International Journal of TROPICAL DISEASE & Health

Volume 45, Issue 3, Page 41-56, 2024; Article no.IJTDH.113693
ISSN: 2278–1005, NLM ID: 101632866

Natural Bioactive Compounds against *Schistosoma haematobium* and *Schistosoma mansoni*

Aristide Ouattara [a*], Harouna Soré [a] and Adama Zida [a,b,c]

[a] Centre National de Recherche et de Formation sur le Paludisme (CNRFP), Ouagadougou, Burkina Faso.
[b] Service de Parasitologie-Mycologie du Centre, Hospitalier Universitaire Yalgado Ouédraogo (CHUYO),Ouagadougou, Burkina Faso.
[c] Département des Sciences Biologiques Appliquées, Unité de Recherche et de Formation en Sciences de la Santé, Université Joseph KI-Zerbo, Ouagadougou, Burkina Faso.

Authors' contributions

This work was carried out in collaboration among all authors. Author AO did the literature search for natural substances with schistosomicide activities and written the manuscript. Authors HS and AZ have made necessary corrections to the manuscript. After the different inputs, all the authors marked their approval on the final version of the manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJTDH/2024/v45i31523

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/113693

Systematic Review Article

Received: 24/12/2023
Accepted: 28/02/2024
Published: 04/03/2024

ABSTRACT

Aim: This documentary review aimed to make a synthesis of bioactive plants or natural compounds on schistosomes. We carried out a review from 2000 to 2022, oriented towards the plants in order to search natural compounds bioactive on schistosomes which can be a great contribution for new drugs discovering.
Terms such as "schistosomiasis and medicinal plants", "natural anti-schistosome compounds", "phytochemical screening", "bioactive compounds on schistosomes" were used for the online literature search through the following sites: PubMed; Google Scholar; ScienceDirect and Hinari.

**Corresponding author: Email: aristouatt378@gmail.com, xyzaristouatt@yahoo.fr;*

Results: There are many plants already used for the traditional treatment of schistosomiasis. This review found nearly 72 families of plants belonging to 228 botanical species have been listed. Some of these have been studied in vitro / in vivo and preliminary results have shown their schistosomicidal properties. Moreover, the results of qualitative phytochemical screening and toxicity testing of these natural compounds provide hope for new drug discoveries.

Conclusion: Even if plants efficacy is proven, we need more in-depth investigations to determine their chemical components in order to minimize the undesirable effects and to guarantee their safety by assessing their toxicity.

Keywords: Schistosomiasis; schistosoma; praziquantel; natural compounds; bioactive.

1. INTRODUCTION

Schistosomiasis or bilharzia, also called "snail fever" is one of the most commonly encountered neglected tropical diseases (NTDs) with high prevalence very often, in low-income countries, especially among schools where hygiene conditions are quite precarious [1,2]. It is a parasitic illness caused by flatworms of the trematode genus. Three species are generally implicated in human pathology. These include: *Schistosoma mansoni*, which is found in the large intestine, *Schistosoma japonicum* which has a preference for the small intestine and *Schistosoma haematobium* with the blader environment as its preferred zone [3]. Schistosomiasis is the second endemic parasitosis worldwide after malaria [4,5]. It affected 230 million people worldwide in 2020 with 80 to 90% of cases in Africa area. This parasitological disease linked both to fecal peril and to certain water activities such as fishing, swimming and agriculture [2,6–8].

Prevention of schistosomiasis through mass chemotherapy, and therapy are the only alternative currently, as there is no known effective vaccine for large-scale use [9]. Some drugs such as metrifonate (introduced in 1960), Amoscanate and Oxamniquine have been used and abandoned either for their side effects, or for their low efficacy or for their hepatotoxicity [10,11].

The management of schistosomiasis cases generally uses praziquantel (PZQ), the anthelmintic which is preferentially used to support schistosomiasis cases [12–14]. After nearly a century of research into schistosomiasis drugs, it was not until 1970 that PZQ was developed [15]. This anthelmintic, produced by Merck and used since 1970 [5] is known as Biltricide® [15,16]. It is the only drug approved by the world health organization (WHO) to treat schistosomiasis [17–19]. Its repeated and frequent use could induce cases of resistance or therapeutic failures [19–22]. Although effective, taking PZQ is often difficult in children with swallowing difficulties, while chewing is contraindicated according to recommendations [5]. This parasitic disease remains so far a heavy burden, with high prevalence especially for developing countries despite mass treatments as a preventive measure [1,12,20,23–26]. In rural areas, where living conditions are precarious, the use of PZQ is not systematic due to poverty [19]. People generally use plants to treat schistosomiasis [19,27,28]. Chemoprevention is an alternative to get away or to eradicate this NTD, but the cost of this operation constitutes a difficulty for its implementation [29,30]. Also, the success of this operation must integrate vector control through the use of molluscicides as recommended by the WHO control strategy [31].

The search for new perspectives for the management or even the eradication of this parasitic disease is an imperative for the researchers. Moreover, one of the major challenges of the WHO is to eradicate schistosomiasis by the year 2030 in countries where this parasitosis remains endemic [32-34]. Indeed one of the WHO objectives in its traditional medicine strategy 2014-2023 is to promote traditional medicine which plays a complementarity role with conventional medicine [35]. For this purpose, research should be directed towards new horizons by involving the plant environment in the search for new medicines as an alternative to the current use of the treatment of schistosomiasis [36,37]. A literature review will allow us to have an overview of some studies conducted on plants or natural bioactive substances that can be potential sources for the development of new drugs against schistosomiasis or others diseases [38]. Phytotherapy can be an effective, accessible and inexpensive solution to effectively control schistosomiasis in addition to water treatment and health education [39,40]. Some advocate that we could modify, or even create a new formulation of PZQ in order to make it more bioactive and bioavailable [41]. Developing a new generation of antischistosomicidal drugs is a necessity for searchers.

However, the lack of information or scientific data on these plants, compound extracts or chemical groups constitutes an obstacle for their use [30,42–44].

2. MATERIALS AND METHODS

We carried out a systematic search for articles deadline from 2000 to 2022 with antischistosomidal plants, extracts or chemical compounds through the following sites: PubMed (https://pubmed.ncbi.nlm.nih.gov/); Google Scholar (https://scholar. google.com); ScienceDirect(https://www.sciencedirect.com/topics/social-sciences/research-article) and Hinari (https://www.emro.who.int/fr/information-resources/hinari/hinari.html)

Terms such as “schistosomiasis and medicinal plants”, “natural anti-schistosome compounds”, “phytochemical screening”, “bioactive compounds on schistosomes” were used for the online literature search. These search terms allowed us to have publications and an overview related to our research topic. The analysis of this documentation allowed us to identify plants and natural compounds active on schistosomes. We noted that *in vitro* and *in vivo* tests were carried out in purebred mice with the different extracts of plants belonging to several families according to the botanical nomenclature.

