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REVIEW ARTICLE

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A narrative review on trypanosomiasis and its effect on food production

Uma revisão narrativa sobre a tripanossomíase e seu efeito na produção de alimentos

Isaac Onyam [a], Manasseh Adorm Otabil [a], Ekow Sekyi Etwire [a], Kenneth Kwansa-Aidoo [a], Samuel Mawuli Adadey [a,b*], William Ekloh [a,c*]

[a] Department of Biochemistry, University of Cape Coast, Cape Coast, Ghana.
[b] School of Medicine and Health Science, Department of Medical Biochemistry, University for Development Studies, P.O. Box TL1350, Tamale, Ghana.
[c] West African Centre for Cell Biology of Infectious Pathogens, College of Basic and Applied Sciences, University of Ghana, P.O. Box LG 54 Accra, Ghana

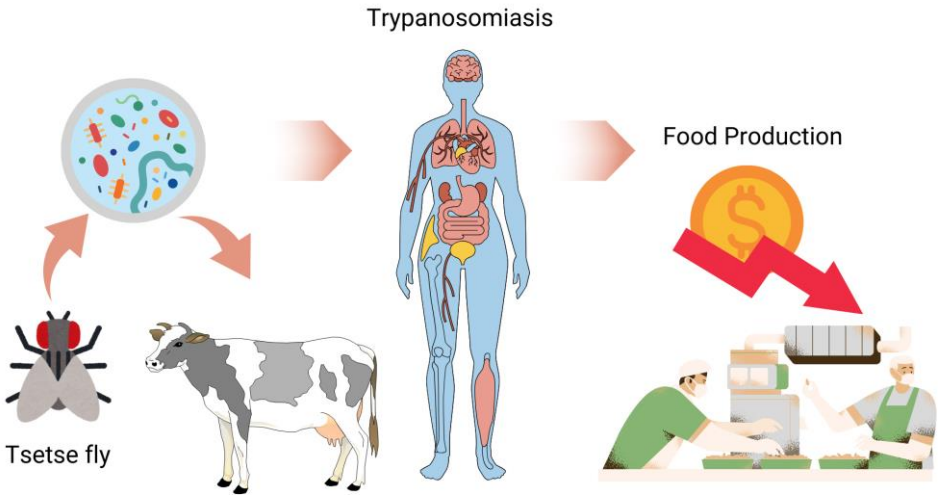
Abstract
Trypanosomiasis is an endemic parasitic disease affecting both humans and animal with a severe negative impact on food production in almost all parts of the world. This review seeks to summarize the history of trypanosomiasis and examine the prevalence of trypanosome infection in animals and its effects on food production. A narrative review was conducted on the history of trypanosomiasis. The literature search was conducted on different databases, and selected articles were screened, data extracted, and analyzed. It is believed that trypanosomiasis has been in existence for several decades dating as far as about 2500 BC during the era of the Egyptian kingdom. Africa was found to have the most common cases of animal trypanosomiasis, with 36 out of 40 articles reporting cases. Cattle among other mammals are the most studied animals and they are the most affected. Hence, milk and meat production are greatly affected by trypanosomiasis. The age of animals and the feed provided to animals also played a role in the prevalence and distribution of the pathogen. This review reveals a wide geographical distribution and diverse host range of trypanosome species. The study also highlights the severity of trypanosomiasis and its impact on food production.

Keywords: Animal trypanosomiasis, food production, prevalence, cattle, trypanosome.

Resumo
A tripanossomíase é uma doença parasitária endêmica que afeta tanto humanos quanto animais, com um impacto negativo severo na produção de alimentos em quase todas as partes do mundo. Esta revisão busca resumir a história da tripanossomíase, examinar a prevalência da infecção por tripanossomas em animais e seus efeitos na produção de alimentos. Uma revisão narrativa foi conduzida sobre a história da tripanossomíase. A pesquisa de literatura foi realizada em diferentes bases de dados, e os artigos selecionados foram avaliados, os dados extraídos e analisados. Acredita-se que a tripanossomíase exista há várias décadas, remontando a cerca de 2500 a.C. durante a era do reino egípcio. A África foi identificada como a região com os casos mais comuns de tripanossomíase animal, com 36 dos 40 artigos relatando casos. O gado, entre outros mamíferos, são os animais mais estudados e os mais afetados. Assim, a produção de leite e carne é amplamente afetada pela tripanossomíase. A idade dos animais e a ração fornecida a eles também desempenharam um papel na prevalência e distribuição do patógeno. Esta revisão revela uma ampla distribuição geográfica e uma diversa gama de hospedeiros das espécies de tripanossomas. O estudo também destaca a gravidade da tripanossomíase e seu impacto na produção de alimentos.

Palavras-chave: Tripanossomíase animal, produção de alimentos, prevalência, bovinos, tripanossoma.

Graphical Abstract



*Corresponding authors: Samuel M. Adadey (smadadey@gmail.com) & William Ekloh (wekloh@ucc.edu.gh)
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ROYALDATASET

1. Introduction

Animal trypanosomiasis, one of the most ubiquitous and neglected diseases, has been a global challenge affecting food production and food security. The disease has been a significant obstacle to the global economy, the health of most mammals, and food production. The disease is caused by a group of vascular protozoans known as trypanosomes. Trypanosome species, a group of unicellular organisms belonging to the genus Trypanosoma, are microorganisms mostly known to cause trypanosomiasis in tropical areas. These protozoans are unicellular, flagellated microorganisms that live and multiply in the hosts' bloodstreams, lymph, and other tissues in a parasitic type of association (Shaw et al., 2014). These microbes are well known for their distinct signatures or behavioral characteristics exhibited in their hosts (Swallow, 2000).

Trypanosome species have been a significant impediment to economic development worldwide, causing diseases that affect a wide range of organisms, ranging from humans to all farm animals, and have a significant negative impact on animal production and human health (Ahmed et al., 2016; Kristjanson et al., 1999). This disease is considered a major constraint on both human health and livestock production all over the globe, with a high number of cases recorded in mainly Africa, Asia, and Latin America (Pritchard, 1966; Seré & Steinfeld, 1996).

