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Review article

A comprehensive exploration of schistosomiasis: Global impact, molecular characterization, drug discovery, artificial intelligence and future prospects

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ABSTRACT

Schistosomiasis, one of the neglected tropical diseases which affects both humans and animals, is caused by trematode worms of the genus *Schistosoma*. The disease is caused by several species of *Schistosoma* which affect several organs such as urethra, liver, bladder, intestines, skin and bile ducts. The life cycle of the disease involves an intermediate host (snail) and a mammalian host. It affects people who are in close proximity to water bodies where the intermediate host is abundant. Common clinical manifestations of the disease at various stages include fever, chills, headache, cough, dysuria, hyperplasia and hydronephrosis. To date, most of the control strategies are dependent on effective diagnosis, chemotherapy and public health education on the biology of the vectors and parasites. Microscopy (Kato-Katz) is considered the golden standard for the detection of the parasite, while praziquantel is the drug of choice for the mass treatment of the disease since no vaccines have yet been developed. Most of the previous reviews on schistosomiasis have concentrated on epidemiology, life cycle, diagnosis, control and treatment. Thus, a comprehensive review that is in tune with modern developments is needed. Here, we extend this domain to cover historical perspectives, global impact, symptoms and detection, biochemical and

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molecular characterization, gene therapy, current drugs and vaccine status. We also discuss the prospects of using plants as potential and alternative sources of novel anti-schistosomal agents. Furthermore, we highlight advanced molecular techniques, imaging and artificial intelligence that may be useful in the future detection and treatment of the disease. Overall, the proper detection of schistosomiasis using state-of-the-art tools and techniques, as well as development of vaccines or new anti-schistosomal drugs may aid in the elimination of the disease.

1. Introduction

Schistosomiasis, also known as Bilharziasis, is a parasitic disease which affects both humans and livestock [1]. It is caused by trematode worms of the genus *Schistosoma* which can cause both acute and chronic diseases in humans. Documentations from the Egyptian and Assyrian medical texts suggested the disease has been with mankind since antiquity [2,3]. Discoveries of the parasites and life cycle by early scientists such as Alpini, Bilharz, Weinland, Mason, Katsurada, Ruffer and Leiper gave more insight about the biology of the parasites and how it is able to spread [3].

The disease is considered as one of the neglected tropical diseases and ranked second after malaria in terms of the number of infected persons and those at risk of the infection [2,4,5] (Fig. 1). It is estimated that about 250 million people are infected and 800 million are at risk of the infection. Out of these numbers, between 280 and 300 thousand individuals are thought to die annually [6–8]. However, there is a marked geographical variation in the prevalence of the disease [9]. In areas of high prevalence and death rates, the disease is normally common among school children, adolescents and young adults of school going age, women, fishermen and farmers using irrigation practices [9–11]. It affects communities with poor access to good drinking water, lack of proper sanitation practices and inadequate health facilities [1].

Human schistosomiasis is thought to be caused by eight species of the genus *Schistosoma* which are responsible for the various types of the disease. These species are *S. haematobium* (urogenital), *S. mansoni* (intestinal/hepatic), *S. japonicum* (arteriovenous), *S. intercalatum* (rectal), *S. mekongi* (arteriovenous), *S. guineensis* (rectal), *S. malevensis* (arteriovenous) and *S. mattheei* (urinary) [13]. Of the eight, *S. haematobium*, *S. mansoni* and *S. japonicum* are the most common and also most pathogenic [3]. Apart from the human infective forms, species such as *S. bovis*, *S. curassoni*, *S. hippopotami*, *S. indicum*, *S. rahhaini* and *S. spindale* have been reported to cause the animal disease [14].

Transmission of schistosomiasis is mostly dependent on certain environmental factors that affect the intermediate host. The main factors responsible for the transmission of schistosomiasis involve how close individuals are to water bodies (dams, irrigation projects) and certain socioeconomic factors (poverty, migration, climate change) [15,16]. The life cycle of an adult schistosome requires an asexual multiplication or development phase within a snail intermediate host. The adult form of the parasite then dwells in the blood vessels around the bladder and intestines of vertebrate hosts [17]. This therefore may suggest that climate change that may alter the aquatic environment of the intermediate host may significantly affect transmission and distribution of the disease [17]. The human

Fig. 1. Global distribution of Schistosomiasis across different endemic regions. The figure shows the approximate minimum (5.10 %) and maximum (85.40 %) mean prevalence, calculated as a percentage of the total global prevalence. About 97 % of the total Schistosomiasis infections occur in Africa. Africa also records 85 % of the global at-risk population [12].

infection occurs when there is contact with water bodies contaminated with free-swimming larvae known as cercariae which are released by the intermediate snail host [18]. In animal schistosomiasis, other mammalian hosts are involved.

According to the Centers for Disease Control and Prevention (CDC), symptoms of the disease are not caused by the worms themselves but by the body's ability to react to the eggs [19]. The disease can progress from mild symptoms to severe complications if left untreated. Most people do not show symptoms of the disease when they are first infected. However, after days or months (1–2 months) of infection, affected individuals may develop rashes or itchy skin and later fever, cough, chills and muscular pains which are also common in some viral, bacteria and protozoan infections [9,19]. Symptoms and clinical signs may vary depending on the nature of the infection. For instance, in patients with urinary schistosomiasis, the classical manifestation is haematuria which is associated with higher frequency of dysuria and urinary incontinence [8,20]. Chronic cases of the urinary disease may be characterized by bladder and urethra fibrosis, hydronephrosis and possibly cancer of the bladder [9,21,22]. Clinical signs and symptoms of intestinal schistosomiasis at the early stages may include abdominal pains, diarrhoea, anorexia, weight loss and blood in stool [8,9]. At the advanced stages, intestinal schistosomiasis is accompanied by anaemia due to excessive bleeding from ulcerations of the colon and rectum [8,23]. Additionally, some affected persons may show signs and symptoms such as hepatosplenomegaly, portal hypertension [18] fibrotic strictures, fistulas and perforations in the bowel [24].

Although the elimination and control of schistosomiasis have been successful in many countries, the disease is still a major public health concern in many other affected areas [25]. The successes have been possible due several strategies that have been adopted to effective control the disease. Some of these measures include vector control, diagnosis and chemotherapy, environmental control, improved health education, provision of clean water, and sanitation and surveillance [26]. Over the years praziquantel has been the drug of choice in treatment and public health strategy to fight schistosomiasis [26]. This drug is thought to increase the membrane permeability of the parasites towards calcium ions leading to muscle contraction and hence paralysis [27]. Although the drug has been used for several years, prevalence rate is still high in some parts of Africa ([28]; Fig. 1). Ideally, vaccines are the surest way to complement the efforts of anti-schistosomal drugs as it would cause a reduction in the rate of transmission and reinfection cases. Currently, no effective vaccines have been developed for schistosomiasis. However, significant progresses have been made on potential vaccine candidates at different phases of clinical development such as *S. mansoni* - TSP-2 [28,29], *S. mansoni* – cathepsin B1 [7], *S. mansoni* p80/GLA-SE [29], *S. mansoni* 14/GLA-SE [30], *S. haematobium* 28 – GST [31] and *S. japonicum* insulin receptor 1 [7].

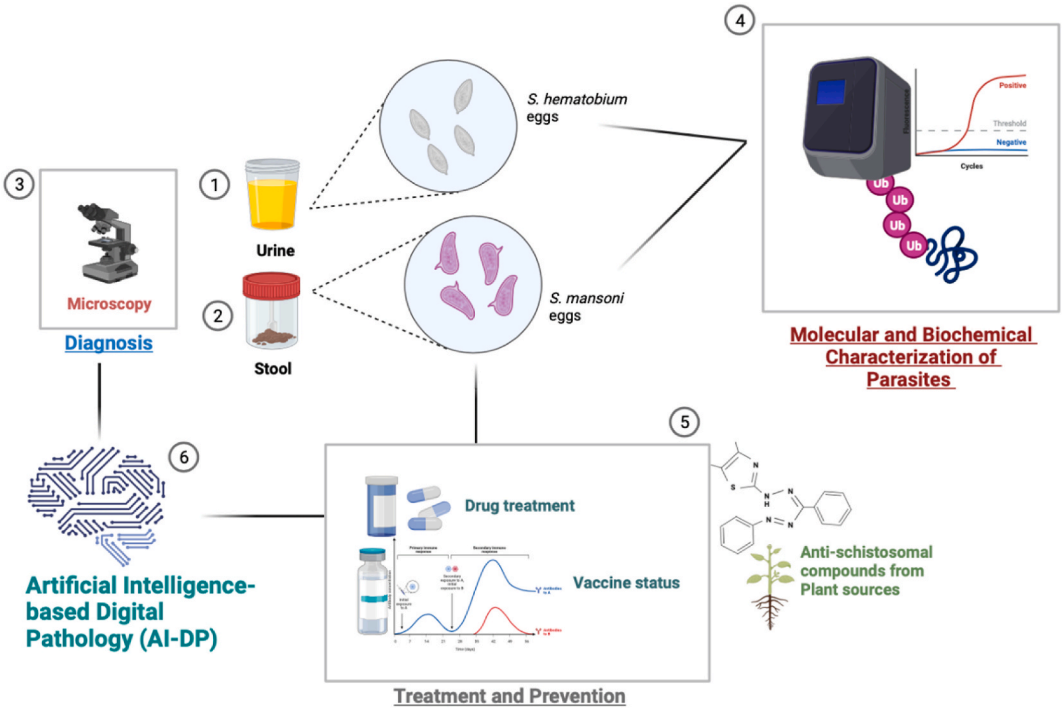

Fig. 2. An illustrative summary of the study. Eggs are screened in (1) Urine samples for *S. haematobium* detection and (2) Stool samples for *S. mansoni*, *S. japonicum*, and *S. mekongi*. (3) Microscopy is used as the gold standard for diagnosis and detection of *Schistosoma* eggs. (4) Molecular and biochemical tools for parasite characterization. Biomarkers such as the partial region of the mitochondrial cox1 gene, the 18S rRNA gene, and the nuclear rDNA (ITS1- 5.8S- ITS2) regions are being explored for *Schistosoma* parasite characterization. (5) Drugs such as Praziquantel are used for the treatment of Schistosomiasis as well as in Mass Drug Administration (MDA) programs. Plant-based compounds with anti-schistosomal activities are currently being explored for use as novel drug candidates for the treatment of schistosomiasis. Progress is currently being made to target candidate schistosomal antigens for the development of vaccines. (6) Artificial Intelligence-based Digital Pathology (AI-DP) has been employed in the detection and automated scanning of helminth eggs in stool, as well as in the clinical diagnosis of Schistosomiasis-associated hepatic fibrosis, and the prediction and prognosis of advanced Schistosomiasis.

Treatment, prevention and control of severe complications are dependent on the proper identification as well as early and accurate diagnosis of the disease. The choice of an appropriate diagnostic method is largely dependent particularly on the stage of the infection and the availability of resources. The disease is diagnosed based on clinical signs and symptoms, identifying the causative organisms and the way the react to certain biochemical tests. Some of the successful diagnostic methods used include parasitological examination (microscopy), serological evaluation (ELISA, RDTs), molecular detection (PCRs, LAMP) and imaging (ultrasonography) [7,32–34].

Over the years, reviews on schistosomiasis have mostly focused on epidemiology, life cycle, diagnosis, control and treatment. Thus, a comprehensive literature synthesis remains lacking. The present review takes into consideration historical perspectives, global economic ramifications, detection methods, molecular characterization, drug discovery, current vaccine status and applications of artificial intelligence (Fig. 2). It also focuses on the prospects of using plants as potential sources of anti-schistosomal agents for the purpose of drug discovery and development. Furthermore, the use of imaging and artificial intelligence in the detection and treatment of the disease and future prospects of the research are highlighted.

2. Methodology

This comprehensive literature synthesis was based on a thorough compilation and analysis of research work carried out on schistosomiasis. Major areas of focus included the historical development, geographical distribution, economic ramifications, mode of transmission and infection, symptoms and mode of detection, drug discovery and applications of artificial intelligence in the detection and treatment of schistosomiasis. Curation of data was based on an extensive literature review conducted with the help of databases and resources such as PubMed, PubChem, DrugBank, protein data bank NCBI, Gene Ontology, UniProt, Prota4u, and String Database. Key words and phrases used in the search process included ''schistosomiasis'', ''schistosoma'', ''anti-schistosomal'', ''praziquantel'', ''cercariae'', ''miracidia'', ''artificial intelligence in schistosomiasis'', ''plants against schistosomiasis'', ''symptoms of schistosomiasis'', ''molecular detection of schistosomiasis'', ''economic impacts of schistosomiasis'', ''drug discovery in schistosomiasis'', ''vaccine development in schistosomiasis'', ''life cycle of schistosomiasis'' and ''global distribution of schistosomiasis''.

3. History and geographical distribution of schistosomiasis

Theodor Maximilian Bilharz, a German pathologist, was the first to discover *S. haematobium* and *S. mansoni* in 1851. He described eggs of *S. mansoni* as rather deformed probably because he observed a few of the *S. mansoni* eggs having a lateral spine relative to the

Table 1
History and geographical distribution of schistosomes.

Region	Year	Species/Strains	Snail Vector	Host	References
Gondwanaland	>120 million years ago	*S. haematobium*, *S. mansoni*	*Bulinus africanus* group, *Bu. forskalii* group, *Bu. truncatus/tropicus* group	Mammals	[36,41]
Asia	70–148 million years ago	*Schistosoma indicum* group, *S. japonicum*	*Onchomelana nosophora*	Mammals	[36,41]
Western Russia and North Eastern Africa	Ice age, post-glacial era, 2000 B.C.	*S. haematobium*	ND	Paleolithic man, neolithic man	[49]
Central and Eastern Africa	Ice age, 12000 B.C., 10000 B.C.-8000 B. C., 2000 B.C.	*S. haematobium*	ND	Human, paleolithic man, neolithic man, and naturally infected animal reservoir	[49]
Far East	3.8 million years ago, 1880s–1980s	*Schistosoma japonicum*, *S. mekongi*	Pomatiopsidae	Pre-Human, Human	[50,51]
North Eastern Africa	c.1184-c.1087 B.C.	*S. haematobium*	ND	Human	[52]
Middle East	c.1650 (Bronze age)	*S. haematobium*	*Bulinus truncatus*	Human	[53]
Eastern Asia	1880s–1980s	*Schistosoma japonicum*	*Onchomelana nosophora*	Human	[36,41,54]
Sub-Saharan Africa	1934	*Schistosoma intercalatum*	*Bulinus forskalii*, *Bu. africanus*	Human	[55,56]
Southern and Western Africa	1969	*S. haematobium* and *S. mansoni*	*Biomphalaria pfeifferi* Krauss, *Bulinus africanus*, and *Bulinus truncatus rohlfsi*	Human	[36]
Latin America	ND	*S. mansoni*	*Biomphalaria glabrata*	Human	[38,39,57]
Africa, Middle East, Central and South America, and Eastern Asia	ND	*S. haematobium*, *S. mansoni*, *S. japonicum*, *S. intercalatum*, *S. guineensis*, *S. mattheei*	Species of *Biomphalaria*, *Bulinus*, *Onchomelania*	Human	[36,58]
Eastern and Western Africa	Unknown	*S. haematobium*	Physidae and Bulinidae	Monkeys and baboons	[59]
Eastern and Western Africa	Unknown	*S. mansoni*	Planorbidae	Monkeys and baboons	[59]

ND = not determined.

numerous *S. haematobium* eggs having a terminal spine. Louis honoured his teacher Sir Patrick Manson (who before then recognized that *S. haematobium* was found in urine while *S. mansoni* was found in faecal matter) by naming this species after him. Robert Leiper in 1916 then confirmed the two species of *Schistosoma* parasites and demonstrated their life cycle [35].

The exact origin of schistosomiasis may be very difficult to predict. Nonetheless, evidence from surviving written records and eggs of *Schistosoma* parasites found in human remains [36] among others have been helpful in estimating to a degree of certainty for the beginnings of these parasitic flatworm infections or disease. While there is lack of hard evidence for the actual onset of schistosomiasis, it is believed that this disease had zoonotic origins that may predate recorded or documented history [37]. Genetic or molecular investigations propose finding *Schistosoma* parasite infections in human hosts around 1–10 million years ago in the savanna regions of Africa [38].

Having a common ancestry, the parasites have experienced diversification through evolution millions of years ago because of geographical separation [39]. It has therefore been speculated that *Schistosoma* evolved 70–120 million years ago on the supercontinent called Gondwanaland comprising present day Africa, Antarctica, Australia, India, and South America [40]. The ancestral *Schistosoma* parasites, *S. indicum* group, after moving to Asia from Africa between 70 and 148 million years ago evolved and later differentiated into *S. japonicum* in the spreading first to the Far East before spreading to other geographical locations [41–43]. The route for the spread of *Schistosoma* ancestral parasites groups from the African continent to the other endemic continents right from the Mesozoic through the Miocene Epoch to the present Cenozoic era was through Madagascar which served as the final connection or link during the era of continental drift. During this continental drift era [44], there was further evidence of the spread of schistosomiasis from Africa through Madagascar to other endemic continents using phylogeny to establish the existence of *Bulinus* snail vectors in Madagascar (*Bulinus bavayii*, *Bu. liratus.* and *Bu. obtusispira*) and their respective closely related species in sub-Saharan Africa (*Bu. africanus* group, *Bu. forskalii* group, and *Bu truncates/tropicus* group [45]. Additionally, australopithecines in order to get access to food preferred living along freshwater bodies which provided them a lot of shellfish. These water bodies also had prehistoric snail vector shells and were suggested to be frequented by baboons who are reservoirs for *S. mansoni* [36]. This demonstrates the coexistence of australopithecines and *Schistosoma* parasites in the Pleiocene era.

Other schools of thought believe schistosomiasis spread through movement of early modern man out of Africa to different endemic continents via the "green Sahara" and Nile Valley during the Holocene era or different times of the Pluvial periods about 120,000 years ago [46–48]. The "green Sahara' had therefore supported the migration of animals and especially humans out of Africa up to about the last interglacial era and with this human migration came the massive dispersal of human *Schistosoma* parasites from Africa to other parts of the world. In modern times, the widespread irrigation projects and construction of dams has significantly increased the spread of schistosomiasis. The disease has been a burden from Antiquity and pre-Antiquity to modern times until the discovery of the anthelmintic, praziquantel, in the 1980s which reduced the menace of schistosomiasis through mass drug administration campaigns [36]. Table 1 summarizes the historical and geographical development of the disease.

4. Economic importance of schistosomiasis

Schistosomiasis poses significant economic impact with inherent tradeoffs between water resources development and public health. While irrigation schemes are one of the most important policy responses designed to reduce poverty, particularly in sub-Saharan Africa, they facilitate the propagation of schistosomiasis and other diseases due to its impact on public health, productivity, healthcare costs, and overall socio-economic development [60].

Firstly, it affects healthcare costs and treatment, demanding long-term management that places a considerable burden on affected healthcare systems. The World Health Organization estimates the annual economic burden of schistosomiasis, including treatment costs and lost productivity, to be around $3.5 billion globally [61]. This diversion of resources hampers healthcare infrastructure improvement and addressing other pressing health issues.

