



Activity of Iranian Medicinal Herbs against Human Intestinal Parasites (HIP): A Systematic Review

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ABSTRACT

Background and objectives: Intestinal parasitic infections are a major public health problem worldwide, especially in developing countries. It is estimated that around 3.5 billion people are infected with intestinal parasites. Human intestinal parasites (HIP) are clinically important due to broad epidemiological distribution, reinfection and drug resistance. In the last decades, bioactive compounds from herbs were used against a wide variety of microorganisms including parasites. We aimed to perform a systematic review on studies on the effects of medicinal herbs on HIPs in Iran.

Methods: Relevant scientific publications until April, 2015 were extracted from five English databases (PubMed, Google Scholar, Ebsco, Science Direct and Scopus) and four Persian databases (Magiran, Irandoc, IranMedex and the Scientific Information Database).

Results: A total of 18 papers and two dissertations met the inclusion criteria. Overall, 22 different plant extracts were used against *Giardia lamblia*, *Entamoeba histolytica*, *Cryptosporidium* and *Hymenolepis nana*. Based on the results, the extracts could exert time- and dose-dependent inhibitory effects against the tested HIPs. Five plants types including *Allium*, *Chenopodium botrys*, *Carum copticum*, *F. asafoetida* and *Artemisia annua* were able to completely inhibit the tested parasites, while *Thymus vulgaris* and *A. paradoxum* showed the lowest inhibitory effect (7%).

Conclusions: Given the findings, it is recommended to conduct in vivo studies on medicinal herbs with favorable in vitro effects against HIPs.

Keywords: Intestinal Parasites, Herbal Medicines, Plant Extracts, In vitro, In vivo

INTRODUCTION

Intestinal helminths and protozoan infections are widely distributed around the world. Human intestinal parasites (HIPs) remain a major public health challenge, affecting millions of people, mainly in tropical and subtropical countries (1). Infections caused by HIPs are highly endemic in populations with poor hygiene and low socioeconomic status, favoring larval skin penetration and oral-fecal transmission (2). Main symptoms and complications of HIP infections include diarrhea, dysentery, hematuria, vomiting, loss of appetite, abdominal distension, mental disorders and allergies (3). Moreover, chronic infections caused by parasites such as *Ascaris lumbricoides* and hookworms can lead to malnutrition and anemia in high risk individuals, particularly children (2). Despite the remarkable scientific advances in health and medicine, parasitic infections are still one of the most common diseases worldwide. Intestinal protozoa are transmitted by the fecal-oral route (water contaminated with feces, soiled hands or ingestion of contaminated food). The most important intestinal protozoan infections are giardiasis (caused by *G. lamblia*), amoebiasis (caused by *Entamoeba histolytica*), cyclosporiasis (caused by *Cyclospora cayetanensis*), isosporiasis (caused by *Isospora belli*) and cryptosporidiosis (caused by *Cryptosporidium sp.*). Prevention and control of these infections have been an important aspect of national health planning (5). Based on estimations, more than 3.5 billion people worldwide are infected with HIPs, of which 450 million are clinically symptomatic and the majority being children (6).

Despite the efforts made on prevention and control of HIPs, the prevalence is still considerable owing to drug resistance, reinfection and broad epidemiological distribution (8). Therefore, novel anti-parasitic drugs are urgently required to treat and control parasitic diseases. Medicinal herbs have recently attracted a lot of attention as suitable alternatives for chemical medicine due to several advantages including fewer side effects, high availability, low cost, and better biocompatibility (9). The history of herbal medicine is as old as the human civilization.

Herbal remedy is still the main preference of 75-80% of people in developing countries (10). In this paper, we conduct a systematic review of previous publications on the activity of medicinal herbs against HIPs in Iran.

