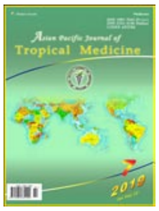

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Potential of herbal constituents as new natural leads against helminthiasis: A neglected tropical disease

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ABSTRACT

The WHO reports that billions of people and animals in tropical and subtropical regions are affected by helminthiasis as neglected tropical disease. It is predominant in underdeveloped areas; nevertheless, the increase in the number of travelers and migrants has made this infection more common. The current mass drug treatment produces severe side effects and many strains of helminths are resistant to them. None of the chemotherapeutic drugs meets the ideal requirements of anthelmintics, such as broad spectrum of activity, single dose cure, free from side effect and cost-effectiveness. Today, many researchers are screening the traditional herbal system in search of the anthelmintic herbal constituents which overcome all the problems of synthetic drugs. Several researchers proclaim anthelmintic activity of herbal medicines by using different experimental models. The present review demonstrates natural product drug discovery, outlining potential of herbal constituents from natural sources as natural leads against helminthiasis.

1. Introduction

Human beings have relied on the Mother Nature throughout the ages for the treatment of a wide range of diseases. In particular, herbal drugs have formed the basis of sophisticated traditional medicinal systems. The earliest records from 2 600 BC, approximately 1 000 plant-derived substances were documented in Mesopotamia. Most of them are still used today for the treatment of ailments like tropical diseases[1].

Neglected tropical diseases (NTDs) are among the seventeen life threatening endemic ailments that occur in tropical and subtropical regions covering 149 countries[2]. Billions of people were affected with the NTDs and people died from these infections is more than half million every year[3-6]. The infections mainly affect peoples who live on less than US$ 2 per day or under the World Bank poverty level of US$ 1.25 per day[7]. Helminthiasis is one of the major public health problems and development challenges, and it is estimated that each species affect more than one billion people all over the world and is classified as neglected tropical disease by WHO[8,9]. It is mainly associated with poverty and is most predominant in the poorest populations of the developing countries. Helminthiasis is one of the major reasons behind poverty of these countries as it affects the pregnancy, child growth, worker productivity, and outcome[10,11]. In these regions, it mainly contributed to malnutrition, anemia, eosinophilia, pneumonia and reduced physical and intellectual abilities[11-13]. Moreover, it offers very less profit for pharmaceutical industries in returns of huge investment on research and development of new chemical entities[14].

Helminthiasis is the most common infection caused by worms, which is mainly divided into two phyla. Nemathelminths are nematodes, *e.g.* hookworms (*Ancylostoma duodenale*) and roundworms (Ascaris lumbricoids). Platyhelminths are flatworms

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divided into the cestode, *e.g.* tapeworms (Taenia solium, Taenia saginata) and the trematode *e.g.* flukes (*Schistosoma mansoni* and Schistosoma hematobolium)[15].

2. Helminths affecting humans

The helminths affect approximately more than 1.45 billion people across the globe. Among them, *Ascaris lumbricoides* affects more than 819 million, *Trichuris trichiura* affects over 465 million and hookworm (*Necator americanus* and/or *Ancylostoma duodenale*) affects over 439 million peoples worldwide[16]. Helminthiasis leads to malnutrition and anemia, which retard children's mental and physical growth[17], significantly contribute to school absenteeism[8]. Helminths mainly reside in gastrointestinal tract and can also infect liver and other organs. The infection is generally spread through contaminated soil with helminths and their eggs in the areas with poor sanitation[18]. Helminths is a large veterinary health problem to farm yard animals and responsible for 3%-8% of their weight loss and 28% of death[19].

Table 1 shows the prevalence of helminthiasis in three major continents. It has been observed that African and Asian are affected more compared to America. This data supports the statement that helminthiasis is more common in developing countries than developed countries.