A study conducted by The Economist Intelligence Unit and The End Fund reveals that Ethiopia, Kenya, Rwanda, and Zimbabwe face significant economic setbacks due to schistosomiasis and soil-transmitted helminthiasis. Complete eradication of these diseases by 2030 could inject over $5 billion into their GDP by 2040, positively impacting education and future earning potential among school-age children [62].

In specific countries, such as Egypt and China, schistosomiasis inflicts substantial economic costs. For instance, in Egypt, the annual cost of treating schistosomiasis exceeds $215 million, impacting agriculture and the labor force [63]. In China's Dongting Lake region, schistosomiasis results in a 5.3 % reduction in rice yields, translating to an annual economic loss of over $80 million [64].

Chronic schistosomiasis infections cause fatigue, anemia, and decreased physical activity, affecting educational attainment and future productivity, especially in children. In Egypt, a historically affected region, schistosomiasis contributes to decreased agricultural productivity and labor force participation [65].

Agricultural productivity suffers as infected individuals experience fatigue and weakness, reducing efficiency in farm work [66]. In Burkina Faso, the poorest households engaged in subsistence agriculture bear a heavy disease burden, experiencing an average yield loss of 32–45 % due to schistosomiasis [60]. The disease's negative impact extends to the tourism industry, deterring tourists and foreign investment in affected regions. High prevalence areas may face economic stagnation due to reduced revenue from tourism. This can impede economic development efforts in these areas [67].

Educational outcomes are also affected as schistosomiasis impacts cognitive function, absenteeism, and school attendance. In Zimbabwe, high prevalence rates lead to reduced educational attainment, hindering human capital development and limiting long-term economic opportunities [68]. Studies have shown that the disease significantly influences school attendance and performance, leading to reduced educational attainment and potential long-term economic consequences [69]. School dropouts are often

unable to attain the economically sustainable livelihoods for themselves and their families and are often left to undertake menial jobs that may not fetch as much.

5. Symptoms of schistosomiasis

When exposed to the schistosomiasis-causing larvae, many people have no symptoms. A general feeling of being unwell may be the disease's initial sign. The irritation at the point of entry may cause a person to experience "swimmer's itch" within 12 h of infection, which is characterized by a tingling feeling or light rash [70]. As the cercariae and eventually the adult worms and their eggs migrate through the body, the symptoms of schistosomal infection change over time. Seizures, paralysis, or spinal-cord inflammation may result from egg migration to the brain or spinal cord [71].

The symptoms of intestinal schistosomiasis, also known as bilharzia, include fever, bloody diarrhoea, body aches, and raised rash at the site of worm penetration. On the other hand, signs of urinary schistosomiasis include blood in the urine (haematuria), pain and irritation, enlarged liver and spleen (occurs in advanced cases), hypertension (linked to liver enlargement), fibrosis, and strictures [72]. The type of species developing the condition might also affect the symptoms of schistosomiasis. The early signs of *S. mansoni* include fever, raised rash, bloody diarrhoea, body aches, and abdominal pain. These symptoms can develop into chronic symptoms of anaemia, liver scarring, and irritation of the bladder. Initial symptoms of *S. japonicum* resemble those of *S. mansoni*, but they can develop into chronic symptoms in the affected organs. For example, the digestive system may experience bloody diarrhoea and abdominal pain, while the heart and lungs may experience continuous coughing and wheezing. Moreover, urinary symptoms of *S. haematobium* infection include bladder irritation, pain during urination, frequent urination, and blood in the urine, while genital symptoms may involve pain or discomfort during sexual intercourse [73].

6. Detection of schistosomiasis

There are several methods of detection for schistosomiasis (Table 2). Sir Patrick Manson used a microscope to show that *S. mansoni* was present in America in 1902 [3]. Several diagnostic methods are available for use during examinations, including the Kato Katz, miracidium hatching test (MHT), formol-ether concentration technique (FECT), circulating cathodic antigen (CCA), point of care test

Table 2
Detection methods of schistosomes and their applications.

Method	Principles/Applications	References
Urine filtration or sedimentation	Use of microscope after filtration or sedimentation of samples to determine the intensity of *Schistosoma mansoni* and *S. haematobium*	[75]
Kato Katz	Use of microscope to examine schistosome eggs to identify the intensity of *S. mansoni* and *S. haematobium* in urine and stool samples	[76]
Polymerase Chain Reaction (PCR)	Use of species-specific primers to determine low levels of DNA from schistosome samples	[3]
Formol-ether concentration technique (FECT)	Use of centrifuge to examine schistosome contaminated stool samples	[74]
Circulating cathodic antigen (CCA) and circulating anodic antigen (CAA)	Use of *Schistosoma* circulating antigens in urine or stool samples to detect decrease in levels from blood circulation into urine after treatment by praziquantel	[77]
Point of care test (POCT)	Diagnostic test for *S. haematobium* and *S. mansoni* in stool samples	[74]
Miracidia hatching technique (MHT)	Use of eggs present in stool samples using microscope by hatching of miracidia from ova to examine eggs in stool samples	[78,79]
Enzyme-Linked Immunosorbent Assay (ELISA)	Use of circulating anodic antigens to examine face, gut or shin samples contaminated with schistosome	[80]
OCTAM	Use of glycol-derivative to image the liver with prolonged infection to evaluate the hepatic function after infection	[81]
Positron emission tomography (PET)	Use of gamma rays produced by radionuclide tracer to detect *in vivo* and the assess worm burden	[81]
Fluorescence molecular tomography (FMT)	Fluorochrome-based infrared probes are used to view intravascular schistosomes	[82]
Intravital microscopy (IVM)	Use of microscopy to study biological systems *in vivo*	[83]
Confocal laser scanning microscopy (CLSM)	Using laser technology for scanning eggs for diagnosing schistosomiasis in mucosa and colons	[84]
Recombinase polymerase amplification (RPA) assay	Using amplification of the Dra1 DNA region of *S. haematobium* to identify low amounts of *S. haematobium* and *S. japonicum*	[85,86]
Computed tomography (CT scan)	Scanning of ascites, dilated collateral arteries, splenomegaly for chronic schistosomiasis that have anomalous patterns of egg calcification and damage to organs	[87]
MR scan	The hepatosplenic changes visualized by scanning of system for spinal and cerebral schistosomiasis	[88]
Indirect immunofluorescence antibody test (IFAT)	Use of antigens such as membrane bound antigens and gut associated antigens and read on a fluorescence microscope to detect schistosome eggs in stool, urine, rectal and bladder biopsies	[89]
Indirect hemagglutination assay (IHA)	Antigens of *S. mansoni* worms based on indirect haemagglutination used in the detection of antibodies in sera of *S. mansoni*	[90]
Colloidal dye immunofiltration assay (CDIFA)	A serological technique to detect *S. japonicum* in serum	[91]
Loop-mediated isothermal amplification (LAMP)	Uses specific primers from both inner and outer parts to target a particular gene for amplification of DNA of schistosomes in stool, urine and serum	[92]
Environmental DNA (eDNA)	Use of species-specific TaqMan quantitative PCR assay to detect the environmental stages of *S. mansoni* in aquatic environment	[93]
Ultrasonography	Demonstrates schistosomal lesions in the hepatic parenchyma to provide direct information about lesions in target organs, their patterns and regression after treatment	[94]

(POCT), and PCR-based [4]. MHT examines the quantity of eggs present in stool samples whereby samples are suspended in distilled water in flasks then hatching of miracidia from ova could indicate infection occurring. This flask examination occurs at 4, 6, 8 and 24 h for the confirmation of the results. On the other hand, the Kato-Katz examination involves the use of slides and a light microscope, with the samples placed on a 200 μm Kato-Katz screen mesh. The sample is transferred into a 6 mm hole on the slide and a glycerol-soaked cellophane strip is used to cover the stool, afterwards examination is done for the presence and number of schistosome eggs [7]. The POCT diagnosis of *S. haematobium* and *S. mansoni* is made using a fast diagnostic test, and stool sample screenings for FECT are conducted using a centrifuge instrument [74].

Primers for the direct detection of tiny fragments of ancient DNA that are specific for either *S. mansoni* or *S. haematobium* have been created. PCR can be useful for the detection of DNA that have low-intensity levels [3]. A schistosome circulating anodic antigen was found using an enzyme-linked immunosorbent assay (ELISA) in the face, gut, and shin of Egyptian mummies in which *S. haematobium* infection was found to be present [80]. The approach has good specificity and can detect haematuria using a dipstick. It can also count the eggs in the urine after it has been filtered or centrifuged [80].

Recently, a glycol-derivative shortened OCTAM imaging method was used to image the function of the hepatocytes in mice afflicted with schistosomes [81]. Other imaging techniques such as the positron emission tomography (PET) are also used to directly identify parasites *in vivo*. PET involves the use of gamma rays produced by a radionuclide tracer which have been injected into the body of the parasites. Subsequently, three-dimensional images of the tracer concentration are created using computer analysis [81].

Fluorescence molecular tomography (FMT) can also be used to observe intravascular schistosomes *in vivo* [82]. Fluorochrome-based near-infrared probes are detected and quantified by FMT [82]. Fluorochrome distribution can be measured and evaluated at all tissue depths via tomographic slicing into a live animal [82]. To evaluate fluorochrome concentration and distribution in three-dimensional regions of interest within the animals, computer software acquires the FMT images. Intravital microscopy (IVM), is a method that uses microscopy to study biological systems *in vivo* at high resolution, has been utilized to directly monitor schistosomes inside of their hosts [83]. Confocal laser scanning microscopy (CLSM), a new diagnostic method for visualizing schistosome eggs, has just been developed [84]. *S. mansoni* eggs were initially found in the mucosa of dissected mouse stomachs and later in the colons of infected mice using a laser technology intended for scanning a living eye [84]. The recombinase polymerase amplification (RPA) assay, another method currently under study and development, has been shown to be effective in identifying low amounts of *S. haematobium* and *S. japonicum* [85].

Cesmeli et al. [87] reported that individuals suffering from chronic schistosomiasis have anomalous patterns of egg calcification and damage to their target organs. On a CT scan, it is easy to see splenomegaly, ascites, and dilated collateral arteries, among other schistosomiasis-related suggestive findings. According to Passos et al. [95], CT exhibits the degree of calcification associated with urogenital schistosomiasis better than other imaging modalities. Ectopic schistosomiasis, such as spinal and cerebral schistosomiasis, can be seen on magnetic resonance imaging (MR) scans [88]. The hepatosplenic changes associated with schistosomiasis, such as heterogeneity of the hepatic parenchyma, the presence of peripheral perihepatic vessels, periportal fibrosis, splenomegaly, siderotic nodules, and the presence of dilated venous collateral veins, can be clearly visualized on an MR scan [88].

Serum antibodies, antigen detection, DNA detection, and stool and urine microscopy for parasite identification are some of the diagnostic techniques for schistosomiasis that are now accessible [32]. In order to find antibodies in the serum of infected individuals, antibody-based procedures such as indirect immunofluorescence (IFAT), enzyme-linked immunosorbent assay (ELISA), and indirect hemagglutination (IHA) are used [96]. Colloidal dye immunofiltration (CDIFA) assay, a serological technique, provides quick, low-cost, and straightforward detection of *S. japonicum* in serum [91].

Detection methods may be advantageous in distinct ways. The Kato-Katz technique has been reported to be specific, easy to use, affordable, less arduous, and acceptable under field conditions [97]. According to Wang et al. [98], traditional parasitological diagnostic methods utilizing microscopy are typically of low-cost and do not require extensive training or advanced facilities. The primary serological test, ELISA, is thought to exhibit high sensitivity, specificity, positive connection with worm load, and ability to estimate the degree of an infection [99]. With a low cross-reaction profile, the colloidal dye immunofiltration (CDIFA) assay provides quick, easy, and affordable detection of *S. japonicum* in serum [91]. PCR can determine the infection density in hosts and detect early infections [100]. Low concentrations of *S. haematobium* and *S. japonicum* have been found using the RPA test [85].

Thatnotwithstanding, choice of technique goes hand in hand with corresponding limitations. For instance, the accuracy of the Kato-Katz technique depends on the species, severity of infection, and quantity of stool samples analyzed [97]. Microscopy is labor-intensive and time-consuming [98], and its applicability in resource-constrained situations is limited by the necessity for skilled microscopists in addition to their low sensitivity for the detection of light infections. Another drawback of using microscopic analysis of eggs in feces or urine is the challenge in tracking the efficacy praziquantel treatment [101]. Moreover, due to the fact that PCR can only process a small volume of sample, it may not offer any meaningful clinical advantage. Hence, the presence or absence of ova in the processed sample is determined by chance. The purification of urine and the preparation of complete DNA samples constitute further restrictions on the field application of DNA-based diagnostics [102]. Molecular screening techniques have been investigated in the majority of low resource settings. However, PCR application is particularly uncommon because of restricted resources and the need for costly technology, cold chain logistics, continuous power supply, and highly skilled labour [103].

7. Transmission and life cycle of schistosomes

The transmission and life cycle of *Schistosoma* involves a complex interaction between the definitive host, the environment and the intermediate host [104] (Fig. 3). The life cycle involves two hosts in which sexual and asexual reproduction occurs. The mammalian host is often the definitive host where sexual reproduction occurs whilst the Molluscan host is the intermediate host where asexual

reproduction occurs [105]. Both the miracidia which emerges from the eggs in fresh water and the cercaria which emerges from infected snails are non-feeding larval stages and they target the molluscan and mammalian hosts respectively [7]. Whilst the cercaria can infect a number of mammals including mice, humans and ruminants, the miracidia infect only snails, and they are highly specific to the genus of snails they infect [17]. For instance, *S. mansoni* would infect snails of the genus *Biomphalaria*, whilst *S. haematobium* and *S. japonicum* would infect snails of the genus *Bulinus* and *Oncomelania* respectively. *S. mekongi* infects snails of the genus *Neotricula* [105].

The eggs of mature schistosomal worms are released by the mammalian host into the external environment through urine or feces [106] (Fig. 3). These eggs are already embryonated before being released into the environment and the embryo goes through several processes in order to hatch into miracidium [107]. The flame cells of the embryo beat to signal the hatching process which leads to the contraction of embryo in preparation towards hatching [108]. The movement cilia of the miracidium begin from the anterior ends and spreads to the whole body, forcing the eggshell to rapture [108]. This occurs when the egg encounters fresh water. Freshwater provides an ideal environment for the intermediate host snails to thrive [109]. These snails are an essential part of the parasite's life cycle, and their presence is necessary for the successful transmission of schistosomiasis. Factors which influence hatching include temperature, light and salinity and freshwater provides the right environment for the eggs to hatch into the miracidium as well as for the miracidium to survive in the water [110].Studies have shown that water with high salt content is deadly to miracidia [109,111,112].

The miracidia must find and infect specific freshwater snail species for the next stage of its life cycle [104]. When the snail is in the water, it releases specific ligands which are picked up by the miracidia receptors [113]. Once the miracidia detect the specific ligands, it induces behavioral change in the miracidia which moves in proximity to the source of the ligand (chemoklinokinesis) [113]. As this happens, there is an increased quantity of miracidia as others also detect the ligands released by the snail [113]. The miracidia then penetrate the snails' tissues and transform into a different larval stage called sporocysts [114]. Studies show that the success of the penetration of the snail by the miracidia is largely dependent on the ability of the miracidia to evade the internal defense system of the snail, comprising largely of hemocytes and soluble components of the hemolymph [115]. After successfully invading the tissues of the snail host, the parasite undergoes several physiological and morphological changes and becomes a primary sporocyst [116]. This sporocyst, also referred to as mother sporocyst, is usually found at the fibromuscular tissue of the host, most often at the site of entry

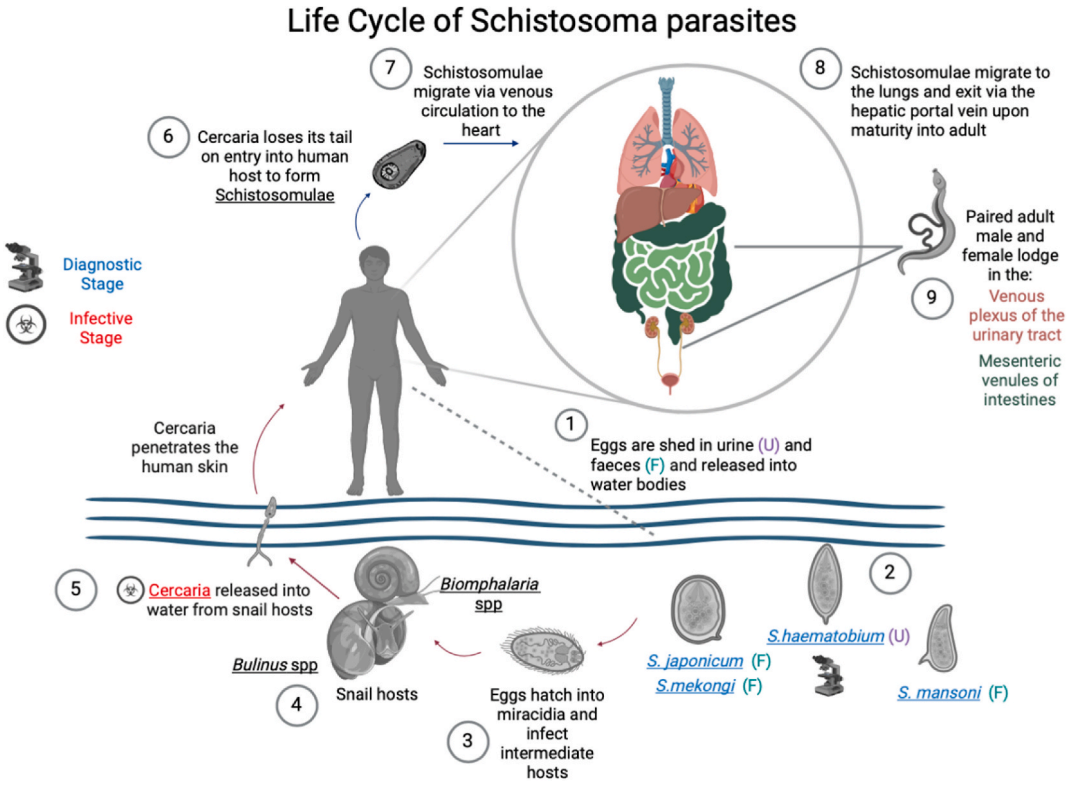

Fig. 3. Life cycle of the *Schistosoma* parasite. (1) *Schistosoma* eggs are introduced into water bodies via urine and stool. (2) *S. haematobium* eggs are shed in urine (U) whilst *S. japonicum*, *S. mekongi,* and *S. mansoni* are shed in stool (F). (3) Upon contact with fresh water, eggs hatch into miracidia and penetrate the tissues of snail hosts. (4) Common intermediate hosts are *Bulinus* and *Biomphalaria* species which have been implicated in the transmission *S. haematobium* of and *S. mansoni* respectively. (5) Free swimming cercariae are released into the water through the skin of snails. (6) Cercariae penetrate host skin and lose tail on entry to form Schistosomulae. (7) Schistomulae migrate to the heart via venous circulation. (8) Schistosomulae migrate to the lungs and leave after maturing into male and female adults. (9) Male adult worms enfold female worms and lodge in either the venous plexus of the urinary tract or the mesenteric venules of the intestines, depending on the species of the schistosome parasite.