MATERIALS AND METHODS

To gather data, a precise and comprehensive search was performed on all scientific publications (full texts and abstracts) and Iranian parasitology theses available from February to April 2015. The search was performed using five English databases (PubMed, Google Scholar, Ebsco, Science Direct and Scopus) and four Persian databases (Magiran, Irandoc, IranMedex and Scientific Information Database). The reference lists of obtained articles were also reviewed for additional relevant studies. The search terms used alone or combined were: "Intestinal parasite", "Plant", "Medicinal plant", "Herbal extract", "Herb", "Traditional", "Protozoa", "Helminth", "*Entamoeba histolytica*", "*Giardia lamblia*", "*Cryptosporidium*", "Natural or Herbal medicine". The synonyms of herbal medicine including "Herbal preparation", "Herbal medication", "Herbal product", "Herbal remedy", "Medicinal herb", and "Phytopharmaceutical" were also searched. Other relevant diseases and topics such as HIP were also reviewed and included if the appropriate outcomes were shown. The language of database search was limited to English and Persian.

All identified studies were independently evaluated for eligibility and inclusion by two different reviewers. Selected papers were studied carefully and repetitive papers were excluded. The following details were extracted from the included publications: year of publication, first author, target parasite, scientific name of the plants, part of the plants used for extraction, type of extract, concentration, exposure time, animal model and outcomes.

RESULTS

A total of 18 papers and two dissertations were retrieved from the databases. Figure 1 shows the study design process. According to the obtained publications, 22 types of plants were used against four intestinal parasites including *G. lamblia*, *Cryptosporidium*, *Entamoeba histolytica* and *Hymenolepis nana*.

Allium, *Chenopodium botrys* and *Ferula asafoetida* were found as the most frequently used plants. Five plants including *Allium*, *Chenopodium botrys*, *Carum copticum*, *F. asafoetida* and *Artemisia annua* were able to completely inhibit the examined parasites, while *Thymus vulgaris* and *A. paradoxum* exhibited low inhibitory properties (7%). In addition, aqueous and hydroalcoholic extracts were the most commonly used type of extract.

The only medicinal herb that was evaluated both in vitro and in vivo was *A. paradoxum*. All in vivo studies had used Balb/c mice as the animal model. Tables 1 and 2 present characteristics of the herbal extracts and parasites used in the retrieved publications. The studies concluded that *Allium*, *Ch. botrys*, *C. copticum*, *F. asafoetida* and *A. annua* are promising source of anti-parasitic agents that could be potentially used for development of novel drugs against HIPs.