3. Conventional drug therapy for helminthiasis

The current mass drug treatment of helminths produces side effects (Table 2) like abdominal disturbances, nausea, vomiting, headache, diarrhea, weight loss and many of the drugs are not recommended to use during pregnancy[20]. Consequently agranulocytosis and teratogenicity are major adverse effects of the conventional medicines. None of the chemotherapeutic drugs meets the ideal requirements of anthelmintic such as broad spectrum of activity, single dose cure, free from side effects and cost effectiveness. Moreover, the increase of resistance[21], toxic residue of synthetic drugs, less availability and high cost requires the search for alternative medicinal system to overcome associated problems.

4. Herbal constituents as new natural leads

The World Medicines Situation 2011[22] reports that all the countries uses traditional medicines at some extent, among these, developing countries accounts for 70%-95%. Moreover, at least 25% of all currents drugs are obtained either directly or indirectly from natural origin. According to the herbal medicine market research report 2018, the global market of herbal medicines increasing exponentially to register a compound annual growth rate of 5.88% to reach US$ 129 million by 2023, which was 50 million in 2017[23]. As per the resolution of World Health Assembly (WHA62.13)[24], the member governments are mandatory to conserve, respect and universally communicate the knowledge of traditional medicines. Also, it prepares regulatory policies for development of new innovative traditional medicines to encourage appropriate, harmless, rational and effective uses.

A survey of plant constituents used as drugs in countries with WHO-Traditional Medicine Centers has identified 122 compounds derived from 94 plants, of which 80% were used for therapeutic purposes[1]. There is no doubt that herbs are among the vital natural sources for synthesis of various molecules from simple skeletal structure to complex one. Many popular components are based on traditional drugs, such as quinine (chloroquine & mefloquine), artemisinin, taxol (paclitaxel), camptothecin,

Table 1. Prevalence of different helminthes in major continents.

Helminths	Regions affected		
	Asia	Africa	America
Ascariasis *Ascariasis lumbricoides* (roundworm)	+	+	+
Trichuriasis *Trichuris trichiura* (whipworm)	+	+	+
Hookworm *Necator americanus*; *Ancylostoma duodenale*	+	+	+
Strongyloidiasis *Strongyloides stercoralis* (threadworm)	+	+	+
LF *Wuchereria bancrofti; Brugia malayi*	+	+	-
Onchocerciasis (river blindness) *Onchocerca volvulus*	-	+	-
Loiasis *Loa loa*	-	+	-
Dracunculiasis (guinea worm) *Dracunculus medinensis*	-	+	-
Schistosomiasis *Schistosoma haematobium*	-	+	-
Schistosoma mansoni	-	+	-
Schistosoma japonicum (blood flukes)	+	-	-
Clonorchis sinensis (liver fluke)	+	-	-
Opisthorchis viverrini (liver fluke)	+	-	-
Paragonimus spp. (lung flukes)	+	-	-
Fasciolopsis buski (intestinal fluke)	+	-	-
Fasciola hepatica (intestinal fluke)	+	-	-
Cysticercosis *Taenia solium* (pork tapeworm)	-	+	-

+ Present; - Absent.

Table 2. WHO-recommended anthelminthic drugs.

Drug	Dosage	Mechanism of action	Adverse effects
Albendazole	400 mg	Albendazole causes changes in cells of the intestine by hindering polymerization and the conversion of tubules into microtubules.	Abdominal pain, agranulocytosis, aplastic anemia, bone marrow suppression causing pancytopenia, dizziness, headache, leukopenia. nausea/vomiting, vertigo, elevated intracranial pressure, meningitis, hair loss, pyrexia, teratogenicity.
Mebendazole	500 mg	Mebendazole inhibits worm microtubule formation and leads to glucose depletion.	Abdominal pain, alopecia, diarrhea, leukopenia, thrombocytopenia, raised liver enzymes and teratogenicity.
Levamisole	150 mg	Levamisole causes worm muscle paralysis by continuous stimulation through nicotinic receptors on worm muscle surface.	Abdominal pain, agranulocytosis, anorexia, diarrhea, dizziness, dysgeusia, fatigue, malaise, mouth sores, nausea, vomiting and skin rashes.
Pyrantel	10 mg/kg	Pyrantel causing excessive depolarization followed by blocking of neuromuscular junction which leads to paralysis of helminthes.	Abdominal discomfort, dizziness, drowsiness, facial swelling, headache, insomnia, rashes, shock, seizures, Teratogenicity.
Ivermectin	150 μg/kg	Ivermectin has high selectivity to bind GABA receptor, so as to mediate GABAnergic mobilization of chlorine ions from chloride channel to cause hyperpolarization of muscles; this effect can cause paralytic death.	Ataxia, dizziness, diarrhoea, fever eye swelling/redness/pain, headache, itching, malaise, nausea, neurotoxicity, rashes, swollen lymph nodes, vision complications, weakness.

