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PARASITOLOGY

Biological control of *Biomphalaria*, the intermediate host of *Schistosoma* spp.: a systematic review

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ABSTRACT: *Schistosomiasis is an important vector-borne disease transmitted by an intermediate host: a freshwater mollusk. Control of these snail vectors is one of the strategies of the World Health Organization against the disease. The present study was based on a systematic review of published scientific papers concerning the biological control of snails (genus Biomphalaria), and identified the ongoing challenges and propose future perspectives. The review methodology was based on the PRISMA statement, the international databases Web of Science and Scopus for the period 1945-2021. In total, 47 papers were analyzed, published by authors from 14 different countries, the majority being from: France, Brazil, the United States, and Egypt. The most widely used strategy for biological control was predation by fish (12 studies). Fourteen papers were published in the most prolific decade 2010-2019; during which there was also a greater diversity of biological control agents in studies. In this context, we believed that one of the principal challenges of this approach is the successful simultaneous use of multiple types of biological control agent: predators, competitors, and/or microbial agents. This new approach may provide important insights for the development of new biological control agents or microbial-based products, with the potential to reduce the parasite load carried by schistosomiasis snail vector and control its transmission in a sustainable way.*
Key words: *schistosomiasis, neglected diseases, predation, competition, microbial control.*

Controle biológico de *Biomphalaria*, hospedeiro intermediário do *Schistosoma* spp.: uma revisão sistemática

RESUMO: *A esquistossomose é uma importante doença transmitida por vetor, um hospedeiro intermediário: um molusco de água doce. O controle desses caramujos vetores é uma das estratégias da Organização Mundial da Saúde para controle da doença. O presente estudo foi baseado em uma revisão sistemática de artigos científicos publicados sobre o controle biológico de caramujos (gênero Biomphalaria), e teve como objetivo identificar os desafios atuais e propor perspectivas futuras. A metodologia de revisão foi baseada na declaração PRISMA, nas bases de dados internacionais, Web of Science e Scopus, entre 1945-2021. No total, foram analisados 47 artigos, publicados por autores de 14 países diferentes, sendo a maioria: França, Brasil, Estados Unidos e Egito. A estratégia mais utilizada para controle biológico foi a predação por peixes (12 estudos). Quatorze artigos foram publicados na década mais produtiva 2010-2019, durante a qual também houve uma maior diversidade de agentes de controle biológico em estudos. Neste contexto, acreditamos que um dos principais desafios desta abordagem é a utilização simultânea bem-sucedida de múltiplos tipos de agentes de controle biológico: predadores, concorrentes e/ou agentes microbianos. Esta nova abordagem fornece importantes subsídios para o desenvolvimento de novos agentes de controle biológico ou produtos de base microbiana, com o potencial de reduzir a carga parasitária transportada pelo vetor esquistossomose de caramujos e controlar sua transmissão de forma sustentável.*
Palavras-chave: *esquistossomose, doenças negligenciadas, predação, competição e controle microbiano.*

INTRODUCTION

Schistosomiasis, caused by *Schistosoma* spp., has the second greatest socioeconomic impact of any parasitic disease (after malaria) and is one of the neglected tropical diseases. Globally, it is the principal freshwater gastropod borne disease, and is present in 78 countries, with an estimated 240 million infected individuals. A further 700 million are at risk worldwide in endemic areas (WHO, 2020). Overall,

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51 of the 78 countries apply preventive chemotherapy annually, and 18 have reported the cessation of transmission; although, this has yet to be confirmed (WHO, 2021). The World Health Roadmap of the World Health Organization (WHO) aimed the eradication of schistosomiasis as a priority public health target.

Species of *Schistosoma* are transmitted through the establishment of interactions between the definitive (human and non-human) and intermediate (snails) hosts in a limnic environment. Transmission to the vertebrate host occurs when the larvae of the parasite (cercariae), are released by infected freshwater snails and penetrate human skin, or in the case of aquatic rodents enter via the interdigital membranes (COLLEY et al., 2014). The snail intermediate host is infected via contamination of the limnic ecosystem, by human and animal feces that contain the parasite eggs. Recently, viable hybridization and introgression have been found under natural conditions in Europe and Africa, both between and within human and animal schistosomes (LÉGER et al., 2016; LÉGER & WEBSTER, 2017; KINCAID-SMITH et al., 2017; LÉGER et al., 2020). This raises important questions in relation to measures for the control of transmission and the elimination of this disease, given its impact on public health, and its potential for rapid adaptation in areas in which it is endemic.

The main types of schistosomiasis control interventions are preventive chemotherapy, individual diagnostic tests, treatment with praziquantel, control of snail populations and health education (WHO, 2021). However, the financial costs of diagnosis and treatment should be considered alongside wider social and environmental costs and benefits when planning a truly integrated disease control strategy (SALARI et al., 2020). However, in addition to the costs of diagnosis and treatment, other social and environmental measures of incalculable value should also be considered when planning a true One Health-based strategy for disease control (CDC, 2020).

