, Bonny-Okoli C, Ojiako OA, Ujowundu CO. and Igwe, CU. *In*
- 1017 *vitro* and *in vivo* Antitrypanosomal Effects of Methanol and Aqueous Extracts of
- 1018 *Picralima nitida*, *British Journal of Pharmaceutical Research*, 4(5): 644-653,
- 1019 2014

- 1020 Ene AC, Atawodi SE. and Apeh YEO. *In vitro* and *In vivo* Antitrypanosomal Effects of
1021 Petroleum Ether, Chloroform and Methanol Extracts of *Artemisia maritima*
1022 Linn. *British Journal of Pharmaceutical Research* 4(6): 751-758,
1023 Ene AC, Atawodi SE, Ameh DA, Nnamani CN, Apeh YEO. Antitrypanosomal effects
1024 of petroleum ether, chloroform and methanol extracts of *Artemisia maciverae*
1025 Linn. *Indian Journal of Experimental Biology*. 2009;47:981-986.
1026 Erasto P, Grierson DS and Afolayan AJ. Bioactive sesquiterpene lactones from the
1027 leaves of *Vernonia amygdalina*. *Journal of Ethnopharmacology* 2006 106:117-
1028 120.
- 1029 Fullas F (2010) Ethiopian medicinal plants in veterinary health care. *Ethiopian e-journal*
1030 *for research and innovation* 2: 48-58
- 1031 Garba MH, Kabir AY, Yusuf AM, Ajayi J, Ega O, and Kabir M. *invivo* anti-
1032 trypanosomal effect of crude methanolic extract of *Boswellia diazelli* stem bark
1033 extract in *T. brucei* infected mice. *Nigerian society of biochemistry and*
1034 *molecular biology*(NSBMB), 11th – 14th November, 2014, Ilorin
- 1035 Ghamba H, Balla LJ, Goje A, Halidu MD. and Dauda E. *In vitro* antimicrobial
1036 activities of *Vernonia amygdalina* on selected clinical isolates, *International*
1037 *Journal of Current Microbiology and Applied Science*, 2014, 3(4): 1103-1113
- 1038 Gurib-Fakim, A. (2006). Medicinal plants: Traditions of yesterday and drugs of
1039 tomorrow. *Molecular Aspects of Medicine* 27: 1–93.
- 1040 Habila N, Abel SA, Zakari L, Isaac A., Bello EH, Monday AD and Taofiq OA .
1041 Evaluation of *In Vitro* Activity of Essential Oils against *Trypanosoma brucei*
1042 *brucei* and *Trypanosoma evansi*. *Journal of Parasitology Research*, 2010 1-5
- 1043 Hassan MI, Emmanuel OO, Kabiru YA, Maimuna UB. and Ilumi JY. Evaluation Of
1044 Antitrypanosomal Activity Of Ethyl Acetate Extract Of *Adansonia Digitata*
1045 Seed Extract In *T.B. Brucei* Infected Albino Mice *Int. J. Drug Res. Tech.* 2012,
1046 Vol. 2 (7), 454-460
- 1047 Herbert WJ, Lumsden WHR. *Trypanosoma brucei*: A Rapid Matching Method for
1048 Estimating the host's Parasitemia. *Experimental Parasitology*. 1976;40:427-431
- 1049 Hoet S, Opperdoes F, Brun R, Quetin-Leclercq J (2004). Natural products active against
1050 African trypanosomes: a step towards new drugs. *Nat. Product Reports* 21: 353-
1051 364.
- 1052 Ibrahim, MA Aliyu AB, Sallau AB, Bashir M, Yunusa I. and Umar TS. *Senna*
1053 *occidentalis* leaf extract possesses antitrypanosomal activity and ameliorates the
1054 trypanosome induced anemia and organ damage *Pharmacognosy Research*,
1055 2010.2;3.175-180
- 1056 Igwe, AC, Onabanjo AO.. Chemotherapeutic effects of *Annona senegalensis* in
1057 *Trypanosoma brucei brucei*. *Annals of Tropical Medicine and*
1058 *Parasitology*.,1989 83 (5): 527- 534.