khellin, sodium chromoglycate, galegine, metformin, papaverine, verapamil[1,25-27]. Therefore, the WHO paid great attention on new chemical entities to manage NTDs including helminthiasis.

Thus, the present review demonstrates the potential of herbal constituents from different plants sources as new natural leads against helminthiasis (Table 3). The method used for compiling following data consist of articles from the National Center for Biotechnology Information during the period 2005-2019.

It was also observed from the data that phytoconstituents from different plants shown their distinct mechanism of action according to the major chemical group. Table 4 summarizes the anthelmintic mechanism of different phytoconstituents.

Figure 1 shows that around 46 families of plants possess anthelmintic activity. Among them, family Asteraceae has the most plants that show anthelmintic potential. The helminthes used for evaluating anthelmintic activity are given in Figure 2. It has been observed that *Haemonchus contortus* was the most frequently used test agent for the study of anthelmintic potential.

Subsequently, Figure 3 shows that the major plant parts possessing anthelmintic potential. Among all these parts, leaves have shown more potential than other plant parts.

Moreover, the Figure 4 shows the various methods of extraction used to obtain anthelmintic phytoconstituents from the plants. The aqueous extract followed by methanolic and ethanolic extract have shown more significant anthelmintic potential.

Nevertheless, the anthelmintic potential depends on the presence of major phytoconstituents present in the plants. It has been observed that, tannins (20%) shows more potential followed by flavonoids (19%), phenolic compounds (18%), saponins (12%), alkaloids (11%), various enzymes (8%), metals (2%), glycosides (2%) terpenoids (2%) and other phytoconstituents (3%) are responsible for anthelmintic activity (Table 3).