Environmental measures for the control of schistosomiasis include reducing environmental contamination and preventing infection of human and non-human hosts. To achieve this, STAUFFER & MADSEN (2018) recommend controlling the snail vector population through chemical or biological means, eliminating cercariae released by snail intermediate hosts without killing the snails, and reducing infection rates in areas of transmission. The current recommendation for snail vector control is a chemical product, niclosamide, but well-structured biological control is also being encouraged, given that chemical control causes problems such as the death of non-target organisms and contamination, preventing the use of the water resource for a period of time, and high cost (WHO, 2017).

History of schistosomiasis control initiatives, focusing on biological control

The control of vector snail populations is one of the strategies recommended by the WHO for the control of schistosomiasis (BARBOSA et al., 2008). In its early reports (WHO, 1961, 1965, 1967), the WHO emphasized the need for the control of snail populations as the most effective measure against endemic schistosomiasis, given the lack of efficacy of the therapeutic drugs available at the time. The application of molluscicides is recommended in combination with the establishment of adequate public sanitation and drinking water supplies.

In the 1970s (WHO, 1973), schistosomiasis control faced challenges worldwide because of a major lack of both resources and qualified personnel (BARBOSA et al., 2008). The most important goal of this period was to reduce the spread of the disease into intermediate areas based on the treatment of infected individuals and the concomitant application of chemical molluscicides, such as niclosamide, in endemic areas. One of the most important aspects of this report was that it discouraged the biological control of snails, particularly where studies of environmental impact were unavailable (WHO, 1973).

Two reports were published in the 1980s (WHO, 1980, 1985). In the first, the emphasis was still on the control of transmission, whereas in the second, the focus shifted to the control of morbidity through the diagnosis and treatment of infected individuals. The 1980 report emphasized biological control by means of predatory snails, such as *Marisa cornuarietis*, which were used to reduce the transmission of schistosomiasis on a large scale in Puerto Rico. However, the committee recommended that snails from endemic areas should not be transferred or maintained in laboratories in other endemic areas for any purpose, discouraging studies on biological control (WHO, 1980).

In the 1990s and 2000s, chemotherapy became the principal control measure for schistosomiasis, in an integrated disease control program that also targeted geohelminthiasis to reduce costs (WHO, 1993). In the 1990s, school-children with a prior diagnosis were the principal targets of treatment, and in the 2000s, treatment focused on high-risk groups (children and adults involved in activities with a high risk of infection) without prior diagnosis.

Over the last 20 years, WHO experts have published three recommendations (2001, 2012, 2017, 2022). The first report broadened the focus on the control of schistosomiasis morbidity (reduction of 75–100% in schoolchildren and women) and made no mention of the control of snail populations. The 2012 resolution focused on public policies to eliminate endemic schistosomiasis in affected countries. It recommended strengthened epidemiological monitoring, preventive chemotherapy, and sanitary interventions, such as public sanitation systems, supplies of clean drinking water, and elimination of vector mollusks, but did not address the avoidance of potential environmental impacts. In 2017 (WHO, 2017), the report recommended integrated vector control, broad studies of vectors and their local transmission patterns, and the development of different biological and other control strategies to assess their impact on the disease when combined with other types of intervention, such as drugs and vaccines. In 2022, the recommendation is directed toward public health campaigns to ensure high acceptance of snail control interventions. With development of snail control programs for the larger and less expensive global supply of molluscicides. In addition, the development and evaluation of new and environmentally friendly molluscicides are encouraged (WHO, 2022).

Schistosomiasis control measures are currently aligned with the One Health approach, which involves integrated vector control measures. There is a clear need for sustainable ecological control measures that preserve the environment, other animals, and local human populations, as mandated by the systemic schistosomiasis control model of the One Health concept (CDC, 2020). In this context, the present study provided a systematic review of the scientific papers published on the biological control of *Biomphalaria*, the intermediate host of schistosomiasis, and evaluates current challenges and future perspectives.

Methods

The present study was based on a systematic literature review, following the PRISMA guidelines (MOHER et al., 2009; PAGE et al., 2021), of the Web of Science and Scopus international databases, covering the 76-year period between 1945 and 2021. The review consisted of three steps: (i) identification of papers in the Web of Science and Scopus databases that contained specific descriptors, in addition to papers from other sources that were not detected by the descriptors but were relevant to this review; (ii) screening (omitting duplicate, reviews, and mathematical models, as well as unavailable papers and those beyond the scope of the present study), of papers in English, Portuguese, and French published in indexed journals and available for download; and (iii) the inclusion of eligible full-text papers that were available online (Figure 1). The search phase looked for the descriptors "schistosomiasis and biological control" or "*Biomphalaria* and biological control", in the titles or keywords of the papers.

All the studies identified through this search were read in full, classified as field or laboratory research, by biological agent analyzed (bacterium, fungus, invertebrate or vertebrate), and by the type of control (predation, competition or microbial control). The studies were analyzed quantitatively in terms of the number of papers per type of biological agent, the decade of publication, and country of origin.

Analysis of the papers included in the present study

In total, 98 papers were identified during the search of the Scopus (46) and Web of Science (52) databases in June 2021. A further 23 papers that were not identified using the descriptors were also added to the list of references. Twenty-one of these papers were excluded due to duplication or failure to satisfy the study's inclusion criteria. Of these, only 47 were available for download and were analyzed for the present review (Figure 1).