Figure 1. Flowchart describing the study design process

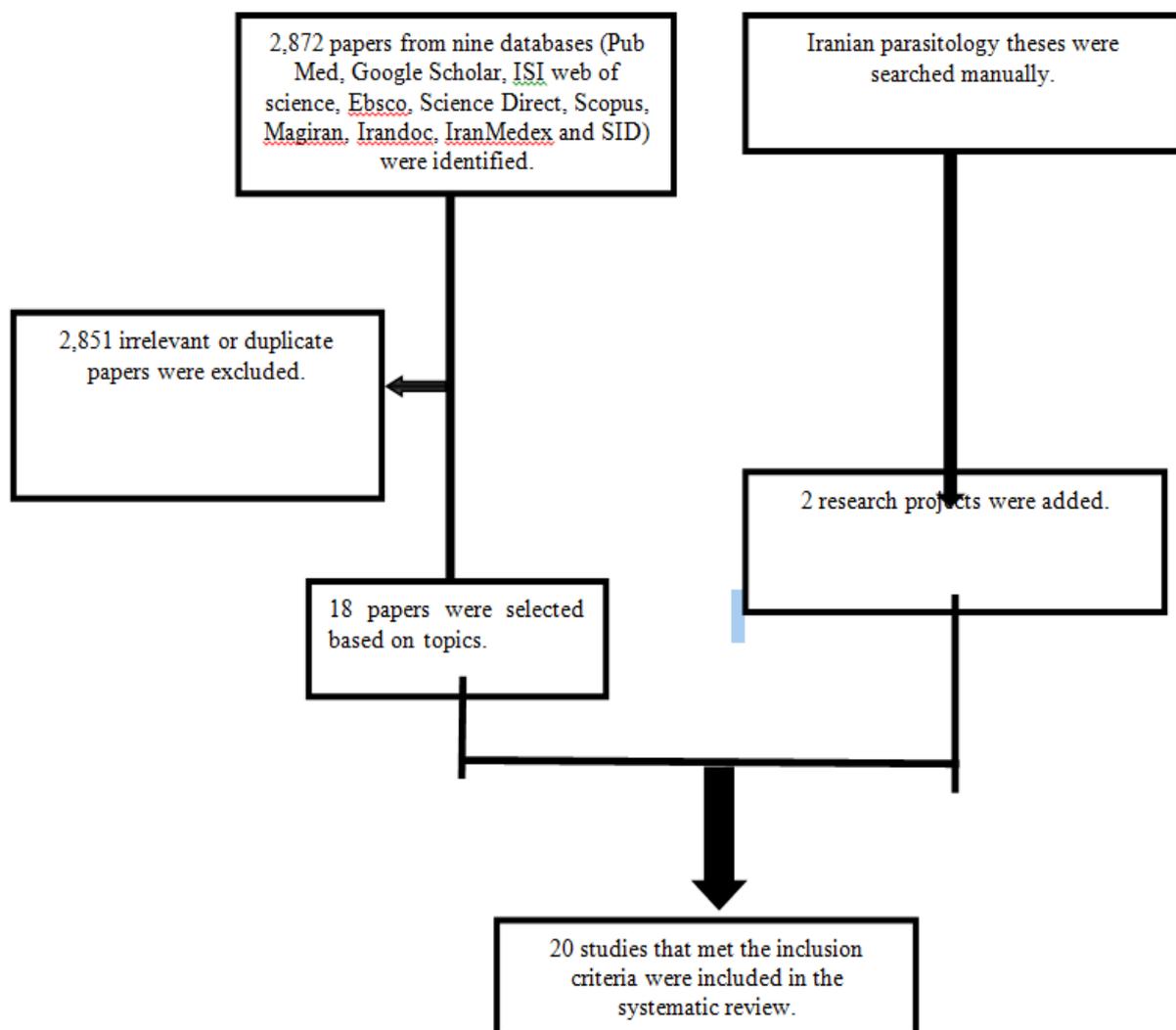


Table 1. Details of studies on the in vitro activity of

No.	Parasite	Plant	Type of parasite	Extract	Part used	Concentration	Exposure time	Re:	Reference
1	<i>Hymenolepis nana</i>	<i>A. sativum</i>	Cyst	—	Garlic tablets	—	—	71.1% effective	[11]
	<i>G. lamblia</i>	<i>A. sativum</i>	Cyst	—	Garlic tablets	—	—	34.6% effective	
2	<i>G. lamblia</i>	<i>Eucalyptus globulus</i>	Cyst	—	—	—	—	IC50 = 0.022 mg/ml	[12]
	<i>E. histolytica</i>	<i>E. globulus</i>	—	—	—	—	—	IC50 = 3.1 mg/ml	
3	<i>G. lamblia</i>	<i>Artemisia annua</i> & <i>Thymus vulgaris</i>	Cyst	Hydroalcoholic	Leaf	1, 10, 50 and 100 mg/ml	30 and 60 min	Highest inhibitory effect at 100 mg/ml for 60 min	[13]
4	<i>G. lamblia</i>	<i>Allium ascalonicum</i> 4° C	Cyst	—	Bulb	—	30 min, 1, 2 and 3 h	The mean giardiacidal activity at 4°C after 3h was 28.46%	[14]
		<i>A. ascalonicum</i> 24° C	—	Bulb	—	30 min, 1, 2 and 3 h	The mean giardiacidal activity at 24°C after 3h was 33.86%		
		<i>A. sativum</i> , 4° C	—	Bulb	—	30 min, 1, 2 and 3 h	The mean giardiacidal activity at 4°C after 3h was 36%		
		<i>A. sativum</i> , 24° C	—	Bulb	—	30 min, 1, 2 and 3 h	The mean giardiacidal activity at 24°C after 3h was 43%		
		<i>A. cepa</i> 4° C	—	Bulb	—	30 min, 1, 2 and 3h	The mean giardiacidal activity at 4°C after 3h was 33.26%		
		<i>A. cepa</i> 24° C	—	Bulb	—	30 min, 1, 2 and 3 h	The mean giardiacidal activity at 24°C after 3h was 41.13%		
5	Amoeba cyst	<i>Acanthophyllum squarrosum</i>	Cyst	Aqueous	Leaf	1, 5, 10, 15 and 20 %	0 and 15 min	IC50 =7.4 mg /ml	[15]
6	<i>G. lamblia</i>	<i>A. sativum</i>	Cyst	Chloroformic	Bulb	4 and 8 mg/ml	1-19h	Complete elimination of <i>Giardia</i> cyst at 4mg/ml after 13h and at 8 mg/ml after 8h	[16]
7	<i>G. lamblia</i>	Lemon juice 4°C	Cyst	Aqueous	—	—	30 min, 1, 2 and 3h	The mean inhibition rate was 18.9% after 180 min	[17]
		Vinifer 4° C		Aqueous	—	—	30 min, 1, 2 and 3h	The mean inhabitation rate was 12.8% after 180 min	
		Vineger 4° C		Aqueous	—	—	30 min, 1, 2 and 3h	The mean inhibition rate was 28.4% after 180 min	
		Lemon Juice 24° C		Aqueous	—	—	30 min, 1, 2 and 3h	The mean inhibition rate was 28.35% after 180 min	
		Vinifer 24° C		Aqueous	—	—	30 min, 1, 2 and 3h	The mean inhibition rate was 16.22% after 180 min	
		Vineger 24° C		Aqueous	—	—	30 min, 1, 2 and 3h	The mean inhibition rate was 40.63% after 180 min	