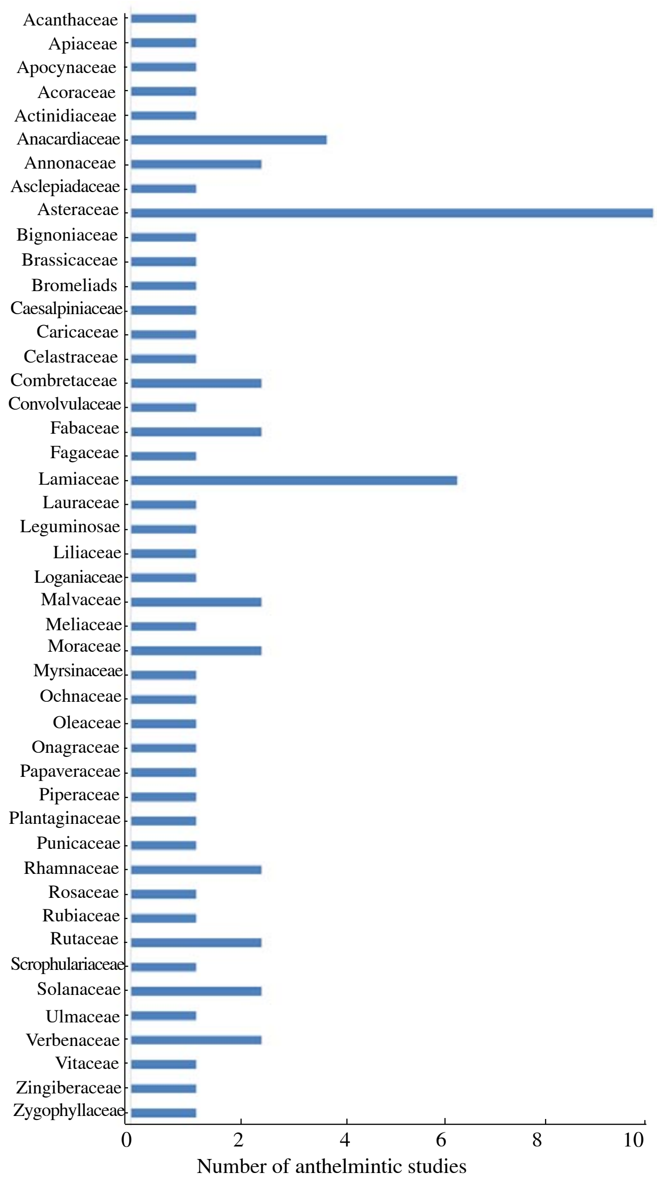

Figure 1. Anthelmintic agents by plant families.

Table 3. Different *in vitro* and *in vivo* anthelmintic studies of herbal constituents.