Authors from 14 different countries produced the 47 papers, with the majority (28) being from four countries: France (8), Brazil (8), the United States (6), and Egypt (6). Three of the papers selected (RUIZ-TIBÉN et al., 1969; JOBIN & BERRÍOS-DURÁN, 1970; PAULINYI & PAULINI, 1972) were published in the Bulletin of the World Health Organization, and had been cited 16, 6 and 19 times, respectively.

The biological strategy most commonly used to control *Biomphalaria* populations throughout the study period was predation using fish (12 papers), with the first paper on this subject being published in 1946. Other types of biological control involved two snail species, *Marisa cornuarietis* (Ampullariidae) (six papers), and *Melanoides tuberculata* (Thiaridae) (five papers). The *Biomphalaria* species most often targeted in the studies was *B. glabrata* (23 papers), followed by *B. pfeifferi* (12 papers). In the case of microbiological and parasitic agents, 5 papers focused on bacteria, four on fungi, and two on helminths.

The most prolific decades in the present study were 2010–2019 (14 papers), 1990–1999 (10 papers), and 1980–1989 (eight papers). In the

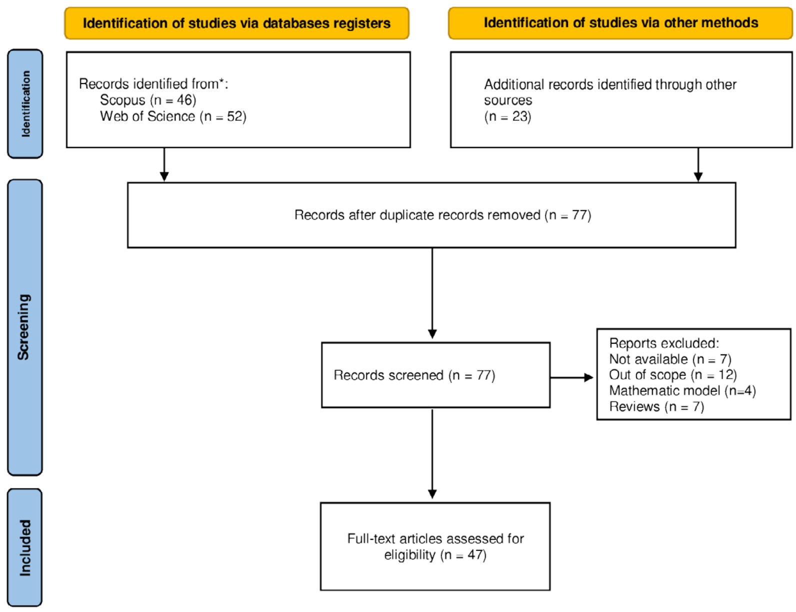

Figure 1: PRISMA 2020 flow diagram in this systematic review.

1980s and 1990s, predation was the biological control strategy evaluated in most studies, i.e., four and five papers, respectively. During this period, six studies focused on snails as both predators and competitors. We highlighted the research on *M. cornuarietis* in Puerto Rico and the studies of thiarids in the West Indian islands of Saint Lucia, Martinique, and Guadeloupe (PRENTICE, 1983; POINTIER, 1989; 1993; GIOVANELLI et al., 2003). It is important to note here that the success of the biological control program in Puerto Rico using *M. cornuarietis*, which began in the 1950s and generated key results in the 1970s and 1980s, led the WHO to recommend the use of this snail as a biological control agent in its reports published in the 1980s. Even after the use of snails became less popular, (POINTIER et al., 1991; SOKOLOW et al., 2015), further research was conducted in the 1990s and early 2000s before being discontinued.

A greater diversity of biological agents, reported in 14 papers, was studied for the control of *Biomphalaria* between 2010 and 2019. The large number of papers published in this most recent period may reflect the WHO recommendations on integrated vector management, which encourage detailed local study of the problem in a given region with the aim of identifying local solutions. Predation was an ongoing theme (seven papers), but new agents such as waterbugs, fly larvae, and prawns were also included. The remaining seven papers discussed microbiological and parasitological agents, including fungi (three papers), bacteria, and helminths (two papers each).

Agents of biological control

The concept of biological control has been redefined many times in recent years; we adopted the following definition, proposed by EILENBERG et al. (2001): “The use of living organisms to suppress the population density or impact of a specific pest organism, making it less abundant or less damaging than it would otherwise be.” *Biomphalaria*, it should be noted, is an organism that acts as a transmitter of a neglected disease, rather than as a pest itself. Biological control in this case has the objective of reducing the transmission of schistosomiasis through the control of this intermediate host.

Over the years, control of *Biomphalaria* snail populations has been attempted, using direct (predation) or indirect (competition for food or habitat) mechanisms or ecological interactions (AROSTEGUI et al., 2019); the various agents can be classified as either microbial control (viruses, fungi, protozoa, and bacteria), predators, or competitors (POINTIER & JOURDANE, 2000) and are detailed below, organized into these three types.