N'gana, or nagana, originated from the Zulu language, which means useless or powerless is the word used to describe trypanosomiasis in sick animals. The name came about because farm animals in tsetse fly-prone areas became weaker and unfit for work. As the name and meaning suggest, animal production in tsetse fly belt areas is extremely difficult (Seshabela, 2003; Steverding, 2008). The disease is known to be transmitted primarily by the vector tsetse fly. These vectors are found in semi-arid and sub-humid areas, with a potential distribution range of over 8.7 million km^2 in 37 countries across the continent of Africa (M'mboyi, 2001; Swallow, 2000). Over the years, Tsetse fly belt areas have been well known to record a high number of trypanosome cases with an overwhelming impact on food production and human health. The disease is said to occur in both tsetse fly and non-tsetse fly areas, and this is due to the movement of certain wild animals, domestic animals, and some hematophagous biting insects. Mostly, specific types of trypanosome protozoan like T. evansi and T. vivax are known to be transmitted by these insects due to their unique characteristics, making it possible for the disease to occur inside and outside tsetse fly-infested areas. The parasite is said to undergo complex metamorphic developmental cycles in the primary vector and an incomplete cycle in some hosts only. The blood-feeding tsetse fly vector, according to taxonomists, belongs to the order Diptera. Bites from these vectors are unique and painful and cannot go unnoticed during the transmission of the parasite (Abdeta et al., 2022; Alingu et al., 2014; Bauer et al., 1999).

Most international bodies, like the Pan-African Tsetse and Trypanosomiasis Eradication Campaign (PATTEC) under the umbrella of the Africa Union (A.U), the Food and Agriculture Organization (F.A.O) of the United Nations (U.N.), the World Health Organization (W.H.O), the International Atomic Energy Agency (IAEA), and the Inter-African Bureau for Animal Resources (AU-IBAR) (AU-IBAR, 2019) have mounted a fight against these endemic diseases with the aim to control the vectors, eliminate the parasites, and reduce their means of spread completely. Other local bodies specific to individual countries, like the Coordinating Office for Control of Trypanosomiasis in Uganda (COCTU) (Kizza et al., 2021) and the Kenya Tsetse and Trypanosomiasis Eradication Council (KENTTEC) has also contributed to the fight by mapping their territories and the developments of the national atlases to avail the tsetse belt and trypanosome area to aid control and properly stop the disease in addition to other innovative methods like livestock protective fencing (LPF) and target technology (Gamba et al., 2021). This mapping is based on certain variables, such as tsetse density, socio-economic and environmental variables, and others. Despite all initiatives and modern strategic methods of fighting the disease, it still survives against all odds, with only a slight reduction in the total number of animal trypanosomiasis cases (Albert et al., 2015).

The complete eradication of the disease has been an unrealistic goal due to the recent alarming issue of the development of resistance against anti-trypanosomal drug treatment (Mamoudou et al., 2006). According to Matthews and his colleagues, it is believed that the extracellular protozoan undergoes an antigenic variation that expresses a large repertoire of antigenically distinct surface coats, which allows the parasite to populate and avoid antibody-mediated elimination (Matthews et al., 2015). Nagana, as it is popularly known in Africa, has been a disease that has been neglected and undermined over the years, with its consequences not being considered a threat. According to research, the acute forms of both sleeping sickness and the Nagana disease are caused by T. congolense and T. vivax, with T. brucei causing the chronic form of the disease (Chamond et al., 2010; Silva et al., 1996).

The incidence of trypanosome cross-transmission across organisms has been a factor in the rise. Transmission across species mostly occurs in areas near game parks and wildlife reserves. This has presented the world with a challenge of new strains of trypanosome parasites that are slightly different in terms of their genetic composition and are partially immune to the sort of treatment that is already in use. The virulent nature of the parasite increases when it is transmitted from one organism to another, as it is known to affect wildlife mildly and domesticated animals severely. This comes from their adaptive mechanisms and changes in environment, i.e., how the host immune system responds to the parasites. Also, the idea of hunting game animals for fun, as a source of food, rearing these animals as livestock and keeping animals as pets can contribute to the cross-transmission of the parasite. These can lead to severe constraints on disease management and subsequently cause negative impacts on food production and the economic growth of many agricultural nations. As such, there is a need for a comprehensive study to review the prevalence of trypanosomes and the effect of trypanosomiasis on food security and human health

Over the years, common drugs such as Isometamidium, Diminazene, and Homidium Bromide have been used in the treatment of trypanosomiasis, but until recent times, these drugs have been ineffective against some trypanosome species (Mamoudou et al., 2006). African livestock owners and farmers mostly administer about 35 million doses of trypanocides and anti-trypanosomal drugs annually to prevent or treat the disease. These drugs are estimated to cost about $500 billion annually. However, the parasites continue to kill approximately 3 million cattle in Africa each year, not to mention the total death rate of animals worldwide (Shaw et al., 2014). Furthermore, bovine trypanosomiasis alone has been reported to cause an economic loss of US$1.5–2 billion per year, and Africa spends at least $30 million every year to control bovine trypanosomiasis in terms of curative and prophylactic treatments. Yet still, the number of cases increases gradually (Jones & Dávila, 2001). This escalating and neglected issue could have a huge impact on the economy, as farmers and livestock owners encounter greater lose and spend huge income in treating infected farm animals and eventually gain nothing from rearing animals. There is a need for a comprehensive

plan to increase research output and research facilities in trypanosomiasis-prone areas to develop better diagnostic and efficacious drug regimens to help fight the disease. Effective disease surveillance, vector control strategies, and sustainable agricultural practices could be implemented to help reduce the disease burden.

2. Methodology

2.1 Literature search to estimate the prevalence of trypanosome infection

The PubMed database was used to generate the information in this review article. A search was conducted on PubMed using the key words: ((effect) OR (outcome) OR (result)) AND ((animal trypanosomiasis) OR (animal trypanosome)) AND (((food production) OR (livestock production)) OR (animal production)) OR (crop cultivation)). **Fig. 1** shows the review's search strategy and the results obtained from the literature search done.