No.	Name of plant	Family	Plant part used	Fraction used	Activity studied against	Chemical constituent responsible	Standard drug used	Ref.
1	*Butea monosperma*	Fabaceae	Seeds	Crude powder	*Haemonchus contortus, Trituris colubriformis, Trituris axei, Trituris ovis*	Palasonin	Levamisole	[28]
2	*Nicotiana tobacum*	Solanaceae	Leaves	Methanolic aqueous extract	*Haemonchus contortus*	Nicotine	Levamisole	[29]
3	*Spigelia anthelmia*	Loganiaceae	Whole plant	Aqueous extract	*Nippostrongylus braziliensis*	-	Albendazole	[30]
				Separated proteins from leaf, stem, root	*Haemonchus contortus*	Prroteins (protease, protease inhibitor, chitinase)	-	[31]
4	Milkweed	Asclepiadaceae	Latex	-	*Heligmosom–oides bakeri, Trichuris muris*	Cysteine proteinases	-	[32]
5	*Ficus carica*	Moraceae	Latex	-	*Heligmosomoides bakeri, Trichuris muris*	Cysteine proteinases	-	
6	*Ananas comosus*	Bromeliads	Fruits	Aqueous extract	*Heligmosomoides bakeri, Trichuris muris*	Cysteine proteinases	-	
7	*Caraca papaya*	Caricaceae	Latex	-	*Heligmosomoides bakeri, Trichuris muris*	Cysteine proteinases	-	
8	*Actinidia deliciosa*	Actinidiaceae	Fruits	Aqueous extract	*Heligmosomoides bakeri, Trichuris muris*	Cysteine proteinases	-	
9	*Ficus benjamina*	Moraceae	Latex	-	*Heligmosomoides bakeri, Trichuris muris*	Cysteine proteinases	-	
10	*Artemisia absinthium*	Asteraceae	Aerial parts	Ethanolic aqueous extract	*Haemonchus contortus*	Thujone (α and β)	Albendazole	[33]
11	*Thespesia lampas*	Malvaceae	Roots	Aqueous extract	*Pheretima posthuma, Ascaridia galli, Raillietina spiralis*	Glycosides, phenolic compounds	Piperazine citrate	[34]
12	*Clerodendrum umbellatum* Poir	Verbenaceae	Leaves	Aqueous extract	*Schistosoma mansoni*	Flavonoids and tannins	Praziquantel	[35]
13	*Chlorophytum borivilianum*	Liliaceae	Root tuber	Saponin extract	*Pheretima posthuma, Ascaridia galli*	Saponins	Piperazine citrate	[36]
14	*Holoptelea integrifolia*	Ulmaceae	Bark	Ethanolic aqueous extract	*Eisenia foetida*	Tannins, polyphenol, saponins,	Piperazine citrate	[37]
			Stem bark	Benzene, chloroform, methanol, aqueous, pet ether	*Pheretima posthuma*	Flavonoids, polyphenol	Piperazine citrate	[38]
15	*Anogeissus Leiocarpus*	Combretaceae	Leaves	Acetone extract	*Haemonchus contortus*	Glucoside, terpenoids	Albendazole	[39]
16	*Acacia nilotica*	Leguminosae	Bark leaves	Ethyl acetate	*Haemonchus contortus*	Flavonoid, tannins	Levamisole	[40]
17	*Ageratum conyzoides*	Asteraceae	Leaves	Ethanolic extract	*Nematode Heligmosomoides bakeri*	Tannins, flavonoids, polyphenol	Mebendazole	[41]
18	*Verbascum thapsus* extracts	Scrophulariaceae	Whole plant	Methanolic extract	*Ascaridia galli)* and *tapeworms (Raillietina spiralis)*	Flavonoids, saponins, tannins	Albendazole	[42]
19	*Annona muricata L.*	Annonaceae	Leaves	Aqueous extract	*Haemonchus contortus* from sheep	Phenolic compounds	Levamisole	[43]
20	*Rubus fruticosus*	Rosaceae	Fruits	Methanolic extract	*Artemia Raillietina spiralis* and *Ascaridia galli*	Flavonoids, saponins, tannins	Albendazole and piperazine citrate	[44]
21	*Solanum violaceum* Ortega	Solanaceae	Whole plant	Methanolic extract	*Pheretima posthuma* mode	Flavonoids, polyphenol	Albendazole	[45]
22	*Enhydra fluctuans* Lour	Asteraceae	Whole plant	Methanolic extracts	*Pheretima posthuma* (earthworm)	Tannins, saponins, alkaloids flavonoids	Albendazole	[46]
23	*Azadirachta indica*	Meliaceae	Leaves	Aqueous extract	*Haemonchus contortus*	Tannins, flavonoids, alkaloids, saponins	Levamisole	[47]
			Leaves seeds	Ethanolic extract	*Leishmania donovani*	Polyphenols, flavonoids, stigmasterol, γ-sitosterol	Pentamidine	[48]
			Leaves	Ethanolic aqueous extracts	*Gastrothylax indicus*	Tannins, flavonoids, steroids, alkaloids saponins	Albendazole	[49]
24	*Embelia schimperi* Vatke	Myrsinaceae	Fruits	Hydro-alcoholic extract	*Hymenolepis nana Necator americanus*	Embelin	Albendazole	[50]
25	*Caesalpinia bonducella*	Caesalpiniaceae	Leaves,	Methanolic extracts	*Hymenolepis diminuta, Syphacia obvelata*	Tannins, flavonoids	Albendazole, praziquantel	[51]
26	*Calotropis procera*	Apocynaceae	Flower	Ethanolic aqueous extracts	*Gastrothylax indicus*	Alkaloids, phenols	Albendazole	[49]
			Flower	Aqueous extract	*Haemonchus contortus*	Alkaloids, flavonoids, phenols	Oxfendazol, levamisole	[52]
27	*Punica granatum*	Punicaceae	Rind	Ethanolic aqueous extracts	*Gastrothylax indicus*	Tannins, saponins	Albendazole	[49]
28	*Onobrychis viciifolia*	Fabaceae	Whole plant	Pellets	*Ostertagia ostertagi, Cooperia oncophora*	Tannins	-	[53]
29	*Acorus calamus Linn*	Acoraceae	Rhizomes	Methanolic extracts	*Hymenolepis diminuta*	β-asarone	Praziquantel	[54]
30	*Zanthoxylum armatum*	Rutaceae	Seed powder	Aqueous extract	*Haemonchus contortus*	Flavonoids, polyphenol, copper,zinc	Levamisole	[55]

Table 3. Different *in vitro* and *in vivo* anthelmintic studies of herbal constituents (continued).