Predators

The earliest attempts at biological control of *Biomphalaria* were based on predation (Tables 1, 2, and 3), by fish (OLIVER-GONZÁLEZ, 1946). Laboratory studies have shown that *Sarotherodon mossambica*, *Tilapia rendalli*, *T. nilotica*, *Gambusia affinis*, *Labeo niloticus*, and *Cyrinus carbio* all prey on the egg masses and neonates of *Biomphalaria* (GRABER et al., 1981; ANDRADE, 1982; SULIEMAN et al., 2015; AFIFI & AHMED, 2018). Other species have been observed to prey on adult snails, and these include: *Sargochromis codringtoni, G. affinis*, *L. niloticus*, *C. carbio*, and *Clarias gariepinus* (CHIMBARI et al., 1996; 1997; GASHAW et al., 2008; SULIEMAN et al., 2015; AFIFI & AHMED, 2018). In the field, *Serranochromis macrocephala* and *Astatoreochromis alluadi* were able to reduce *Biomphalaria* populations (DE BONT & DE BONT, 1952; MCMAHON et al., 1977). Notably, *Geophagus brasiliensis* was also tested under both laboratory and semi-natural conditions and fed on snails in both locations, even when a variety of other foods was also available (WEINZETTL & JURBERG, 1990).

Two species of snail, *Marisa cornuarietis* and *Pomacea* sp., have been tested as potential predators of *Biomphalaria*. In the laboratory, CHERNIN et al. (1956a) evaluated the conditions under which *M. cornuarietis* could limit the growth of *Biomphalaria* populations by preying on egg masses and newly hatched snails. In 1956, owing to the high cost of the chemicals used to control schistosomiasis, the Puerto Rican government decided to implement a biological control project that focused on irrigation ponds, using *M. cornuarietis* as the control agent. It was possible to confirm the effectiveness of *M. cornuarietis* as a predator/competitor of *B. glabrata* in the field, and obtain a 60-fold reduction in the cost of controlling *B. glabrata* (RUIZ-TIBÉN et al., 1969). Two decades later, POINTIER et al. (1991) introduced *M. cornuarietis* to the West Indian island of Guadeloupe; POINTIER & DAVID (2004) monitored the effect of the subsequent 13 years and reported convincing evidence that *M. cornuarietis* played an important role in the disappearance of *B. glabrata* in the region.

Leeches of the genus *Helobdella* have also been tested as potential predators of *Biomphalaria*. CHERNIN et al. (1956b) found that *H. fusca* could control the snail population. Other authors have reported that *H. triserialis* is a predator of new hatched, juvenile, as well as adult, *B. glabrata*, *B. straminea* and *B. tenagophila* (GUIMARÃES et al., 1983; 1984). Crayfish (*Procambarus clarkii*) reduced the abundance of *B. pfeifferi* (HOFKIN et al., 1991; 1992). The same was observed for *B. alexandrina* both in field experiments and in the laboratory (KHALIL & SLEEM, 2011).

Freshwater prawns of the genus *Macrobrachium* have been studied in relation to their potential for regulating *Biomphalaria* populations in the field. SAVAYA et al. (2014) suggested restocking male prawns as a means of controlling local snail populations and reducing the prevalence of schistosomiasis in a region affected by dam construction. SOKOLOW et al. (2015) confirmed that reintroduction of the prawn after its extirpation resulted in a significant reduction in not only the population of infected snails but also the prevalence of schistosomiasis in the region; the prawns feed on the eggs, newly hatched snails, and other small individuals. Larvae of the fly *Sepedon ruficeps* have been tested as biological control agents for *B. pfeifferi*. The larvae have a high predation capacity, with one larva consuming up to 40 snails (AGBOHO et al., 2017). Waterbugs (*Sphaerodema urinator*) can find, attack, and devour snails, preferring small individuals of *B. alexandrina* (YOUNES et al., 2017).

Competitors

The first studies focusing on the competitors of *Biomphalaria* were published in the 1950s; although, papers on this topic are still scarce. These competitors (Tables 4 and 5) consist of a number of other snail species. Several studies have verified the effects of the interspecific competition between *M. cornuarietis* and *Biomphalaria* in the field. FERGUSON et al. (1958) reported that *Biomphalaria* had disappeared completely from ponds two years after the introduction of *M. cornuarietis*. Similar results were obtained by OLIVER-GONZALEZ & FERGUSON (1959), who recorded the almost complete elimination of *Biomphalaria* from streams 18 month after the introduction of *M. cornuarietis* and, more importantly, the absence of new schistosomiasis infections in a study group of preschool children. RUIZ-TIBÉN et al. (1969) reported the implementation of a *M. cornuarietis* biological control program for *B. glabrata* populations in natural ponds on the island of Puerto Rico, as an alternative to chemical controls. The 20-year follow-up showed

Table 1 - Summary of the content of the peer-reviewed papers on biological control of *Biomphalaria* species using predators from 1946 to 1984.

