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Anthelmintic Activity of Plants Especially of *Aristolochia* Species in Haemonchosis: A Review

[1]K.P. Mini, [2]K.V. Venkateswaran, [2]S. Gomathinayagam, [2]S. Bijargi and [1]P.K. Mandal
[1]Rajiv Gandhi Institute of Veterinary Education and Research, Pondicherry, 605009, India
[2]Madras Veterinary College, Tamil Nadu Veterinary and Animal Sciences University, Chennai, 600007, India

Corresponding Author: P.K. Mandal, Rajiv Gandhi Institute of Veterinary Education and Research, Pondicherry, 605009, India Tel: 919489585699

ABSTRACT

Haemonchosis is one of the common helminthic diseases of ruminants which causes high mortality. Course of infection depends on the worm burden, age and nutrition of the host. The principal feature of *Haemonchus* species infection is anaemia. Anthelmintics with different modes of action are the necessity of the hour, which has changed the focus to other sources like plants. Screening of medicinal plants for their anthelmintic activity has become great scientific interest. Ethnopharmacological surveys provide the rationale for selection and scientific investigation of medicinal plants. Herbal drugs are extensively used as anthelmintics in the developed world before the era of broad spectrum drugs. Many currently available therapeutic compounds are plant derived or synthetic analogues derived from those compounds. Plants of the genus *Artemisia* were used against the nematodes *Ascaris suum* and *Toxocara* spp. as well as cestodes of poultry. From time immemorial, plant derivatives like *Nicotiana tabaccum* have been used against *Moneizia*, *Ascaridia* and several species of GI nematodes including *Cooperia, Haemonchus, Nematodirus* and *Trichostrongylus*. Arecoline and several other alkaloids from the dried ripe seeds of *Areca catechu* were found to be active against tapeworms in dogs and poultry. *Aristolochia* species of plant are traditionally used for neatodiasis in India. In this review an effort is made to compile the available reports and studies about the anthelmintic activity and use of different plants especially of *Aristolochia* with special reference to Haemonchosis.

Key words: Anthelmintic, haemonchosis, *Aristolochia,* ruminants, plants

INTRODUCTION

Livestock, especially small ruminants, represent a major asset among resource-poor small holder farmers particularly the pastoralist communities (Mini, 2012; Alemu *et al*., 2014). Diseases caused by helminth parasites in small ruminants continue to be a major productivity constraint both in the tropics and subtropics (Perry *et al*., 2002; Verissimo *et al*., 2012; Mini *et al*., 2013). In the developed countries, the greatest impact is on the costs of control of helminth parasitoses, whereas, in the developing countries, the impact is on direct and potential productivity losses (Perry and Randolph, 1999; Ombasa *et al*., 2012). Among different types of helminths, nematodes are the most important as far as their prevalence and adverse effects on animal health and productivity are concerned. They cause retarded growth (Ashraf, 1985; Kochapakdee *et al*., 1995; Mini, 2012), lowered productivity (Ombasa *et al*., 2012), mortality (Sykes, 1994; Mohammed *et al*., 2013) and high economic losses (Irfan, 1984; Iqbal *et al*., 1993; Alemu *et al*., 2014), which adversely affect the livelihood of small farmers.

Haemonchus is the highly pathogenic nematode parasite of livestock, especially small ruminants capable of causing acute disease and high mortality (Perry *et al*., 2002; Soulsby, 2006; Ombasa *et al*., 2012). Haemonchosis is characterized by haemorrhagic anaemia due to the blood sucking activities of the worms in the abomasum (McKenna *et al*., 1995; Chartier *et al*., 2001; Soulsby, 2006; Mohammed *et al*., 2013). This is one of the most important parasites causing reduced production in livestock throughout the tropics and in most countries (Walle *et al*., 1995; Alemu *et al*., 2014). Over the past five decades, the control of this parasite has been achieved mainly through intensive chemo prophylaxis based on the repeated use of anthelmintic drugs (Mohammed *et al*., 2013). The emergence of nematode population resistant to one or more of the currently available broad spectrum anthelmintics is a worldwide phenomenon and is particularly severe in small ruminants (Chandrawathani *et al*., 1999; Leethwick *et al*., 2001; Ombasa *et al*., 2012).

Misuse of synthetic antiparasitic products has led to the development of Anthelmintic Resistance (AR) (Lans and Brown, 1998; Arunachalam, 2008; Mohammed *et al*., 2013). In developing countries, production and availability of these drugs are highly variable and often too expensive. Moreover, this approach has become a source of public concern in terms of both the use of proprietary drugs in farm production and the risk of chemical residues in food products (Muhammad *et al*., 2004; Mohammed *et al*., 2013). Hence, novel approaches to nematode parasite control are needed for small ruminants in the tropics and sub-tropics to counteract the problem of AR (Waller, 1997, 1999; Ombasa *et al*., 2012) creating a trend towards organic farming and sustainable animal husbandry (Waller, 2003; Mohammed *et al*., 2013). Development of livestock breeds resistant to parasites and the use of plants with anti-parasitic properties as well as the use of traditional herbal remedies, or Ethnoveterinary Medicine (EVM) are becoming more relevant (Waller, 1999; Ferreira *et al*., 2013).

Ethnoveterinary medicine refers to people's beliefs, knowledge, skills and practices relating to care of their animals (McCorkle, 1986). Even now, in human healthcare, 80-90% of the planet's inhabitants still rely mainly on traditional treatments and practitioners (Plotkin, 1992; Ferreira *et al*., 2013). Similar figures appear to hold for animal health care (McCorkle *et al*., 1996; McCorkle *et al*., 1996; Mini, 2012).