No.	Name of plant	Family	Plant part used	Fraction used	Activity studied against	Chemical constituent responsible	Standard drug used	Ref.
31	*Combretum mucronatum*	Combretaceae	Leaves,	Hydro-ethanolic (1:1) extract	*Caenorhabditis elegans*	Oligomeric procyanidins	-	[56]
32	*Annona senegalensis*	Annonaceae	Roots, stem, bark, fruits	Methylene chloride-methanol (1:1) extract	*Heligmosomoides bakeri*	Alkaloids, tannins, polyphenols, saponins	-	[57]
33	*Nauclea latifolia*	Rubiaceae	leaves			Tannins, polyphenols, saponins	-	
34	*Lophira lanceolata*	Ochnaceae	Leaves, Trunk bark and Root bark	Ethanolic and methanolic-methylene chloride extract	*Onchocerca ochengi*, *Caenorhabditis elegans*	Tannins, polyphenols, flavonoids and saponins	Ivermectin, levamisole albendazole	[58]
35	*Cissus quadrangularis*	Vitaceae	Aerial parts	Methanolic extract	*Haemonchus contortus*	Alkaloids, tannins, flavonoids, phenols	Albendazole	[59]
			Root	Aqueous, ethanol extract	*Pheretima posthuma*	Tannins, flavonoids, phenols	Piperazine citrate	[60]
36	*Schinus molle*	Anacardiaceae	Leaves	Methanolic extract	*Haemonchus contortus*	Alkaloids, tannins	Albendazole	[59]
37	*Maytenus senegalensis*	Celastraceae	Stem bark	Aqueous extract	*Haemonchus contortus*	Tannins, polyphenols	Albendazole	[61]
38	*Rhamnus alaternus*	Rhamnaceae	Leaves	Ethanolic extract	*Teladorsagia circumcincta*, *Trichostrongylus colubriformis*	Tannins, polyphenols	-	[62]
39	*Epilobium hirsutum*	Onagraceae	Leaves	Ethanolic extract	*Teladorsagia circumcincta*, *Trichostrongylus colubriformis*	Tannins, polyphenols	-	
40	*Rhamnus. palaestinus*	Rhamnaceae	Leaves	Ethanolic extract	*Teladorsagia circumcincta*, *Trichostrongylus colubriformis*	Tannins, polyphenols	-	
41	Herbmix							
	Althaea officinalis	Malvaceae	Roots	Herbmix is a powder mixture of dry herbs	*Haemonchus contortus*	Flavonoids, diterpenes, phenolic acids	-	[63]
	Petasites hybridus	Asteraceae	Butterbur					
	Inula helenium	Plantaginaceae	Butterbur					
	Plantago lanceolata	Lamiaceae	Leaves					
	Rosmarinus officinalis	Lamiaceae	Leaves					
	Solidago virgaurea	Asteraceae	Stem					
	Laricifomes officinalis	Papaveraceae	Stem					
	Hyssopus officinalis	Lamiaceae	Stem					
	Foeniculum vulgare	Apiaceae	Seeds					
42	*Andrographis paniculata*	Acanthaceae	Leaves	Ethanol, Methanol, Ethyl acetate Petroleum ether extract	*Ancylostoma duodenale*	Andrographolide, Neoandrographolide and Andrograpanin	Albendazole	[64]
43	*Cryptocarya novoguineensis*	Lauraceae	Leaves	Methanolic Extract	*Haemonchus contortus*	Goniothalamin	Monepantel and Moxidectin	[65]
44	*Piper methysticum*	Piperaceae	Leaves	Methanolic extract	*Haemonchus contortus*	Dihydrokavain, Desmethoxyyangonin and Yangonin	Monepantel and Moxidectin	
45	*Castanea sativa*	Fagaceae	Leaves, Bark	Aqueous extract	*Haemonchus contortus*	Hydrolysable tannins	-	[66]
46	*Ipomoea chilliantha*	Convolvulaceae	Aerial parts	Ethano: water (7:3)	*Haemonchus placei*	Phenylpropanoid, triterpene, saponin	Thiabendazole	[67]
47	*Lantana canescens*	Verbenaceae	Aerial parts			Phenylpropanoid, flavonoid		
48	*Aspilia latissima*	Asteraceae	Leaves			Phenylpropanoid, triterpene, saponin		
49	*Handroanthus serratifolius*	Bignoniaceae	Flowers			Phenylpropanoid,		
50	*Elettaria cardamomum*	Zingiberaceae	Seeds	Methanolic Extract	*Teladorsagia circumcincta*	Phenols, tannins	Thiabendazole	[68]
51	*Sisymbrium irio*	Brassicaceae	Aerial parts	Aqueous extract		Phenols, tannins		
52	*Jasminum polyanthum*	Oleaceae	Aerial parts	Methanol & aqueous extract		Phenols, tannins		
53	*Anacardium occidentale*	Anacardiaceae	Nut shell	Hexane extract	*Echinococcus multilocularis*, *Echinococcus granulosus*	Anacardic acid	Albendazole, Dihydroartemisinin	[69]
54	*Baccharis conferta*	Asteraceae	Aerial parts	Methanolic extract	*Haemonchus contortus*	Flavonol, isokaempferide, Hydroxycinamic acid	Thiabendazole	[70]
55	*Marrubium vulgare*	Lamiaceae	Leaves	Ethanol & aqueous extract	*Digestive strongyles*	-	Albendazole dimethyl sulfoxide	[71]
56	*Citrus aurantifolia*	Rutaceae	Fruit peel	Hydrodistillation	*Haemonchus contortus*	Limonene, β-pinene and γ-terpinene	Levamisole	[72]
57	*Anthemis nobile*	Asteraceae	Flowers			Isobutyl angelate, isoamyl Angelate and α-thujene		
58	*Lavandula officinalis*	Lamiaceae	Flowers			Linalool acetate, trans-sabinene hydrate and camphor		
59	*Myracrodruon urundeuva*	Anarcadiacea	Seed exudates	Aqueous extract	*Haemonchus contortus*	Proteins (SEX, SEXF1, and SEXF2)	-	[73]
60	*Balanites aegyptiaca*	Zygophyllaceae	Fruit	Methanolic extract	*Toxocara canis*	Saponins (Balanitin-7)	-	[74]