Our literature review focused on articles published from January 2001 to December 2022 and we sorted articles that best met our selection criteria. The documentation collection period is from September 2022 to April 2023.We also searched the libraries of the WHO and the West African Health Organization (WAHO) on plants with schistosomicidal properties.

The selected articles had to meet one of the following criteria: deal with plants or natural bioactive compounds effective on schistosomiasis; *in vitro* and *in vivo* tests on schistosomes involving natural substances; the phytochemical profile of plant extracts against schistosomiasis; toxicity testing of plant extracts effective against schistosomiasis. We proceeded to a full reading of each article in order to take stock of the research work already done and to establish the link with our research topic.

3. REVIEW

3.1 Years of Publications

Between 2001 and 2022, more than two hundred articles were submitted to us based on the keywords and expressions used with the aim of taking stock of the existing plants repertory may possibly be explored in the search for bioactive substances on schistosomes.

Among the documentation proposed through our research, around one hundred articles met our selection criteria (see Fig. 1).

The highest rate of publication of the documentation was recorded between 2019 and 2020, followed by the last two years with a slight decline. This could be explained by a motivation of researchers in view of emergence of NTDs in recent years. It could be due to the funding allocated by WHO to researchers in achieving its considerable reduction objectives for burden of morbidity and mortality, or even eradication of NTDs by 2030 [32,33].

3.2 Schistosomicidal Plants

The plant environment is increasingly explored in search of new alternatives in the search for solutions against schistosomiasis which has become a real challenge in the response to NTDs [45].

This approach is in line with the objectives of the WHO in its program for NTDs eradication by 2030 [33].

The documentary review allowed us to know that there are a lot of schistosomicidal plants belonging to different botanical families. This plant environment is a potential source of natural substances as an alternative which can contribute to the development of new antischistosomal drugs, and which will strengthen the capacity to treat this parasitosis on a global scale [46]. The plant material listed is the result of ethnobotanical surveys that have made it possible to inventory plants used in traditional medicine and with anthelmintic potential in general and antischistosomal particularly [47,48]. The listed plants belong to 72 families containing a total of 229 botanical species (see Tables 1 and 2). The majority of plants have been listed through ethnobotanical surveys [48], on the shelves of the WAHO [47] and the WHO libraries.

3.3 Preparation of Plant Material

In search of plant extracts bioactive on schistosomiasis, the researchers proceeded to collect plants that had been previously identified by botanist experts. All harvested plants were fully dried in the shade for at least two weeks before being sprayed for the various extractions with different solvents. Virtually all plant parts have been used to search for bioactive substances on schistosomes: leaves, barks, roots, fruits, stems, branches, bulbs, pods, rhizomes, or even the whole plant.

The solvents used for the different extractions were: distilled water, hydro-alcohol, ethanol, methanol (in varying percentages), acetone, chloroform, ethyl-acetate, acetonitrile, ether, methane, olive oil and hexane [49].

3.4 Antischistosomal Activity of Natural Substances

We noticed that there is a varied range of plants with antischistosomal and antimolluscicidal properties [47,50] and therefore, the ability to neutralize the parasite [51].

All the strains of schistosomes used for the different tests were acquired through research institutions, and *S. mansoni* has been the subject of most studies unlike other species of schistosomes [52,53]. Obtaining cercariae for *in vitro* and *in vivo* testing required collection of intermediate host snails that were maintained and infected for their excretion of cercariae in many laboratories such as the Schistosome Biological Supply Center (SBSC), Theodor Bilharz Resaech Institute (TBRI), Gisa, Egypt; in Medical Parasitology Department, Faculty of Medicine, Menoufia University, Giza, Egypt.

3.5 *In vitro* Study of the Antischistosomal Activity of Plants

Several researchers have carried out work on the *in vitro* anti schistosome activity of plants. Most authors focused on one or at most three plants and priority was given to *in vitro* tests. *In vivo* testing remained a challenge [54]. Others, on the other hand, have shown the effectiveness of natural substances by taking these two aspects into account [52,55].

For most authors *in vitro* activity was evaluated in the culture RPMI-1640 medium. This medium has been used either in combination with serum or with antibiotics such as Gentamicin, Streptomycin, Penicillin and many others as supplements [56]. All *In vitro* tests were incubated for 24 or 48 hours at 37°C with 5% of CO_2. The concentrations of the different extracts tested were between 62.25 µg/ml and 500 µg/ml in search of lethal concentrations of the extract. The lethal concentrations that we observed varied between 125 µg/ml to 500 µg/ml [57]. Those concentrations below 125 µg/ml had a reduced activity on the parasites because they let perceive the mobility of certain parasites with microscopy [57].

The *In vitro* test was the most common and all results were promising, as they all showed efficacy of crude plant extracts on at least one stage of the parasite and even on the intermediate host snail [52,54,58].

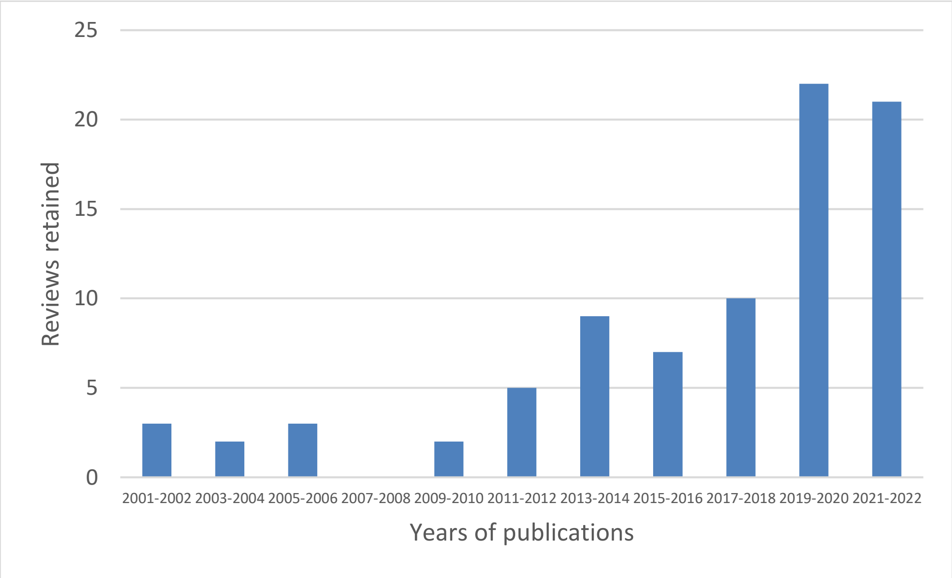

Fig. 1. Number of publications exploited and interval of year of appearance

The antischistosomal activity of a plant extracts may be linked to a chemical substance or to a combination of chemical groups which should be identified [59,60].