- 1059 J. A. Abedo*, O. A. Jonah, R. S. Abdullahi, M. R. Mazadu, H. Y. Idris, H. Muhammed,
1060 F. T. Shettima, S. Ombugadu, M. Daudu, J. Garba, U. Abdulmalik, B. A. Kugu
1061 and A. O. Usman. Evaluation of trypanosomal activity of *Tapinanthus*
1062 *globiferus* and *Gongronema latifolium* on *Trypanosoma congolense* *Bioscience*
1063 *Research*, 10(1): 20-28, 2013
- 1064 . Abedo J. A O. A. Jonah, R. S. Abdullahi, M. R. Mazadu, H. Y. Idris, H. Muhammed,
1065 F. T. Shettima, S. Ombugadu, M. Daudu, J. Garba, U. Abdulmalik, B. A. Kugu
1066 and A. O. Usman. Evaluation of trypanosomal activity of *Tapinanthus*

- 1067 *globiferus* and *Gongronema latifolium* on *Trypanosoma congolense* Bioscience
- 1068 Research, 10(1): 20-28, 2013
- 1069 John OI , Ngozichukwuka PI, Alexander IG, Carol JC, Nzekwe U, and Rajeev K S.
- 1070 Scientific Investigation of Antitrypanosomal Activity of *Crateva Adansonii* DC
- 1071 Leaves Extracts Indo Global Journal of Pharmaceutical Sciences, 2012; 2(3):
- 1072 226-229
- 1073 Josephine A. Abedo, Alice Jonah, Rakiya Abdullahi, Melelem Mazadu, Hamza Idris,
- 1074 Hafsat Muhammed, Fatima Shettima, Sunday Ombugadi, Mercy Daudu, Jabiru
- 1075 Garba, Umaru Abdulmalik and Bashir Kagu, Comparative Studies of *In vitro*, *In*
- 1076 *vivo* Trypanocidal Activity and Phytochemical Screening of *Tapinanthus*
- 1077 *globiferus* and *Gongronema latifolium*, International Journal of Animal and
- 1078 Veterinary Advances, 2013, 5(3): 120-124,
- 1079 Kabiru YA, Ogbadoyi EO, Okogun JI, Gbodi TA, and Makun HA. Anti-trypanosomal
- 1080 Potential of Eucalyptus Camaldulensis, British Journal of Pharmacology and
- 1081 Toxicology, 2013 4(2): 25-32
- 1082 Kabiru YA, Okogun JI, Gbodi TA, Makun HA, and Ogbadoyi EO. Evaluation of the
- 1083 efficacy of combination therapy in *T. b .brucei* – infected mice using extracts of
- 1084 *annona senegalensis* and *eucalyptus camaldulensi*. IOSR Journal of Pharmacy
- 1085 ,2012 Volume 2 Issue 4;32-37 32
- 1086 Kabiru YA, Okogun JI, Samuel O, Agada EG , Ogbadoyi EO. Antitrypanosomal
- 1087 potential of *Deterium senegalensis*. Programme Book. 3rd Stakeholders Meeting
- 1088 of the African Network for Drugs and Diagnostics Innovation 11-13 October
- 1089 2010 United Nations Office in Nairobi UNON, Kenya
- 1090 Kifleyohannes T, Getachew T, Yacob HT, Mirutse G. and Nigatu Kebede3Effect of
- 1091 crude extracts of *Moringa stenopetala* and *Artemisia absinthium* on parasitaemia
- 1092 of mice infected with *Trypanosoma congolense* BMC Research Notes 2014,
- 1093 7:390
- 1094 Kobo PI, Erin PJ, Suleiman MM, Aliyu, H, Tauheed M. Muftau, S. and Mamman M.
- 1095 Antitrypanosomal effect of methanolic extract of *Zingiber officinale* (ginger) on
- 1096 *Trypanosoma brucei brucei*-infected Wistar mice. Veterinary World, EISSN:
- 1097 2231-0916. 770-775
- 1098 Lejon V., Boclaert M., Jannin J., Moore A and Buscher P. (2003). The challenge of
- 1099 *Trypaosoma brucei gambiense* sleeping sickness diagnosis outside Africa Lancet
- 1100 infectious disease. 3:804-808
- 1101 Maikai VA, Nok JA, Auda AO. and Alawa CBI.*In vitro* antitrypanosomal activity of
- 1102 aqueous and methanolic crude extracts of stem bark of *Ximenia americana* on
- 1103 *Trypanosoma congolens*. Journal of Medicinal Plants Research, 2008. 2(3), pp.