[115]. Within 14–21 days, the primary sporocyst (mother sporocysts) generate secondary sporocysts (daughter sporocysts) which then move to the digestive gland or the hepatopancreas of the snail and this is where the cercariae are generated [117].

In response to sunlight, numerous cercariae exit through the snail's body after approximately one month into the water, resulting in the leakage of hemolymph and thus damaging the snail [115]. The released cercariae possess a tail and are able to swim freely in the fresh water where it can survive up to 48 h [109]. When individuals come into contact with freshwater contaminated with cercariae during activities such as swimming, bathing, fishing, or washing clothes, cercariae penetrate the skin, leading to infection [109]. Individuals who engage in activities like rice farming, fishing, or irrigation are at an increased risk of exposure due to prolonged contact with infested water sources [118]. In certain cases, transmission can occur through the use of contaminated water for domestic purposes, leading to the ingestion of cercariae [119]. Stagnant or slow-moving freshwater bodies are particularly conducive to the transmission of *Schistosoma* parasites and the spread of schistosomiasis [120]. For schistosomiasis transmission to occur, humans need to come into contact with contaminated water. Stagnant or slow-flowing water bodies often serve as sources of water for domestic, recreational, and agricultural purposes, increasing the likelihood of exposure to infected water [121]. Stagnant water bodies also provide an environment where cercariae can remain suspended in the water and come into contact with individuals entering or using the water, facilitating their penetration into the skin [120]. Furthermore, in slow-moving or stagnant water bodies, there is less dilution of parasites released by infected snails compared to swiftly flowing water [120]. This can increase the concentration of cercariae in the water and the chances of successful transmission to humans [118].

The cercariae enter the skin of the human host losing their tails in the process and transform into schistosomulae [122]. These schistosomulae make their way into the venous blood vessels, either directly or by infiltrating the lymphatic system [123]. From there, they are carried to the lungs through the right heart before progressing to the left heart, eventually entering the arterial circulation [124]. Once they reach the hepatic portal system, the schistosomulae migrate to the mesenteric veins in the liver. These adult worms each have a ZZ chromosome and the ZW chromosome pair in males and females respectively and so they mature into adult worms of separate sexes [125]. The male worm holds onto the female worm within the gynaecophoral canal, and together, they migrate to various locations specific to each species of the parasite [124]. *S. haematobium* migrates to the mesenteric veins of the bladder and

Table 3
The gender-associated (expressed highly in the associated gender) proteomic profile of adult *Schistosoma* spp.

Genes/Proteins	Adult female worms	Adult male worms	Reference
Gender associated	Epididymal secretory protein E1 Female-specific 800 protein Tyrosinases 1 and 2 Eggshell proteins (p14, p19, p34, p48, chorion, etc.)	Gynecophoral canal protein	[129,134]
Cytoskeleton and motor proteins		Actin 2 Troponins Dynein light chain 3 Myosin Myosin regulatory light chain Paramyosin Tropomyosin Alpha-actinin ′ Fimbrin Microtubule associated protein 1B Desmoyokin	[135]
Transporters		SGPT2 Fatty acid-binding protein	
Nutrient associated	Ferritin-1 heavy chain Cathepsin D Adenylosuccinate lyase	Cathepsin B	[135,136]
Growth associated	Elongation factor 1-alpha Polo-like kinase1 Ribosomal proteins Translationally controlled tumor protein Stathmin-like protein		[135]
Redox associated	Superoxide dismutase (SOD) Glutathione peroxidase Extracellular superoxide dismutase	28 kDa glutathione-S-transferase	[135]
Calcium signalling		Calponin Calpain	[135]
Tegument associated		Sj25, Sm23, Sm8, Sm15, Sm20 22.6kD tegumental antigen	[96,135] [137]
Membrane associated	23K integral membrane protein (SJ23) Annexin B13a Vesicular integral membrane protein Vip36 CD36 antigen Tetraspanin	Annexin Collagens Extensin class I Echinonectin	[135]
Immune associated	Cyclophilin B Immunophilin Mucin-like protein		[135]
Others	sm16 Histidine-rich proteins Asparagine-rich proteins	14-3-3 protein	[136]

ureters whilst *S. japonicum* more frequently migrates to the mesenteric veins of the small intestine whilst *S. mansoni* worms can exist in either large or small intestine [126].

The transmission of the disease relies heavily on environmental conditions, particularly those influencing the intermediate host, the snail [127]. It is conceivable that alterations in the environment due to factors like climate change could impact aquatic ecosystems, thereby leading to changes in the transmission of schistosomiasis [118].

8. Biochemical and molecular characterization of the schistosome

Schistosomes possess a pair of sex chromosomes and seven pairs of autosomes, totalling eight pairs of chromosomes [128]. *S. mansoni* and *S. japonicum* were targeted by the *Schistosoma* Genome Project instituted by the WHO in 1994 to promote novel chemotherapeutics discovery [129]. Consequently, draft sequences of *S. mansoni* (haploid genome ~300 Mbp) and *S. japonicum* (haploid genome ~397 Mbp) have been elucidated and are available in curated databases (http://www.genedb.org/genedb/smansoni/index.jsp; http://lifecenter.sgst.cn/schistosoma/en/schistosomaCnIndexPage.do). Phylogenetically, *S. mansoni* and *S. japonicum* belong to Lophotrochozoa in the clade *Schmidtea* under whole metazoan phylogeny [129].

Cercarial glycocalyx, egg glycolipids and glycoproteins, as well as glycoproteins secreted from the gut and in the membrane of adult *Schistosoma* are antigenic glycoconjugates [130]. *S. mansoni* and *S. haematobium* which produce ~1 and ~2 eggs respectively every 10 min share many carbohydrate-based egg antigens [130], compared to *S. japonicum* (~10 eggs per 10 min). Characteristically, schistosome glycoproteins contain a single residue of N-acetylglucosamine (GlcNAc) in O-linkage to either serine (Ser) or threonine (Thr) similar to subcellular modifications in mammalian nuclear or intracellular glycoproteins [130]. Further similarities between mammalian glycoproteins and schistosome surface localized glycoproteins is evident in the simple mucin-type O-glycans present in both. Important mammalian glycoproteins of this nature that mediate immune response to schistosomes include 2-deoxy-2--acetamido-*d*-galactose α-*O*-linked to Ser/Thr (GalNAcα1-Ser/Thr) constituting Tn antigens, and Galβ1-3GalNAcα1-ser/Thr which make up T antigens [130]. In mammalian hosts, adult schistosomes absorb glucose relying on glucose transporter proteins (SGTPs) while at various stages of the parasite both in the snail and mammal, fatty-acid binding proteins (FABPs) facilitate the uptake of host-derived fatty acids [129]. It is likely that other transporters such as a CD36-like class B scavenger receptor [131] and very-low

Table 4
Representative studies using RNA interference to manipulate schistosome genes.

RNAi Strategy	Development stage	Target gene(s)	Outcome	Reference
dsRNA[a] incubated with miracidia	Miracidia and sporocytes	CD36-like class B scavenger receptor (SRB)	Significant reduction in acetylated low-density lipoprotein binding to sporocysts	[131]
dsRNA incubated with miracidia	Miracidia and sporocytes	SGTP1	40 % reduction in Larval glucose uptake capacity.	[116]
dsRNA incubated with cercariae	Cercariae and transformed schistosomula	Cathepsin B	Potent suppression of cognate enzyme	[83]
dsRNA or siRNA[b] incubation with or electroporation of the worm	Cercariae, transformed schistosomula and adults	Cathepsin B	Cathepsin B was significantly suppressed up to 40 days	[138]
dsRNA incubation with 3-week-old worms	Adults	Cathepsins B1, L1 (=F), D and asparaginyl endopeptidase (legumain)	Synergistic inhibition of cathepsins D and B; reduced hemoglobin and albumin degradation, respectively.	[139]
dsRNA electroporation into schistosomula	Schistosomula	Cathespin B (SmCB1)	Significant growth retardation	[140]
dsRNA electroporation into schistosomula	Cultured schistosomula	Cathepsin D (Clan AA, Family A1) aspartic protease	Significant growth retardation *in vitro*; absence of accumulation of gut-localized hemozoin (lethal phenotype) *in vivo*	[141]
dsRNA and siRNA incubation or electroporation into worms	Cultured schistosomula and adults	Alkaline phosphatase (SmAP)	A >70 % reduction in Alkaline phosphatase enzyme activity achieved.	[142]
shRNA[c] electroporation into schistosomula	Transformed schistosomula	Mago nashi gene of *S. japonicum*	Morphological change in testicular lobes in male worms	[143]
dsRNA incubation with schistosomula	Transformed schistosomula	Thioredoxin glutathione reductase (TGR)	Death of parasites *in vitro*, within 4 days of silencing TGR	[144]
dsRNA incubation with pairs of adult worms and eggs	Adults and eggs	Inhibin/Activin (SmInAct)	SmInAct dsRNA–treated eggs failed to develop	[145]
siRNA electroporation into adults	Adults	Asparaginyl endopeptidase (SmAE) and cathepsin B1	SmAE silenced and cathepsin B1 fully processed and active	[146]
Particle bombardment of siRNA into 26–33 day old worm pairs	Adults	[d]TGF-β type II receptor (SmTβRII)	Reduction of gynecophoral canal protein	[147]
dsRNA incubation	Cultured schistosomula	Prx 1	Lowered survival of cultured parasites due to reduction in total enzyme activity	[148]

[a] dsRNA -Double stranded RNA.
[b] siRNA -Short interfering RNA.
[c] shRNA -Short/Small hairpin RNA.
[d] Transforming growth factor.

density lipoproteins [132] actively partake in uptake and utilization of other metabolites required for parasite cell function and development.

Schistosoma proteomic profile has been found to differ across developmental cycles and gender [129]. Proteomic and transcriptomic approaches have been used to study the differential gene regulation in male and female *Schistosoma* worms (Table 3), and inform the foray into gene manipulation studies with RNA interference techniques (Table 4). It has also been reported that the speed of movement of *S. haematobium* to the dermis after contact is similar in *S. mansoni* while it is much faster in *S. japonicum* [133]. Investigations using murine models reported that the inflammatory response leading to cercarial dermatitis is ordered by a local production of pro-inflammatory cytokines; interleukins (IL-1β, IL-6, IL-12), tumor necrosis factor alpha (TNFα) and monocyte chemoattractant protein-1 (M1P1α) [133]. Other immunoregulatory mediators, IL-10 and prostaglandins (PG) E_2 and D_2 are additionally released.

Schistosome parasites migrating into host hepatic mesenteries experience oxidative stress from two sources. The first being from immune generated radicals formed as part of the immune response and the other resulting from the parasite's own metabolism which involves breaking down and consuming host haemoglobin to release toxic heme and ferrous ions [149]. Evidence indicates that schistosomes lack catalase, the main enzyme required to neutralize the reactive oxygen species (ROS) hydrogen peroxide (H_2O_2), while their phospholipid classed glutathione peroxidases exhibit poor reactivity to H_2O_2 [149]. The parasites rely on peroxiredoxins (Prx) as an alternative for enzymatically disintegrating H_2O_2. The characteristically oxidative resistant adult stage was found to express higher amounts of Prx proteins than other stages in the life cycle of the parasite [149]. Generally, Prx proteins contain a reactive cysteine (Cys) in the N-terminal protein and are classed into three families; typical 2-Cys Prx, atypical 2-Cys Prx, and 1-Cys Prx [149]. *S. mansoni* expresses three typical 2-Cys Prx proteins which are approximately 65 % identical to each other and to mammalian typical 2-Cys Prx [148].

Beyond resistance to peroxidation, the outcomes of lipid peroxidation also contribute to disease progression and the inflammation process [150]. By-products such as cyclic peroxides and malondialdehyde are highly mutagenic and genotoxic as they cause mutations not limited to DNA-strand breaks and sister chromatid exchange [150]. Specifically, *S. haematobium* worms and eggs secret an estrogen-like metabolite that turns highly genotoxic after peroxidation. Catechol estrogens such as 4-hydroxyestrone (estradiol) (4-OHE_1 (E_2)), and 2-hydroxyestrone(estradiol) (2-OHE_1(E_2)) are further oxidized to their quinone forms, estrone (estradiol) 3, 4-quinone (E_1(E_2)-3, 4Q) leading to redox cycling and ROS production [151]. The ROS interaction with DNA causes formation of depurinating adducts that generate apurinic sites which eventually, over several potentially mutagenic cell generations, become cancerous [151].

Pioneering research identified circulating anodic antigen (CAA) and circulating cathodic antigen (CCA) from the gut of the schistosome [130]. CAA and CCA, together with GlcNAc, GalNAc, LacNAc (N-acetyllactosamine), and egg glycoproteins such as ICAM-1 (intercellular adhesion molecule 1), MEA (major egg antigen), OPN (osteopontin), SEA (soluble egg antigen), and SWA (soluble worm antigen) have become targeted biomarkers [152] for detecting schistosomiasis. A recent study reported that plasma concentrations of IL-6, eotaxin-1, LPS (lipopolysaccharide) and FABP (fatty-acid binding protein) did not significantly vary in uninfected and schistosome-infected children [153]. However, concentrations of sTREM (soluble triggering receptor expressed on myeloid) cells and sCD23 (soluble CD23) cells were significantly different ($p = 0.046$ and $p = 0.05$ respectively) for the two groups, being higher in schistosome-infected children [153].

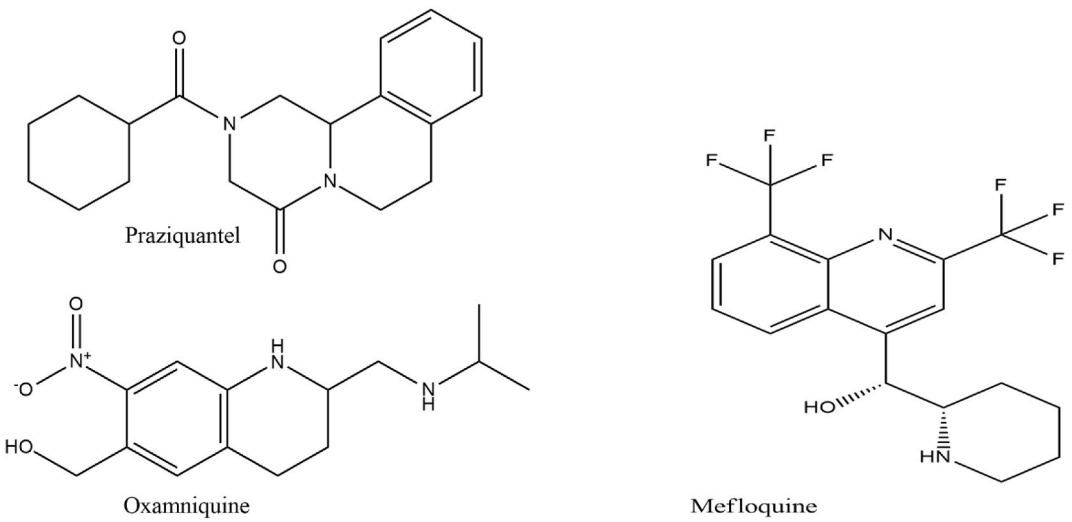

Fig. 4. Chemical structures of praziquantel, oxamniquine and mefloquine.

9. Current drugs and vaccines employed in *Schistosoma* infection

Currently, the preferred drug for schistosomiasis is praziquantel [154]. In Africa, it is largely employed in preventative chemotherapy (PCT) programs to treat intestinal and urogenital schistosomiasis illnesses caused by *S. mansoni* and *S. haematobium* parasites [155]. Discovered for its anthelminthic properties in 1972, the drug was originally intended for animal use. However, its effectiveness against all known human-infecting schistosome species and cestodes as well as tolerance by humans made it the ideal choice [156]. Praziquantel (PZQ) has been administered widely (mass drug administration) in PCT to treat schistosome infection and lessen related morbidity (Fig. 4), with an estimated 235 million people receiving Praziquantel treatments in 2018 alone [157]. Approximately 80 % of the drug is absorbed in the gastrointestinal tract [158]. Praziquantel (PZQ) is a racemic drug, with the standard dose comprising of an equal 1:1 mixture of two enantiomers. The (R) enantiomer, referred to as Levo-PZQ, L-PZQ, or (−)-PZQ, possesses the anti-schistosomal activity. In contrast, the (S) enantiomer, known as Dextro-PZQ, D-PZQ, or (+)-PZQ, lacks antischistosomal action but contributes to some known adverse side effects of PZQ [159]. The exact mechanism of PZQ's antiparasitic action is not fully understood. However, research indicates that the (R)-PZQ enantiomer disrupts the parasite's calcium ion homeostasis, leading to uncontrolled muscle contraction and eventual death of the parasite [27]. A meta-analysis showed that praziquantel monotherapy had a 76 % protection rate against schistosomiasis [160]. However the efficiency of the drug increased with higher dosages, with a protection rate of 91 % when the dosage was increased to 60/80/100 mg/kg divided into two or more doses [160].

Artemisinin derivatives, such as artemether and artesunate, have also been employed in the treatment of schistosomiasis in addition to praziquantel [160]. The meta-analysis found that the combination of praziquantel and artemisinin derivatives resulted in higher protection rates than praziquantel when used alone [160]. Praziquantel and artemether or artesunate together had a protection rate of 84 % for treating schistosomes and 96 % for preventing them. Multiple doses of artemether or artesunate have been recommended to be taken to prevent schistosome infection with 1- or 2-week intervals [160]. Praziquantel is effective in killing adult schistosomes, but it does not prevent re-infection and is unable to kill developing schistosomes [154]. This limitation of praziquantel highlights the need for alternative treatment options or strategies, such as vaccines, to control and eliminate schistosomiasis.

Another antimalarial drug that has been reported to have antischitosomal activity is mefloquine [161,162] (Fig. 4). Similar to the action of other artemisinin derivatives, mefloquine action is higher in immature *Schistosoma* as compared to adults with dose ranging from 200 to 400 mg/kg [162]. A study indicates a 70–100 % reduction with regards to parasite load [161]. Similar to mefloquine, trioxaquine was initially developed for the treatment of malaria but due to its dual mechanism which include alkylation of the heme group and the inhibition of hemoglobin formation it is employed against *S. mansoni* [161].

Two enzymes glutathione reductase and thrioreoxinareductase are responsible for antioxidant defense in vertebrates. The parasite schistosome also possesses the single, multifunctional enzyme thioredoxin reductase. The enzyme's penultimate amino acid at the C-terminal that is vital for the parasite's survival is selenocysteine, and this has been targeted by researchers to develop potent inhibitors with anti-schistosomal activity [163,164]. One of the identified compounds, furoxan, has shown activity against the parasite in micromolar concentrations [162,165] and was effective *in vivo* studies when given once daily for five days through intraperitoneal injections. However, furoxan compound has limitation due to its higher toxicity as compared to PZQ in mammalian cells [162,165].