8	<i>E. histolytica</i>	<i>A. sativum</i>	trophozoite	Hydroalcoholic		15, 30, 45 and 60 mg/ml	24 and 48h	MIC was 60 mg/ml after 24h	[18]
		<i>A. sativum</i>		Hexanic	—	1, 2, 3 and 4 mg/ml	24 and 48 h	MIC was 4mg /ml after 24 h MIC was 3mg/ml after 48 h	
9	<i>G. lamblia</i>	<i>Carum copticum</i>	Cyst	Essence	Fruit	2, 4, 6 and 8 mg/ml	1, 2 and 3 h	Complete inhibition at 8 mg/ml for 60 min and at 6 mg/ml for 120 min	[19]
		<i>C. copticum</i>		Hydroalcoholic	Fruit	25, 50, 75 and 100 mg/ml	1, 2 and 3 h	Complete inhibition at 100 mg/ml for 60 min and at 75 mg/ml for 120 min	
10	<i>Cryptosporidu m oocyst</i>	<i>Vccinium corymbosum</i>	Oocyst	—	Fruit	0.25, 0.5, 1 and 2 mg/ml	24 and 48 h	The highest fatality rate (45.8%) on <i>Cryptosporidu m</i> oocyst was seen at concentration of 2mg/ ml after 48 h	[20]
		<i>A. sativum</i>		—	Commercial tablet	0.3, 0.6, 1.2 and 2.4 mg/ml	24 and 48 h	The highest inhibitory effect (53%) was seen at 2.4 mg/ml after 48h	
11	<i>G. lamblia</i>	<i>Ar. annua</i>	Cyst	Hydroalcoholic	Leaf	1, 10, 50 and 100 mg/ml	1, 5, 30 min and 1, 3, 24 h	Maximum lethal effect on <i>Giardia</i> cyst was observed at 50 and 100 mg/ml of the extract after 3 and 24 h	[21]
12	<i>G. lamblia</i>	<i>Eucalyptus</i>	Cyst	Methanolic	Leaf	10, 100 and 200 mg/ml	30 and 60 min	The highest inhibitory effect (63.3%) on <i>Giardia</i> was observed at 200 mg/ml after 60 min	[22]
		<i>Satureia hortensis</i>		Methanolic	Leaf	10, 100 and 200 mg/ml	30 and 60 min	The highest inhibitory effect (84.3%) on <i>Giardia</i> was seen at 200 mg/ml after 60 min	
		<i>Heracleum glabrescens</i>		Methanolic	Leaf	10, 100 and 200 mg/ml	30 and 60 min	The highest inhibitory effect (63.3 %) on <i>Giardia</i> was seen at 200 mg/ml after 60 min	
13	<i>G. lamblia</i>	<i>Ferula asafoetida</i>	Cyst	Alcoholic 4°C	Resinate	1, 1.25, 2.5, 5, 10 and 20 mg/ml	1, 2, 3, 4 and 5 h	<i>A. safoetida</i> ethanol extract completely inhibited <i>Giardia</i> at 20 mg/ml after 4 h	[23]
				Alcoholic 24° C	Resinate	1, 1.25, 2.5, 5, 10 and 20 mg/ml	1, 2, 3, 4 and 5 h		
				Alcoholic 37° C	Resinate	1, 1.25, 2.5, 5, 10 and 20 mg/ml	1, 2, 3, 4 and 5 h		
				Aqueous 4° C	Resinate	1, 1.25, 2.5, 5, 10 and 20 mg/ml	1, 2, 3, 4 and 5 h		
		Aqueous 24° C	Resinate	1, 1.25, 2.5, 5, 10 and 20 mg/ml	1, 2, 3, 4 and 5 h	The highest inhibitory effect (57.23%) was observed at 20 mg/ml after 5 h			
		Aqueous 37° C	Resinate	1, 1.25, 2.5, 5, 10 and 20 mg/ml	1, 2, 3, 4 and 5 h				
		Aqueous 4° C	Fruit	1, 1.25, 2.5, 5, 10 and 20 mg/ml	1, 2, 3, 4 and 5 h				
		Aqueous 24° C	Fruit	1, 1.25, 2.5, 5, 10 and 20 mg/ml	1, 2, 3, 4 and 5 h				
Aqueous 37° C	Fruit	1, 1.25, 2.5, 5, 10 and 20 mg/ml	1, 2, 3, 4 and 5 h	The highest giardicidal effect (66.1%) as observed at concentration of 20 mg/ml after 5 h					