Biological control agent	*Biomphalaria* species	Target stage	Effect on *Schistosoma* assessed	Main results	Reference
Lebistes reticulatus (guppy)	*B. glabrata*	Egg mass/ young	No	Preference for eggs masses to hatch and snails shedding cercariae	OLIVER-GONZÁLEZ (1946)
Serranochromis macrocephala (fish)	*Biomphalaria* sp.	All stages	No	After three months, the tank was drained and no small snails were found in it	DE BONT & DE BONT (1952)
Marisa cornuarietis (snail)	*B. glabrata*, *B. pfeifferi*	Egg masses/ young	No	*M. cornuarietis* devoured egg masses and young *Biomphalaria*	CHERNIN et al. (1956a)
Helobdella fusca (leech)	*Australorbis glabratus* = *B. glabrata*	Young and newly hatched	No	Adult leeches anchor themselves in the shell until the snail is devoured	CHERNIN et al. (1956b)
M. cornuarietis (snail)	*B. glabrata*	Adults	No	The disappearance of *B. glabrata* coincided with the introduction of *Marisa*	RUIZ-TIBEN et al. (1969)
Pomacea sp. (snail)	*B. glabrata*	Egg mass/ newly hatched	No	*Pomacea* sp. caused a reduction in the number eggs and impeded the establishment of *B. glabrata* colonies	PAULINYI & PAULINI (1972)
Astatoreochromis alluandi, Tilapia leucosticta, T. Zillii, Gambusia affinis (fishs)	*B. pfeifferi*	Adults	No	*A. alluaudi* reduced the number of *B. pfeifferi*. *T. zilliie* and *T. leucosticta* did not appear to be associated with reduction in the snail populations	MCMAHON et al. (1977)
T. rendalli and *Sarotherodon mossambica* (fishs)	*B. glabrata*	All stages	No	*S. mossambica* preyed on snails occasionally. *T. rendalli* reduced the snail population	GRABER et al. (1981)
T. nilotica (fish)	*B. glabrata*	Adult	No	The fish impeded hatching and thus limited the growth of the four study populations	ANDRADE (1982)
H. triserialis lineata (leech)	*B. glabrata*	All stages	No	No predation of egg masses, but young specimens preyed on more than adults	GUIMARÃES et al. (1983)
H. triserialis lineata (leech)	*B. straminea, tenagophila*	All stages	No	Velocity of predation inversely proportional to the size of the snails, no predation of egg masses	GUIMARÃES et al. (1984)

that *B. glabrata* populations declined gradually, and were eventually replaced by *M. cornuarietis*. While this may have been beneficial in terms of disease control, the authors felt that the introduction of *M. cornuarietis* may eventually have led to ecological disruptions due to the elimination of *B. glabrata* populations. JOBINS & BERRIOS-DURAN (1970) discussed the competitive relationship between

Table 2 - Summary of the content of the peer-reviewed papers on biological control of *Biomphalaria* species using predators from 1990 to 2011.

Biological control agent	*Biomphalaria* species	Target stage	Effect on *Schistosoma* assessed	Main results	Reference
Geophagus brasiliensis (fish)	*B. tenagophila*	Juvenile/ adult	No	The predator fed on the snails in both conditions, preying preferentially on snails of 5–11 cm	WEINZETTL & JURBERG (1990)
Procambarus clarkii (crayfish)	*B. pfeifferi*	Adult	No	*P. clarkii* reduced the abundance of snails by 5 days, after 30 days there were no live snails in the tanks containing 4 crayfish.	HOFKIN et al. (1991)
M. cornuarietis and *Ampullaria glauca* (snails)	*B. glabrata*	All states	Yes	*M. cornuarietis* colonization was rapid, and all *B. glabrata* were eliminated, as was *S. mansoni* infection in local mice	POINTIER et al. (1991)
P. clarkii (crayfish)	*B. pfeifferi* *B. glabrata*	Adult All stages	No	Crayfish consumed adult *Biomphalaria*, affecting the survival of juveniles snails	HOFKIN et al. (1992)
T. rendalli, *Sargochromis codringtoni* (fishes)	*B. pfeifferi*	Adult	No	*T. rendalli* was primarily herbivorous and *S. codringtoni* was malacophagous	CHIMBARI et al. (1996)
Sargochromis codringtoni (fish)	*B. pfeifferi*	Adult	No	Each fish consumed approximately 800 snails within 1 week	CHIMBARI et al. (1997)
M. cornuarietis (snail)	*B. glabrata*	All stages	No	*B. glabrata* disappeared from the ponds with *M. cornuarietis*	POINTIER & DAVID (2004)
Clarias gariepinus (fish)	*B. pfeifferi*	Adult/ egg mass	No	It took 32 days to consume all the snails (with proper food) and 16 days (with limited food)	GASHAW et al. (2008)
P. clarkii (crayfish)	*B. alexandrina*	Adult	No	Laboratory: all snails were consumed; Field: reduction/ absence of snail	KHALIL & SLEEM (2011)

of introducing the competitor and the simplicity of this strategy of biological control. However, no other studies of this species in different localities were identified by our search strategy, nor were there any current studies on the program implemented in Puerto Rico using *M. cornuarietis.*

A relationship between *Melanoides* (=*Thiara*) *tuberculata* and *Biomphalaria* has also been observed in the field. POINTIER (1989; 1993) reported a rapid spread of *M. tuberculata*, that resulted PRENTICE (1983) and MKOJI et al. (1992) have suggested that *Thiara granifera* and *B. glabrata* compete for both space and food, and that *B. glabrata* in the field.