Another drug that has been employed for treatment is oxamniquine (Fig. 4). This drug is effective against *Schistosoma mansoni* despite being relatively ineffective against other schistosome species [166]. A study carried out in Brazil have compared the effectiveness of oxamniquine to praziquantel [167]. The study showed that oxamniquine had comparable efficacy to praziquantel in the treatment of schistosomiasis [167]. However, in Brazil, oxamniquine has been replaced by praziquantel due to its cost-effectiveness [167]. The mechanism of action of the drug involves its activation by the enzyme *S. mansoni* sulfotransferase (SmSULT) that oxamniquine binds to and is transiently sulfated to a hydroxy-methyl group. The activated form of the drug then undergoes nucleophilic attack on macromolecules such as DNA, resulting in death of *S. mansoni* [168,169]. Alternately, the sulfur group will decay, followed by the activated oxamniquine acting as an electrophile, producing adducts with macromolecules and interfering with the metabolism of schistosomes. Apart from its narrow spectrum of activity, this drug has other shortcomings such as its potential for resistance development and the occurrence of side effects such as nausea, vomiting and abdominal pain [167]. These factors emphasize the need for alternate treatment options and the significance of implementing comprehensive control measures for schistosomiasis.

Schistosomiasis vaccines have been the subject of continuing research and development [154]. However, there are currently no licensed vaccines for the prevention of schistosomiasis. The complex life cycle of the parasite and the host immune response make it challenging and difficult to develop an effective schistosomiasis vaccine [154]. However, in preclinical and clinical investigations, a number of vaccine candidates have demonstrated promise. These include live attenuated vaccines, DNA vaccines, and recombinant proteins [154]. In animal models, some of the potential vaccines showed reduced pathology or partial protection against schistosome infection [154].

One such candidate is the large subunit of calpain (Sm-p80) from *S. mansoni* [170]. *S. mansoni* challenge infections in mice and baboons have been effectively averted by vaccines based on Sm-p80 [171]. This vaccine may be helpful in addressing various degrees of infection, illness, and transmission due to the differential expression of Sm-p80/Sm-p80 protein orthologs in different life cycle stages of the parasite [170].

Another vaccine candidate is the recombinant 28-kDa glutathione S-transferase of *S. haematobium* (rSh28GST) [31]. In a phase 3 trial conducted in Senegal, children aged 6–9 years received three subcutaneous injections of rSh28GST/Alhydrogel or Alhydrogel alone after clearing ongoing schistosomiasis infection with praziquantel [31]. The vaccine was found to be safe albeit with limitations as it did not demonstrate significant efficacy in preventing reinfection. The low levels of IgA and IgE as well as the lack of specific IgG3 antibodies in the vaccination group may have contributed to the vaccine's ineffectiveness [31].

10. Plants as anti-schistosomal agents

There have been reports of using *Asparagus stipularis* roots to cure schistosomiasis [172]. Additionally, the cercaricidal and adulticidal effects of five plant extracts (*Phyllanthus amarus, Morinda lucida, Nauclea latifolia, Vernonia amygdalina*, and *Azadirachta indica*) against *S. mansoni*, were compared in a study conducted by Acheampong et al. [173]. Results from the study showed that *V. amygdalina* had the best schistosomicidal activity *in vivo*, whereas *A. indica* had the most cercaricidal and adulticidal properties *in vitro*. Given the medicinal potential of these plant extracts, further research is required to identify the precise compounds causing the anti-schistosomal actions and to determine the underlying molecular pathways [173].

Furthermore, in acute murine schistosomiasis mansoni, a phenol derivative of turmeric spice known as curcumin therapy significantly reduced liver damage and parasite burden while also modulating the cellular and humoral immune responses of infected mice [174]. By downregulating fibrinogenic signaling in mice, other plants like Ziziphus spina-christi leaf extract have been shown to improve schistosomiasis-infected liver granuloma, fibrosis, and oxidative stress ([175]). Additionally, soluble glycoprotein fraction from *Allium sativum* purified by size exclusion chromatography was effective on murine schistosomiasis mansoni [176]. Additionally, the evaluation of the schistosomicidal properties of *Styrax camporum* and *Styrax pohlii* revealed that fractions from these species contain compounds capable of separating adult *S. mansoni* worms that are paired. Furthermore, *S. pohlii* and *S. camporum* may exhibit considerable potential as a source of active chemicals for future research because these compounds killed adult schistosomes *in vitro* [177].

Solasonine and solamargine, two glycoalkaloids from the fruits of *Solanum lycocarpum* A. St.-Hill. (Solanaceae), have shown effects on *S. mansoni* infection *in vitro*. Exposure to these substances impacted adult *S. mansoni* worm survival, split worm pairs, and accelerated the parasite's tegument desquamation in less than a day [178]. Furthermore, *Nigella sativa* by itself was able to lower the overall number of eggs and the quantity of *S. mansoni* worms in the liver. Even though the combination of *N. sativa* and PZQ had positive outcomes the observed parameters were even more intensified, with a total worm load reduced by up to 99 % [179]. Furthermore, after 24 h of *in vitro* exposure, piplartine's schistosomicidal activity, obtained from *Tuber tuberculatum* Jacq., Piperaceae, resulted in a decrease in the amount of eggs expelled through the feces and was as effective as praziquantel in killing adult stage *S. mansoni* worms [1]. *A. indica,* Meliaceae, which contains triterpenoids like limonin and nimbin, may be effective in reducing the survival rate of *S. mansoni* worms and thus induce tegumentary alterations *in vitro* [173]. Vernodalin, a sesquiterpene lactone with promising schistosomicidal activity, found in *Gymnanthemum amygdalinum*, Delile, Sch. Bip, Asteraceae, was able to completely eradicate the motor activity and ovipositioning of adult *S. mansoni* worms after 24 h of exposure [180]. Moreover, *A. indica* (3 h IC_{50} 27.62 μg/ml) and *G. amygdalinum* (3 h IC_{50} 35.84 μg/ml) both exhibited time- and concentration-dependent cercaricidal action. Following treatment *in vivo* with *G. amygdalinum, A. indica*, and praziquantel, the corresponding worm recoveries were 48.8, 85.1, and 59.9 %. Consequently, these plants and the active ingredients in them may be effective substitutes for treating schistosomiasis [179].

Quercetin, a flavonoid present in *Styrax ca*mporum Pohl., Styracacea, selectively inhibits the NAD^+ catabolizing enzyme of

Table 5
Plants with reported anti-schistosomal properties.

Family	Plant species	Plant part	Reference
Asparagaceae	*Asparagus stipularis*	Roots	[172]
Phyllanthaceae	*Phyllanthus amarus*	Leaves and stem	[173]
Rubiaceae	*Morinda lucida*	Stem and bark	[173]
Asteraceae	*Vernonia amygdalina*	Stem	[173]
Meliaceae	*Azadirachta indica*	Leaves, bark and root	[173,179]
Zingiberaceae	*Curcuma longa*	Roots	[174]
Rhamnaceae	*Ziziphus spina-christi*	Leaves	[175]
Amaryllidaceae	*Allium sativum*	Leave and stems	[176]
Styracaceae	*Styrax pohlii*	Leaves, stems and bark	[177]
Styracaceae	*Styrax camporum*	Leaves, stems and bark	[177]
Solanaceae	*Solanum lycocarpum*	Fruits	[178]
Ranunculaceae	*Nigella sativa*	Whole plant	[179]
Piperaceae	*Tuber tuberculatum Jacq.*	Leaves	[1]
Asteraceae	*Gymnanthemum amygdalinum*	Stems and leaves	[180,179]
Anacardiaceae	*Ozoroa pulcherrima*	Whole plant	[186,187]
Amaryllidaceae	*Allium cepa* L.	whole plant	[182,189]
Asteraceae	*Artemisia annua*	Roots	[184,185]
Asphodelaceae	*Hemerocallis fulva*	leaves	[186]
Malvaceae	*Melochia Pilosa*	Bark and stems	[186]
Fabaceae	*Millettia thonningii*	Leaves and stems	[189]
Asteraceae	*Berheya speciose*	Leaves	[190]
Ebenaceae	*Euclea natalensis*	Leaves	[190]
Meliciae	*Trichilia ematica*	Leave	[190]
Phyllanthaceae	*Phyllanthus amarus*	Whole plant	[191]
Asteraceae	*Eremanthus erythropappus*	Leaves	[192]
Malvaceae	*Sida pilosa*	Aerial parts	[193]
Pedaliaceae	*Harpagophytum procumbens*	Flower, leaves and stems	[189]
Verbenaceae	*Clerodendrum umbellatum*	Aerial part	[194]
Asteraceae	*Ambrosia maritima.*	Leaves	[195]

S. mansoni with an IC_{50} value of 3.9 and has moderately decreased its motor activity [177]. *In vitro*, the separation of mature worms from *S. mansoni* is triggered by kaempferol, a flavonoid that can also be extracted from *Styrax pohlii* A.DC and *S. camporum* Pohl., Styracacea, at a concentration of 100 μM [177]. From the Amaryllidaceae family, garlic (*Allium sativum* L.) and onion (*Allium cepa* L.) can significantly lower the worm load and egg count by restoring liver function enzymes and enhancing the antioxidant status of *S. mansoni* infection [181,182]. When *S. mansoni* was experimentally infected with an ethanolic extract of *Mentha piperita* L., Lamiaceae, also known as peppermint, 100 mg/kg of the extract showed parasitic and immunomodulatory properties, significantly increasing levels of IgG2a, IgG1, and IL-10 in comparison to the positive control (PZQ = 500 mg/kg) [183].

Since the 1980s, it has been demonstrated that *Artemisia annua*, a member of the artemisinin family of sesquiterpene trioxane lactones, is effective against *Schistosoma* species [184,185]. Artemisinin is the original component in this family. When a *S. mansoni* infection was treated with a methanolic extract of the roots of *Ozoroa pulcherrima*, at an average dose of 200 mg/kg, the host's anti-inflammatory and antioxidant capacities increased along with the load of eggs and worms [186]. Secondary metabolites such as anthraquinones and cardiac glycosides are responsible for *O. pulcherrima's* protective effects on the liver tissues of *S. mansoni*-infected animals [187,188]. Finally, another literature reports on the *in vitro* efficaciousness of norobtusifoline and kwanzoquinone, which are derived from the roots of *Hemerocallis fulva*, Asphodelaceae, in the treatment of schistosomiasis. All *S. mansoni* cercariae were totally immobilized by these compounds, and all adult worms' motor activity was stopped. The chemical components included in *Melochia pilosa* (Mill.) Fawc. & Rendle, Malvaceae, include alkaloids, phenols, tannins, and terpenoids, which are responsible for the extract's anti-schistosomal activity [189]. Table 5 provides a selected list of plants with reported anti-schistosomal properties.

11. Applications of artificial intelligence in the detection of disease

Traditional manual screening for parasites in fecal samples demands expensive equipment and significant expertise, limiting its applicability in resource-limited settings and contributing to the overuse of prophylactic medication. The integration of artificial intelligence (AI) in parasite detection and treatment seeks to address this challenge [196] (Table 6).

The AiDx Assist machine is an automated digital microscope that swiftly screens blood samples for microfilaria worms and detects *Schistosoma* eggs in urine. Designed for prompt parasitic worm detection in blood samples, it also reveals evidence of other Neglected Tropical Diseases (NTDs) during urine sample analysis [197]. Operating with a CMOS sensor, the multi-diagnostic AiDx Assist Microscope exhibits high precision in identifying S. *haematobium* and *S. mansoni* eggs in urine and stool samples. A study by Makau-Barasa et al. [198] attests to its comparable sensitivity and specificity, offering semi-automated and fully automated modes. In the semi-automated mode, operators visually confirm parasite presence after autofocusing, scanning, and registration, reducing time and errors. Conversely, the fully automated AiDx Assist employs AI for autofocusing, scanning, registration, processing, and automatic parasite count, streamlining the detection process [198].

The reversed-lens CellScope is another form of AI diagnostic tool for *Schistosoma*. This is a mobile phone-based microscope made up of a reversed iPhone 4S lens attached to an iPhone 4S that digitizes images for storage, cataloging, or sharing clinical information. It incorporates remarkable features, including the ability to save geographic coordinates for tracing infectious disease regions. The CellScope demonstrates over 95 % sensitivity in diagnosing *Schistosoma* parasites, with about four times improvement in sensitivity compared to the standard microscopy due to its wide image area (4 mm^2) [199]. In a study conducted by Coulibaly et al. [200], the reversed-lens CellScope exhibited sensitivities of 50.0 % *for S. mansoni* and 35.6 % for *S. haematobium*, along with specificities of 99.5 % and 100 % respectively. Similarly, in a study by Ephraim et al. [201], the mobile phone-mounted reversed-lens CellScope demonstrated sensitivity of 67.6 %, and 100.0 % specificity, compared to conventional light microscopy for diagnosing S. *haematobium*

Table 6
Methods and applications of artificial intelligence in schistosomiasis.

AI Tool	Application	Reference
AiDx Assist Microscope	Uses CMOS sensor; high precision in detecting S. *haematobium* and S. mansoni eggs in urine and stool samples; semi-automated and fully automated modes for parasite detection.	[197,198]
Reversed-lens CellScope	Mobile microscope digitizes images for diagnosing S. *haematobium*, mapping infectious disease regions; exhibits high specificity for S. mansoni and S. *haematobium*. Manual operation may affect sensitivity.	[199–201]
AINA	Diagnosing Female Genital Schistosomiasis (FGS); recognizes FGS-related lesions in patient photos, provides educational support, and continuously enhances diagnostic accuracy.	[202]
Schistoscope	Uses AI with a UNET-based deep neural network for automatic detection of *Schistosoma* haematobium eggs in urine. Operates semi- or fully automated, offering reliability and precise counting	[202,203, 204]
3S Technology	Integration of GPS, Remote Sensing, and Geographical Information System (GIS) for identifying *Schistosoma* risk factors, mapping prevalence areas, and evaluating *O. hupensis* habitat and transmission risks.	[205–208]
AI-DP Prototype	AI-based digital pathology for detecting soil-transmitted helminth and intestinal *Schistosoma* eggs; involves whole slide imaging (WSI) scanner, deep learning and data reporting system.	[209,210]
On-Chip Imaging	Employs CMOS sensor; visualized by transferring image captured by the camera imaging software unto a computer version. Utilizes direct on-chip imaging on a webcam sensor for identifying *Schistosoma haematobium* eggs.	[211]
Portable Robotic Microscope	Scans entire McMaster chamber, captures high-resolution images of fecal samples, autonomously identifies and counts egg species using a trained convolutional neural network.	[196]
Kubic FLOTAC Microscope (KFM)	Versatile and portable digital microscope designed for fecal specimens prepared with Mini-FLOTAC or FLOTAC. Proven efficient in detecting gastrointestinal parasites, validated for fecal egg count.	[212,213]
FECPAKG2	Uses the MICRO-I device to capture and digitize images of helminth-containing samples. Images are stored, transferred to online-based laboratories, and analyzed for expert diagnosis.	[214]

infection making the Cellscope a promising AI-diagnostic device for *Schistosoma* parasite.

AINA is an AI-driven app for diagnosing Female Genital Schistosomiasis (FGS). Developed with a human-centered approach, it aids healthcare professionals by recognizing FGS-related lesions in patient photos and providing educational support. The app employs a reinforcement learning feedback loop to continuously enhance diagnostic accuracy. Operating in rural African areas where FGS is endemic, AINA's user-friendly interfaces cater to local doctors, nurses, and midwives and FGS images captured in the field contribute to refining AI models [202].

The Schistoscope is another field application of AI in detection of *Schistosoma*. It is an affordable digital microscope tailored for on-the-spot diagnostics, particularly for schistosomiasis. It integrates Artificial Intelligence (AI) through a UNET-based deep neural network, facilitating automatic detection of *Schistosoma haematobium* eggs in urine samples. It can operate as either a semi-automated or a fully automated digital microscope with integrated AI for the identification and quantification of S. *haematobium* eggs [203]. Utilizing a Raspberry Pi camera module and a trained deep neural network, it automatically identifies and quantifies parasitic eggs in urine [203,215]. The AI algorithm in the Schistoscope excels in segmenting and counting, demonstrating reliability in resource-limited settings and diverse real-world conditions. Extensive experiments, including repeatability tests, show its comparability to conventional microscopes, capturing high-quality egg images. The designed autofocusing system enhances microscopic capabilities, surpassing alternative methods [204].

The 3S technology, comprising GPS, Remote Sensing, and Geographical Information System, streamlines *Schistosoma* risk factor identification [205]. The application of remote sensing and geographical information systems aid risk assessment in neglected rural areas, effectively warns remote residents, and maps high-risk zones for efficient environmental data extraction. This is similar to the role of Sentinel-1A satellite SAR image which is essential in extracting data from water bodies in risk assessment [206]. Integrating environmental factors and patient data allows detailed snail distribution analysis, aiding in identifying schistosomiasis risk areas. High-resolution remote sensing plays a crucial role in the spatio-temporal analysis of disease, monitoring, and prediction, advancing our understanding and control of *Schistosoma*, particularly *O. hupensis* habitat and risks [207,208].

AI-based digital pathology (AI-DP) transforms conventional microscopic approaches, revolutionizing clinical pathology and neglected tropical disease (NTD) programs. It addresses reproducibility and manual error issues through a system comprising a whole slide imaging (WSI) scanner, deep learning AI model, and data reporting system. While promising, its challenges include the lack of interpretability in deep neural networks, WSI scanner affordability, achieving comparable diagnostics, and ensuring reliable operation in resource-limited areas. A proof-of-concept AI-DP prototype, proved effective in detecting eggs of helminths in Kato-Katz thick stool smear. This demonstrates potential in monitoring and evaluating control programs for soil-transmitted helminth and intestinal *Schistosoma*, offering insights for effective integration [209,210].

Similar to the AiDX, On-Chip Imaging also employs the use of a CMOS sensor but in this case, visualized by transferring image captured by the camera imaging software unto a computer version. Utilizing direct on-chip imaging on a webcam sensor, two algorithms are employed to detect *Schistosoma haematobium*. Algorithm 1 is pattern recognition-based, while Algorithm 2 utilizes a sequence of 45 classifiers. The comparison assesses their effectiveness in identifying parasite eggs in images, with each stage of Algorithm 2 rejecting false positive samples passed through the preceding stages [211].

Another form of an AI diagnostic tool is the portable robotic microscope. This efficiently scans the entire McMaster chamber, capturing high-resolution images of fecal samples. With a trained convolutional neural network, it autonomously identifies and counts egg species, showcasing exceptional accuracy compared to manual counts by a trained operator [196].

Recently, the Kubic FLOTAC microscope (KFM), a versatile and portable digital microscope designed to analyze fecal specimens prepared with Mini-FLOTAC or FLOTAC, has emerged for use in the field and laboratory. In both field and laboratory settings, KFM has proven efficient in detecting gastrointestinal parasites and validated for fecal egg count [212,213]. KFM captures images, which can be transmitted online to parasitological or to a diagnostic hub for identification. This coupled with other features enables it to be remotely controlled in visualizing, identifying and counting structures relating to the parasite of interest [212].