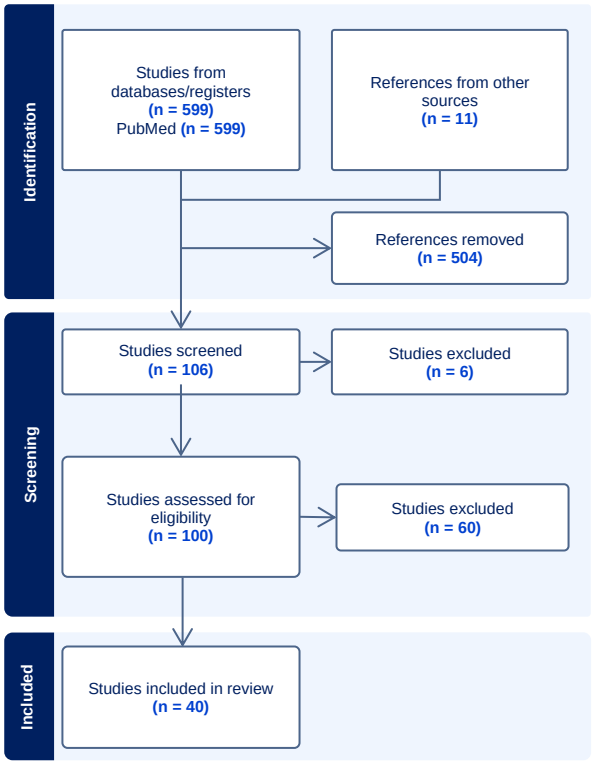

Fig. 1 Flow diagram of literature screening and data extraction.

PubMed provided with 599 articles that matched the search terms used. Examples of topics investigated include disease history, disease prevention, treatment, economic effects, socio-cultural effects, drug use, dosages and modes of action, perception, commonly reported trypanosome species, vector control, and transmission intensity. The search was conducted regardless of the year. These results were upload unto the endnote reference manager for the screening process. All publications resulting from these searches were screened using Endnote, a web-based bibliography database manager, and all documents that met the inclusion criteria of the review paper were retrieved and evaluated by three authors. While the authors attempted to identify all relevant documents, some literature, such as reviewed articles, was inadvertently omitted.

English-language documents and past and most recent publications providing context on the following topics related to animal trypanosomiasis management, vector control, and others were included in this review: While the review focused primarily on the disease's impact on food production globally, it also included relevant research on species distribution (prevalence) and its relevance to specific factors. Two reviewers used a data extraction form to extract and record findings from each paper related to the topics.

2.2 Data extraction

Endnote was used to collect 40 published pieces of literature relevant to the topic from a pool of 610 searches. The retrieved records were mainly from Africa and America with most of them published in the year 2022 (**Fig. 2**). Data was extracted from all articles that met the selection criteria. These articles were reviewed, and data was collected using Microsoft Office Excel with the following parameters: name of the first author, last author, DOI number, diagnostic method used in identifying the presence of the trypanosome species, type of trypanosome species identified, treatments used in the articles, doses, countries, year of publication, sample size used, number of infected animals, type of breed of animals infected, and preventions used. The types of diagnostic tests used were grouped into three broad categories. The types of trypanosome species identified in the article were also categorized based on the year of publication. The prevalence of the disease was determined from the number of infected animals over the total sample size. SPSS and GraphPad prism were statistical tools used for the graphical presentation of the result.

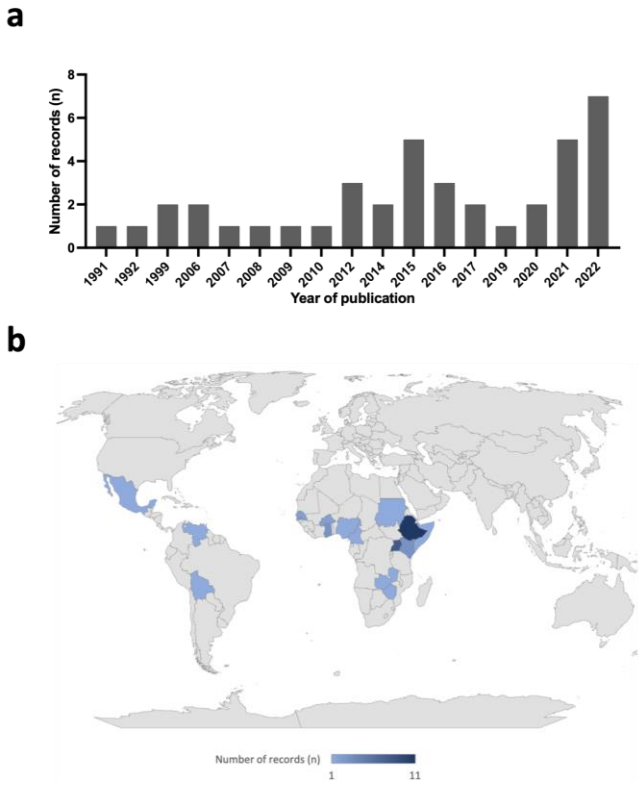

Fig. 2 Characteristics of records retrieved. Year of publication (a) and geographical distribution of publications considered in this study (b).

3. Results and Discussion

3.1 Trypanosomes

Trypanosomes are flagellated unicellular organisms with elongated, cigar-shaped bodies with distinct anterior and posterior ends, surrounded by a plasma membrane and an enclosed cytoplasm containing other organelles (Kershaw, 1983). They are polymorphic species with two developmental forms: epimastigotes and crithidials. In tsetse fly, the trypanosome is long but slender in the midgut, while in the salivary gland, it is short and stumpy (Lawyer & Perkins, 2000; Simpson, 1972). The crithidial form is only found in the salivary glands of the tsetse fly. Pellicles, which surrounds the entire body on all sides, are flexible and thin covers held together by fine fibrils known as microtubules, which help the organism maintain its shape while swimming in its hosts' blood plasma (Kovalenko, 2017; Puranik & Bhate, 2007; Rudzinska & Vickerman, 1968). They have a single flagellum that protrudes from the organism's posterior ends (Vaughan et al., 2008).