According to many authors, the lethal dose LC_{50} (the dose of the plant substance at which 50% of the parasites die) can vary according to the part of the plant used for the same incubation period: *Pterocarpus angolensis* DC; LC_{50} (T=1 hour): leaves 102 mg/mL; stem 51.3 mg/mL and bark 33.8 mg/mL [53]. Also, the effectiveness of the active substance may depend on the solvent used: *Calotropis procera* (at 25 mg/mL): the ethanolic extract caused the death of all adult forms of *S.mansoni* in ½ hour while the aqueous extract didn't become effective until 4 hours later [61,62] ; *Clerodendrum umbellatum:* LC_{50} of the aqueous extract= 805.21µg/mL against 343.10 µg/mL for the methanolic extract [28].

3.6 *In vivo* Study of the Antischistosomal Activity of Plants

As far as *In vivo* tests are concerned, some research conducted has shown some shortcomings in their effectiveness. Some natural compounds with high *in vitro* mortality, on the other hand, exhibited low mortality rates in mice [57]. This is the case of *Allicin* which has been tested *In vitro* and *In vivo* [52]. Others, on the other hand have given interesting results *In vitro* and *In vivo* [63].

Many authors have carried out *In vivo* tests by taking PZQ as control. In the majority of cases for the results obtained, this drug had the greatest parasiticidal activity, compared to the different crude extracts [64–70]. Furthermore, it could also be noted that there was no statistically significant difference between PZQ and other plant extracts in terms of efficacy on schistosomes [71]. Many studies have shown that PZQ, in combination with plant extracts gave very good results in the treatment of schistosomiasis [62,72]. Others, on the other hand, had as a control group infected and untreated mice in comparison with infected mice and treated with crude plant extracts to research the lethal activity of the extract [52].

Many authors recommend better exploring the *in vivo* activity of plant extracts that have shown conclusive results *in vivo* [54,73–76]. Others still advocate conducting studies on the biology of intermediate hosts and considering breaking the chain of transmission of schistosomiasis [77]. Also, it would be interesting to conduct more in-depth studies on plants that have shown their effectiveness on schistosomes using a variety of solvents at concentrations. In addition, the schistosomicidal activity of a plant or a bioactive substance is undoubtedly linked to a chemical substance or group that is important to identify, isolate and quantity ; which also makes it possible to better understand the mechanism of action of these plants or bioactive substance [78,79].

It should also be noted that some authors have carried out *In vitro / In vivo* tests on mice, with other drug groups such as antimalarial drugs [15]. Some molecules have shown higher mortality rates on adults than cercariae: Arthemeter at 300mg/kg/day for 2 days caused the death of 85.4-98.3% of *S. mansoni* adults and 70% cercariae. Others, on the other hand, were less effective on adult forms: Chlorambucil at 25 mg/kg for 5 days caused the death of 22.7% of adults against 75.8% of cercariae [37].

3.7 Phytochemical Screening

We noticed that the compounds of the natural substances were detected qualitatively. Among plants with potential schistosomicidal activity, their active ingredients are mostly unknown. The technic of spectrophotometry through gas chromatography for the detection of chemical compounds of crude extracts was used [51,71,80–82].

It should be noted that some chemical groups are more present than others in terms of percentage as we notice at the Fig. 2. We have alkaloids and terpens groups with almost equal proportion, followed by flavonoids and saponins groups with the same trends. The chemical compounds present in high proportion could be explained by the fact that some authors have sought them especially [51,71,80–82]. These include alkaloids, flavonoids, saponins, tannins, terponoids, steroids and quinones.

Indeed, plants are a huge source of chemical compound belonging to several chemical groups with a lot of medicinal properties such as anti-oxidant, anti-inflammatory, antimicrobial etc [83].

3.8 Cytotoxicity Tests

The search for bioactive substances in the plant environment must also take into account their harmful effects or their toxicity. The toxicity test is

Table 1. The different families of plants encountered in the literature

Botanic family		Botanic family		Botanic family	
Agavaceae	[21,47]	Cannabinaceae	[58]	Ochnaceae	[48]
Amaranthaceae	[21,22,30]	Ebenaceae	[10,27]	Olacaceae	[46]
Amaryllidaceae	[3, 36]	Euphorbiaceae	[30,47,74]	Papaveraceae	[54]
Anacardiaceae	[27,36]	Fabaceae	[9,48,60]	Sterculiaceae	[44]
Annonaceae	[30,47,48]	Liliaceae	[63]	Phyllanthaceae	[21]
Apiaceae	[17]	Asteroideae	[79]	Phytolaccaceae	[3]
Apocynaceae	[3,27,36]	Hypericaceae	[47]	Pinaceae	[21]
Asclepiadaceae	[36,46]	Bombacaceae	[44]	Piperaceae	[17]
Asparagaceae	[27,30,36]	Hypoxidaceae	[44]	Poaceae	[43,48]
Asphodelaceae	[27]	Lamiaceae	[18,30,43]	Polygalaceae	[27,30]
Asteraceae	[3,22,30]	Leguminosae	[44]	Punicaceae	[36]
Bignoniacea	[27,43]	Loganiaceae	[48]	Renonculaceae	[36]
Boraginaceae	[27,43]	Caesalpiniacaceae	[50]	Rhamnaceae	[18,22]
Balanitaceae	[30]	Myrsinaceae	[50]	Rosaceae	[3,13,44]
Burseraceae	[75]	Lythraceae	[3,21]	Rubiaceae	[43,47]
Capparaceae	[36, 43]	Malpighiaceae	[36]	Rutaceae	[10,22,71]
Caricaceae	[21]	Malvaceae	[43]	Sapindaceae	[57]
Celastraceae	[27,43,48]	Primulaceae	[50]	Chrysobalantaceae	[50]
Clusiaceae	[48, 56]	Meliaceae	[3,10,30]	Flacourtiaceae	[50]
Cochlospermaceae	[47]	Pedaliaceae	[44]	Nympheaceae	[50]
Combretaceae	[27,30,36]	Moraceae	[48]	Solanaceae	[53]
Cucubitaceae	[22,36,48]	Moringaceae	[43,68]	Verbenaceae	[21,43,4]
Ancistrocladaceae	[44]	Myrtaceae	[46,53,82]	Zingiberaceae	[3,67,78]
Dipterocarpaceae	[48]			Zygophyllaceae	[36,48]