- 1104 055-058,
- 1105 Mann A, Egwim EC, Barnabas B, Nda-Umar A, Mohammed G. and Ekanem JT
- 1106 Efficacy of *Dissotis rotundifolia* on *Trypanosoma brucei brucei* infection in rats.
- 1107 African Journal of Biochemistry Research, 2009 Vol.3 (1), pp. 005-008
- 1108 Mann M, Oluwaseyi RI, Abdulfatai TA, Chidiebere U, Ekpenyong EU, Isaac IO,
- 1109 Mohammed SS, Dauda RI, Yusuf AY, Kabir AY, and Ogbadoyi, EO. *In Vivo*
- 1110 Antitrypanosomal Effects Of Some Ethnomedicinal Plants From Nupeland Of
- 1111 North Central Nigeria. J Tradit Complement Altern Med. (2011) 8(1):15-21 15
- 1112 Martins GZ, Guimarães NO, Silva FAJ, . Velásquez AMA, Rodrigues DF, Kohatsu
- 1113 AAN, Almeida AE, Planeta CS, Cicarelli RMB. and Moreira RRD.
- 1114 Trypanocidal activity of fruits extracts of *Solanum lycocarpum* St. Hill. on
- 1115 *Trypanosoma brucei* strain. Book of abstract.13th Congress of the International
- 1116 Society for Ethnopharmacology in collaboration with the Society for Medicinal

- 1117 Plant and Natural Product Research And Eurasia-Pacific Uninet Graz, Austria
- 1118 September 2 - 6, 2012. P327
- 1119 Maundu, PM , Ngugi GW, and Kabuye HIS. Traditional food plants of Kenya
- 1120 KENRIK(Kenya Resource Centre for Indigenous Knowledge) National museum
- 1121 of Kenya , Nairobi. 1999
- 1122 Mbaya A, Aliyu M, Ibrahim U. The clinico-pathology and mechanisms of
- 1123 trypanosomosis in captive and free-living wild animals: a review. Veterinary
- 1124 Research Communications 337,793–809.
- 1125 Mekonnen Y, V Yardley, P Rock, S Croft (1999) In vitro antitrypanosomal activity of
- 1126 *Moringa stenopetala* leaves and roots. *Phytotherapy Research* 13: 538-539.
- 1127 ANT
- 1128 Mercy G., Ahmed H, Joseph K, Patrick K, Grace M, Mary N. and Gathu N.
- 1129 Antitrypanosomal Tetranotriterpenoids from *Toona ciliata* roots. Agric. Biol. J.
- 1130 N. Am., 2011, 2(7): 1042-1047
- 1131 Mercy G., Ahmed H, Joseph K, Patrick K, Grace M, Mary N. and Gathu N.
- 1132 Antitrypanosomal Tetranotriterpenoids from *Toona ciliata* roots. Agric. Biol. J.
- 1133 N. Am., 2011, 2(7): 1042-1047
- 1134 Mergia E, Workineh S, Getachew T, and Tilahun T. Phytochemical Screening and *In*
- 1135 *Vitro* Antitrypanosomal Activity of Aqueous and Methanol Leaf Extract of
- 1136 *Verbascum sinaiticum* (Scrophulariaceae) against *Trypanosoma congolense*
- 1137 Field Isolate. J Clin Exp Pathol 2014, 4:4, 1-8
- 1138 Mohammed Auwallbrahim a,n, Aminu Mohammeda, Murtala Bindawa Isah b, Abubakar
- 1139 Babando Aliyu Anti-trypanosomal activity of African medicinal plants: A
- 1140 review update Journal of Ethnopharmacology 154(2014)26–54
- 1141 Molyneux DH: Current public health status of the trypanosomiasis and leishmaniasis.
- 1142 In: *Trypanosomiasis and Leishmaniasis: Biology and Control*. Hide G, Mottram
- 1143 JC, Coombs GH, Holmes PH (Eds), CAB International, Wallingford, Oxon, UK
- 1144 (1997):39-50.