The FECPAKG2 is also a sensitive, accurate and precise tool initially restricted for use in detecting helminths in animals. This protozoan diagnosis platform employs the MICRO-I device to capture and digitize images of helminths in helminth-containing samples. The captured image can be stored and uploaded online from remote settings for evaluation. Uploaded images are then sent to the laboratory for expert analysis and interpretation of results [214].

12. Conclusions and future prospects

The primary objective of reducing schistosomiasis morbidity, as stated by WHO, revolves around controlling the disease's spread [216–218]. WHO's strategy for schistosomiasis control centers on periodic and targeted praziquantel treatment for affected populations [61]. However, dependence solely on the medication may lead to the emergence of resistant strains as well as challenges primarily stemming from the frequency and rapid reinfection [219]. To effectively prevent and manage the disease, additional measures worth considering include large-scale treatment for all at-risk groups, provision of clean water, enhanced sanitation, hygiene awareness, behavior change, alongside efforts in snail control and environmental management [61].

Additionally, integrating a vaccine into a comprehensive approach aimed at controlling and preventing schistosomiasis could result in synergistic advantages when combined with chemotherapy. Viewing a vaccine as the logical next step in the pursuit of eradicating the disease is warranted [219]. Although many potential vaccine candidates have been identified, only a select few have advanced to the clinical trial stage, and these candidates may not provide the requisite level of protective immunity. There is an urgent requirement for an inventive and efficient pipeline aimed at developing an anti-schistosomal vaccine. This pipeline must prioritize the swift development and evaluation of new vaccine components on a large scale. This involves pinpointing and carefully choosing suitable

vaccine candidates through the application of cutting-edge technologies. Leveraging the mRNA vaccine platform, which has demonstrated exceptional efficacy in producing COVID mRNA vaccines, is a pivotal aspect. Furthermore, augmenting this initiative involves employing suitable animal models for immunological analysis and assessing vaccine efficacy [28].

Moreover, recent advancements in sequencing methods have significantly transformed biomedical research, introducing new techniques and refining existing ones. Notably, technologies like single cell RNA sequencing (scRNA-seq) [220–222] and related methods, such as CITE-seq [223–225] and chromatin profiling [224,226], offer valuable tools for profiling and identifying potential vaccine candidates and diagnostic targets for schistosomiasis [26]. Since, development of a vaccine is a time-consuming process that might extend over several decades, as well as the constrained financial resources allocated to vaccine development for neglected parasitic diseases commonly found in tropical areas, it is crucial to enhance funding and embrace a thorough and meticulously devised approach [219].

Currently, nanomaterials are being harnessed in the field of biomedicine to address the treatment, detection, and prevention of various human parasitic diseases. Due to their distinctive characteristics, nanomaterials have garnered notable attention and are being applied to enhance diagnostic techniques, refine therapeutic targets, and propel advancements in both the prevention of schistosomiasis and vaccine development [227]. Nanoparticles are relatively simple to develop, exhibit limited toxicity, amplify the efficacy of drugs by modifying solubility, and enhance drug absorption across biological barriers. Nanotechnology also amplifies the sensitivity and effectiveness of diagnostic tools. Consequently, the convergence of these innovations centered around nanomaterials holds the potential to transform the present landscape of medical treatment, disease management, and diagnostic approaches [227].

Modeling the impact of external and internal factors on the transmission dynamics of schistosomiasis is another approach to controlling the disease. A mathematical model suggests that an effective approach to managing the prevalence of schistosomiasis transmission involves a combination of interventions, including treatment, public health education, and chemical control strategies [228]. Climate change is predicted to indirectly affect the risk of schistosomiasis transmission through its interactions with factors like poverty, rural subsistence livelihoods, absence of clean water and sanitation, inadequate sewage systems, increased human mobility, limited access to affordable healthcare, expansion of agriculture and dam construction [229,230]. Consequently, the impact of climate change on schistosomiasis could combine with the outcomes of changes in land use, an expanding human population, and subsistence livelihoods in unforeseen ways. To address the uncertainty associated with potential shifts in schistosomiasis distribution due to climate change, novel research endeavors are essential. While investigating crucial questions concerning the interaction between climate change and schistosomiasis, public health agencies, non-governmental organizations, decision-makers, and communities have a range of choices to prepare for projected alterations in the propagation of schistosomiasis driven by the cumulative effect of climate fluctuations and changes in land utilization. Establishing comprehensive surveillance and response systems in regions where models suggest a substantial likelihood of schistosomiasis becoming endemic is of utmost importance [230].

Therefore, in the pursuit of eliminating schistosomiasis, a comprehensive approach is vital, which integrates treatment, diagnostics, a better understanding of disease pathogenesis, novel research tools like sequencing and nanotechnology, and the utilization of experimental models to evaluate new approaches for drug discovery process such as AI tools and QSAR models [26,227,231]. In addition, the WHO's roadmap emphasizes the importance of establishing a collection of biological samples (blood, urine, and feces) to develop, validate, and assess new diagnostic targets, which will play a pivotal role in the elimination of schistosomiasis [218].

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All data generated and used in the study can be found in this manuscript.

CRediT authorship contribution statement

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Declaration of competing interest

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References

[1] O.P. Aula, D.P. McManus, M.K. Jones, C.A. Gordon, Schistosomiasis with a focus on Africa, Tropical Medicine and Infectious Disease 6 (3) (2021), https://doi.org/10.3390/tropicalmed6030109.

[2] R.M.R. Barakat, Epidemiology of schistosomiasis in Egypt: travel through time: review, J. Adv. Res. 4 (5) (2013) 425–432, https://doi.org/10.1016/j.jare.2012.07.003.

[3] S. Di Bella, N. Riccardi, D.R. Giacobbe, R. Luzzati, History of schistosomiasis (bilharziasis) in humans: from Egyptian medical papyri to molecular biology on mummies, Pathog. Glob. Health 112 (5) (2018) 268–273, https://doi.org/10.1080/20477724.2018.1495357.

[4] M. Alemu, E. Zigta, A. Derbie, Under diagnosis of intestinal schistosomiasis in a referral hospital, North Ethiopia, BMC Res. Notes 11 (1) (2018) 245, https://doi.org/10.1186/s13104-018-3355-0.

[5] I. Mohamed, S. Kinung'hi, P.N.M. Mwinzi, I.O. Onkanga, K. Andiego, G. Muchiri, M.R. Odiere, B.J. Vennervald, A. Olsen, Diet and hygiene practices influence morbidity in schoolchildren living in Schistosomiasis endemic areas along Lake Victoria in Kenya and Tanzania—a cross-sectional study, PLoS Neglected Trop. Dis. 12 (3) (2018) e0006373.

[6] M.K. Sundaraneedi, B.A. Tedla, R.M. Eichenberger, L. Becker, D. Pickering, M.J. Smout, S. Rajan, P. Wangchuk, F.R. Keene, A. Loukas, Polypyridylruthenium (II) complexes exert anti-schistosome activity and inhibit parasite acetylcholinesterases, PLoS Neglected Trop. Dis. 11 (12) (2017) e0006134.

[7] M.L. Nelwan, Schistosomiasis: life cycle, diagnosis, and control, Curr. Ther. Res. 91 (2019) 5–9.

[8] C. Carbonell, B. Rodríguez-Alonso, A. López-Bernús, H. Almeida, I. Galindo-Pérez, V. Velasco-Tirado, M. Marcos, J. Pardo-Lledías, M. Belhassen-García, Clinical spectrum of schistosomiasis: an update, J. Clin. Med. 10 (23) (2021) 5521.

[9] H.A.H.A. Ismail, S.-T. Hong, A.T.E.B. Babiker, R.M.A.E. Hassan, M.A.Z. Sulaiman, H.-G. Jeong, W.-H. Kong, S.-H. Lee, H.-I. Cho, H.-S. Nam, C.H. Oh, Y.-H. Lee, Prevalence, risk factors, and clinical manifestations of schistosomiasis among school children in the White Nile River basin, Sudan, Parasites Vectors 7 (1) (2014) 478, https://doi.org/10.1186/s13071-014-0478-6.

[10] M.J. Mutsaka-Makuvaza, Z. Matsena-Zingoni, A. Katsidzira, C. Tshuma, N. Chin'ombe, X.-N. Zhou, B. Webster, N. Midzi, Urogenital schistosomiasis and risk factors of infection in mothers and preschool children in an endemic district in Zimbabwe, Parasites Vectors 12 (1) (2019) 427, https://doi.org/10.1186/s13071-019-3667-5.

[11] L.S. Maseke, V. Mushi, D. Tarimo, G. Kwesigabo, H. Mazigo, Adolescents and young adults excluded from preventive chemotherapy for schistosomiasis control in Northern Tanzania: are they at risk and reservoirs of infection? Prevalence and determinants of transmission in Northern Tanzania, IJID Regions 4 (2022) 111–119, https://doi.org/10.1016/j.ijregi.2022.07.008.

[12] P. Steinmann, J. Keiser, R. Bos, M. Tanner, J. Utzinger, Schistosomiasis and water resources development: systematic review, meta-analysis, and estimates of people at risk, Lancet Infect. Dis. 6 (7) (2006) 411–425, https://doi.org/10.1016/S1473-3099(06)70521-7.

[13] C.K. Bisangamo, Epidemiology and control of schistosomiasis, in: New Horizons for Schistosomiasis Research, IntechOpen, 2022.

[14] C.J. Standley, L. Mugisha, A.P. Dobson, J.R. Stothard, Zoonotic schistosomiasis in non-human primates: past, present and future activities at the human–wildlife interface in Africa, J. Helminthol. 86 (2) (2012) 131–140.

[15] A.F. Adenowo, B.E. Oyinloye, B.I. Ogunyinka, A.P. Kappo, Impact of human schistosomiasis in sub-Saharan Africa, Braz. J. Infect. Dis. 19 (2015) 196–205.

[16] N. McCreesh, G. Nikulin, M. Booth, Predicting the effects of climate change on Schistosoma mansoni transmission in eastern Africa, Parasites Vectors 8 (2015) 1–9.

[17] D.P. McManus, D.W. Dunne, M. Sacko, J. Utzinger, B.J. Vennervald, X.-N. Zhou, Schistosomiasis, Nat. Rev. Dis. Prim. 4 (1) (2018) 13, https://doi.org/10.1038/s41572-018-0013-8.

[18] B. Gryseels, Schistosomiasis, Infect. Dis. Clin. 26 (2) (2012) 383–397, https://doi.org/10.1016/j.idc.2012.03.004.

[19] Centers for Disease Control and Prevention, Schistosomiasis: Diseases, Centers for Disease Control and Prevention, 2018, April 11. https://www.cdc.gov/parasites/schistosomiasis/disease.html.

[20] J. Salas-Coronas, J. Vázquez-Villegas, A.B. Lozano-Serrano, M.J. Soriano-Pérez, I. Cabeza-Barrera, M.T. Cabezas-Fernández, A. Villarejo-Ordóñez, J. C. Sánchez-Sánchez, J.I. Abad Vivas-Pérez, S. Vázquez-Blanc, M. Palanca-Giménez, J.A. Cuenca-Gómez, Severe complications of imported schistosomiasis, Spain: a retrospective observational study, Trav. Med. Infect. Dis. 35 (2020) 101508, https://doi.org/10.1016/j.tmaid.2019.101508.

[21] P. Pallangyo, S. Bhalia, N.N. Simelane, F. Lyimo, H.J. Swai, Z.S. Mkojera, N.R. Hemed, N. Misidai, J. Millinga, M. Janabi, Massive bilateral hydroureteronephrosis and end-stage renal disease ensuing from chronic schistosomiasis: a case report, Journal of Investigative Medicine High Impact Case Reports 8 (2020) 2324709620910912.

[22] B. Efared, A.B.A. Bako, B. Idrissa, D. Alhousseini, H.S. Boureima, H.C. Sodé, H. Nouhou, Urinary bladder Schistosoma haematobium-related squamous cell carcinoma: a report of two fatal cases and literature review, Tropical Diseases, Travel Medicine and Vaccines 8 (1) (2022) 3.

[23] A. Beltrame, M. Guerriero, A. Angheben, F. Gobbi, A. Requena-Mendez, L. Zammarchi, F. Formenti, F. Perandin, D. Buonfrate, Z. Bisoffi, Accuracy of parasitological and immunological tests for the screening of human schistosomiasis in immigrants and refugees from African countries: an approach with Latent Class Analysis, PLoS Neglected Trop. Dis. 11 (6) (2017) e0005593.

[24] T.W. Schafer, B.R. Hale, Gastrointestinal complications of schistosomiasis, Curr. Gastroenterol. Rep. 3 (4) (2001) 293–303, https://doi.org/10.1007/s11894-001-0052-1.

[25] M.T. Inobaya, R.M. Olveda, T.N.P. Chau, D.U. Olveda, A.G.P. Ross, Prevention and control of schistosomiasis: a current perspective, Res. Rep. Trop. Med. (2014) 65–75.

[26] P. Ogongo, R.K. Nyakundi, G.K. Chege, L. Ochola, The road to elimination: current state of schistosomiasis research and progress towards the end game, Front. Immunol. 13 (2022) 846108.

[27] C. Thomas, D. Timson, The mechanism of action of praziquantel: can new drugs exploit similar mechanisms? Curr. Med. Chem. 25 (2018) https://doi.org/10.2174/0929867325666180926145537.

[28] A.J. Molehin, D.P. McManus, H. You, Vaccines for human schistosomiasis: recent progress, new developments and future prospects, Int. J. Mol. Sci. 23 (4) (2022) 2255.

[29] W.A. Keitel, G.E. Potter, D. Diemert, J. Bethony, H.M. El Sahly, J.K. Kennedy, S.M. Patel, J.L. Plieskatt, W. Jones, G. Deye, A phase 1 study of the safety, reactogenicity, and immunogenicity of a Schistosoma mansoni vaccine with or without glucopyranosyl lipid A aqueous formulation (GLA-AF) in healthy adults from a non-endemic area, Vaccine 37 (43) (2019) 6500–6509.

[30] M. Santini-Oliveira, R.N. Coler, J. Parra, V. Veloso, L. Jayashankar, P.M. Pinto, M.A. Ciol, R. Bergquist, S.G. Reed, M. Tendler, Schistosomiasis vaccine candidate Sm14/GLA-SE: phase 1 safety and immunogenicity clinical trial in healthy, male adults, Vaccine 34 (4) (2016) 586–594.

[31] G. Riveau, A.-M. Schacht, J.-P. Dompnier, D. Deplanque, M. Seck, N. Waucquier, S. Senghor, D. Delcroix-Genete, E. Hermann, N. Idris-Khodja, Safety and efficacy of the rSh28GST urinary schistosomiasis vaccine: a phase 3 randomized, controlled trial in Senegalese children, PLoS Neglected Trop. Dis. 12 (12) (2018) e0006968.

[32] K.G.A.D. Weerakoon, G.N. Gobert, P. Cai, D.P. McManus, Advances in the diagnosis of human schistosomiasis, Clin. Microbiol. Rev. 28 (4) (2015) 939–967.

[33] O. Ajibola, B.H. Gulumbe, A.A. Eze, E. Obishakin, Tools for detection of schistosomiasis in resource limited settings, Medical Sciences 6 (2) (2018) 39.

[34] B. Chala, Advances in diagnosis of schistosomiasis: focus on challenges and future approaches, Int. J. Gen. Med. (2023) 983–995.

[35] R.T. Leiper, On the relation between the terminal-spined and lateral-spined eggs of bilharzia, Br. Med. J. 1 (2881) (1916) 411.

[36] R. Bergquist, H.K.A. Adugna, Schistosomiasis: paleopathological perspectives and historical notes, in: Schistosoma, CRC Press, 2017, pp. 17–41.

[37] P.B. Adamson, Schistosomiasis in antiquity, Med. Hist. 20 (2) (1976) 176–188.

[38] L. Despres, D. Imbert-Establet, C. Combes, F. Bonhomme, Molecular evidence linking hominid evolution to recent radiation of schistosomes (Platyhelminthes: trematoda), Mol. Phylogenet. Evol. 1 (4) (1992) 295–304.

[39] J.A.T. Morgan, R.J. Dejong, G.O. Adeoye, E.D.O. Ansa, C.S. Barbosa, P. Brémond, I.M. Cesari, N. Charbonnel, L.R. Corrêa, G. Coulibaly, Origin and diversification of the human parasite Schistosoma mansoni, Mol. Ecol. 14 (12) (2005) 3889–3902.