14	<i>G. lamblia</i>	<i>Sambucus ebulus</i>	Methanolic	Fruit	1, 10, 50 and 100 mg/ml	5, 10, 30 and 60 min	The highest inhibitory effect against <i>Giardia</i> (78%) was observed at 100 mg/ml after 60 min	[24]	
15	<i>G. lamblia</i>	<i>Ch. botrys</i>	Cyst	Alcoholic 4° C	Fruit	1, 1.25, 2.5, 5 10 and 20 mg/ml	1, 2, 3, 4 and 5 h	Complete elimination of <i>Giardia</i> at 37 °C, with 20 mg/ml after 5 h	[25]
				Alcoholic 24° C	Fruit	1, 1.25, 2.5, 5 10 and 20 mg/ml	1, 2, 3, 4 and 5 h		
				Alcoholic 37° C	Fruit	1, 1.25, 2.5, 5 10 and 20 mg/ml	1, 2, 3, 4 and 5h		
			Cyst	Aqueous 4° C	Fruit	1, 1.25, 2.5, 5 10 and 20 mg/ml	1, 2, 3, 4 and 5 h	The highest giardicidal effect (66.1%) as observed at concentration of 20 mg/ml after 5 h	
				Aqueous 24° C	Fruit	1, 1.25, 2.5, 5 10 and 20 mg/ml	1, 2, 3, 4 and 5 h		
16	<i>G. Lamblia cyst</i>	<i>Ar. annua</i>	Chloroformic	—	1, 1.25, 2.5, 5 10 and 20 mg/ml	5, 10, 30, 60 and 180 min	The highest inhibitory effect (86%) was observed at concentration of 100 mg/ml after 60 min	[26]	
	<i>G. lamblitroph</i>	<i>Ar. annua</i>	Chloroformic	—	1, 1.25, 2.5, 5 10 and 20 mg/ml	5, 10, 30, 60 and 180 min	Complete inhibition at 100 mg/ml after 60 min		
	<i>G. lamblia Cyst</i>	<i>Tanacetum parthenium</i>	Chloroformic	—	1, 10, 50 and 100 mg/ml	5, 10, 30, 60 and 180 min	The highest inhibitory effect (87%) was observed at concentration of 100 mg/ml after 60 min		
	<i>G. lamblia troph</i>	<i>T. parthenium</i>	Chloroformic	—	1, 10, 50 and 100 mg/ml	5, 10, 30, 60 and 180 min	Complete inhibition at concentration of 100 mg/ml after 60 min		
17	<i>G. lamblia</i>	<i>A. paradoxum</i>	Hydroalcoholic	Leaf	5, 10, 50 and 100 mg/ml	1.5, 10, 30 and 60, 180 min	Complete inhibition at concentration of 100 mg/ml after 180 min	[27]	
		<i>A. paradoxum</i>	Chloroformic	Leaf	5, 10, 50 and 100 mg/ml	1, 5, 10, 30 and 60, 180 min	Complete inhibition at concentration of 100 mg/ml after 180 min		
18	<i>G. lamblia</i>	<i>Olea europaea</i>	Hydroalcoholic 37° C	Leaf	2 and 5 mg/ml	2 and 4 h	The highest inhibitory effect (45.34%) was observed at concentration of 2 mg/ml after 4 h	[28]	
			Hydroalcoholic 4° C	Leaf	2 and 5 mg/ml	2 and 4 h			
		Cyst	<i>S. khuzestanica</i>	Hydroalcoholic 37° C	Leaf	2 and 5 mg/ml	2 and 4 h		The highest inhibitory effect was observed at 5 mg/ml, 4 °C, after 4 h
				Hydroalcoholic 4° C	Leaf	2 and 5 mg/ml	2 and 4 h		
			<i>A. sativum</i>	Hydroalcoholic 37° C	Leaf	2 and 5 mg/ml	2 and 4 h		The highest inhibitory effect (36.69%) was observed at concentration of 5 mg/ml after 4 h at 37 °C
				Hydroalcoholic 4° C	Leaf	2 and 5 mg/ml	2 and 4h		