Table 2. Directory of botanical families and species bioactive on schistosomes

Agavaceae family	***Asteraceae family***	***Ebenaceae family***
Agave americana	*Ageratum conyzoides*	*Euclea divinorum*
Agave lophantha	*Ageratum conyzoides L*	*Euclea natalensis*
Asclepias sinaica	*Ambrosia maritima*	*Euphorbiaceae family*
Asimina triloba	*Arteisia annua*	*Alchornea cordilfolia,*
Solanum nigrum	*Artemisia absinthium*	*Antidesma venosum*
Solanum nigrum (L)	*Artemisia afra*	*Euphorbia mauritanica*
Amaranthaceae family	*Baccharis dracunculifolia*	*Euphorbia peploides (A)*
Chenopodium album (L)	*Baccharis trimera*	*Euphorbia royleana*
Dysphania ambrosioides	*Berkheya speciosa*	*Euphorbia tirucalli (L)*
Amaryllidaceae family	*dracunculifolia DC*	*Jatropha curcas*
Allium cepa	*Echinops kebericho*	*Fabaceae family*
Allium cepa (L)	*Taraxacum officinale*	*Abrus precatorius*
Allium sativum	*Vernonia amygdalina*	*Abrus precatorius (L)*
Allium sativum (L)	*Vernonia colorata*	*Acacia nilotica*
Anacardiaceae family	*Vernonia shirensis*	*Acacia polyacantha*
Lannea barteri	*Bignoniaceae family*	*Albizia adianthifolia*
Lannea chimperi	*Kigelia aethiopum*	*Albizia antuneziana*
Mangifera indica	*Boraginaceae family*	*Albizia versicolor*
Orozoa pulcherrima	*Alkanna orientalis*	*Bauhinia reticulata*
Schinopsis brasiliensis	*Balanitaceae family*	*Bauhinia variegata L*
Scierocarya birrea	*Balanites aegyptiacca*	*Bobgunnia madagascarien*
Searsia longipes	*Burseraceae family*	*Cassia petersiana*
Annonaceae family	*Commiphora molmol*	*Cassia sieberiana*
Annona senegalensis	*Capparaceae family*	*Cratylia mollis*
Anonidium mannii	*Cleome droserifolia*	*Dichrostachys cinerea (L)*
Asimina triloba	*Caricaceae family*	*Emilia javanica*
Xylopia aethiopica	*Carica papaya (L)*	*Eminia poladenia*
Xylopia ochrantha	*Carica papya*	*Eriosema griseum*
Apiaceae family	*Celastraceae family*	*Erythrina abyssinica*
Apium graveolens (L)	*Maytenus senegalensis*	*Erythrina senegalensis*
Coriandrum sativum	*Clusiaceae family*	*Isoberlinia angolensis*
Foeniculum vulgare	*Garcinia huilensis*	*Piliostigma thonningii*
Apocynaceae family	*Cochlospermaceae family*	*Pterocarpus angolensis*

Agavaceae family	***Asteraceae family***	***Ebenaceae family***
Alstonia boonei	*Cochlospermum tinctorium*	*Pterodon pubescens*
Calotropis procera	*Combretaceae family*	*Rhynchosia insignis*
Cryptostegia grandiflora	*Anogeissus leiocarpus*	*Tetrapleura tetraptera*
Diplorynchus condlocarpoum	*Combretum angustifolium*	*Liliaceae family*
Landolphia kirkii	*Combretum glutinosum*	*Allium sativum L*
Nerium oleander	*Combretum mucronatum*	*Asteroideae family*
Nerium oleander (L)	*Combretum mucronatum*	*Artemisia afra*
		Artemisia annua
Picralima nitida	*Combretum sp*	*Hypericaceae family*
Rauwolfia vomitoria	*Terminalia mollis*	*Harungana madagascariensis*
Asclepiadaceae family	*Cucubitaceae family*	*Bombacaceae family*
Pergularia tomentosa	*Cucurbita pepo*	*Adansonia digitata*
Asparagaceae family	*Cucurbita pepo L*	*Hypoxidaceae family*
Asparagus stipularis (R)	*Cucurbitaceae family*	*Hypoxis hemerocallidae*
Furcraea selloa	*Momordica charantia*	*Lamiaceae family*
Furcraea selloa (L)	*Ancistrocladaceae family*	*Coleus kilimandscharica*
Ledebouria ovatifolia	*Ancistrocladus korupensis*	*Ocimum americanum*
Scilla natalensis	*Dipterocarpaceae family*	*Origanum majorana*
Asphodelaceae family	*Monotes katangensis*	*Plectranthus neochilus*
Aloe vera	*Monotes kerstingii*	*Plectranthus tenuiflorus*
	Cannabinaceae family	*Tetradenia riparia*
Lamiaceae family	*Nigella sativa*	
Coleus kilimandscharica	*Myrtaceae family*	*Rutaceae family*
Ocimum americanum	*Melaleuca armillaris*	*Cissus quadrangularis (L)*
Origanum majorana	*Melaleuca leucadendron*	*Citrus limon (L)*
Plectranthus neochilus	*Pimenta racemosa*	*Citrus reticulata*
Plectranthus tenuiflorus	*Syzygium aromaticum*	*Citrus sinensis (L)*
Tetradenia riparia	*Syzygium guineense*	*Pilocarpus microphyllus*
Leguminosae family	*Ochnaceae family*	*Zanthoxyllum leprierii*
Cassia senna	*Ochna schweinfurthiana*	*Zanthoxylum naranjillo*
Loganiaceae family	*Olacaceae family*	*Sapindaceae family*
Buddleia lindleyana	*Olax subscorpioidea*	*Dodonaea viscosa*
Strychnos inocua	*Ximenia americana*	*Paulina pinnata*
Strychnos spinosa	*Papaveraceae family*	*Chrysobalanaceae family*