The parasitic family Trypanosomatidae contains over 50 different parasitic protozoan species. The protozoan severely infects domestic animals but only mildly in wild animals. The species of trypanosomes can be classified based on the categories of organisms they infect, namely Animal trypanosomes (AT), Human trypanosomes (HT), and the group that includes both. These extracellular parasites have geographical footprints in both tsetse fly and non-tsetse fly areas. The major Trypanosoma species are listed in **Table 1**. There are several sub-species of the same trypanosome species, each of which affects or attacks a different type of organism. T. brucei, for example, has three sub-species, and each has preference for specific a host organism. T. brucei gambiense and T. brucei rhodesiense have been identified as having the ability to infect humans, whereas T. brucei chelonian is only infects non-human animals (Berberof et al., 1995).

Table 1 Major Trypanosoma species

Trypanosoma species	Reference
T. vivax	Garcia et al. (2014)
T. congolense	Garcia et al. (2014)
T. evansi	Garcia et al. (2014)
T. brucei rhodesiense	Garcia et al. (2014)
T. brucei gambiense	Garcia et al. (2014)
T. cruzi	Kasozi et al. (2021)
T. brucei crazy	Kasozi et al. (2021)
T. dionisii	Kasozi et al. (2021)
T. equiperdum	Kasozi et al. (2021)
T. thomasbancrofti	Kasozi et al. (2021)
T. elephantis	Kasozi et al. (2021)
T. vegrandis	Thompson et al. (2014)
T. pteropi	Thompson et al. (2014)
T. copemani	Thompson et al. (2014)
T. irwini	Thompson et al. (2014)
T. suis	Caro et al. (2022)
T. copemani, T. gilletti	Caro et al. (2022)
T. theileri	Kasozi et al. (2021)
T. godfreyi	Kasozi et al. (2021)
T. simiae	Kasozi et al. (2021)
T. Megatrypanum pestanai	Kasozi et al. (2021)
T. grayi	Cao et al.(2013)
T.parva	Cao et al.(2013)
T. musculi	Cao et al.(2013)
T. lewisi	Wheeler et al. (2013)
T. uniforme	Wheeler et al. (2013)
T. binneyi	Wheeler et al. (2013)
T. chelodina	Wheeler et al. (2013)

The genus Trypanosoma can also be grouped into two forms of families based on the parts of the hosts in which they reside; these groups are salivaria and stercoraria (Hughes & Piontkivska, 2003). Salivaria are groups of trypanosome species that reside in the salivary gland or anterior part of their vectors. Humans and mostly large animals are infected by these group Salivaria vectors (Malele, 2002). The salivaria group mostly emerges as mammalian infective forms in tsetse's mouthparts, such as the proboscis and salivary glands, and includes the causal agents of African animal trypanosomiasis (AAT), nagana, or human African trypanosomiasis (HAT) that are present across Sub-Saharan Africa (Aksoy et al., 2003). The second form are the stercoraria group. These are groups of trypanosome species that develop and reside in the posterior section of the digestive tracts of vectors (Malele, 2002). Mostly, the stercoraria group consist of trypanosome species that have footprints outside of Africa. These include the causal agents of Chagas disease, common in Latin America, which are T. cruzi and members of the Megatrypanum, such as T. theileri, T. parva, and others (Aksoy et al., 2003).

3.2 Life cycle of trypanosomes

Trypanosome species are known to undergo a complex life cycle that is extremely different in both primary and secondary hosts. Protozoan develops into a promastigote or epimastigote form in the gut of its primary vector. The epimastigote form is transmitted into the secondary vector through a bite from the primary vector (Zhang et al., 2010). Once in the secondary host, the metacyclic trypomastigotes and amastigotes adapt to the new environment as they circulate in the bloodstream. Upon adapting, they begin to undergo proliferation and differentiation via binary fission into new daughter cells. They then spread through body fluids like the spinal fluid, blood, and lymph (Milligan, 1996). This movement occurs in the initial stage of the disease, called the Neurological stage. Mostly, they become undetected at this stage of the disease.

The development of the protozoan can occur in two ways: (1) by migrating into the cerebrospinal part of its secondary host or (2) by developing in its primary host after taking a blood meal from an infected secondary host. If the development occurs in the secondary host, then the protozoan migrates into the cerebrospinal fluids of its secondary host, where it develops into procyclic trypomastigotes and becomes more virulent than in the initial phase of the disease (Vickerman, 1985). Here, the protozoan develops more rapidly and undergoes spontaneous division to enhance its chances of survival via binary fission (Laybourn-Parry, 1984). In the second phase of the disease in the vector, the protozoan develops into procyclic trypomastigotes and undergoes exponential cell division. After a more successful cell division, the procyclic trypomastigotes leave the midgut of the vector and migrate into the mouthparts of the insects, specifically the salivary glands, where they develop into the epimastigote form (Moussa, 2021). In the salivary gland, the protozoan continues to multiply and then changes its form from epimastigote to metacyclic trypomastigotes (Vickerman, 1985).

3.3 History of trypanosomiasis

In human history, trypanosomiasis has been around for centuries. The disease-causing agents existed ages ago, according to evolutionary and biological theories. Because of the presence of trypanosomiasis during the Egyptian old kingdom, it was believed that shepherds and livestock breeders kept both their cattle and game animals together (Steverding, 2008). The practices resulted in a trypanotolerant strain of organisms. In the second millennium, a veterinary Papyrus of the Kahun Papyri identified a disease in Horses and organisms that shared similar features as the Nagana disease, and a cure for this disease was an ointment extracted from the fats of a peculiar bird (Ebbell, 1937; Griffith, 1898). Reports and articles about the disease were officially documented during the Middle Ages. One of the first reports of the disease was made by the famous Arabian geographer Abu Abdullah Yaqut during his journey into the village

of Wangara (Gold Country) in the years 1179–1229 (Kea, 2004; Winkle, 2005).

The first case of the disease was reported after the era of the famous Ibn Khaldun. According to the Arabian, a countryman described a disease with the same modus operandi as a sleeping sickness that killed the emperor Sultan Mari Jata, Emperor of Mali, in his historical document. Mari Jata was possessed and died after two years of suffering from the disease with strange symptoms (Cox, 1996). The Fulbe clan, known as the Fulani tribe, was believed to have played a significant role in the discovery of the disease. They were thought to have identified the disease during their migration from Egypt or Ethiopia to the northern part of West Africa, the present-day location (Winkle, 2005). As known in modern times, the tribe was well known for their intensive rearing of animals, especially cattle. Their rearing activities revealed certain signs and symptoms of a strange disease that was identified and linked to the Nagana disease, which occurred around the 13th century (Winkle, 2005).