Table 2. Details of studies on the in vivo activity of medicinal herbs against HIPs in Iran.

No	Parasite	Plant	Kind of parasite	Extract	Part used	Concentration	Exposure time (days)	Animal model	Results	Ref.
1	<i>G. lamblia</i>	<i>A. paradoxum</i>		Hydroalcoholic	Leaf	20, 50 and 100 mg/ml	3	Balb/c	The highest inhibitory effect (7%) was observed at concentration of 100 mg/ml after 3 days	[29]
	<i>G. lamblia</i>	<i>A. paradoxum</i>		Hydroalcoholic	Leaf and bulb	20, 50 and 100 mg/ml	3	Balb/c	The highest inhibitory effect (71%) was observed at concentration of 100 mg/ml after 3 days	
	<i>G. lamblia</i>	<i>A. paradoxum</i>	Cyst	Hydroalcoholic	Bulb	20, 50 and 100 mg/ml	3	Balb/c	The highest inhibitory effect (66%) was observed at concentration of 100 mg/ml after 3 days	
2	<i>G. lamblia</i>	<i>Tanacetum parthenium</i>	Cyst	Chloroformic	Bulb	20, 50 and 100 mg/ml	3	Balb/c	Treatment with 100 mg/ml for 3 days treated 90% of infected mice	[30]

DISCUSSION

The present systematic review is the first to present valuable data about the efficacy of plant extracts against HIPs in Iran during 1998-2015.

The majority of investigations were conducted on *G. lamblia*, which may be due to the fact that this parasite is the main causative agent for persistent parasitic diarrhea throughout the world. This flagellate parasite is also the most common (14.7%) pathogenic protozoan in Iran (31).

Climate is an important variable of parasitic infections. Iran is located in West Asia and borders the Persian Gulf, Caspian Sea and Gulf of Oman. The country has a variable climate, but in the northwestern areas, winters are cold with subfreezing temperatures and heavy snowfall during December and January. Spring and fall are relatively mild, while summers are dry and hot. In the south, winters are mild and the summers are very hot, having daily average temperatures exceeding 38 °C (100.4 °F) in July. In most parts of the country, annual precipitation averages 250 mm (9.8 inch) or less. The north usually has a humid climate with temperatures seldom below freezing in winter (33). Considering all the above mentioned facts, Iran has a favorable condition for the activity of intestinal parasites.