Agavaceae family	***Asteraceae family***	***Ebenaceae family***
Strychnos stuhlmannii	*Fumaria officinalis*	*Licania tomentosa*
Caesalpiniaceae family	*Sterculiaceae family*	*Flacourtiaceae family*
Afzelia quanzensis	*Cola nitida*	*Flacourtia indica*
Myrsinaceae family	*Phyllanthaceae family*	*Nympheaceae family*
Maesa lanceolata	*Phyllanthus muellerianus*	*Nymphae micrantha*
Lythraceae family	*Phyllanthus niruri*	*Solanaceae family*
Punica granatum	*Phyllantus amarus*	*Brugmansia munamensis*
Malpighiaceae family	*Phyllantaceae family*	*Solanum elaeagnifolium*
Flabellaria paniculata	*Hymenocardia acida*	*Solanum incanum (L)*
Malvaceae	*Phytolaccaceae family*	*Solanum lypocarpum*
Brachychiton rupestris	*Phytolacca dodecandra*	*Solanum nigrum*
Sida pilosa	*Pinaceae family*	*Solanum solamargine (F)*
Primulaceae family	*Pinus canariensis*	*Solanum tuberosum*
Anagallis arvensis L	*Piperaceae family*	*Verbenaceae family*
Meliaceae family	*Piper nigrum*	*Cleome droserifolia*
Azadirachta indica	*Piper tuberculatum*	*Clerodendrum umbellatum*
Khaya grandifoliola	*Poaceae family*	*Stachytarpheta cayennensis*
Khaya nyasica	*Cymbopogon densiflorus*	*Zingiberaceae family*
Khaya senegalensis,	*Imperata cylindrica (L)*	*Aframomum alboviolaceum*
Swietenia mahogani	*Polygalaceae family*	*Curcuma longa*
Trichila monadelpha	*Securidaca longipedunculata*	*Curcuma longa (L)*
Pedaliaceae	*Eriogonum umbellatum*	*Zingiber officinale*
Harpagophytum procumbens	*Punicaceae family*	*Zygophyllaceae family*
Moraceae family	*Prunica granatum*	*Balanites aegyptiaca*
Chlorophora excelsa	*Renonculaceae family*	*Balanites aegyptiaca (L)*
Ficus carica	*Nigella sativa*	*Fagonia mollis Delile*
Moringaceae family	*Pulsatilla chinensis*	*Rubiaceae family*
Moringa oleifera	*Rhamnaceae family*	*Craterispermum caudatum*
Myrtaceae family	*Ziziphus spina-christi*	*Crossopteryx febrifuga*
Callistemon umbellatum	*Ziziphus spina-christi (L)*	*Gardenia jovis-tonantis*
Callistemon rigidus	*Zizyphus mauritiana*	*Mitracarpus frigidus*
Callistemon speciosus		*Mitragyna stipulosa*
Cadaba glandulosa	*Rosaceae family*	*Morinda lucida*
Cajanus cajan (L)	*Malus domestica*	*Nauclea latifolia*

Agavaceae family	***Asteraceae family***	***Ebenaceae family***
Callistemon citrinius		*Pavetta owariensis*
Callistemon viminalis		*Permacoce verticillata*
Callistemon viridiflorus (L)		
Eucalyptus citriodora		
Eucalyptus rostrata		
Eucalyptus species		
Eugenia edulis		
Melaleuca styphelioides		

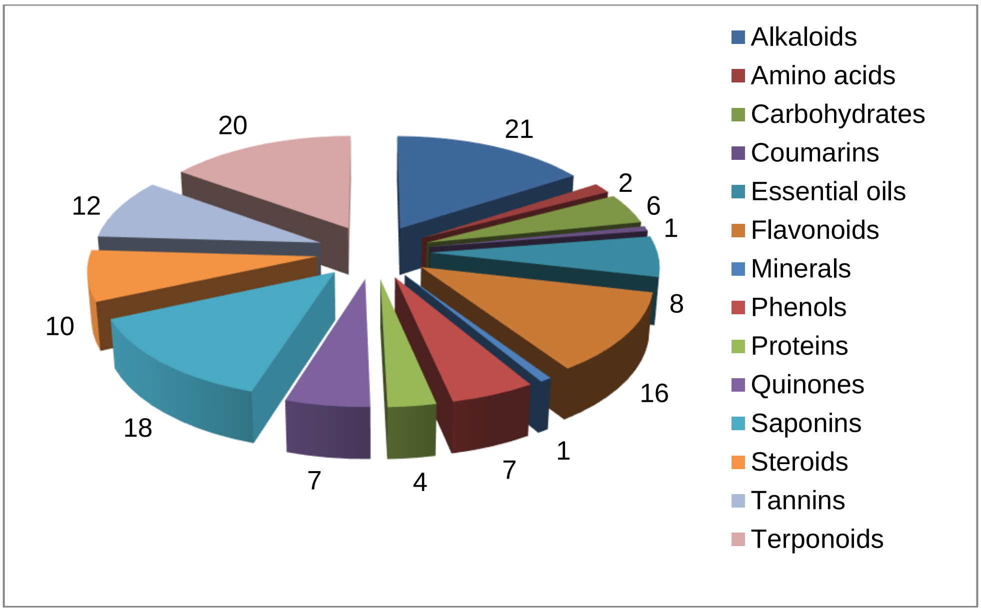

Fig. 2. Proportion in percentages of chemical compounds

also an essential step in the process of researching new drugs in general. We can note that many authors have demonstrated the non-toxicity of plant extracts on “Vero cells” through different types of active extracts at varying concentrations. There are similarities between toxicity test and *in vivo* test. The toxicity test is also carried out in RPMI-1640 medium, supplemented with fetal bovine serum and/or antibiotics. The extracts to be tested are brought into contact with the “Vero cells”. Incubation is also done with 5% CO_2 at 37°C for 24 to 48 hours [55]. Several studies have shown promising results as the toxicity of the herbal extracts used was extremely low or non- existent [84]. Others, however, have shown their effectiveness, but their toxicity remains to be investigated.

4. CONCLUSION

According to many studies, plants could be an alternative in the treatment of schistosomiasis. Several plants are already used by traditional healers, but very few have been analyzed in the laboratory.

Many schistosomicidal plants have been cited in the literature. However, we can note that among the multitude of schistosomicide plants, more appropriate tests are required through clinical trials in order to determine the most effective.

It is also necessary to study the phytochemical profiles in a qualitative and quantitative approach of these natural compounds for the implementation of new molecules against schistosomiasis through clinical research trials.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Bagayan M, Zongo D, Oueda A, Sorgho H, Savadogo B, Drabo F et al. Prevalence of schistosomiasis and soil-transmitted helminth infections among schoolchildren in Burkina Faso. 2016;(July). DOI: 10.1684/mst.2016.0570
2. Angora Etienne K, Menan H, Rey Olivier, Karim Tuo, Andre O Tour, Jean T. Coulibaly. Prevalence and Risk Factors for Schistosomiasis among Schoolchildren in two Settings of Côte d’Ivoire. Published online; 2019.
3. Basha H, Mamo H. The Activity of Plant Crude Extracts against Schistosoma Mansoni; 2021
4. Ly B, Yaro AS, Sodio B. Persistence of urinary schistosomiasis in endemic areas subjected to repeated mass treatments in Mali. 2019;13(February):369-381.