Trypanosomiasis was associated with slave trading in the nineteenth century. Trading became difficult because slave traders had an issue with their cargo being infected with the illness trypanosomiasis (Cox, 1996). Slave masters during the slave trade pressed their doctors to investigate the disease because of its negative impacts. Among these doctors was the famous surgeon, John Atkins. Atkins, in the periods of (1685–1757), reported the neurological aspects of the disease, describing the acute symptoms. Following John Atkins' report, another scientist named Thomas Winterbottom published a report in 1803 describing the symptom of a swollen lymph gland along the back neck, which was associated with the early stages of the disease (Cox, 1996). Certain symptoms described by the Arabs in prehistoric times were not documented (Cox, 1996; Winkle, 2005). Although the disease was well known until this point, individuals could not connect the dots between the disease and how it was being transmitted. Late in the eighteenth century, in the year 1852, a report published indicated that a Scottish missionary and explorer, David Livingstone, drew the line between the disease Nagana and the mode of transmission, which was a bite from the vector tsetse fly. David Livingstone was the first person to discover this after several cattle died from being bitten by the vectors (Bruce, 1895; Cox, 1996). The disease was at the time believed to be transmitted by both male and female tsetse flies. This incident occurred in the valley of the Limpopo and Zambezi rivers, as well as at the banks of the lakes Nyasa and Tanganyika (Winkle, 2005). After this major discovery, it took almost half a century for trypanosome species to be discovered as the causative agents of both nagana and sleeping sickness (Cox, 1996, 2004). The Scottish made a massive improvement towards the discovery of the disease. In the late 1850s, the interest of researchers took a new direction in the understanding of the disease. Identification of certain species of trypanosomes became the new path of development that was later investigated.

In the years 1874–1905, an English physician named Joseph Everett Dutton identified the causal agent as trypanosomes and proposed the species name Trypanosoma gambiense (now T. b. gambiense) in 1902 (Dutton, 1902). In 1895, another Scottish microbiologist and pathologist by the name of David Bruce contributed by discovering some specific species of trypanosome organisms. He discovered that T. brucei, one of the trypanosome species which can also cause nagana in cattle. This created a new development in this field because the specific species in question was already known to cause sleeping sickness in humans only (Ilemobade, 2009). In 1902, the Italian physician and pathologist Aldo Castellani made a breakthrough by discovering trypanosomes in the cerebrospinal fluid of sleeping sickness patients and made a conclusion that they cause sleeping sickness by living in the cerebrospinal fluid (Castellani, 1903; Cox, 1996).

3.4 Trypanosome epidemic and drug discovery

Africa is one of the continents to record the highest number of cases of the disease. Over the past centuries, Africa has experienced three severe trypanosome epidemics (Smith et al., 1998; Steverding, 2008). The continent recorded the first epidemic in 1896, which lasted for ten years and had a serious negative impact on countries like Congo, Kenya, and Uganda. It was estimated that about 300,000 to 500,000 individuals lost their lives, with very negative impacts on both human health and animal production (Cox, 2004; Hide, 1999). The spread caused an immediate investigation into the diseases, which was ordered by the colonial masters in search of a cure. One of the earlier drugs developed to battle the disease was sodium arsenate. This discovery was dedicated to two scientists named Charles Louis Alphonse Laveran and Félix Mesnil in 1902, and the drug was a cure for sleeping sickness based on their research in the years between 1845 and 1938 (Cox, 2004; Winkle, 2005).

The atoxyl form of the drugs was suggested to be effective on infected animals, and experimental research was conducted in 1904 led by a Canadian doctor named Harold Wolferstan Thomas and an Austrian doctor and zoologist named Anton Breinl, but unfortunately, these suggestions were disproved by Robert Koch (Cox, 1996). He investigated the trypanocidal activities of the atoxyl arsenate drug on the island of Ssese, located northwest of Lake Victoria, and came to the bold conclusion that the drugs were toxic and had adverse side effects after observing that out of 1622 patients suffering from sleeping sickness who were treated with the atoxyl form of the drugs, 22 of these suffered from optic nerve issues with complete blindness as a result of the treatments (Winkle, 2005). He then encouraged Paul Ehrlich, who had developed an interest in trypanosomiasis chemotherapy and had made a breakthrough in this area in 1904 by developing a dye called trypan red that was used to test for the presence of T. equinum, which causes sleeping sickness in mice and horses and was known as Mal de Caderas in Central and Southern America (Vickerman, 1997; Winkle, 2005). He was encouraged to continue Robert Koch's research and improve on the atoxyl drug, but unfortunately, the final breakthrough was made by Wilhelm Roehl, Paul Ehrlich's assistant, in 1906. He was able to improve the atoxyl form of the drug with the assistance of a small team of chemists and with the support of the German chemical and pharmaceutical company May and Baker. The drug became the first most effective and accepted drug for treating sleeping sickness, and the name of the drug was Suramin, or Bayer 205. The drug was highly effective against T. b. rhodesiense, and as such, it is still used to treat the early stages of the disease (Winkle, 2005).

This drug was investigated to produce a regimen for Nagana. A year earlier, Michael Heidelberger and Walter A. Jacobs, two scientists, discovered organo-arsenical tryparsamide, which was one of the major breakthroughs because it was the first drug used to treat nagana on a large scale. It was used to improve treatment outcomes and primarily combat the disease in its late stages, either alone or in combination with suramin. This contribution aided in the fight against the influenza epidemic of 1920 (Steverding, 2008). Sudan recorded their first case of AAT in 1904 in the veterinary department's annual report (Elkarib, 1961). In Central and South America, although trypanosomiasis has been around for millennia, it was not discovered in humans until 1909. T. cruzi, a distinct species of trypanosome, was identified as causing acute febrile illness in railway workers (Bonney, 2014). Other contributions were towards developing novel methods of

controlling the vectors and discovering drugs to combat the disease. Sir David Bruce was the one who recommended the practices of game destruction and reservoir host control. These practices drastically reduced the vector population, lowering the number of cases in East Africa (Lyons, 2002). In 1937, chemist Authur James Ewins developed pentamidine for the treatment of sleeping sickness, and later, DDT was first used to control vectors in endemic areas in 1949 (Steverding, 2008).