The relationship between *Pomacea* spp. and *Biomphalaria* has also been studied. Initially, *Pomacea* prevents the establishment of active colonies of *B. glabrata*, causing mortality among the newly hatched *B. glabrata* snails and reducing the number of *B. glabrata* feeding on its own egg masses

Table 3 - Summary of the content of the peer-reviewed papers on biological control of *Biomphalaria* species using predators from 2014 to 2018.

Biological control agent	*Biomphalaria* species	Target stage	Effect on *Schistosoma* assessed	Main results	Reference
Macrobrachium vollenhovenii (prawn)	*Biomphalaria* sp.	All stages	Yes (theoretically)	Reintroduction of male shrimp controlled snail, decreasing the prevalence of schistosomiasis	SAVAYA et al. (2014)
M. vollenhovenii (prawn)	*B. pfeifferi*	Not specified	Yes	80% reduction of infected snails, prevalence of human schistosomiasis 50% lower and egg load 50% lower	SOKOLOW et al. (2015)
Gambusia affinis (fish)	*B. pfeifferi*	All stages	No	All egg masses and neonate snails were preyed, and number of adult snails reduced	SULIEMAN et al. (2015)
Sepedon ruficeps (larva of Diptera)	*B. pfeifferi*	Not specified	Yes	Parasitized *B. pfeifferi* were attacked more frequently	AGBOHO et al. (2017)
Sphaerodema urinator (water bug)	*B. alexandrina*	Not specified	No	The predator attacked and ingested the snails, preferring small snails	YOUNES et al. (2017)
Labeo niloticus and *Cyrinus carbio* (fishes)	*B. pfeifferi*	All stages	No	Both fish are efficient predators of the egg mass and neonates, and reduce the number of adult snails	AFIFI & AHMED (2018)

(PAULINYI & PAULINI, 1972). The accidental introduction of *Ampullaria glauca* into a natural lake led to a marked decline in the local *B. glabrata* population, until only a small colony remained. The presence of *A. glauca* may also have caused a marked decline in the presence of *Pistia stratiotes*, a floating plant that provides a favorable habitat for *B. glabrata*. Another consequence was a decline of *S. mansoni* in the local rat population (POINTIER, 1988; POINTIER et al., 1991).

COELHO et al. (2004) also proposed a biological control model using the Taim strain of *B. tenagophila*, which is resistant to *S. mansoni* infection. However, the proposed model is based on the introduction of a resistant strain following the application of a chemical molluscicide. The authors also generated transgenic *B. glabrata* harboring the *S. mansoni* resistance gene. The use of genetic techniques to manipulate schistosomiasis host snails has been indicated as a potential complementary tool to reduce or even interrupt transmission. The CRISPR-Cas9 system is an alternative that has been explored for schistosomiasis control, although, mentioning *Biomphalaria* spp. is scarce (FAMAKINDE, 2018; 2020).

Microbial control

Entomopathogenic agents, such as fungi, bacteria and nematodes, have been successfully used to control a number of arthropod pests, including *Mahanarva fimbriolata*, *Deois flavopicta*, *Cornitermes cumulans*, and *Rhipicephalus microplus* (FERNANDES & ALVES, 1991; FERNANDES & BITTENCOURT, 2008; PEREIRA et al., 2008; LOUREIRO et al., 2012). Such agents have also been used recently for the microbial control of *Biomphalaria* snails (DUARTE et al., 2015; DUVAL et al., 2015; OKONJO et al., 2015; SAAD et al., 2016; ABD EL-GHANY & ABD EL-GHANY, 2017; ABDEL-WARETH et al., 2019). Entomopathogenic fungi, bacteria, and nematodes are environmentally friendly and are thus considered a sustainable method for the

Table 4 - Summary of the content of the peer-reviewed papers on biological control of *Biomphalaria* species using competitors from 1958 to 1989.

Biological control agent	*Biomphalaria* species	Target stage	Effect on *Schistosoma* assessed	Main results	Reference
M. cornuarietis (snail)	*B. glabrata*	Young/adults	No	After 2 years, the ponds with *M. cornuarietis* had no *A. glabratus*	FERGUSON et al. (1958)
M. cornuarietis (snail)	*B. glabrata*	Young/adults	No	*A. glabratus* disappeared after 1.5 years, there are no schistosomiasis infections in preschool children	OLIVER-GONZALEZ & FERGUSON (1959)
M. cornuarietis (snail)	*B. glabrata*	Adults	No	The disappearance of *B. glabrata* coincided with the introduction of *Marisa*	RUIZ-TIBEN et al. (1969)
M. cornuarietis (snail)	*B. glabrata*	Adults	No	The study emphasized the low cost and simplicity of the method	JOBIN & BERRÍOS-DURÁN (1970)
Pomacea sp. (snail)	*B. glabrata*	Egg mass/ newly hatched	No	*Pomacea* sp. caused a reduction in the number eggs and impeded the establishment of *B. glabrata* colonies	PAULINYI & PAULINI (1972)
T. granifera (snail)	*B. glabrata*	All stages	No	*B. glabrata* was eliminated from 22 months after *T. granifera* was introduced	PRENTICE (1983)
Ampullaria glauca (snail)	*B. glabrata*	All stages	Yes	*A. glauca* decimated the plant Pistia stratiotes (habitat of *B. glabrata*), reducing the population snails and *S. mansoni*	POINTIER (1988)
Thiara tuberculata (snail)	*B. glabrata* and *B. straminea*	All stages	No	Decline of *Biomphalaria* populations and the complete after two years	POINTIER et al. (1989)

control of agricultural insect pests, with a number of commercial products already available (MASCARIN & JARONSKI, 2016; MASCARIN et al., 2019).