5. Amara R, Saadawi S. Praziquantel as The Gold Standard of Schistosomiasis Control Drug Delivery and Nanotechnological Strategies; 2022(April).
6. Professor Pierre Aubry. Doctor Bernard-Alex Gaüzère. Schistosomiasis or bilharzia. Published online. 2021:1-10.
7. World Health Organization. Weekly epidemiological record. Weekly Epidemiological Report. 2021;(48):585-596.
8. High Authority of Health. Update of medical biology procedures relating to the diagnosis of schistosomiasis (bilharzia). Published online; 2017.
9. Nicolas BA, Anthropologies S, Isad DD. Antibilharzia Control in Rural Areas in Ivory Coast: Between Modern, Traditional Treatment and Medical Syncretism. Published online. 2019:181-190.
10. Abaza S. Treatment of Schistosomiasis: From Praziquantel to Development of New Drug Targets Treatment of Schistosomiasis: From Praziquantel to Development of New Drug Targets; 2015(December).
11. Ferrari MLA, Coelho PMZ, Antunes CMF, Tavares CAP, Cunha AS. Efficacy of oxamniquine and praziquantel in the treatment of Schistosoma mansoni infection: A controlled trial. 2003;81(02):190-196.
12. Egie E Enabulele, Roy N Platt, Ehizogie Adeyemi, Esther Agbosua, 1016/j.actatropica. Urogenital schistosomiasis in Nigeria post receipt of the largest single praziquantel donation in Africa. 2021;105916.
13. Ndegwa FK, Kondam C, Aboagye SY. Traditional Kenyan herbal medicine: Exploring natural products' therapeutics against schistosomiasis; 2022(March). DOI: 10.1017/S0022149X22000074
14. Corrêa SDAP, Oliveira RN De, Mendes TMF, Rodrigues K. In vitro and in vivo evaluation of six artemisinin derivatives against Schistosoma mansoni. Published online; 2019.
15. Rodriguez-morales EAJ. Current topics in tropical medicine; 2012.
16. Rosimeire Nunes De O Oliveira, Sierpe Jeraldo Vernonica De Lourdes, Tarsila Fernaz Frezza, Claudia Melo. Epidemiology, Chemotherapy and New Therapeutics; 2014.
17. El-nour Mohamed F Abdoul. Antischistosomal Activity of Zingiber officinale, Piper nigrum, and Coriandrum sativum Aqueous Plant Extracts on Hamster Infected with Schistosoma mansoni; 2021.
18. Abdal Y, Fadladdin J. Antischistosomal Activity of Origanum majorana, Ziziphus spina-christi, and Salvia fruticosa Plant Extracts on Hamster Infected with Schistosoma haematobium; 2021.
19. Ibezim A, Olubiyi OO, Mbah C, Nwodo NJ. Current Computer-Aided Drug Design.; 2017(January). DOI:10.2174/157340991366617011911485 9
20. In DEM, Bassin LE, Fleuve DU, Abdellahi M, Ndir O, Niang S. Assessment of the prevalence of bilharzia among children aged 5 to 14 years after several years of mass treatment in the Senegal River basin Assessment of schistosomiasis prevalence among children 5 to 14 years old after several years of m. Published online; 2016. DOI: 10.3917/spub.164.0535
21. Balahbib A, Omari N El, Ghchime R, Hakkour M, Bouyahya A. Anti-Schistosomal Activity of Medicinal Plants: 2021;10(3):2352-2360.
22. Ali SA. Natural Products as Therapeutic Agents for Schistosomiasis; 2011. DOI: 10.3923/rjmp.2011.1.20
23. Atalabi TE, Lawal U, Ipinlaye SJ. Prevalence and intensity of genito-urinary schistosomiasis and associated risk factors among junior high school students in two local government areas around Zobe Dam in Katsina State, Nigeria. Parasite Vectors. Published online. 2016:1-12. DOI: 10.1186/s13071-016-1672-5
24. Nyasa L, Mazigo H.D, Uisso C, Kazyoba P, Nshala A. Prevalence, Infection intensity and geographical distribution of schistosomiasis among pre-school and school aged children in surrounding villages. SciRep. 2021;(0123456789): 1-11. DOI: 10.1038/s41598-020-80317-x
25. Joof E, Sanyang AM, Camara Y, Sey AP. Prevalence and risk factors of schistosomiasis among primary school children in four selected regions of The Gambia. Published online. 2021:1-15. DOI: 10.1371/journal.pntd.0009380
26. Natalie G Exum, Simon PS Kibira, Ssenyonga Ronald, Julien Nobili, Alexandra K Shannon, John C, et al. The prevalence of schistosomiasis in Uganda:

A nationally representative population estimate to inform control programs and water and sanitation interventions. 2019;(Ci):1-21.