3.5 Signs, and symptoms of trypanosomiasis

The disease is primarily caused by the bite(s) from certain insects harboring the protozoan. Tsetse flies are the primary vector of this disease.The causative agent can be transmitted by a wide range of blood-feeding vectors, which include Heamatopota, submoristans (Abdeta et al., 2022), and hard-ticks (Böse et al., 1987). They are also transmitted by mechanical transmitters like tabanus and stomoxys (Vieira et al., 2017). The spread of the disease can be aided by the movements of certain mammals from one area to the other. Animals suffering from Nagana exhibit mild to severe symptoms based on the stage of the disease. The World Health Organization (WHO) suggests the use of a two-phase classification, haemolymphatic and meningocephalitic stages, which was accepted and used by the scientific community. The signs and symptoms vary based on the host and infecting trypanosome species. Differences in the immune response of the host organisms play a critical role in the rate of spread of the parasites and the severity of the disease (Amaral et al., 2006; Raoult & Roux, 1999).

The haemolymphatic stage is the first phase of the disease. Here, trypanosome species get introduced into the host system via a bite. The parasite gets adapted to its new environment and circulates into the bloodstream of its hosts. The circulation comes with the proliferation and differentiation of the parasite into new daughter cells. The affected hosts exhibit mild symptoms of headache, joint pain, confusion, and itching (Steverding, 2008). Fever, disturbed sleeping pattern, and eye discharge (Kapasi, 2024; Steverding, 2008). Sometimes, the animal suffers some symptoms that are non-specific, like pruritus, rashes, and weight loss (Kirchhoff & Rassi, 2011; Steverding, 2008), swelling of the face and hind limbs (Schmidt et al., 2011), malaise, arthralgia, hemostatic abnormalities, Leucopenia, and neutropenia (Mylan Pharmaceuticals ULC, 2015; Steverding, 2008). At this stage, the parasite adapts and multiplies intra and extracellularly in the host's bloodstream. The adaptation of the parasite is aided by a structure of glycoproteins and other proteins around the membrane that allows them to thrive (Mandal et al., 2013).

Migration of the parasites into the central nervous system (CNS), specifically the cerebrospinal fluid, marks the onset of the second phase of the disease, called the meningocephalitic or cerebrospinal stage. Here the parasite's virulent nature increases, giving rise to severe symptoms such as hair loss, oedema, anaemia, paralysis, coma, extreme lethargy, sensory disturbances, emaciation, listlessness, and disturbed sleep patterns in its host (Kristoffersen, 2002; Lopez, 2013). Other severe conditions set in as the parasite was not controlled, and some of these symptoms were immunosuppression. thrombocytopenia, microthrombi formation, and haemorrhage suggestive of disseminated intravascular coagulation (Perez et al., 2016; Steverding, 2008). Lacrimation, conjunctival petechiae, anorexia, enlarged lymph nodes, abortion, decreased fertility, and loss of body weight (Alanazi, 2018). Disruptions of the neuroendocrine system can also lead to impotence and infertility in both male and female mammals, respectively. The ultimate penalty is the death of the organism. From a microscopic point of view, some of these animals suffer from lymphoid hyperplasia of both lymph nodes and spleen, varying degrees of necrosis, and associated inflammation in the liver (Abd El-Baky & Salem, 2011).

3.6 Prevalence of animal trypanosomiasis on the individual continents.

Literature search was conducted to examine the global prevalence of trypanosomiasis, its threat to food security, and the frequency of host organisms studied. The host organisms studied, and the molecular approach used to screen for trypanosomes are summarized in **Fig. 3a** and **Fig. 3b**. Our review identified cattle as the most studied animal. Animals such as cattle, goats, and sheep are mostly reared under the extensive or semi-intensive system of farming (Lawal-Adebowale, 2012; Shivakumara & Kiran, 2019). In most African countries, housing for these animals is inadequate, hence the animals are exposed to flies and other organisms in the environment (Kiggundu et al., 2021; Nasiru et al., 2012). Also, the feeding activities (grazing) of these reared animals are done early in the morning and after sunset (Ayantunde et al., 2001). These are periods during which most of the vectors feed, creating a lot of exposure time between the animals and the vectors (Owaga et al., 1993).

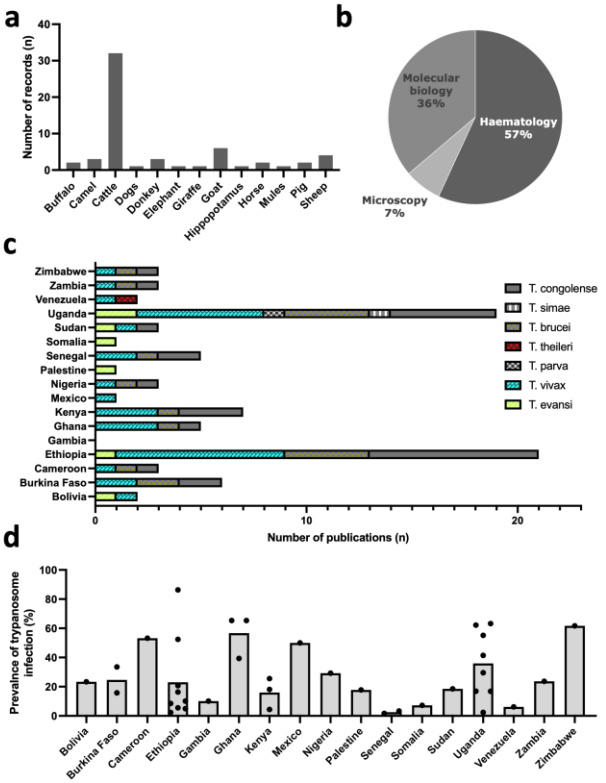

Fig. 3 Trypanosome infections reported by the studies reviewed. Types of animal studies (a). Methods used to investigate trypanosome infections (b). Geographical distributions of trypanosome species identified (c). Prevalence of trypanosome infections compared across countries (d).