[40] S.A. Beer, M.V. Voronin, O.P. Zazornova, G.G. Khrisanfova, S.K. Semenova, Phylogenetic relationships among schistosomatidae, Meditsinskaia Parazitologiia i Parazitarnye Bolezni 2 (2010) 53–59.
[41] G.M. Davis, Evolution of prosobranch snails transmitting Asian Schistosoma; coevolution with Schistosoma: a review, Prog. Clin. Parasitol. III (1993) 145–204.
[42] S.D. Snyder, E.S. Loker, Evolutionary relationships among the schistosomatidae (Platyhelminthes: Digenea) and an Asian origin for schistosoma, J. Parasitol. 86 (2) (2000) 283–288.
[43] S.P. Lawton, H. Hirai, J.E. Ironside, D.A. Johnston, D. Rollinson, Genomes and geography: genomic insights into the evolution and phylogeography of the genus Schistosoma, Parasites Vectors 4 (1) (2011) 131, https://doi.org/10.1186/1756-3305-4-131.
[44] D.J.J. Van Hinsbergen, P.C. Lippert, G. Dupont-Nivet, N. McQuarrie, P.V. Doubrovine, W. Spakman, T.H. Torsvik, Greater India basin hypothesis and a two-stage Cenozoic collision between India and Asia, Proc. Natl. Acad. Sci. USA 109 (20) (2012) 7659–7664.
[45] L. Andriamaro, P. Brémond, D. Rollinson, B. Sellin, E. Sellin, J.R. Stothard, Bulinus species on Madagascar: molecular evolution, genetic markers and compatibility with Schistosoma haematobium, Parasitology 123 (7) (2001) 261–275, https://doi.org/10.1017/S003118200100806X.
[46] A.H. Osborne, D. Vance, E.J. Rohling, N. Barton, M. Rogerson, N. Fello, A humid corridor across the Sahara for the migration of early modern humans out of Africa 120,000 years ago, Proc. Natl. Acad. Sci. USA 105 (43) (2008) 16444–16447.
[47] I.S. Castañeda, S. Mulitza, E. Schefuß, R.A. Lopes dos Santos, J.S. Sinninghe Damsté, S. Schouten, Wet phases in the Sahara/Sahel region and human migration patterns in North Africa, Proc. Natl. Acad. Sci. USA 106 (48) (2009) 20159–20163.
[48] N.A. Drake, R.M. Blench, S.J. Armitage, C.S. Bristow, K.H. White, Ancient watercourses and biogeography of the Sahara explain the peopling of the desert, Proc. Natl. Acad. Sci. USA 108 (2) (2011) 458–462, https://doi.org/10.1073/pnas.1012231108.
[49] C.F.A. Bruijning, Water, health and economic progress, Trans. Roy. Soc. Trop. Med. Hyg. 65 (Supplement_4) (1971) S47–S52, https://doi.org/10.1016/0035-9203(71)90080-0.
[50] L. Liu, G.-N. Huo, H.-B. He, B. Zhou, S.W. Attwood, A phylogeny for the pomatiopsidae (Gastropoda: Rissooidea): a resource for taxonomic, parasitological and biodiversity studies, BMC Evol. Biol. 14 (1) (2014) 29, https://doi.org/10.1186/1471-2148-14-29.
[51] C.J. Standley, A.P. Dobson, J.R. Stothard, Out of animals and back again: schistosomiasis as a zoonosis in Africa. Schistosomiasis, InTech, 2012, pp. 209–230.
[52] M.A. Ruffer, Note on the presence of "Bilharzia haematobia" in Egyptian mummies of the twentieth dynasty [1250-1000 BC], Br. Med. J. 1 (2557) (1910) 16.
[53] E.V. Hulse, Joshua's curse and the abandonment of ancient Jericho: schistosomiasis as a possible medical explanation, Med. Hist. 15 (4) (1971) 376–386.
[54] A.R. Bay, Total prevention: a history of schistosomiasis in Japan, Med. Hist. 66 (2) (2022) 95–115.
[55] A.C. Fisher, A study of the schistosomiasis of the Stanleyville district of the Belgian Congo, Trans. R. Soc. Trop. Med. Hyg. 28 (3) (1934) 277–306, https://doi.org/10.1016/S0035-9203(34)90066-3.
[56] L.-A. Tchuem Tchuenté, V.R. Southgate, J. Jourdane, B.L. Webster, J. Vercruysse, Schistosoma intercalatum: an endangered species in Cameroon? Trends Parasitol. 19 (9) (2003) 389–393, https://doi.org/10.1016/S1471-4922(03)00193-4.
[57] R.J. DeJong, J.A.T. Morgan, W.L. Paraense, J.-P. Pointier, M. Amarista, P.F.K. Ayeh-Kumi, A. Babiker, C.S. Barbosa, P. Brémond, A. Pedro Canese, C.P. de Souza, C. Dominguez, S. File, A. Gutierrez, R.N. Incani, T. Kawano, F. Kazibwe, J. Kpikpi, N.J.S. Lwambo, E.S. Loker, Evolutionary relationships and biogeography of Biomphalaria (Gastropoda: Planorbidae) with implications regarding its role as host of the human bloodfluke, schistosoma mansoni, Mol. Biol. Evol. 18 (12) (2001) 2225–2239, https://doi.org/10.1093/oxfordjournals.molbev.a003769.
[58] D.G. Colley, A.L. Bustinduy, W.E. Secor, C.H. King, Human schistosomiasis, Lancet 383 (9936) (2014) 2253–2264.
[59] M.G. Taylor, G.S. Nelson, B.J. Andrews, A case of natural infection of S. haematobium in a Senegalese baboon (Papio sp,), Trans. Roy. Soc. Trop. Med. Hyg. 66 (1) (1972) 16–17, https://doi.org/10.1016/0035-9203(72)90028-4.
[60] D. Rinaldo, J. Perez-Saez, P. Vounatsou, J. Utzinger, J.-L. Arcand, The economic impact of schistosomiasis, Infectious Diseases of Poverty 10 (1) (2021) 134, https://doi.org/10.1186/s40249-021-00919-z.
[61] World Health Organization (WHO), Schistosomiasis. https://www.who.int/news-room/fact-sheets/detail/schistosomiasis, 2023.
[62] A. Gouvras, What Is the Economic Impact of Schistosomiasis? A One Health Question, BugBitten, 2022, May 6. https://blogs.biomedcentral.com/bugbitten/2022/05/06/what-is-the-economic-impact-of-schistosomiasis-a-one-health-question/.
[63] T. El-Khoby, N. Galal, A. Fenwick, R. Barakat, A. El-Hawey, Z. Nooman, M. Habib, F. Abdel-Wahab, N.S. Gabr, H.M. Hammam, M.H. Hussein, N.N. Mikhail, B. L. Cline, G.T. Strickland, The epidemiology of schistosomiasis in Egypt: summary findings in nine governorates, Am. J. Trop. Med. Hyg. 62 (2_suppl) (2000) 88–99, https://doi.org/10.4269/ajtmh.2000.62.88.
[64] L. Zou, S. Ruan, Schistosomiasis transmission and control in China, Acta Trop. 143 (2015) 51–57.
[65] I.F. Abou-El-Naga, Towards elimination of schistosomiasis after 5000 years of endemicity in Egypt, Acta Trop. 181 (2018) 112–121.
[66] O. Combary, S. Traore, Impacts of health services on agricultural labor productivity of rural households in Burkina Faso, Agric. Resour. Econ. Rev. 50 (1) (2021) 150–169.
[67] E. Leshem, Y. Maor, E. Meltzer, M. Assous, E. Schwartz, Acute schistosomiasis outbreak: clinical features and economic impact, Clin. Infect. Dis. 47 (12) (2008) 1504–1506, https://doi.org/10.1086/593191.
[68] A.E. Ezeamama, A.L. Bustinduy, A.K. Nkwata, L. Martinez, N. Pabalan, M.J. Boivin, C.H. King, Cognitive deficits and educational loss in children with schistosome infection—a systematic review and meta-analysis, PLoS Neglected Trop. Dis. 12 (1) (2018) e0005524.
[69] A.E. Ezeamama, C.-L. He, Y. Shen, X.-P. Yin, S.C. Binder, C.H. Campbell, S. Rathbun, C.C. Whalen, E.K. N'Goran, J. Utzinger, A. Olsen, P. Magnussen, S. Kinung'hi, A. Fenwick, A. Phillips, J. Ferro, D.M.S. Karanja, P.N.M. Mwinzi, S. Montgomery, D.G. Colley, Gaining and sustaining schistosomiasis control: study protocol and baseline data prior to different treatment strategies in five African countries, BMC Infect. Dis. 16 (1) (2016) 229, https://doi.org/10.1186/s12879-016-1575-2.
[70] E.J. Pearce, A.S. MacDonald, The immunobiology of schistosomiasis, Nat. Rev. Immunol. 2 (7) (2002) 499–511, https://doi.org/10.1038/nri843.
[71] D.J. Gray, A.G. Ross, Y.-S. Li, D.P. McManus, Diagnosis and management of schistosomiasis, BMJ 342 (2011), https://doi.org/10.1136/bmj.d2651.
[72] C. Kokaliaris, A. Garba, M. Matuska, R.N. Bronzan, D.G. Colley, A.M. Dorkenoo, U.F. Ekpo, F.M. Fleming, M.D. French, A. Kabore, Effect of preventive chemotherapy with praziquantel on schistosomiasis among school-aged children in sub-Saharan Africa: a spatiotemporal modelling study, Lancet Infect. Dis. 22 (1) (2022) 136–149.
[73] J. Coia, H. Cubie, Schistosoma species, in: J. Coia, H. Cubie (Eds.), The Immunoassay Kit Directory, The Immunoassay Kit Directory, 2/1/3, Springer, Dordrecht, 1995, https://doi.org/10.1007/978-94-009-0359-3_32.
[74] N. Nausch, E.M. Dawson, N. Midzi, T. Mduluza, F. Mutapi, M.J. Doenhoff, Field evaluation of a new antibody-based diagnostic for Schistosoma haematobium and S. mansoniat the point-of-care in northeast Zimbabwe, BMC Infect. Dis. 14 (1) (2014) 1–9.
[75] P.A. Peters, A.A.F. Mahmoud, Ks Warren, J.H. Ouma, T.K.A. Siongok, Field studies of a rapid, accurate means of quantifying Schistosoma haematobium eggs in urine samples, Bull. World Health Organ. 54 (2) (1976) 159.
[76] N. Katz, A. Chaves, J. Pellegrino, A simple, device for quantita tive stool thick-smear technique in schistosomiasis mansoni, Revista Do Instituto de Medicina Tropical de São Paulo 14 (6) (1972) 397–400.
[77] A.O. Kildemoes, B.J. Vennervald, E.M. Tukahebwa, N.B. Kabatereine, P. Magnussen, C.J. de Dood, A.M. Deelder, S. Wilson, G.J. van Dam, Rapid clearance of Schistosoma mansoni circulating cathodic antigen after treatment shown by urine strip tests in a Ugandan fishing community–Relevance for monitoring treatment efficacy and re-infection, PLoS Neglected Trop. Dis. 11 (11) (2017) e0006054.
[78] Y. Shen, R. Ji, M. Yang, J. Lin, H. Wang, C. Zhu, Q. Xu, Establishment of a fluorescence staining method for Schistosoma japonicum miracidia, Sci. Rep. 10 (1) (2020) 16766.
[79] P. He, C.A. Gordon, G.M. Williams, Y. Li, Y. Wang, J. Hu, D.J. Gray, A.G. Ross, D. Harn, D.P. McManus, Real-time PCR diagnosis of Schistosoma japonicum in low transmission areas of China, Infectious Diseases of Poverty 7 (1) (2018) 25–35.
[80] L. Le, M.H. Hsieh, Diagnosing urogenital schistosomiasis: dealing with diminishing returns, Trends Parasitol. 33 (5) (2017) 378–387.
[81] P. Cheng, P. Chiang, K. Lee, C. Yeh, K. Hsu, S. Liu, L. Shen, C. Peng, C. Fan, T. Luo, Evaluating the potential of a new isotope-labelled glyco-ligand for estimating the remnant liver function of schistosoma-infected mice, Parasite Immunol. 35 (3–4) (2013) 129–139.

[82] G. Krautz-Peterson, D. Ndegwa, K. Vasquez, H. Korideck, J. Zhang, J.D. Peterson, P.J. Skelly, Imaging schistosomes in vivo, Faseb. J. 23 (8) (2009) 2673.
[83] P.J. Skelly, Imaging schistosomes in vivo, Faseb. J. 23 (8) (2009) 2673.
[84] M.C. Holtfreter, O. Stachs, M. Reichard, M. Loebermann, R.F. Guthoff, E.C. Reisinger, Confocal laser scanning microscopy for detection of Schistosoma mansoni eggs in the gut of mice, PLoS One 6 (4) (2011) e18799.
[85] W. Xing, X. Yu, J. Feng, K. Sun, W. Fu, Y. Wang, M. Zou, W. Xia, Z. Luo, H. He, Y. Li, D. Xu, Field evaluation of a recombinase polymerase amplification assay for the diagnosis of Schistosoma japonicum infection in Hunan province of China, BMC Infect. Dis. 17 (1) (2017) 164, https://doi.org/10.1186/s12879-017-2182-6.
[86] N.A. Tanner, Y. Zhang, T.C. Evans Jr, Simultaneous multiple target detection in real-time loop-mediated isothermal amplification, Biotechniques 53 (2) (2012) 81–89.
[87] E. Cesmeli, D. Vogelaers, D. Voet, P. Duyck, R. Peleman, M. Kunnen, M. Afschrift, Ultrasound and CT changes of liver parenchyma in acute schistosomiasis, Br. J. Radiol. 70 (835) (1997) 758–760, https://doi.org/10.1259/bjr.70.835.9245889.
[88] A.S.A. Bezerra, G. D'Ippolito, R.P. Caldana, A.O. Cecin, M. Ahmed, J. Szejnfeld, Chronic hepatosplenic schistosomiasis mansoni: magnetic resonance imaging and magnetic resonance angiography findings, Acta Radiol. 48 (2) (2007) 125–134, https://doi.org/10.1080/02841850601105833.
[89] B. Tarp, F.T. Black, E. Petersen, The immunofluorescence antibody test (IFAT) for the diagnosis of schistosomiasis used in a non-endemic area, Trop. Med. Int. Health 5 (3) (2000) 185–191.
[90] A.A. Yameny, Evaluation of health centers laboratory results for schistosoma haematobium infection in el-fayoum governorate, Egypt, Journal of Bioscience and Applied Research 2 (12) (2016) 788–796, https://doi.org/10.21608/jbaar.2016.10975.
[91] X. Xiang, W. Tianping, T. Zhigang, Development of a rapid, sensitive, dye immunoassay for schistosomiasis diagnosis: a colloidal dye immunofiltration assay, J. Immunol. Methods 280 (1) (2003) 49–57, https://doi.org/10.1016/S0022-1759(03)00196-0.
[92] N. Lodh, K. Mikita, K.M. Bosompem, W.K. Anyan, J.K. Quartey, J. Otchere, C.J. Shiff, Point of care diagnosis of multiple schistosome parasites: species-specific DNA detection in urine by loop-mediated isothermal amplification (LAMP), Acta Trop. 173 (2017) 125–129, https://doi.org/10.1016/j.actatropica.2017.06.015.
[93] D. Bass, G.D. Stentiford, D.T.J. Littlewood, H. Hartikainen, Diverse applications of environmental DNA methods in parasitology, Trends Parasitol. 31 (10) (2015) 499–513, https://doi.org/10.1016/j.pt.2015.06.013.
[94] G.G. Cerri, V.A. Alves, A. Magalhães, Hepatosplenic schistosomiasis mansoni: ultrasound manifestations, Radiology 153 (3) (1984) 777–780.
[95] M.C.F. Passos, L.C. Silva, T.C.A. Ferrari, L.C. Faria, Ultrasound and CT findings in hepatic and pancreatic parenchyma in acute schistosomiasis, Br. J. Radiol. 82 (979) (2009) e145–e147, https://doi.org/10.1259/bjr/90266783.
[96] S. Annie, G.Y.J. François, I. Arezki, V. Caroline, D. Pascal, van G. Tom, D. Francis, Development and evaluation of a western blot kit for diagnosis of schistosomiasis, Clin. Vaccine Immunol. 12 (4) (2005) 548–551, https://doi.org/10.1128/CDLI.12.4.548-551.2005.
[97] Y.B. Zhou, M.X. Yang, Q.Z. Wang, et al., Field comparison of immunodiagnostic and parasitological techniques for the detection of Schistosomiasis japonica in the People's Republic of China, Am. J. Trop. Med. Hyg. 76 (6) (2007) 1138–1143, https://doi.org/10.4269/ajtmh.2007.76.1138.
[98] C. Wang, L. Chen, X. Yin, et al., Application of DNA-based diagnostics in detection of schistosomal DNA in early infection and after drug treatment, Parasites Vectors 4 (2011) 1–9, https://doi.org/10.1186/1756-3305-4-164.
[99] H. El-Morshedy, B. Kinosien, R. Barakat, et al., Circulating anodic antigen for detection of Schistosoma mansoni infection in Egyptian patients, Am. J. Trop. Med. Hyg. 54 (2) (1996) 149–153, https://doi.org/10.4269/ajtmh.1996.54.149.
[100] H.M. Hussein, M.M. El-Tonsy, R.A. Tawfik, et al., Experimental study for early diagnosis of prepatent Schistosomiasis mansoni by detection of free circulating DNA in serum, Parasitol. Res. 111 (2012) 475–478, https://doi.org/10.1007/s00436-012-2822-0.
[101] P.L.A.M. Corstjens, P.T. Hoekstra, C.J. de Dood, G.J. van Dam, Utilizing the ultrasensitive Schistosoma up-converting phosphor lateral flow circulating anodic antigen (UCP-LF CAA) assay for sample pooling-strategies, Infectious Diseases of Poverty 6 (2017) 155, https://doi.org/10.1186/s40249-017-0368-1.
[102] N.P. Pai, C. Vadnais, C. Denkinger, et al., Point-of-care testing for infectious diseases: diversity, complexity, and barriers in low- and middle-income countries, PLoS Med. 9 (2012) e1001306, https://doi.org/10.1371/journal.pmed.1001306.
[103] L. Van Lieshout, M. Roestenberg, Clinical consequences of new diagnostic tools for intestinal parasites, Clin. Microbiol. Infection 21 (6) (2015) 520–528, https://doi.org/10.1016/j.cmi.2015.03.015.
[104] M. Viana, C.L. Faust, D.T. Haydon, J.P. Webster, P.H.L. Lamberton, The effects of subcurative praziquantel treatment on life-history traits and trade-offs in drug-resistant Schistosoma mansoni, Evolutionary Applications 11 (4) (2018) 488–500.
[105] G. Mouahid, A. Rognon, R. de Carvalho Augusto, P. Driguez, K. Geyer, S. Karinshak, N. Luviano, V. Mann, T. Quack, K. Rawlinson, G. Wendt, C. Grunau, H. Mon, Transplantation of schistosome sporocysts between host snails: a video guide [version 1; peer review: 2 approved], Wellcome Open Research 3 (3) (2018), https://doi.org/10.12688/wellcomeopenres.13488.1.
[106] A. Shuja, J. Guan, C. Harris, A. Alkhasawneh, M. Malespin, S. De Melo, Intestinal schistosomiasis: a rare cause of abdominal pain and weight loss, Cureus 10 (1) (2018) e2086, https://doi.org/10.7759/cureus.2086.
[107] K.K. Geyer, S.E. Munshi, M. Vickers, M. Squance, T.J. Wilkinson, D. Berrar, C. Chaparro, M.T. Swain, K.F. Hoffmann, The anti-fecundity effect of 5-azacytidine (5-AzaC) on Schistosoma mansoni is linked to dis-regulated transcription, translation and stem cell activities, Int. J. Parasitol.: Drugs Drug Resist. 8 (2) (2018) 213–222, https://doi.org/10.1016/j.ijpddr.2018.03.006.
[108] Y.-Z. Xu, M.H. Dresden, The hatching of schistosome eggs, Exp. Parasitol. 70 (2) (1990) 236–240, https://doi.org/10.1016/0014-4894(90)90104-K.
[109] L. Braun, J.E.T. Grimes, M.R. Templeton, The effectiveness of water treatment processes against schistosome cercariae: a systematic review, PLoS Neglected Trop. Dis. 12 (4) (2018) e0006364.
[110] S. Steinfelder, J.F. Andersen, J.L. Cannons, C.G. Feng, M. Joshi, D. Dwyer, P. Caspar, P.L. Schwartzberg, A. Sher, D. Jankovic, The major component in schistosome eggs responsible for conditioning dendritic cells for Th2 polarization is a T2 ribonuclease (omega-1), J. Exp. Med. 206 (8) (2009) 1681–1690, https://doi.org/10.1084/jem.20082462.
[111] J.E.T. Grimes, D. Croll, W.E. Harrison, J. Utzinger, M.C. Freeman, M.R. Templeton, The roles of water, sanitation and hygiene in reducing schistosomiasis: a review, Parasites Vectors 8 (1) (2015) 156, https://doi.org/10.1186/s13071-015-0766-9.
[112] A. Yu, J.T. Vannatta, S.O. Gutierrez, D.J. Minchella, Opportunity or catastrophe? effect of sea salt on host-parasite survival and reproduction, PLoS Neglected Trop. Dis. 16 (2) (2022) e0009524.
[113] C.E. Fogarty, P. Phan, M.G. Duke, D.P. McManus, R.C. Wyeth, S.F. Cummins, T. Wang, Identification of Schistosoma mansoni miracidia attractant candidates in infected Biomphalaria glabrata using behaviour-guided comparative proteomics, Front. Immunol. 13 (2022). https://www.frontiersin.org/articles/10.3389/fimmu.2022.954282.
[114] B. Zimmerman, B. Kelly, B.J. McMillan, T.C.M. Seegar, R.O. Dror, A.C. Kruse, S.C. Blacklow, Crystal structure of a full-length human tetraspanin reveals a cholesterol-binding pocket, Cell 167 (2016), https://doi.org/10.1016/j.cell.2016.09.056.
[115] D. Negrão-Corrêa, A.C.A. Mattos, C.A.J. Pereira, R.L. Martins-Souza, P.M.Z. Coelho, Interaction of *Schistosoma mansoni* sporocysts and hemocytes of *Biomphalaria*, Journal of Parasitology Research 2012 (2012) 743920, https://doi.org/10.1155/2012/743920.
[116] J.P. Boyle, X.-J. Wu, C.B. Shoemaker, T.P. Yoshino, Using RNA interference to manipulate endogenous gene expression in Schistosoma mansoni sporocysts, Mol. Biochem. Parasitol. 128 (2) (2003) 205–215, https://doi.org/10.1016/S0166-6851(03)00078-1.
[117] T.P. Yoshino, J.R. Laursen, Production of schistosoma mansoni daughter sporocysts from mother sporocysts maintained in synxenic culture with Biomphalaria glabrata embryonic (BGE) cells, J. Parasitol. 81 (5) (1995) 714–722, https://doi.org/10.2307/3283960.
[118] Y.-B. Zhou, M.-X. Yang, P. Tao, Q.-L. Jiang, G.-M. Zhao, J.-G. Wei, Q.-W. Jiang, A longitudinal study of comparison of the Kato–Katz technique and indirect hemagglutination assay (IHA) for the detection of schistosomiasis japonica in China, 2001–2006, Acta Trop. 107 (3) (2008) 251–254, https://doi.org/10.1016/j.actatropica.2008.06.009.
[119] S.-Y. Guo, L. Li, L.-J. Zhang, Y.-L. Li, S.-Z. Li, J. Xu, From the one health perspective: schistosomiasis japonica and flooding, Pathogens 10 (12) (2021), https://doi.org/10.3390/pathogens10121538.