- 1145 Musuyu MD, Fruth, BI, Nzunzu J, Lami GK, Mesiaa OK, Kambu GL, Tona R,
- 1146 Cimanga K, Cos LM, Apers S. and Pieters L. In vitro antiprotozoal and
- 1147 cytotoxic activity of 33 ethnopharmacologically selected medicinal plants from
- 1148 Democratic Republic of Congo. Journal of Ethnopharmacology 141 (2012) 301–
- 1149 308
- 1150 Nilza de Lucas RB, Tânia U, Benedito PF, Celso, V N. Antitrypanosomal Activity of a
- 1151 Semi Purified Subfraction Rich in Labdane Sesquiterpenes, Obtained from
- 1152 Flowers of *Anthemis tinctoria*, against *Trypanosoma cruzi*, *Pharmacology and*
- 1153 *Pharmacy*, 2011, 2, 47-55
- 1154 Norhayati I, Getha K, Muhd Haffiz J, Mohd Ilham A, Lili Sahira H, Siti Syarifah Mm
- 1155 and Muhd Syamil A.. *In vitro* antitrypanosomal activity of Malaysian
- 1156 plants. 2013 *Journal of Tropical Forest Science* 25(1): 52–59
- 1157 Nwakaego EN, *In vitro* anti-trypanosomal activity of *Morinda lucida* leaves. African
- 1158 Journal of Biotechnology , 2012 11(7), pp. 1812-1817, 24
- 1159 Nwanjo HU. Efficacy of aqueous leaf extract of *Vernonia amygdalina* on plasma
- 1160 lipoprotein and oxidative status in diabetic rat models. Nig. J. Physiol. Sci. 2005
- 1161 20(1-2):30-42
- 1162 Obboh A, Lawal M, and Malann Y.D. Anti-trypanosoma Activity of the Ethanolic Leaf
- 1163 Extract of *Senna occidentalis* (Fabaceae) on *Trypanosoma brucei brucei* Infected
- 1164 Mice. *I. 2. No. 1. 2013. Pp. 32-37*

- 1165 Ogbunugafor HA, Okochi VI, Okpuzor J Adedayo T. and Esue S. *Mitragyna ciliata* and
1166 its trypanocidal activity. African Journal of Biotechnology Vol. 6 (20), pp. 2310-
1167 2313,
- 1168 Okeniyi JAO. Comparison of healing of incised abscess wounds with honey and eusol
1169 dressing. J. Alter. Compl. Med. 2005 11: 511-513.
- 1170 Okpuzor J, Okochi VI, Okubena MO, Awoyemi AK. The influence of African Herbal
1171 Formula on the haematological parameters of trypanosome infected rats. African
1172 Journal of Biotechnology , 2003 Vol. 2 (9), pp. 312-316,
- 1173 Olukunle, J. O.1; Abatan, M. O, Soniran, O. T.2; Takeet, M. I.3; Idowu O. A2.; Akande,
1174 F. A3.; Biobaku, K. T1 and Jacobs, E. B. In-vivo Antitrypanosomal Evaluation
1175 Of Some Medicinal Plants Extracts From Ogun State, Nigeria. *Science World*
1176 *Journal Vol 5 (No 1) 2010*
- 1177 Omafuvbe BO, Abiose SH, and Adaraloye OO. The production of 'Kpaye'--a fermented
1178 condiment from *Prosopis africana* (Guill and Perr) Taub. Seeds. *Int J Food*
1179 *Microbiol.* 1999, 51:183-186
- 1180 Omale J. and Joseph JE. Comparative evaluation of trypanocidal activities of *Cissus*
1181 *multistriata* and *Saba florida* (benth) leaf extracts J Biosci Tech, Vol 2
1182 (1), 2011, 197-204
- 1183 Orhue N, Nwanze E and Okafor A. 2009. *Scoparia dulcis* protects against *Trypanosoma*
1184 *brucei* induced immunosuppression in experimentally infected rabbits. *Afri. J.*
1185 *Food Sci.*, 3: 172-175.