Out of the 40 articles retained for analysis, 36 recorded trypanosome infections from Africa, making Africa the continent with the highest prevalence. Zimbabwe recorded the highest mean prevalence of (62%) followed by Ghana (57%) and Cameroon (53%). However, the highest number of reports (9 records) and prevalence (86%) were from Ethiopia (**Fig. 3c**). Next to Africa was South America, which had three reports, and Asia had only one report, with a prevalence of 18% in Palestine. The mean prevalence of animal trypanosomiasis was 27% in South America,

and these were recorded in 3 countries, namely Bolivia, Mexico, and Venezuela, with prevalence of 23%, 50%, and 6%, respectively (**Fig. 3d**). The reports from Mexico were on goats, while cattle were reported on from Bolivia and buffaloes in Venezuela.

The variations in the prevalence of trypanosome infection observed in our review suggest that geographical location may contribute to the distribution of vectors and trypanosome species. Only one strain of trypanosome was reported in Mexico, Palestine, and Gambia. On the other hand, T. vivax and T. congolense were reported in most countries (**Fig. 3a**). Trypanosomes are known to thrive in tropical regions, which may explain the variety of species observed from tropical countries. A previous report stated that distributions of the trypanosome species may be influenced by the type, sex, and age of the host animal, vector control strategies, and accessibility of trypanosome species to the hosts (Tehseen & Ramayah, 2015). The presence of a suitable mammalian host remains the most likely factor determining the spread and abundance of trypanosome species. The disease is known to affect female mammals more than male mammals (Kizza et al., 2022). The age of animals may also contribute to the variation, as calves are commonly affected by the disease compared to adults. Animal trypanosomiasis was reported as the cause of high calf mortality (> 70%) (Ahmed et al., 2016).

3.7 Effect trypanosome infection on food production

The disease has been a major challenge that the food industry faces. The food industry has been the backbone of economic development, contributing at least 20% of most country's total income (Azam & Shafique, 2017). Due to the high prevalence of the disease in Africa, especially in countries in the sub-Saharan region, farmers are faced with the challenge of maintaining healthy animal populations to maintain constant milk and meat production. An estimate of about $5 billion was calculated as annual estimated loss in livestock production due to trypanosomiasis (Murray & Gray, 1984; Williams et al., 1993). This clearly shows the number of agricultural products that are annually affected as raw materials for industrial processes, and commodities for exportation. The reduction in these individual agricultural products collectively causes a huge economic loss and eventually leads to poverty in rural areas, as they are the major source of income for farmers (Neil Adger, 1999). The disease also poses a great threat to food security as agricultural targets are not met by countries that heavily rely on agricultural activities as their major source of revenue. At the industrial level, low productivity is observed because of inadequate raw materials. Additionally, the extensive use of trypanocidal drugs has not been successful in controlling the disease due to drug resistance, leading to further economic losses as farmers spend a lot on these drugs without proper returns. Most countries are unable to meet their target of food supply, hence the need to rely on imported meat, dairy products, and canned foods, putting a strain on the economy (Afewerk et al., 2000; Buzby, 2001).

3.8 Effect trypanosome infection on crop production

Trypanosome infections have been reported in a wide range of animals like donkeys, camels, bulls, cattle, and horses used for crop farming (**Fig. 3**). These animals are used in farm practices like ploughing, planting grains, hunting, and transportation. Most rural areas in Africa, like northern Karamoja in Uganda (Muhanguzi et al., 2017) and other parts of the world use these as the main means of transporting agricultural products from farms to marketplaces and storage places. It is worth noting that trypanosome-infected (sick) animals cannot work effectively on the farm. Droppings from both domestic and farm animals serve as a rich source of manure for crop production. There is a reduction in the dropping of sick animals, which subsequently affects the quality and quantity of manure produced. Trypanosome infection results in the reduction of some essential nutrients in the animals and these include proteins (Holmes et al., 2000), carbohydrates (Aksoy et al., 2003), fats and some vitamin specifically vitamin E together with some minerals iron as the require folic acids (Aboko-Cole & Lee, 1974). Farm crops produce low-quality food as a result of stunted growth, and some crops eventually die due to a lack of essential nutrients (Karlen et al., 1992).

3.9 Effect trypanosome infection on meat and milk production

Farm animals reared in areas with less trypanosome presence as compared to those reared in a trypanosome-infected environment are mostly anaemic with stunted growth due to the trypanosomiasis infection (Connor, 1992; Ganyo et al., 2018). These animals often suffer from the disease, which eventually leads to an increase in weight loss, affecting the quality of the meat produced by these animals, and a reduction in nutrient composition. Exportation of the meats and meat products obtained from infected animals is considered of low quality and, as such, leads to rejection of these products (Deckers, 2011; Varnam & Sutherland, 1995). Such contamination can lead to severe health issues if not identified earlier, and these can lead to an unstable economy and an elevated poverty level as the impact on farmers will be massive (Briggs, 2003). The infected animals are mostly anaemic with low levels of proteins (Holmes et al., 2000), carbohydrates (Aksoy et al., 2003), fats and some vitamins, specifically vitamin E, together with some minerals, such as iron, and as well as folic acids (Aboko-Cole & Lee, 1974). Milk produced from animals infected with trypanosomiasis is of low quality as the disease is known to interfere with growth, metabolic, and hormonal activities (Matthewman et al., 1993). The effect of the interference of these biochemical changes affects both the quantity and quality of milk, as the milk produced lacks certain nutrients, and some strains of the trypanosome species are likely to cause contamination of the milk produced as traces of them can be identified in these products (Aboko-Cole & Lee, 1974; Leak, 1999). A study conducted reveals a 25% reduction in milk production when these animals are infected, indicating the severity of the disease (Ahmed et al., 2016).