27. Sparg SG, Staden JVan, Ja AK, Efficiency of traditionally used South African plants against schistosomiasis. 2001;73:209-214.
28. Kenfack Mérimé Christian, Jatsa Hermine Boukeng, Feussom Nestor Gipwe, Emilienne Tienga Nkondo, Ulrich Membe Femoe, Christelle Dongmo Tsague et al. In vitro Antischistosomal Activity of Clerodendrum umbellatum Poir (Labiateae) Leaves Aqueous Extract and Derived Fractions against Schistosoma mansoni Adult Worms. 2020;22(December):40-49.
DOI: 10.9734/JAMPS/2020/v22i1030199
29. Rugel Anastasia R, Guzman Meghan A, Taylor Alexander B, Frédérick D Chévalier, Reid S Tarpley, Stanton F McHardy et al. Drugs and Drug Resistance Why does oxamniquine kill Schistosoma mansoni and not S. haematobium and S. japonicum? IJP Drugs Drug Resist. 2020;13(April):8-15.
DOI: 10.1016/j.ijpddr.2020.04.001
30. Rousseau JJ, Dickens C. Indigenous plants and schistosomiasis control in south africa : Molluscicidal activity of some zulu medicinal plants. Published online; 2004.
31. World Health Organization. Field Use of Molluscicides in Schistosomiasis Control Programs; 2020.
32. Guang Zang and Weizhong Yang. Prevention and Control of Infectious Diseases in BRI Countries; 2021.
33. World Health Organization. Fighting Neglected Tropical Diseases to Achieve the Sustainable Development Goals; 2021.
34. Alan Fenwick, David Rollinson and Vaughan Southgate, Schistosomiasis Implementation of Human schistosomiasis control: Challenges and prospects; 2006.
35. World Health Organization (WHO). WHO Traditional Medicine Strategy 2014-2023. World Heal Organ. Published online. 2013:1-76.
DOI: 2013
36. Yousif Fouad, Wassel Gamila, Boulos Loutty, and Therese Labib, Contribution to in vitro screening of Egyptian plants for schistosomicidal activity Contribution to *in vitro* screening of Egyptian plants for schistosomicidal activity. 2012;0209.
DOI: 10.3109/13880209.2011.625952
37. Bergquist R, Utzinger J, and Keiser J. Controlling schistosomiasis with praziquantel : How much longer without a viable alternative? Published online. 2017:1-10.
DOI: 10.1186/s40249-017-0286-2
38. Evelyn Asante Kwatia, Lord Gyimah, Abraham, Yeboah Mensah, and Arnold Forkuo Donkor. The Ghanaian Flora as a Potential Source of Anthelmintic and Antischistosomal Agents; 2021.
39. Nelwan Martin L. Prevention of schistosomiasis; 2021.
40. David Rollinsona, Stefanie Knoppb, Sarah Levitza, Russell Stothardd J, Louis-Albert Tchuem Tchuentée, Amadou Garbab et al. Time to set the agenda for schistosomiasis elimination.2013.
41. Zanolla D, Perissutti B, Passerini N et al. A new soluble and bioactive polymorph of praziquantel. 2018;(January):1-10.
42. Nicolas J Pierre. Medicinal plants of northern Madagascar Ethnobotanical antakarana and scientific informations; 2012.
43. Ledoux A, Nicolas J pierre, Gallé J baptiste, Gro S. Some plants used in the south west of Madagascar; 2017.
44. Hostettmann K, Marston A, Ndjoko K, Wolfender J luc. The Potential of African Plants as a Source of Drugs. Published Online. 2001:973-1010.
45. Emmanuella Bema Twumasi, Pearl Ihuoma Akazue, Kwaku Kyeremeh, Theresa Manful Gwira, Jennifer Keiser, Fidelis Cho-Ngwa et al. Antischistosomal , antionchocercal and antitrypanosomal potentials of some Ghanaian traditional medicines and their constituents. Published online 2020:1-21.
DOI: 10.1371/journal.pntd.0008919
46. Diego Ricardo, Galhardo Duarte, Mahomoodally Mohamed Faouzi, Lobine Devina, Suroowan Shano, and Rengasamy Kana R R. Botanical Products in the Treatment and Control of Schistosomiasis: Recent Studies and Distribution of Active Plant Resources According to Affected Regions; 2020.
47. West African Health Organization. West African Pharmacopeia; 2020.
48. Muya Kalunga, Kalonji Monique, Kahumba Byanga, Ethnobotanical overview of some plants used against urogenital schistosomiasis in Lubumbashi and surroundings. 2014;(August).
DOI: 10.1007/s10298-014-0877-z

49. Rolland Kipré Gueyraud, Offoumou Rostand M'Bai, Dieudonné Kigbafori Silué, Allico Djaman Joseph, Guédé Noel Zirihi. Technique for flavonoid extraction by solvents. 2019;d:141-142.
50. Esham R El-Seedi, Shaden AM Khalifa, Azza H Mohamed, Nermeen Yorsi, Chao Zhao, Nabil El-Wakeil, et al. Plant extracts and compounds for combating schistosomiasis; 2022.
51. Bhatia Manisha and Siddiqui Nasir Ali. Abrus Precatorius (L.): An Evaluation of Traditional Herb; 2014.
52. Fakahany Amany Fakahany El, Abdelmaabood Amina I, Abd Atef Hamid, Amira T Morsi, Abououf Eman A. *In Vitro* and in Vivo Activity of Allicin against Schistosoma Mansoni. Published online; 2020.
53. Sadek Gehan S, Harba Nancy M, Faheem Mona Faheem, *In vitro* assessment of Schistosoma mansoni cercaricidal activities of Solanum nigrum and Callistemon citrinius leaves extracts and cercarial genetic changes by RAPD-PCR. Published online; 2019.
DOI: 10.21608/puj.2019.7468.1029
54. Elizondo-luévano Joel H, Castro-ríos Rocio, Vicente Belen, Pedro Fernadez Soto, JulioLopez Aban, Antonio Muro et al. *In Vitro* Antischistosomal Activity of the Argemone Mexicana Methanolic Extract and Its Main Component Berberine. 2021;16(1):91-100.
55. Nunes Rosimeire Oliveira, Lúcia Vera Garcia Rehder, Adriana Silva Santos Oliveira, Veronica de Lourde Sierpe Jeraldo, Aricio Xavier Linhares, and Silmara Marque Allgretti, Anthelmintic activity in vitro and in vivo of Baccharis trimera (Less) DC against immature and adult worms of Schistosoma mansoni. Exp Parasitol. 2014;139:63-72.
DOI: 10.1016/j.exppara.2014.02.010
56. Aline Pereira Castro, Ana Carolina Alves de Mattos, Neusa Araújo Pereira, Naira Ferreira Anchieta, Matheus Siqueira Silva, Danielle Ferreira Dias et al. Potent Schistosomicidal Constituents from Garcinia brasiliensis. Published online; 2015.
DOI: 10.1055/s-0035-1545927
57. Bawazir Salwa S, Ibtihal H Badawi, and Ehssan A. Hassan, Effects of Dodonaea viscosa on experimental schistosomiasis in mice extract. 2020;1(1):11-19.
58. Mohamed Azza M, Metwally NM, Mahmoud SS. Sativa seeds against Schistosoma mansoni different stages. 2005;100(April):205-211.
59. Marwa I Ezzat, Mona M Okba, Sherif H Ahmed, Hossny A El-Banna, Abdelbary Prince, Shanaz O Mohamed et al. In-depth hepatoprotective mechanistic study of Phyllanthus niruri: In vitro and in vivo studies and its chemical characterization. Published online. 2020:1-23.
60. Klev Gaitan Sikam, Gervais Mouté Appl, Ntabo Virginia Klen, Wansi Jean Duplex, Chemistry and pharmacological aspects of Aridanin, a lead compound from Tetrapleura tetraptera (Fabaceae). 2022;(September).
DOI: 10.53365/nrfhh/152273
61. Azzam M Ahmed, Aboueldahab MM, Haidar Mohammad, Taha Hoda. *In vitro* effects of the stem extracts of the plant Calotropis procera on Schistosoma mansoni adult worms. 2016;(August 2018).
62. Ahmed H Ngm, Marwa Abou Eldahab, Lotfia M Khalil, Rhama BM Juroud, Ahmad M Azzam, Hoda H Taha et al. Ameliorative effect of calotropis procera and/or praziquantel on schistosoma mansoni infected mice. 2019;49(3):529-538.
63. Behnaz Asianipour, Mehmet Caian, Determination and Comparison of In Vitro Radical Scavenging Activity of Both Garlic Oil and Aqueous Garlic Extracts and Their In Vivo Antioxidant Effect on Schistosomiasis Disease in Mice. 2018;6(7):820-827.
64. Ibrahim Aly, Hanan Taher, Faten EL-Feky. Antischistosomal and antioxidant protective role of Carica papaya fruit extracts against Schistosoma mansoni. 2020;16(1):107-117.
65. El-shabasy Shrouk MAEl-morsy, Sayed AM El- Tantawy, Eman A El Shabasy. Antischistosomal effects of Ficus carica leaves extract and/or PZQ on Schistosoma mansoni infected mice. J Parasite Dis. Published online; 2021.
DOI: 10.1007/s12639-021-01417-7
66. Rizk M, Ibrahim N, El-Rigal N. Comparative in vivo antioxidant levels in Schistosoma mansoni infected mice treated with Praziquantel or the essential oil of Melaleuca armillaris leaves; 2012.
67. Hussein Atef, Rashed Samira, Hayawan Ibrahim El, El-sayed Rabab, and Ali Hemat. Evaluation of the anti-schistosomal effects of Turmeric (Curcuma longa)

versus praziquantel in Schistosoma mansoni infected mice. 2017;12(4):587-596.