- 1186 Oyeibanji BO. Preliminary studies on the effect of *Mangifera indica* extract on
1187 trypanosomiasis infection. Programme Book. 3rd Stakeholders Meeting of the
1188 African Network for Drugs and Diagnostics Innovation 11-13 October 2010
1189 United Nations Office in Nairobi UNON, Kenya
- 1190 Patrick OE, Canice C A. and Augustine OO. Response of *Trypanosoma brucei brucei*--
1191 induced anaemia to a commercial herbal preparation. African Journal of
1192 Biotechnology Vol. 2 (9), pp. 307-311, September 2003
- 1193 Peni IJ, Ajagbonna OP, Elinge CM, Agaie BM, Elsa AT, Yusuf H and Ribah IM. Effects
1194 of *Allium sativum* Bulb Extract, Diminazene Aceturate and Their Combination
1195 on Parasitaemia, and Biochemical Indices in Rats Experimentally Infected with
1196 *Trypanosoma Brucei Brucei*. *Journal of Applied Pharmaceutical Science* 02
1197 (06); 2012: 112-115
- 1198 Peter O, Magiri, E., Auma J, Magoma G, Imbuga M and Murilla G. 2009 Evaluation of
1199 in vivo antitrypanosomal activity of selected medicinal plant extracts. *J. Med.*
1200 *Plants Res.*, 3: 849-854.
- 1201 Santos KKA, Edinardo F.F. Matias a, Saulo R. Tintino a, Celestina E.S. Souza a, Maria
1202 F.B.M. Braga a Anti-*Trypanosoma cruzi* and cytotoxic activities of *Eugenia*
1203 *uniflora* L. *Experimental Parasitology* 131 (2012) 130–132
- 1204 Scott IM, Jensen HR, Philogene BJR., Arnason JT (2008). A review of *Piper* spp.
1205 (Piperaceae). *Phytochemistry*, insecticidal activity and mode of action.
1206 *Phytochem. Rev* 7: 65-75.
- 1207 Sepide, M., Alireza, O., Majid, M., Vahide, E.A. and Laleh, P. Anti-inflammatory
1208 effects of *Zingiber officinale* in type 2 diabetic patients. *Adv. Pharm. Bull.*, 2013,
1209 3(2): 273-276.
- 1210 Shaba P, Pandey NN, Sharma OP, Rao JR. and Singh RK. Anti-trypanosomal Activity
1211 of *Piper Nigrum* L (Black pepper) Against *Trypanosoma Evansi* *J Vet Adv*
1212 2012, 2(4): 161-167

- 1213 Shaba P, Pandey NN, Sharma OP, Rao JR. and Singh RK. Antitrypanosomal Effects of
1214 Brassica Oleracea (Cabbage) Fruits and Leaves. J. Vet. Adv., 2012, 2(7):304-
1215 401
- 1216 Shittu OK and Elekwechi U. Therapeutic potentials of methanol extracts of honey bee
1217 (*Apis mellifera*) against trypanosome *brucei* infection. *Nigerian society*
1218 *of biochemistry and molecular biology*(NSBMB), 11th – 14th November, 2014,
1219 Ilorin
- 1220 Shittu OK, and Tanimu M. Proximate analysis of wheat supplemented diet and its anti-
1221 trypanosomal effect on infected rat. International Journal of Applied Biological
1222 Research 2012, 4(1and2): 109 - 103
- 1223 Shittu OK, Habibat U, Usman YU.Effect of methanolic leaf extract of *Thymus vulgaris*
1224 on some biomarker enzymes in *Trypanosoma brucei* infected rats. *Int J Pharm*
1225 *Biomed Res* 2013b, 4(2), 83-87
- 1226 Shittu OK, and Bashir L. Activity Of Methanolic Extract Of *Musca Domestica* Against
1227 *Trypanosoma Bruceibrucei* Infected Rats. *Nigerian society of biochemistry and*
1228 *molecular biology*(NSBMB), 11th – 14th November, 2014, Ilorin.
- 1229 Shittu OK., Musa F. and Gbadamosi DF. Trypanocidal Activity And Heamatological
1230 Changes In T. Brucei Infected Rats Treated With Methanolic Leaf Extract Of
1231 *Thymus Vulgaris* . *Ijabr* Vol.2013 5(1and2): 109 – 114.
- 1232 Sibibe M and Williams JT . “*Baobab-Adansonia Digitata. Fruits For The Future*”,
1233 International Centre for under utilised Crops, Southampton, UK, 96, 2002
- 1234 SubhadhirasakulS, JankeawB and Malinee A. Chemical constituents and antioxidative
1235 activity of extracts from *Dyera costulata* leaves. *Songklanakarin Journal of*
1236 *Science Technology*, 2003 25: 351–357.