Allium: *Allium* species grow in temperate climates of the northern hemisphere. This perennial plant belongs to the *Liliaceae* family. It has been known to possess medicinal and dietary properties (39).

The anti-helminthic (40, 41), anti-protozoal (42, 43), antibacterial (44), anti-tumor (45), antioxidant (46) and anti-fungal (47) activities of *A. sativum* (garlic) have been well-demonstrated.

According to the reviewed publications, most studies have been carried out on the effects of *Allium* against HIPs. *A. sativum* has long been used by humans due to its numerous health benefits. This complex herb contains an unusually high concentration of sulfur-containing compounds (1–3%), 17 amino acids, enzymes and minerals such as selenium. The sulfur-containing compounds are responsible for garlic's strong odor and many of its medicinal effects.

Allicin (diallyl thiosulfinate or diallyl disulfide) is the most biologically active ingredient of garlic. Kaempferol and quercetin also have inhibitory effects against microorganisms including parasites, especially *Giardia* (48).

In a study by Ankri and Mirelman, a low concentration (5 µg/mL) of allicin inhibited virulence of 90% of *E. histolytica* trophozoites (49). Based on the results of previous studies, the extract of *A. sativum* could be considered as a proper candidate for protozoal treatment and inhibition of *G. lamblia* and *E. histolytica*. Studies have also investigated the anti-mycotic properties of *A. sativum* against clinically important dermatophytes, *Candida albicans* and *Aspergillus niger* (50).

Artemisia: *Artemisia* is a large, diverse genus of herbs with more than 200 species belonging to the daisy family (*Asteraceae*). Most species of *Artemisia* contain secondary metabolites such as sesquiterpenes, monoterpenes, especially sesquiterpene lactones that could be responsible for the biological activities of *Artemisia* species. *Artemisia* has long been used in traditional medicine, particularly Chinese medicine. Artemisinin (a semi-synthetic derivative of *Artemisia*) is thought to be responsible for the anti-malaria activity of *Artemisia* against *Plasmodium vivax* and *P. falciparum* (51). Furthermore, the anti-malaria activity of *Artemisia* has been demonstrated in primate models (52). Recent studies indicate that *Artemisia* can become cytotoxic in the presence of iron influx and ferrous iron, which are abundant in cancer cells. Some studies have reported the efficacy of artemisinin against various cancers (53, 54). Santonin, the active component of *A. nilagirica*, has been shown to have anti-parasitic effects against *Trichinella spiralis* larvae. *Artemisia* is effective against a wide range of pathogenic protozoan including *Pneumocystis carini* (56) and causative agents of cryptosporidiosis, amoebiasis, schistosomiasis, giardiasis and leishmaniasis (57). According to Ridley and Hudson (1998), the anti-parasitic activity of artemisinin relies on alkylation and oxidation of membrane proteins and lipids as well as inactivation of protein channels through generation of highly reactive oxygen-based free radicals or electrophilic intermediates (58). A study in 2012 reported that 100 mg/ml of *A. annua* extract can inhibit 97% and 100% of giardia cysts and trophozoites, respectively (21).

Ferula asafoetida: *Asafoetida* is the oleogum-resin exuded from the roots and stems of several *Ferula* species. This plant is widely distributed in the Mediterranean region and Central Asia and is native to the deserts of Iran. *Asafoetida* has been used as an antimicrobial agent in traditional medicine (59). The plant contains calcium, phosphorus, iron, carotene, riboflavin, niacin, resinous materials composed of ferulic acid, umbel-liferone, asaresinotannols, farnesiferols A, B and C, and about 25% gum composed of glucose, galactose, l-arabinose, rhamnose, and glucuronic acid and volatile oil (3-17%) consisting of disulfides as its major components, notably 2-butyl propenyl disulfide (E- and Z-isomers) and monoterpenes (α - and β -pinene, etc.). Extract of this plant was effective against *Trichomonas vaginalis*, *Leishmania major* (*in vitro*) and *Schistosoma mansoni* (*in vivo*) (60, 61). El Deeb et al. reported phytomedicine *asafoetida* as a suitable natural remedy for *Blastocystis* sp. infection (62). In a study by Rezaeiemanesh and Shirbazou, exposure to 20 mg/ml of *f. asafoetida* ethanol extract at 37 °C for four hours had 100% giardicidal effect (23).