DUARTE et al. (2015) reported the action of two well-known entomopathogenic fungi (*Beauveria* and *Metarhizium*) against *B. glabrata* egg masses: the fungi penetrated the eggs and reached the embryos, thus impairing egg maturation. OKONJO et al. (2015) recorded up to 70% mortality in adult *B. pfeifferi* exposed for 28 days to entomopathogenic nematodes. Several bacteria have also been shown to exhibit molluscicidal activities. DUVAL et al. (2015) described a novel *Paenibacillus* strain that affects both the adult and embryonic stages of *B. glabrata*, causing significant mortality. These microbial control studies reflect the considerable global momentum attained by biopesticide research, in recent years, which has been supported by both social and governmental demands for more sustainable invertebrate pest control methods (Table 6).

Table 5 - Summary of the content of the peer-reviewed papers on biological control of *Biomphalaria* species using competitors from 1991 to 2004.

Biological control agent	*Biomphalaria* species	Target stage	Effect on *Schistosoma* assessed	Main results	Reference
M. cornuarietis and *Ampullaria glauca* (snails)	*B. glabrata*	All states	Yes	*M. cornuarietis* colonization was rapid, and all *B. glabrata* were eliminated, as was *S. mansoni* infection in local mice	POINTIER et al. (1991)
Melanoides (=*Thiara*) *tuberculata* (snail)	*B. pfeifferi*	All stages	No	Both species persisted over the study period, with *M. tuberculata* more abundant	MKOJI et al. (1992)
M. tuberculata (snail)	*B. glabrata*	All stages	No	Reduction of *B. glabrata* populations to very low levels, reducing/eliminating *S. mansoni*	POINTIER (1993)
M. tuberculata (snail)	*B. glabrata*	All stages	No	*B. glabrata* population was reduced until it disappeared	POINTER et al. (1993)
M. tuberculata (snail)	*B. glabrata*	All stages	No	The population of *B. glabrata* reached lower density in the 4th year	GIOVANELLI et al. (2003)
B. tenagophila Taim strain (resistant to *S. mansoni*)	*B. tenagophila* susceptible to *S. mansoni*	Adult	Yes (theoretically)	The introduction of the Taim strain would produce resistant descendants	COELHO et al. (2004)
M. cornuarietis (snail)	*B. glabrata*	All stages	No	*B. glabrata* disappeared from the ponds with *M. cornuarietis*	POINTIER & DAVID (2004)

Challenges

There is no single species capable of controlling populations of *Biomphalaria* spp. in the various local endemics settings, wherefore concurrent use of a few species, depending on the ecosystem, should be considered. The development of multi-agent solutions is one of the challenges for the control of these vectors and should reduce the population and have an impact on the transmission of schistosomiasis. Each location will require a solution that accommodates the characteristics and unique diversity of that location, that is, there is no single solution.

However, the introduction of an exotic species into an ecosystem may threaten its environmental integrity (WHO, 1980), and the introduction of more than one species into the same ecotope could be disastrous. In the face of this, developing sustainable biological controls that can be used to impede disease transmission will be difficult. Further clear challenges are the need to compile a detailed database of the organisms reported in the principal areas of disease transmission and to enhance the application of natural local biological agents affecting vector snails in each region. SOKOLOW et al. (2015), who used a local population of prawns that naturally consume newly hatched snails, to develop a sustainable local control strategy, adopted this approach. From this perspective, biological control has the advantage of not only controlling the host of *S. mansoni*, but also improving the quality of life of the local human population affected by schistosomiasis, using natural predators, competitors, parasites, or established biocontrol agents (SOKOLOW et al., 2017).

Table 6 - Summary of the content of the peer-reviewed papers on biological control of *Biomphalaria* species using microbial control.