[120] N.G. Exum, S.P.S. Kibira, R. Ssenyonga, J. Nobili, A.K. Shannon, J.C. Ssempebwa, E.M. Tukahebwa, S. Radloff, K.J. Schwab, F.E. Makumbi, The prevalence of schistosomiasis in Uganda: a nationally representative population estimate to inform control programs and water and sanitation interventions, PLoS Neglected Trop. Dis. 13 (8) (2019) e0007617.
[121] F. Reitzug, J. Ledien, G.F. Chami, Associations of water contact frequency, duration, and activities with schistosome infection risk: a systematic review and meta-analysis, PLoS Neglected Trop. Dis. 17 (6) (2023) e0011377.
[122] T.B. Duguet, A. Glebov, A. Hussain, S. Kulkarni, I. Mochalkin, T.G. Geary, M. Rashid, T. Spangenberg, P. Ribeiro, Identification of annotated bioactive molecules that impair motility of the blood fluke Schistosoma mansoni, Int. J. Parasitol.: Drugs Drug Resist. 13 (2020) 73–88, https://doi.org/10.1016/j.ijpddr.2020.05.002.
[123] Y.-N.T. Tian-Bi, B. Webster, C.K. Konan, F. Allan, N.R. Diakité, M. Ouattara, D. Salia, A. Koné, A.K. Kakou, M. Rabone, J.T. Coulibaly, S. Knopp, A. Meïté, J. Utzinger, E.K. N'Goran, D. Rollinson, Molecular characterization and distribution of Schistosoma cercariae collected from naturally infected bulinid snails in northern and central Côte d'Ivoire, Parasites Vectors 12 (1) (2019) 117, https://doi.org/10.1186/s13071-019-3381-3.
[124] T. Hailegebriel, E. Nibret, A. Munshea, Prevalence of *Schistosoma mansoni* and *S. haematobium* in snail intermediate hosts in Africa: a systematic review and meta-analysis, J. Trop. Med. 2020 (2020) 8850840, https://doi.org/10.1155/2020/8850840.
[125] D. Gurarie, N.C. Lo, M.L. Ndeffo-Mbah, D.P. Durham, C.H. King, The human-snail transmission environment shapes long term schistosomiasis control outcomes: implications for improving the accuracy of predictive modeling, PLoS Neglected Trop. Dis. 12 (5) (2018) e0006514.
[126] C.S. Nation, A.A. Da'dara, J.K. Marchant, P.J. Skelly, Schistosome migration in the definitive host, PLoS Neglected Trop. Dis. 14 (4) (2020) e0007951.
[127] L. Chitsulo, D. Engels, A. Montresor, L. Savioli, The global status of schistosomiasis and its control, Acta Trop. 77 (1) (2000) 41–51, https://doi.org/10.1016/S0001-706X(00)00122-4.
[128] G. Oliveira, D.A. Johnston, Mining the schistosome DNA sequence database, Trends Parasitol. 17 (10) (2001) 501–503.
[129] Z.-G. Han, P.J. Brindley, S.-Y. Wang, Z. Chen, Schistosoma genomics: new perspectives on schistosome biology and host-parasite interaction, Annu. Rev. Genom. Hum. Genet. 10 (1) (2009) 211–240, https://doi.org/10.1146/annurev-genom-082908-150036.
[130] R.D. Cummings, A.K. Nyame, Glycobiology of schistosomiasis, Faseb. J. 10 (8) (1996) 838–848.
[131] N. Dinguirard, T.P. Yoshino, Potential role of a CD36-like class B scavenger receptor in the binding of modified low-density lipoprotein (acLDL) to the tegumental surface of Schistosoma mansoni sporocysts, Mol. Biochem. Parasitol. 146 (2) (2006) 219–230, https://doi.org/10.1016/j.molbiopara.2005.12.010.
[132] J. Fan, X. Gan, W. Yang, L. Shen, D.P. McManus, P.J. Brindley, A Schistosoma japonicum very low-density lipoprotein-binding protein, Int. J. Biochem. Cell Biol. 35 (10) (2003) 1436–1451, https://doi.org/10.1016/S1357-2725(03)00105-5.
[133] S. Jenkins, J.P. Hewitson, G.R. Jenkins, A. Mountford, Modulation of the host's immune response by schistosome larvae, Parasite Immunol. 27 (2005) 385–393, https://doi.org/10.1111/j.1365-3024.2005.00789.x.
[134] I. Ebersberger, J. Knobloch, W. Kunz, Cracks in the shell—zooming in on eggshell formation in the human parasite Schistosoma mansoni, Dev. Gene. Evol. 215 (5) (2005) 261–267, https://doi.org/10.1007/s00427-005-0467-z.
[135] J.M. Fitzpatrick, D.A. Johnston, G.W. Williams, D.J. Williams, T.C. Freeman, D.W. Dunne, K.F. Hoffmann, An oligonucleotide microarray for transcriptome analysis of Schistosoma mansoni and its application/use to investigate gender-associated gene expression, Mol. Biochem. Parasitol. 141 (1) (2005) 1–13.
[136] J.M. Fitzpatrick, K.F. Hoffmann, Dioecious Schistosoma mansoni express divergent gene repertoires regulated by pairing, Int. J. Parasitol. 36 (10) (2006) 1081–1089, https://doi.org/10.1016/j.ijpara.2006.06.007.
[137] K.F. Hoffmann, D.A. Johnston, D.W. Dunne, Identification of Schistosoma mansonigender-associated gene transcripts by cDNA microarray profiling, Genome Biol. 3 (8) (2002), https://doi.org/10.1186/gb-2002-3-8-research0041 research0041.1.
[138] G. Krautz-Peterson, M. Radwanska, D. Ndegwa, C.B. Shoemaker, P.J. Skelly, Optimizing gene suppression in schistosomes using RNA interference, Mol. Biochem. Parasitol. 153 (2) (2007) 194–202, https://doi.org/10.1016/j.molbiopara.2007.03.006.
[139] M. Delcroix, M. Sajid, C.R. Caffrey, K.-C. Lim, J. Dvořák, I. Hsieh, M. Bahgat, C. Dissous, J.H. McKerrow, A multienzyme network functions in intestinal protein digestion by a platyhelminth parasite, J. Biol. Chem. 281 (51) (2006) 39316–39329, https://doi.org/10.1074/jbc.M607128200.
[140] J.M. Correnti, P.J. Brindley, E.J. Pearce, Long-term suppression of cathepsin B levels by RNA interference retards schistosome growth, Mol. Biochem. Parasitol. 143 (2) (2005) 209–215, https://doi.org/10.1016/j.molbiopara.2005.06.007.
[141] M.E. Morales, G. Rinaldi, G.N. Gobert, K.J. Kines, J.F. Tort, P.J. Brindley, RNA interference of Schistosoma mansoni cathepsin D, the apical enzyme of the hemoglobin proteolysis cascade, Mol. Biochem. Parasitol. 157 (2) (2008) 160–168, https://doi.org/10.1016/j.molbiopara.2007.10.009.
[142] D. Ndegwa, G. Krautz-Peterson, P.J. Skelly, Protocols for gene silencing in schistosomes, Exp. Parasitol. 117 (3) (2007) 284–291, https://doi.org/10.1016/j.exppara.2007.07.012.
[143] P. Amiri, M. Haak-Frendscho, K. Robbins, J.H. McKerrow, T. Stewart, P. Jardieu, Anti-immunoglobulin E treatment decreases worm burden and egg production in Schistosoma mansoni-infected normal and interferon gamma knockout mice, J. Exp. Med. 180 (1) (1994) 43–51.
[144] A.N. Kuntz, E. Davioud-Charvet, A.A. Sayed, L.L. Califf, J. Dessolin, E.S.J. Arnér, D.L. Williams, Thioredoxin glutathione reductase from Schistosoma mansoni: an essential parasite enzyme and a key drug target, PLoS Med. 4 (6) (2007) e206.
[145] T.C. Freitas, E. Jung, E.J. Pearce, TGF-β signaling controls embryo development in the parasitic flatworm Schistosoma mansoni, PLoS Pathog. 3 (4) (2007) e52.
[146] G. Krautz-Peterson, P.J. Skelly, Schistosoma mansoni: the dicer gene and its expression, Exp. Parasitol. 118 (1) (2008) 122–128.
[147] A. Osman, E.G. Niles, S. Verjovski-Almeida, P.T. LoVerde, Schistosoma mansoni TGF-β receptor II: role in host ligand-induced regulation of a schistosome target gene, PLoS Pathog. 2 (6) (2006) e54.
[148] A.A. Sayed, D.L. Williams, Biochemical characterization of 2-Cys peroxiredoxins from Schistosoma mansoni, J. Biol. Chem. 279 (25) (2004) 26159–26166.
[149] A.A. Sayed, S.K. Cook, D.L. Williams, Redox balance mechanisms in schistosoma mansoni rely on peroxiredoxins and albumin and implicate peroxiredoxins as novel drug targets, J. Biol. Chem. 281 (25) (2006) 17001–17010, https://doi.org/10.1074/jbc.M512601200.
[150] P. Masamba, A.P. Kappo, Immunological and biochemical interplay between cytokines, oxidative stress and schistosomiasis, Int. J. Mol. Sci. 22 (Issue 13) (2021), https://doi.org/10.3390/ijms22137216.
[151] J. Santos, M.J. Gouveia, N. Vale, M. de L. Delgado, A. Gonçalves, J.M.T. Da Silva, C. Oliveira, P. Xavier, P. Gomes, L.L. Santos, Urinary estrogen metabolites and self-reported infertility in women infected with Schistosoma haematobium, PLoS One 9 (5) (2014) e96774.
[152] R.R. Lima, J.V. Lima, J.F. Ribeiro, J.B. Nascimento, W.F. Oliveira, P.E. Cabral Filho, A. Fontes, Emerging biomedical tools for biomarkers detection and diagnostics in schistosomiasis, Talanta 124900 (2023).
[153] B.N. Ondigo, R.E. Hamilton, E.O. Magomere, I.O. Onkanga, P.N. Mwinzi, M.R. Odiere, L. Ganley-Leal, Potential utility of systemic plasma biomarkers for evaluation of pediatric schistosomiasis in western Kenya, Front. Immunol. 13 (2022). https://www.frontiersin.org/articles/10.3389/fimmu.2022.887213.
[154] B.M. Tebeje, M. Harvie, H. You, A. Loukas, D.P. McManus, Schistosomiasis vaccines: where do we stand? Parasites Vectors 9 (1) (2016) 528, https://doi.org/10.1186/s13071-016-1799-4.
[155] S. Brooker, D. De Savigny, E.K. N'goran, G. Raso, B.H. Singer, M. Tanner, J. Utzinger, N. Ørnbjerg, Schistosomiasis and neglected tropical diseases: towards integrated and sustainable control and a word of caution, Parasitology 136 (13) (2009) 1859–1874, https://doi.org/10.1017/S0031182009991600.
[156] M.R. Reich, R. Govindaraj, K. Dumbaugh, B. Yang, A. Brinkmann, S. El-Saharty, W.H. Organization, International Strategies for Tropical Disease Treatments: Experiences with Praziquantel, World Health Organization, 1998.
[157] World Health Organization, Sustaining the drive to overcome the global impact of neglected tropical diseases: second WHO report on neglected diseases, Retrieved from, http://www.who.int/iris/handle/10665/77950, 2013.
[158] T. Fürst, K.D. Silué, M. Ouattara, D.N. N'Goran, L.G. Adiossan, Y. N'Guessan, F. Zouzou, S. Koné, E.K. N'Goran, J. Utzinger, Schistosomiasis, soil-transmitted helminthiasis, and sociodemographic factors influence quality of life of adults in côte d'Ivoire, PLoS Neglected Trop. Dis. 6 (10) (2012) 1–12, https://doi.org/10.1371/journal.pntd.0001855.
[159] T. Meyer, H. Sekljic, S. Fuchs, H. Bothe, D. Schollmeyer, C. Miculka, Taste, A new incentive to switch to (R)-Praziquantel in schistosomiasis treatment, PLoS Neglected Trop. Dis. 3 (1) (2009) 1–5, https://doi.org/10.1371/journal.pntd.0000357.