3.10 Recommendation for control and prevention of trypanosome infection

3.10.1 Housing and grazing strategies

Changing the time and location of the grazing activities of farm animals can minimize their exposure to tsetse fly bites. Feeding periods for rearing animals in areas of tsetse fly belts can be controlled. The vector is known to be active in the early morning and evening. Feeding activities for these animals can be done during the afternoon to reduce exposure to these flies. Also, grazing in areas with dense vegetation should be avoided, as these are preferred habitats for tsetse flies and can also be beneficial (Swallow, 2000). Changes can be made to the type of housing systems used in rearing animals, as it is known that most farmers in Africa and Asia use extensive management systems instead of intensive management systems. Provision of a well-constructed house for these animals can be made with materials like screens, insect-proof netting, and treated curtains in addition to the basic and common wooden or plastic structure frame. Also, for livestock protective fences, high black nets treated with insecticide can be

attached to the fences of animal pens, kraal, stables, and others; this will help create a physical barrier against tsetse flies and reduce animal exposure. Regular cleaning of animal housing is encouraged, as the larvae of these parasites are known to survive in waste from infected animals. These practices are necessary to prevent the spread of the disease, and proper ventilation is necessary to prevent overheating of the housing system in hot climates (Dias & Schofield, 1999).

3.10.2 Vector control

Controlling vector density can be achieved by destroying the habitat of flies by regular weeding of brushy and marshy areas around human settlements. Also, using insecticide-treated traps, target technology, and screens to attract or repel tsetse flies away from the animal-rearing areas plays a vital role in preventing diseases. Insecticide-treated nets or curtains are used to protect animals during resting periods, especially at night. Activities of such nature can create a conducive environment where animals can thrive with minimal exposure to trypanosomes (Allsopp, 2001).

The application of pheromonal-induced chemosterilant drugs like pyriproxyfen and deltamethrin are able to induce infertility in female vectors. This prevents the organism from reproducing (Hargrove et al., 2012; Okoth et al., 1991), ending the progressive life cycle of the parasite. Also, some of these drugs target the male vectors by rendering them impotent or sterile, preventing them from mating and reproducing new offspring with the female insect specifically the queen. These drugs are applied in sprays, drones, and plane sprays forms to distribute droplet of these drugs in solution forms (Mangan, 2005). This aid farmers to covers vase areas and enhance effective control.

Insecticides are applied with the aim of killing and incapacitating the vectors carrying trypanosome. Spraying DDT as an insecticide has been an excellent strategy in the fight against the Nagana disease (Williams & Williams, 1992). DDT drastically reduces the vector, lowering the number of cases associated with the disease. Spraying with organophosphorus drugs such as diazinon and carbamate, as well as pyrethroid-containing drugs such as flumethrin and permethrin, is also effective against the vectors known to mechanically transmit the disease. These drugs are applied in the form of pour-ons, sprays, whole-body dips and baths, and sprays and showers.

3.10.3 Chemotherapy

Regularly administering trypanocidal drugs, chemotherapeutic and chemoprophylactic treatment (**Table 2**) in collaboration with boosters and other drugs for the prevention and management of the nagana disease have been employed over the years to help prevent the spread of the disease (Kalule, 2010; Vytalis, 2013). Consultation with veterinarian and other professionals is essential to determine the appropriate drugs, dosages, and treatment intervals for the specific type of trypanosomiasis prevalent in a particular region. The use of these practices has created new avenue and modern strategies in effectively controlling the disease (Muhanguzi et al., 2017).

Table 2 Anti-Trypanosoma drugs reported by the studies reviewed

Drug	N	Mode of action	Reference
Isometamidium	4	When in the system of the infected animal, it rapidly concentrates in the mitochondrion of trypanosome species lyses the parasite.	Ardelli & Woo (2001)
Deltamethrin	1	Deltamethrin is effective against insects both through ingestion and through direct contact. Pyrethroids, in general, disrupt normal nerve signal production and transmission in the nervous system. Deltamethrin act on nerve membranes by delaying the closing of the sodium ion channel gate and creating ion imbalance on the membranes of these species leading to death.	Narahashi (1996)
Diminazene aceturate	8	The main biochemical mechanism of the trypanocidal actions of Diminazene aceturate is by binding to trypanosomal kinetoplast DNA (kDNA) in a non-intercalative manner through specific interaction with sites rich in adenine-thymine base pairs. This causes destruction of genes and knockout of some protein at the gene level before transcription.	Ayantunde et al. (2019); Ibrahim et al. (2015)
Homidium bromide	1	It binds to DNA by intercalating between base pairs, which causes the DNA helix to partially unwind preventing protein synthesis and DNA replication leading to death of the trypanosome species.	Newton (1957); Waring (1965)
Veriben B12	1	This Diminazene aceturate drug incorporated with vitamin B12 and binds trypanosomal kinetoplast DNA (kDNA) in a non-intercalative manner through specific interaction with sites rich in adenine-thymine base pairs which can cause the destruction of genetic materials in the trypanosome species.	Ayantunde et al. (2019); Ibrahim et al. (2015)
Samorin R	1	Samorin R is an improved version of Isometamidium. When this drug is administered, it is transported into the mitochondrion of the trypanosome species. In the mitochondrion, it accumulates in the kinetoplasts and causes disruption and lyses of the kDNA, killing the powerhouse of the organism and leading to death.	Ardelli & Woo (2001); Kratzer et al. (1992)

N, Number of publications that reported on use of drug

3.10.4 Cross breeding

Some livestock breeds exhibit natural resistance or tolerance to trypanosomiasis. Crossing susceptible breeds with trypanotolerant breeds of animals has been an ancient practice. This application aids in producing new breeds of organisms that can resist these trypanosome species and are effective in tsetse fly belts. Careful breeding and selecting animals that are genetically resistant or more tolerant to the disease can reduce the susceptibility of the herd. This method also plays an important part in an integrated control strategy for controlling the spread of diseases in many African and Asian countries (Soudré et al., 2013).

4. Conclusion

Here, we provided comprehensive information on the life cycle and history of trypanosomes with special focus of trypanosomiasis and its effect food security. The results confirm the wide geographical distribution and diverse host range of trypanosome species. This study revealed a high prevalence of trypanosome infection in Africa.

Authors' Contributions

S.M.A., W.E.: Conceptualization; S.M.A., I.O.: Data Curation; I.O., M.A.O., E.S.E., K.K.: Original Draft preparation; S.M.A., W.E.: Supervision; All authors: Writing - Review & Editing. All authors read and approved the final manuscript.

Conflict of interest

The authors declare no conflict of interest.

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