- 1237 Sweeney CJ, Mehrotra S, Sadaria MR, Kumar S, Shortle NH, Roman Y, Sheridan C,
1238 Campbell RA, Murray DJ, Badve S, Nakshatri H. The sesquiterpene lactones
1239 parthenolide in combination with docetaxel reduces metastasis and improves
1240 survival in a xenograft model of breast cancer. *Mol. Canc. Ther.*2005, 4(6):1004
- 1241 Taylor, J.L.S., T. Rabe, L.J. McGaw, A.K. Jäger and J. van Staden (2001). Towards the
1242 scientific validation of traditional medicinal plants. *Plant Growth Regulation* 34:
1243 23–37.
- 1244 Teka F, Getachew T, and Workineh S.Evaluation of in vivo antitrypanosomal activity of
1245 crude extracts of *Artemisia abyssinica* against a *Trypanosoma congolense* isolate.
1246 *BMC Complementary and Alternative Medicine* 2014, 14:117
- 1247 Teklehaymanot T (2009) Ethnobotanical study of knowledge and medicinal plants use
1248 by the people in Dek Island in Ethiopia. *J Ethnopharmacol* 124: 69-78.
- 1249 Tijani AY, Uguru MO, Salawu OA, Abubakar A, Onyekwelu NO. and Akingbasote JA.
1250 Effect of *Faidherbia albida* on some biochemical parameters of rats infected
1251 with *Trypanosoma brucei brucei*. *African Journal of Pharmacy and*
1252 *Pharmacology*, 2009 Vol. 3(1). pp. 026-030,
- 1253 Ubik, “A New Flavonoid: Tinctosid from *Anthemis tinc- toria* L,” *Short*
1254 *Communications Pharmazie*, Vol. 60, No. 12, 2005, pp. 956-957.
- 1255 Weldegerima B, Teferra A, Muthuswamy R (2008) Ethno-Veterinary use of medicinal
1256 plants by traditional healers in Dabat District, Northwestern Ethiopia. *Phcog*
1257 *Mag* 4(15).
- 1258 WHO: African trypanosomiasis or sleeping sickness. *World Health Org. Fact Sheet*
1259 (2001) 259.<http://www.who.int/mediacentre/factsheets/fs259/en/>
- 1260 Williams-Blangero S, Vandeberg JI, Blangero J, Corrêa-Oliveira R: Genetic
1261 epidemiology of *Trypanosoma cruzi* infection and Chagas’ disease. *Front.*
1262 *Biosci.* (2003) 8:e337-e345.

1263 Wurochekke AU, Chechet G, Nok AJ. *In-vitro* and *In-vivo* antitrypanosomal brucei
1264 infection in mice. J Med Sci. 2004; 4 (3):236-239
1265 Wurochekke AU, Nok AJ. *In vitro* anti trypanosomal activity of some medicinal plants
1266 used in the treatment of trypanosomosis in Northern Nigeria. Afr. J. Biotechnol.
1267 20043(9):481-483.
1268 Yamamoto, T. 1997. Chemistry and application of green tea. CRC Press, Inc., Boca
1269 Raton, Fla.
1270 Yineger H, Kelbessa E, Bekele T, Lulekal E (2007) Ethnoveterinary medicinal plants at
1271 Bale Mountains National Park, Ethiopia. J Ethnopharmacol 112: 55-70.
1272 Yusuf AB, Umar IA, and Nok AJ. Effects of methanol extract of *Vernonia amygdalina*
1273 leaf on survival and some biochemical parameters in acute *Trypanosoma brucei*
1274 *brucei* infection African Journal of Biochemistry Research, 2012 6(12), pp. 150-
1275 158,

1276 Yusuf OK. Evaluation of Anti-trypanosomal Activities of Fermented Wheat germ and
1277 Garlic bulb Extracts in *T. brucei*-infected rats. A Phd Thesis Submitted To the
1278 Department Of Biochemistry, University Of Ilorin, Ilorin, Nigeria.2010.
1279
1280
1281
1282
1283
1284
1285
1286
1287
1288
1289