Biological control agent	*Biomphalaria* species	Target stage	Effect on *Schistosoma* assessed	Main results	Reference
Bacillus TSB (terminal spore *Bacillus)*	*B. glabrata*	Not specified	No	Mortality of snails was more than 99% in the different trials	DIAS (1954)
B. thuringiensis (bacterium)	*B. alexandrina* and *B. truncatus*	Adult	No	Molluscicidal activity observed in both snail species	OSMAN & MOHAMED (1991)
Bacillus sp. (bacterium)	*B. glabrata*	Adult	No	LC50 of the suspensions ranged from 2.6 to 2.8	SINGER et al. (1997)
Plagiorchis elegans (trematode)	*B. glabrata*	Young, juvenile/ adult	No	Snail survivorship and reproductive reduced only at the higher exposure levels	DAOUST et al. (2010)
Metarhizium anisopliae and *Beauveria bassiana* (fungi)	*B. glabrata*	Egg mass	No	Hyphal bodies of both fungi inhibited embryogenesis completely, with no juveniles hatching whatsoever	DUARTE et al. (2015)
Paenibacillus glabratella (bacterium)	*B. glabrata*	Juvenile	No	The bacterium isolated from *B. glabrata* is infectious, highly lethal to the snail and reduces the number of offspring by impacting the embryonic stages	DUVAL et al. (2015)
Phasmarhabditis hermaphrodita (nematode)	*B. pfeifferi*	Juvenile	No	Mortality of up to 70%, *B. pfeifferi* susceptible to *P. hermaphrodita*	OKONJO et al. (2015)
236 fungal isolates	*B. alexandrina*	Adult	No	20 fungal species presented molluscicidal activity, killing 100% of the snails, *Penicillium janthinellum* had the lowest LC50	SAAD et al. (2016)
B. thuringiensis (bacteria)	*B. alexandrina*	Adult	No	Four isolates presented a high level of molluscicidal activity against *B. alexandrina*. Qalyubia was the most potent, with the lowest LC_{50} value	ABD EL-GHANY & ABD EL-GHANY (2017)
B. bassiana, *M. anisopliae*, and *Paecilomyces lilacinus*	*B. alexandrina*	Adult	No	Acetone extracts of *B. bassiana* and *P. lilacinus* had a molluscicidal effect on *B. alexandrina*, with *P. lilacinus* being more toxic	ABDEL-WARETH et al. (2019)

As mentioned above, biocontrol agents, particularly fungi and bacteria, have attracted increasing attention over the past 10 years (DUARTE et al., 2015; DUVAL et al., 2015; SAAD et al., 2016; ABD EL-GHANY & ABD EL-GHANY, 2017). These microorganisms, some of which are natural to the microbiome of either the target animal or its aquatic environment, may function as disruptors of either physiological mechanisms or microbial biodiversity. From this perspective, the microbiome of snails and other freshwater organisms may play an important role in control, shaping the ability of these organisms to transmit disease (CHEVALIER et al., 2020). According to PORTET et al. (2021), microorganisms influence and are influenced by *S. mansoni* infection in *B. glabrata*.

Given this, one further challenge for effective biological control is to use microorganisms as the active ingredient of a product that can be used for the indirect control of schistosomiasis transmission. This would be a natural product intended to provoke a homeostatic imbalance in snails, particularly, those infected with *S. mansoni*. This imbalance would reduce the parasite load of the vector or provoke its death, culminating in a selective control. However, it is necessary to identify, test, and study in minute detail the impact of different microorganisms, at different concentrations, on the dynamics of the *Biomphalaria*/*Schistosoma* interaction.

Future perspectives

Despite the effectiveness of schistosomiasis control programs based on the large-scale treatment of populations with drugs, the disease persists as a major public health problem in most endemic areas. Fundamental to success will be a holistic understanding of the disease. Schistosomiasis is a systemic disease that involves intermediate hosts (snails) and definitive hosts, such as rodents, cattle, and humans that can migrate and spread the disease to new areas. The disease cycle also involves the limnic environments inhabited by host snails, which are also the final destination of domestic, medical, and industrial effluents in many countries with endemic diseases. While a holistic perspective, which relates the links in the epidemiological chain systematically, is essential to combat schistosomiasis effectively, it has yet to be put into practice. Based on the One Health concept, we suggested a differentiated approach and the implementation of strategies that protect not only public health, but also the integrity of the environment. Integrated, effective, and sustainable control should focus primarily on the control of transmission rather than morbidity, and be based on the application of local knowledge.

Based in the papers analyzed in this study, biological control is a promising measure for the control of schistosomiasis transmission, in contrast to the use of chemical molluscicides, which are expensive, environmentally unsafe, and toxic to many non-target organisms. However, to use this strategy we suggest ecological studies to identify possible competing organisms, predators, and/or microorganisms in the water or microbiota of mollusks in the region. These studies could be conducted in partnership with researchers from local research institutions and the affected community. It is important to maximize the avoidance of products, substances, and biological control agents that could in any way destabilize the local ecosystem or harm the local population. In this scenario, biological control constitutes an important complementary measure to be integrated with systemic controls, such as chemotherapy, large-scale environmental and sanitation programs, and the implementation of environmental and health education for populations at higher risk of the disease.

CONCLUSION

Based on the findings of our review, we encourage further research into the microbiota of the snail vectors. This would involve not only the identification of the microorganisms present in the normal microbiota, but also those associated with the susceptibility of the snails to *Schistosoma* infection We also encouraged research into local free-living microorganisms or those present in the microbiota of other aquatic organisms, which may interact with the snail vectors. These microbial agents may have potential as physiological disruptors and reproductive and/or epigenetic agents that could be used to alter the dynamics of the interaction between *Biomphalaria* and *Schistosoma*. This approach may reveal potential biological control agents or other microbial products that can reduce the parasite load of schistosomiasis vectors and control their transmission in a sustainable manner.

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DECLARATION OF CONFLICT OF INTERESTS

We have no conflict of interest to declare.

AUTHORS' CONTRIBUTIONS

GF conducted the research, collect data, analysed the results and wrote the manuscript. AMRA collect datas, analysed the results and wrote the manuscript. SQ analysed the results and wrote the manuscript. PG analysed the results and designed and wrote the manuscript. CMS designed and conducted the research, analysed the results and wrote the manuscript. All authors revised the manuscript and approved of the final version.

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