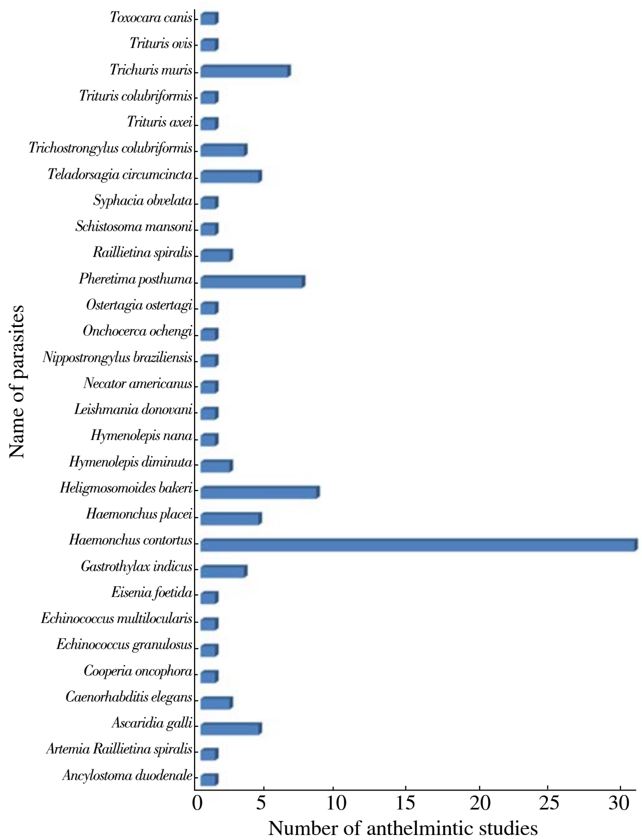

Figure 2. Anthelmintic studies of various plants.