[160] R. Liu, H.-F. Dong, Y. Guo, Q.-P. Zhao, M.-S. Jiang, Efficacy of praziquantel and artemisinin derivatives for the treatment and prevention of human schistosomiasis: a systematic review and meta-analysis, Parasites Vectors 4 (1) (2011) 201, https://doi.org/10.1186/1756-3305-4-201.
[161] R.A.F. El Ridi, H.A.-M. Tallima, Novel therapeutic and prevention approaches for schistosomiasis: review, J. Adv. Res. 4 (5) (2013) 467–478, https://doi.org/10.1016/j.jare.2012.05.002.
[162] D. Cioli, L. Pica-Mattoccia, A. Basso, A. Guidi, Schistosomiasis control: praziquantel forever? Mol. Biochem. Parasitol. 195 (1) (2014) 23–29, https://doi.org/10.1016/j.molbiopara.2014.06.002.
[163] F. Angelucci, A.A. Sayed, D.L. Williams, G. Boumis, M. Brunori, D. Dimastrogiovanni, A. Bellelli, Inhibition of Schistosoma mansoni thioredoxin-glutathione reductase by auranofin: structural and kinetic aspects, J. Biol. Chem. 284 (42) (2009) 28977–28985.
[164] F. Angelucci, D. Dimastrogiovanni, G. Boumis, M. Brunori, A.E. Miele, F. Saccoccia, A. Bellelli, Mapping the catalytic cycle of Schistosoma mansoni thioredoxin glutathione reductase by X-ray crystallography, J. Biol. Chem. 285 (42) (2010) 32557–32567.
[165] G. Rai, C.J. Thomas, W. Leister, D.J. Maloney, Synthesis of oxadiazole-2-oxide analogues as potential antischistosomal agents, Tetrahedron Lett. 50 (15) (2009) 1710–1713, https://doi.org/10.1016/j.tetlet.2009.01.120.
[166] S.-H. Xiao, J. Sun, M.-G. Chen, Pharmacological and immunological effects of praziquantel against Schistosoma japonicum: a scoping review of experimental studies, Infectious Diseases of Poverty 7 (1) (2018) 9, https://doi.org/10.1186/s40249-018-0391-x.
[167] G.F. Cota, R.A. Pinto-Silva, C.M.F. Antunes, J.R. Lambertucci, Ultrasound and clinical investigation of hepatosplenic schistosomiasis: evaluation of splenomegaly and liver fibrosis four years after mass chemotherapy with oxamniquine, Am. J. Trop. Med. Hyg. 74 (1) (2006) 103–107.
[168] C.L.L. Valentim, D. Cioli, F.D. Chevalier, X. Cao, A.B. Taylor, S.P. Holloway, L. Pica-Mattoccia, A. Guidi, A. Basso, I.J. Tsai, Genetic and molecular basis of drug resistance and species-specific drug action in schistosome parasites, Science 342 (6164) (2013) 1385–1389.
[169] A.B. Taylor, K.M. Roberts, X. Cao, N.E. Clark, S.P. Holloway, E. Donati, C.M. Polcaro, L. Pica-Mattoccia, R.S. Tarpley, S.F. McHardy, Structural and enzymatic insights into species-specific resistance to schistosome parasite drug therapy, J. Biol. Chem. 292 (27) (2017) 11154–11164.
[170] A.J. Molehin, J.U. Rojo, S.Z. Siddiqui, S.A. Gray, D. Carter, A.A. Siddiqui, Development of a schistosomiasis vaccine, Expet Rev. Vaccine 15 (5) (2016) 619–627.
[171] G. Ahmad, W. Zhang, W. Torben, C. Haskins, S. Diggs, Z. Noor, L. Le, A.A. Siddiqui, Prime-boost and recombinant protein vaccination strategies using Sm-p80 protects against Schistosoma mansoni infection in the mouse model to levels previously attainable only by the irradiated cercarial vaccine, Parasitol. Res. 105 (2009) 1767–1777.
[172] W.A. Chisamile, M.A. Sonibare, J.F. Kamanula, Ethnobotanical Study of Traditional Medicinal Plants Used for the Treatment of Infectious Diseases by Local Communities in Traditional Authority (T/A) Mbelwa, Mzimba District, Northern Region, Malawi 6 (1) (2023) 115–139, https://doi.org/10.3390/j6010009. J.
[173] D.O. Acheampong, N. Owusu-Adzorah, F.A. Armah, E. Aninagyei, E.A. Asiamah, A.K. Thomford, W.K. Anyan, Ethnopharmacological evaluation of schistosomicidal and cercaricidal activities of some selected medicinal plants from Ghana, Trop. Med. Health 48 (1) (2020) 19, https://doi.org/10.1186/s41182-020-00205-y.
[174] G. Allam, Immunomodulatory effects of curcumin treatment on murine schistosomiasis mansoni, Immunobiology 214 (8) (2009) 712–727, https://doi.org/10.1016/j.imbio.2008.11.017.
[175] R.S. Almeer, M.F. El-Khadragy, S. Abdelhabib, A.E. Abdel Moneim, Ziziphus spina-christi leaf extract ameliorates schistosomiasis liver granuloma, fibrosis, and oxidative stress through downregulation of fibrinogenic signaling in mice, PLoS One 13 (10) (2018) e0204923.
[176] E.M. Al-Olayan, M.F. El-Khadragy, R.A. Alajmi, M.S. Othman, A.A. Bauomy, S.R. Ibrahim, A.E. Abdel Moneim, Ceratonia siliqua pod extract ameliorates Schistosoma mansoni-induced liver fibrosis and oxidative stress, BMC Compl. Alternative Med. 16 (1) (2016) 434, https://doi.org/10.1186/s12906-016-1389-1.
[177] C.G. Braguine, C.S. Bertanha, U.O. Gonçalves, L.G. Magalhães, V. Rodrigues, V.M. Melleiro Gimenez, M. Groppo, M. L. A. e Silva, W.R. Cunha, A.H. Januário, P. M. Pauletti, Schistosomicidal evaluation of flavonoids from two species of Styrax against Schistosoma mansoni adult worms, Pharmaceut. Biol. 50 (7) (2012) 925–929, https://doi.org/10.3109/13880209.2011.649857.
[178] G.L. Abuelenain, Z.H. Fahmy, A.M. Elshennawy, E.H.A. Selim, M. Elhakeem, K.M.A. Hassanein, S.M. Awad, Phenotypic changes of treated by, and Albendazole: study, Helminthologia 59 (1) (2022) 37–45.
[179] M.R. Mahmoud, H.S. El-Abhar, S. Saleh, The effect of Nigella sativa oil against the liver damage induced by Schistosoma mansoni infection in mice, J. Ethnopharmacol. 79 (1) (2002) 1–11, https://doi.org/10.1016/S0378-8741(01)00310-5.
[180] K. Stete, S.J. Krauth, J.T. Coulibaly, S. Knopp, J. Hattendorf, I. Müller, L.K. Lohourignon, W.V. Kern, E.K. N'Goran, J. Utzinger, Dynamics of Schistosoma haematobium egg output and associated infection parameters following treatment with praziquantel in school-aged children, Parasites Vectors 5 (1) (2012) 298, https://doi.org/10.1186/1756-3305-5-298.
[181] D.M. Metwally, E.M. Al-Olayan, M. Alanazi, S.B. Alzahrany, A. Semlali, Antischistosomal and anti-inflammatory activity of garlic and allicin compared with that of praziquantel in vivo, BMC Compl. Alternative Med. 18 (2018) 1–11.
[182] R.N. De Oliveira, V.L.G. Rehder, A.S.S. Oliveira, V. de L.S. Jeraldo, A.X. Linhares, S.M. Allegretti, Anthelmintic activity in vitro and in vivo of Baccharis trimera (Less) DC against immature and adult worms of Schistosoma mansoni, Exp. Parasitol. 139 (2014) 63–72, https://doi.org/10.1016/j.exppara.2014.02.010.
[183] N.N. Dejani, L.C. Souza, S.R.P. Oliveira, D.M. Neris, J.M.A. Rodolpho, R.O. Correia, V. Rodrigues, L.V.S. Sacramento, L.H. Faccioli, A. Afonso, F.F. Anibal, Immunological and parasitological parameters in Schistosoma mansoni-infected mice treated with crude extract from the leaves of Mentha x piperita L, Immunobiology 219 (8) (2014) 627–632, https://doi.org/10.1016/j.imbio.2014.03.015.
[184] B. Ivanescu, A. Miron, A. Corciova, Sesquiterpene lactones from *Artemisia* genus: biological activities and methods of analysis, Journal of Analytical Methods in Chemistry 2015 (2015) 247685, https://doi.org/10.1155/2015/247685.
[185] Y. Meng, N. Ma, H. Lyu, Y.K. Wong, X. Zhang, Y. Zhu, P. Gao, P. Sun, Y. Song, L. Lin, Recent pharmacological advances in the repurposing of artemisinin drugs, Med. Res. Rev. 41 (6) (2021) 3156–3181.
[186] H.B. Jatsa, N.G. Feussom, E.T. Nkondo, M.C. Kenfack, N.D. Simo, J.B.K. Fassi, U.M. Femoe, C. Moaboulou, C.D. Tsague, E. Dongo, P. Kamtchouing, L.-A. Tchuem Tchuente, Efficacy of Ozoroa pulcherrima Schweinf methanolic extract against Schistosoma mansoni-induced liver injury in mice, Journal of Traditional and Complementary Medicine 9 (4) (2019) 304–311, https://doi.org/10.1016/j.jtcme.2017.08.009.
[187] T.F. Frezza, C.N.F.D. Oliveira, V.L.G. Rehder, S. Boaventura Junior, S.M. Allegretti, T.M. Banin, Tegumentary changes in two diferent strains of schistosoma mansoni treated with artemisinin and artesunic acid, Rev. patol. trop (2013) 309–321.
[188] H.B. Jatsa, R.C. Russo, C.A. de J. Pereira, E.C. Aguilar, C.C. Garcia, E.S. Araújo, J.L.R. Oliveira, V.F. Rodrigues, V.G. de Oliveira, J.I. Alvarez-Leite, F.C. Braga, Tchuem Tchuente Louis-Albert, P. Kamtchouing, D.A. Negrão-Corrêa, M.M. Teixeira, Improvement of the liver pathology by the aqueous extract and the n-butanol fraction of Sida pilosa Retz in Schistosoma mansoni-infected mice, J. Ethnopharmacol. 180 (2016) 114–123.
[189] A.P. Castro, A.D. Mattos, R.L.M. Souza, M.J. Marques, M.H.D. Santos, Medicinal plants and their bioactive constituents: a review of bioactivity against Schistosoma mansoni, J. Med. Plants Res. 7 (21) (2013) 1515–1522.
[190] S.G. Sparg, J. Van Standen, A.K. Jager, Efficiency of traditionally used South African plants against Schistosomiasis, J. Ethnopharmacol. 73 (2000) 209–214.
[191] S. Khatoon, V. Rai, A.K.R.S. Rawat, S. Mehrota, Comparative pharmacognostic studies of three Phyllantus species, J. Ethnopharmacol. 104 (2006) 79–86.
[192] L.M. Almeida, P.G. Farani, L.A. Tosta, M.S. Silvério, O.V. Sousa, A.C. Mattos, P.M. Coelho, E.G. Vasconcelos, P.F. Pinto, In vitro evaluation of the schistosomicidal potential of Eremanthus erythropappus (DC) McLeisch (Asteraceae) extracts, Nat. Prod. Res. 26 (2012) 2137–2143.
[193] H.B. Jatsa, C.A.J. Pereira, E.S. Araújo, J.L. Rodrigues, V.G. Oliveira, V.F. Rodrigues, F.M. Rosa, F.C. Braga, M.M. Teixeira, D.N. Corrêa, Biological activity of Sida pilosa plant extract on Schistosoma mansoni, in: 12° International Symposium on Schistosomiasis, 2010, p. 184. Rio de Janeiro.
[194] H.B. Jatsa, Sock E.T. Ngo, L.A. Tchuem Tchuente, P. Kamtchouing, Evaluation of the in vivo activity of different concentrations of Clerodendrum umbellatum poir against Schistosoma mansoni infection in mice, Afr. J. Tradit., Complementary Altern. Med. 6 (2009) 216–221.
[195] A. El-Ansary, A.M. Mohamed, S.S. Mahmoud, S. El-Bardicy, On the pathogenicity of attenuated Schistosoma mansoni cercariae released from metabolically disturbed Biomphalaria alexandrina, J. Egypt. Soc. Parasitol. 33 (2003) 777–794.

[196] Y. Li, R. Zheng, Y. Wu, K. Chu, Q. Xu, M. Sun, Z.J. Smith, A low-cost, automated parasite diagnostic system via a portable, robotic microscope and deep learning, J. Biophot. 12 (9) (2019) e201800410.

[197] T.E. Agbana, A.A. Onasanya, Performance Evaluation of AiDx Assist in the Diagnosis of Lymphatic Filariasis (LF) in Field Settings: A Field Study Conducted by the INSPiRED NWO Project-Dec. 2021, 2022.

[198] L. Makau-Barasa, L. Assefa, M. Aderogba, D. Bell, J. Solomon, R.O. Urude, O.J. Nebe, J. A-Enegela, J.G. Damen, S. Popoola, J.-C. Diehl, G. Vdovine, T. Agbana, Performance evaluation of the AiDx multi-diagnostic automated microscope for the detection of schistosomiasis in Abuja, Nigeria, Sci. Rep. 13 (1) (2023) 14833, https://doi.org/10.1038/s41598-023-42049-6.

[199] N.A. Switz, M.V. D'Ambrosio, D.A. Fletcher, Low-cost mobile phone microscopy with a reversed mobile phone camera lens, PLoS One 9 (5) (2014) e95330.

[200] J.T. Coulibaly, M. Ouattara, M.V. D'Ambrosio, D.A. Fletcher, J. Keiser, J. Utzinger, E.K. N'Goran, J.R. Andrews, I.I. Bogoch, Accuracy of mobile phone and handheld light microscopy for the diagnosis of schistosomiasis and intestinal protozoa infections in Côte d'Ivoire, PLoS Neglected Trop. Dis. 10 (6) (2016) e0004768.

[201] R.K.D. Ephraim, E. Duah, J.S. Cybulski, M. Prakash, M.V. D'Ambrosio, D.A. Fletcher, J. Keiser, J.R. Andrews, I.I. Bogoch, Diagnosis of schistosoma haematobium infection with a mobile phone-mounted foldscope and a reversed-lens CellScope in Ghana, The American Society of Tropical Medicine and Hygiene 92 (6) (2015) 1253–1256, https://doi.org/10.4269/ajtmh.14-0741.

[202] N.J. Lehmann, M.-U. Karagülle, P. Meurer, E. Niedermeyer, P. Vidishiqi, L. Pysz, M. Kreß, L.R. Muth, H. Feldmeier, B.R. Sahondra, O.R.T. Onintsoa, A. Voisard, A. Schuster, Designing AINA - intercultural human-centered design of an AI-based application for supporting the diagnosis of female genital schistosomiasis. 2022 IEEE 10th International Conference on Healthcare Informatics (ICHI), 2022, pp. 431–441, https://doi.org/10.1109/ICHI54592.2022.00065.

[203] B. Meulah, P. Oyibo, M. Bengtson, T. Agbana, R.A.L. Lontchi, A.A. Adegnika, W. Oyibo, C.H. Hokke, J.C. Diehl, L. van Lieshout, Performance evaluation of the schistoscope 5.0 for (Semi-)automated digital detection and quantification of schistosoma haematobium eggs in urine: a field-based study in Nigeria, Am. J. Trop. Med. Hyg. 107 (5) (2022) 1047–1054, https://doi.org/10.4269/ajtmh.22-0276.

[204] P. Oyibo, S. Jujjavarapu, B. Meulah, T. Agbana, I. Braakman, A. van Diepen, M. Bengtson, L. van Lieshout, W. Oyibo, G. Vdovine, J.-C. Diehl, Schistoscope: an automated microscope with artificial intelligence for detection of schistosoma haematobium eggs in resource-limited settings, Micromachines 13 (5) (2022), https://doi.org/10.3390/mi13050643.

[205] M.E. Bavia, J.B. Malone, L. Hale, A. Dantas, L. Marroni, R. Reis, Use of thermal and vegetation index data from earth observing satellites to evaluate the risk of schistosomiasis in Bahia, Brazil, Acta Trop. 79 (1) (2001) 79–85, https://doi.org/10.1016/S0001-706X(01)00105-X.

[206] X.I.A. Shang, X.U.E. Jing-bo, G.A.O. Feng-hua, L.V. Shan, X.U. Jing, Z. Shi-qing, L.I. Shi-zhu, Sentinel-1A radar remote sensing-based modeling for quick identification of potential risk areas of schistosomiasis transmission after flood, Chin. J. Parasitol. Parasit. Dis. 38 (4) (2020) 417.

[207] J.-B. Xue, S. Xia, L.-J. Zhang, E.M. Abe, J. Zhou, Y.-Y. Li, Y.-W. Hao, Q. Wang, J. Xu, S.-Z. Li, X.-N. Zhou, High-resolution remote sensing-based spatial modeling for the prediction of potential risk areas of schistosomiasis in the Dongting Lake area, China, Acta Trop. 199 (2019) 105102, https://doi.org/10.1016/j.actatropica.2019.105102.

[208] L. Shi, J.-F. Zhang, W. Li, K. Yang, Development of new technologies for risk identification of schistosomiasis transmission in China, Pathogens 11 (Issue 2) (2022), https://doi.org/10.3390/pathogens11020224.

[209] P. Ward, P. Dahlberg, O. Lagatie, J. Larsson, A. Tynong, J. Vlaminck, M. Zumpe, S. Ame, M. Ayana, V. Khieu, Affordable artificial intelligence-based digital pathology for neglected tropical diseases: a proof-of-concept for the detection of soil-transmitted helminths and Schistosoma mansoni eggs in Kato-Katz stool thick smears, PLoS Neglected Trop. Dis. 16 (6) (2022) e0010500.

[210] S. Shafi, A.V. Parwani, Artificial intelligence in diagnostic pathology, Diagn. Pathol. 18 (1) (2023) 109, https://doi.org/10.1186/s13000-023-01375-z.

[211] E. Linder, A. Grote, S. Varjo, N. Linder, M. Lebbad, M. Lundin, V. Diwan, J. Hannuksela, J. Lundin, On-chip imagingst o of Schistosoma haematobium eggs in urine for diagnosis by computer vision, PLoS Neglected Trop. Dis. 7 (12) (2013) e2547.

[212] G. Cringoli, L. Rinaldi, M.P. Maurelli, J. Utzinger, FLOTAC: new multivalent techniques for qualitative and quantitative copromicroscopic diagnosis of parasites in animals and humans, Nat. Protoc. 5 (3) (2010) 503–515, https://doi.org/10.1038/nprot.2009.235.

[213] B.D. Barda, L. Rinaldi, D. Ianniello, H. Zepherine, F. Salvo, T. Sadutshang, G. Cringoli, M. Clementi, M. Albonico, Mini-FLOTAC, an innovative direct diagnostic technique for intestinal parasitic infections: experience from the field, PLoS Neglected Trop. Dis. 7 (8) (2013) e2344.

[214] M. Ayana, J. Vlaminck, P. Cools, S. Ame, M. Albonico, D. Dana, J. Keiser, H. Manly, L.F. Matoso, Z. Mekonnen, Modification and optimization of the FECPAKG2 protocol for the detection and quantification of soil-transmitted helminth eggs in human stool, PLoS Neglected Trop. Dis. 12 (10) (2018) e0006655.

[215] J.C. Diehl, P. Oyibo, T. Agbana, S. Jujjavarapu, G.-Y. Van, G. Vdovin, W. Oyibo, Schistoscope: smartphone versus Raspberry Pi based low-cost diagnostic device for urinary Schistosomiasis. 2020 IEEE Global Humanitarian Technology Conference (GHTC), 2020, pp. 1–8, https://doi.org/10.1109/GHTC46280.2020.9342871.

[216] World Health Organization, The World Health Report 2002: Reducing Risks, Promoting Healthy Life, World Health Organization, 2002.

[217] World Health Organization, Helminth Control in School-Age Children: a Guide for Managers of Control Programmes, World Health Organization, 2011.

[218] World Health Organization, Ending the Neglect to Attain the Sustainable Development Goals: a Rationale for Continued Investment in Tackling Neglected Tropical Diseases 2021–2030, World Health Organization, 2021.

[219] T. Eyayu, A.J. Zeleke, L. Worku, Current status and future prospects of protein vaccine candidates against Schistosoma mansoni infection, Parasite Epidemiology and Control 11 (2020) e00176.

[220] T.M. Gierahn, M.H. Wadsworth, T.K. Hughes, B.D. Bryson, A. Butler, R. Satija, S. Fortune, J.C. Love, A.K. Shalek, Seq-Well: portable, low-cost RNA sequencing of single cells at high throughput, Nat. Methods 14 (4) (2017) 395–398.

[221] R. Salomon, D. Kaczorowski, F. Valdes-Mora, R.E. Nordon, A. Neild, N. Farbehi, N. Bartonicek, D. Gallego-Ortega, Droplet-based single cell RNAseq tools: a practical guide, Lab Chip 19 (10) (2019) 1706–1727.

[222] C. Gao, M. Zhang, L. Chen, The comparison of two single-cell sequencing platforms: BD rhapsody and 10x genomics chromium, Curr. Genom. 21 (8) (2020) 602–609.

[223] M. Stoeckius, C. Hafemeister, W. Stephenson, B. Houck-Loomis, P.K. Chattopadhyay, H. Swerdlow, R. Satija, P. Smibert, Large-scale simultaneous measurement of epitopes and transcriptomes in single cells, Nat. Methods 14 (9) (2017) 865.

[224] E.P. Mimitou, A. Cheng, A. Montalbano, S. Hao, M. Stoeckius, M. Legut, T. Roush, A. Herrera, E. Papalexi, Z. Ouyang, Multiplexed detection of proteins, transcriptomes, clonotypes and CRISPR perturbations in single cells, Nat. Methods 16 (5) (2019) 409–412.

[225] A. Nathan, J.I. Beynor, Y. Baglaenko, S. Suliman, K. Ishigaki, S. Asgari, C.-C. Huang, Y. Luo, Z. Zhang, K. Lopez, Multimodally profiling memory T cells from a tuberculosis cohort identifies cell state associations with demographics, environment and disease, Nat. Immunol. 22 (6) (2021) 781–793.

[226] E. Swanson, C. Lord, J. Reading, A.T. Heubeck, P.C. Genge, Z. Thomson, M.D.A. Weiss, X. Li, A.K. Savage, R.R. Green, Simultaneous trimodal single-cell measurement of transcripts, epitopes, and chromatin accessibility using TEA-seq, Elife 10 (2021) e63632.

[227] A. Qadeer, H. Ullah, M. Sohail, S.Z. Safi, A. Rahim, T.A. Saleh, S. Arbab, P. Slama, P. Horky, Potential application of nanotechnology in the treatment, diagnosis, and prevention of schistosomiasis, Front. Bioeng. Biotechnol. 10 (2022) 1013354.

[228] T. Kamara, M. Byamukama, M. Karuhanga, Modelling the role of treatment, public health education, and chemical control strategies on transmission dynamics of schistosomiasis, J. Math. (2022) 2094979, https://doi.org/10.1155/2022/2094979, 2022.

[229] A. Garchitorena, S.H. Sokolow, B. Roche, C.N. Ngonghala, M. Jocque, A. Lund, M. Barry, E.A. Mordecai, G.C. Daily, J.H. Jones, Disease ecology, health and the environment: a framework to account for ecological and socio-economic drivers in the control of neglected tropical diseases, Phil. Trans. Biol. Sci. 372 (1722) (2017) 20160128.

[230] G.A. De Leo, A.-S. Stensgaard, S.H. Sokolow, E.K. N'Goran, A.J. Chamberlin, G.-J. Yang, J. Utzinger, Schistosomiasis and climate change, BMJ 371 (2020).

[231] J.T. Moreira-Filho, A.C. Silva, R.F. Dantas, B.F. Gomes, L.R. Souza Neto, J. Brandao-Neto, C.H. Andrade, Schistosomiasis drug discovery in the era of automation and artificial intelligence, Front. Immunol. 12 (2021) 642383.