Chenopodium botrys: This plant is native to the Mediterranean region and is an important member of the *Chenopodiaceae* family, which is important for phytochemical medicinal evaluation. Phytochemically chenopods contain minerals, primary metabolites, aromatic cytokinins, amino acids, hormones, carbohydrates, proteins and secondary metabolites such as lignans, catechins, flavonols, organic acids, coumarines, carotenoid terpenoids, isoflavones, phenol derivatives, sterols, saponins, sesquiterpenoids, triterpenes, glycosides, monoterpenes, vitamins, amides, amines and alkaloids. A study reported that the essential oil from *C. botrys* has significant activity against gram positive and gram negative bacteria. Besides, oil of *Chenopodium* fruits and flowers has anti-helminthic properties against hookworms, roundworms and tapeworms (63). Boiled and infusion of the roots, leaves and inflorescences of this medicinal plant are used for elimination of intestinal worms.

The decoction of this plant containing up to 300 mg dry plant material per kg body weight is reported to be effective for treatment of ascariasis (64).

Carum copticum (Ajwain): *C. copticum* is an annual herb from the family *Apiaceae* that has been widely used in traditional medicine. It contains terpinene, o-cymene, terpinolene, nerolidol, etc. Moreover, thymol and carvacrol are two major components of this plant. Previous studies have demonstrated the anti-parasitic, anti-fungal, antioxidant, antibacterial and hypolipidemic effects of *C. copticum* (65). The *C. copticum* extract had in vitro macrofilaricidal properties against adult bovine filarial worm *S. digitata*. Furthermore, *C. copticum* increased infertility and mortality rate of human filarial worm *Brugia malayi* in vivo (66). Another study reported the inhibitory effects of *C. copticum* essential oil against protoscoleces of hydatid cyst (67). Moreover, ethyl acetate extract of *C. copticum* (25 µg/mL) showed in vitro antimalarial and anti-leishmanial activity (68). Hydroalcoholic extract of *C. copticum* showed leishmaniacidal activity with IC₅₀ of 15.625 M which was less than the IC₅₀ of a macrophage cell line (43.76 M) (69).

Shahabi et al. showed that the hydroalcoholic extract and essence of *C. copticum* had inhibitory effects on *G. lamblia* cysts (70). In another study, *C. copticum* powder showed more significant dose-dependent anti-parasitic and anti-helminthic effects compared to levamisole (an immunomodulator drug and anti-helminthic agent) on sheep infected with mixed nematodes (71). Extracts of *C. copticum* can eliminate nematodes owing to its high carvacrol and thymol content (72, 73). The extract of this plant also exerted favorable

effects against *Eimeria tenella*, the causative agent for coccidiosis in chicken (74).

Limitations and drawbacks: Most studies have evaluated the efficacy of medicinal plants against *Giardia*, and little attention has been paid to other HIPs. Some major factors have been neglected including concentration, exposure time and part of the herb used for extraction. In addition, only one study has been carried out to evaluate the in vivo effects of medicinal plants against HIPs. This could be due to lack of suitable laboratory animals for HIPs, while mice and hamsters are suitable for other parasites, such as *Toxoplasma* and *Leishmania*.

In addition, monitoring infected animals with intestinal parasites is relatively difficult. Furthermore, conducting preclinical investigations is more costly compared to in vitro investigations. Last but not least, none of the reviewed studies was conducted on active components of the extracts.

CONCLUSION

To our knowledge, this study is the first systematic review on the efficacy of medicinal herbs against intestinal parasites in Iran. Given the findings, it is recommended to conduct in vivo studies on medicinal herbs with favorable in vitro effects on HIPs.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding publication of this study.

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