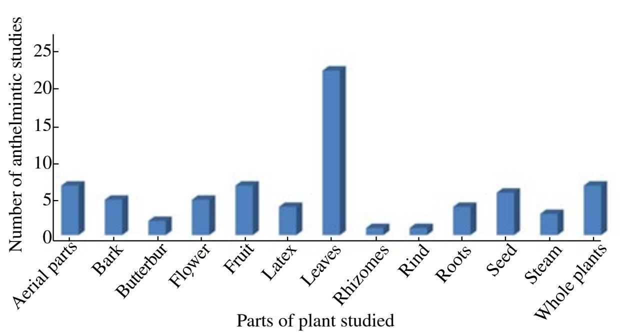

Figure 3. Anthelmintic activity studied in different parts of plants.

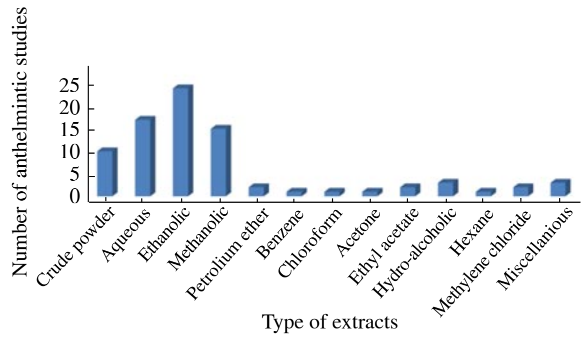

Figure 4. The anthelmintic activity of crude powder and different fractions obtained from plants.

5. Conclusions

The available conventional drugs fails to meet the ideal requirements of anthelmintic effect on all species of helminthes, single dose cure, free from side effects and cost-effective. Moreover, the increase of resistance, toxic impurities from synthetic drugs, less availability with higher cost requires the search for alternative system of medicine to overcome associated problems. The old classical systems of medicine and ethno medical surveys described the use of plants for the treatment of helminthic infection. This traditional knowledge of active herbs revealed effectiveness and safety of medicinal plants. However, their mode of action and the phytoconstituents responsible for the activity is not clearly known. The crude plant extracts, essential oils and isolates containing active principle show significant anthelmintic activity using *in vitro* and *in vivo* models. Moreover, to explore bioactivity of anthelmintic plants, further studies are needed, so as to discover different natural sources to emerge cost effective treatment of helminthic infection. The present review surveys literature that report name of plants, their anthelmintic activity and possible constituent that responsible for the bioactivity. The special attention is desired in order to standardize the bioactive plant with quantitative anthelmintic activity. Consequently, the design of palatable herbal preparations is needed to overcome side effects. Hence further study must be carried out to explore different plants of higher efficiency and negligible side effects.

Table 4. Anthelmintic mechanism of different phytoconstituents.

Phytoconstituents	Mechanism of action
Alkaloids	Alkaloids act on CNS and cause paralysis of parasites. Alkaloids act as antioxidant and consist of steroids and oligoglycosides, which reduces the sugar transport and reduces nitrate generation thereby reducing homeostasis which is required for larval development[75].
Benzyl isothiocyanate	Benzyl isothiocyanate Inhibit energy metabolism and affecting motor activity of the helminths[76].
Cysteine proteinases	Proteolytic activity of plant cysteine proteinases like papain and chymopapain digest the nematode cuticle thereby causing larval death[77].
Isoflavones	Inhibit the enzymes of glycolysis and glycogenolysis and disturb the Ca_2^+ homeostasis in the helminths[78].
Phenolic compounds	Phenolic compounds interfere with oxidative phosphorylation and thereby reduces energy production and also inhibit the glycoproteins on cell surface of the parasites resulting into their death[79].
Saponins	Affect the permeability of the cell membrane of helminths and cause vacuolization and disintegration of teguments[80].
Tannins	Reduces the larval nutrition by binding with the free proteins causing starvation of larvae and also by directly inhibiting the oxidative phosphorylation to reduce gastrointestinal metabolism resulting in death of larvae[81,82].

Conflict of interest statement

We declare that we have no conflict of interest.

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