68. Ilona Jean A Almanzor, Dianabelle E Clemente, Raffy Jay C Fornillos, Maricel A Gomez and Facundo Rey M, Ladiao. In Vivo Trials of Moringa oleifera Lam. Extracts as Antischistosomal Treatment on Schistosoma japonicum Infected Mice. 2014;56:49-56.
69. Jatsa BH, Ngo Sock TE, Tchuem Tchuente AL, and Kamtchouing P. Evaluation of the in vivo activity of different concentrations of clerodendrum umbellatum powder against schistosoma mansoni infection in mice. 2009; 6:216-221.
70. Domo GA and Kela SL. The efficacy of *Maytenus senegalensis (L*) extracts on experimentally infected rats with Schistosoma mansoni. 2009;5(4): 157-163.
71. Muema Jackson M, Obonyo Meschack A, Njeru Sospeter N, and Mwatha Joseph K. Mwatha. Antischistosomal Effects of Selected Methanolic Plant Extracts in Swiss Albino Mice Infected with Schistosoma mansoni. 2015;9(1):1-11. DOI: 10.9734/EJMP/2015/16953
72. Nicolaus O Mbugi, Geoffrey Maina, Musa Chacha. Schistosomacidal Activity of Lannea Schimperi and Searsia Longipes against Chronicles of Pharmaceutical Science Schistosomacidal Activity of Lannea Schimperi and Searsia Longipes against Cercariae, Schistosomula and Adult Stage of Schistosoma Mansoni; 2019;(June).
73. Abou M Marwa El Dahab, Shahat Sondos M, Mahmoud Soheir SM, and Mahana Noha A. Experimental Parasitology *In vitro* effect of curcumin on Schistosoma species viability, integument ultrastructure and egg hatchability. Exp Parasitol. 2019;199(January):1-8. DOI: 10.1016/j.exppara.2019.02.010
74. Rayan Rubens da Silva Alves, João Gustavo Mendes Rodrigues, Andrea Teles-Reis, Ranielly Araújo Nogueira, Irlla Correia Lima Licá, Maria Gabriela Sampaio Lira et al. Antiparasitic effects of ethanolic extracts of Piper arboreum and Jatropha gossypiifolia leaves or cercariae and adult worms of Schistosoma mansoni; 2020. DOI: 10.1017/S003118202000181X2020
75. Zaki Sheir, Amira A Nasr, Ahmed Massoud, Osama Salama, Gamal A Badra, Hassan El-Shennawy et al. A safe, effective, herbal antischistosomal therapy derived from Myrrh; 2001.
76. Bagayan M, Zongo D, Savadogo B, Oueda A, Sorgho H, Kabre GB et al. Prevalence of urinary schistosomiasis in a school environment in a peri-urban neighborhood of the city of Ouagadougou; 2014.
77. Narin Preyavichyapugdee, Manao Sangfuang, Saowa Park Chaiyapum, Suwatcharaporn Sriburin, Yupa Pootaeng-on, Phiraphol Chusongsang et al. Schistosomicidal activity of the crude extract of Artocarpus lakoocha Published online. 2006:1-15.
78. Ali Hussein Abu Almaaty, Hadeer Abd El-Hak Rashed, Maha Farid Mohammed Soliman, Eman Fayad, Fayez Althobaiti, and Nahla Soliman El-Shenawy. Parasitological and Biochemical Efficacy of the Active Ingredients of Allium sativum and Curcuma longa in Schistosoma mansoni Infected Mice. Published online; 2021.
79. Jerome Munyangia, Lucile Cornet-Vernetb , Michel Idumboc, Chen Lud, Peter Lutgen , Christian Platform et al. Effect of Artemisia annua and Artemisia afra tea infusions on schistosomiasis in a large clinical trial. Phytomedicine. 2018;51(October):233-240. DOI: 10.1016/j.phymed.2018.10.014
80. Loyana Silva Godinho, Lara Soares Alexo de Carvalho, Clarissa Fields Barbosa de Castro, Mirna Meana Dias, Priscilla Faria Pinto, Anthony Eduardo Miller Crotti et al. Anthelmintic Activity of Crude Extract and Essential Oil of Tanacetum vulgare (Asteraceae) against Adult Worms of Schistosoma Mansoni; 2014
81. Tianshan Wang, Xiaopeng Wu, Yanping Liu, Youping Luo, Xiang Li, Yujie Zhou et al. Chemical constituents from ethanol extract of Polyalthia rumphii branches and their cytotoxicity evaluation. Rev Bras Pharmacogn. 2018;28(2):235-238. DOI: 10.1016/j.bjp.2018.03.004
82. Mariana Araújo Vieira do Carmo, Marina Fidelis, Caroline Andolfato Sanchez, Aline Pereira Castro, Ihosvany Camps, Fabio Antonio Colombo et al. Camu-camu (Myrciaria dubia) seeds as a novel source of bioactive compounds with promising antimalarial and antischistosomicidal properties. Food Res Int. 2020; 136:109334. DOI: 10.1016/food.2020.109334

83. Ana C Mengarda, Polyana S Mendonca, Christiane S Morais, Ramon M Cogo, Susana F Mazloum, Maria C Salvadori et al. Antiparasitic activity of piplartine (piperlongumine) in a mouse model of schistosomiasis, 2020:105350. DOI: 10.1016/j.actatropic.2020.105350
84. Hermine Boukeng Jatsa, Nestor Gipwe Feussom, Emilienne Tienga Nkondo, Merime Christian Kenfack, Nadege Distele Simo, Joseph Bertin Kadji Fassi, et al. Efficacy of methanolic extract of Ozoroa pulcherrima schweinf against schistosoma mansoni- induced liver injury in mice. Published online. 2018:4-11. DOI: 10.1016/j.jtcme.2017

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/113693