Anthelmintics with different modes of action are the necessity of the hour, which has changed the focus to other sources like plants (Ombasa *et al*., 2012). Screening of medicinal plants for their anthelmintic activity has become the scenario of great scientific interest (Alemu *et al*., 2014). Ethnopharmacological surveys provide the rationale for selection and scientific investigation of medicinal plants, since some of these indigenous remedies are already in use by significant population over extended periods of time (Lans, 2001; Ferreira *et al*., 2013). Most of the pharmaceutical companies have some form of research programs investigating plants with the aim of creating allelochemicals (bioactive secondary compounds) and new marketable drugs. The use of EVM is limited by the seasonal availability of certain plants, the scarcity of treatment against infectious disease, the ineffectiveness of some treatments and the often inadequate ethno-diagnosis (McCorkle *et al*., 1996; Ferreira *et al*., 2013).

In this context, it is important to realise that herbal drugs were also extensively used as anthelmintics in the developed world before the era of broad spectrum drugs. Some herbal remedies in the British veterinary codex (1965) include oil of chenopodium (frequently combined with a laxative), derived from *Chenopodium ambrosioides* (De Bairacli, 1991; Ombasa *et al*., 2012), which was used for many years in the UK and the US to treat nematode parasite infections

(*Strongylus*, *Parascaris* and *Ascaris* spp.) in monogastric animals including humans (Gibson, 1965). A monoterpene (ascaridole) is believed to be the active ingredient in the oil of this plant (Okuyama *et al*., 1993; Ketzis *et al*., 2002). Many currently available therapeutic compounds are plant derived or synthetic analogues derived from those compounds (Farnsworth *et al*., 1985; Ferreira *et al*., 2013).

Plants of the genus *Artemisia* were used against the nematodes *Ascaris suum* and *Toxocara* spp. as well as cestodes of poultry (Hammond *et al*., 1997). From time immemorial, plant derivatives like *Nicotiana tabaccum* have been used against *Moneizia*, *Ascaridia* and several other species of GI nematodes including *Cooperia, Haemonchus, Nematodirus* and *Trichostrongylus* (Iqbal *et al*., 2004; Tariq *et al*., 2009). Arecoline and several other alkaloids from the dried ripe seeds of *Areca catechu* were found to be active against tapeworms in dogs and poultry (Tariq *et al*., 2009).

In this review efforts have been made to compile the available reports and studies about haemonchosis including its lifecycle, pathogenesis and clinical signs, the anthelmintic activity of different class of plants against nematodes, especially against *Haemonchus*. Details about the *Aristolochia* species of plants and their anthelmintic activity with special reference to haemonchosis have been highlighted.

HAEMONCHOSIS

Gastrointestinal (GI) nematode infections are seen almost in all the higher species of animals (Soulsby, 2006; Ombasa *et al*., 2012). The GI nematodes have developed novel strategies to adapt to the host animal (Alemu *et al*., 2014). The evolution of these parasites in recent decades involved development of resistance to many chemicals used as anthelmintics (Sharma *et al*., 1971; Mohammed *et al*., 2013). A study conducted on such helminths gives an insight on the chemotherapy of these helminths considering development of resistance, targeting new pharmacophores and also developing strategies where more than one classical pathway of anthelmintic action are exhibited (Yadav and Uppal, 1992; Alemu *et al*., 2014).

Haemonchosis is one of the most common and serious helminth diseases of ruminants (Soulsby, 2006; Ombasa *et al*., 2012). Haemonchus, the causative agent has gained considerable attention for research from different parts of the world (Githiori *et al*., 2002; Iqbal *et al*., 2005; Costa *et al*., 2006; Eguale *et al*., 2007a; Mini *et al*., 2013) as it is a species showing development of resistance with different mechanisms and also adversely affects economy.

Anthelmintic resistance in nematodes of sheep and goats has been reported from different states in India (Yadav, 1990; Singh *et al*., 1995; Srivastava *et al*., 1995; Swarnkar *et al*., 2001; Dhanalakshmi *et al*., 2003; Das and Singh, 2005; Ponnuduari *et al*., 2005; Verissimo *et al*., 2012).

Haemonchus contortus: *Haemonchus contortus* is the predominant nematode of small ruminants followed by *Oesophagostomum columbianum*, *Trichostrongylus colubriformis, Trichuris ovis*, *Bunostomum trigonocephalum* and *Cooperia* spp. Gastrointestinal nematodes in sheep and goats are high during monsoon seasons in most of the agroclimatic zones (Meenakshisundaram, 1999; Jeyathilakan *et al*., 2003; Arunachalam, 2008; Hussain *et al*., 2011).

Haemonchus contortus is preponderant during June-November and rare during December-May in Southern India (Sanyal, 1991; Arunachalam, 2008). *Haemonchus contortus* occurs in the abomasum of sheep, goats, cattle and numerous other ruminants in most parts of the world (Costa *et al*., 2006; Eguale *et al*., 2007a; Foster *et al*., 2011). It is commonly known as the 'Stomach worm or 'Wireworm' of ruminants and is one of the most pathogenic parasites (Soulsby, 2006; Eguale *et al*., 2011). Males are 10-20 mm long and females 18-30 mm. The male has an even reddish colour, while in the female the white ovaries are spirally wound around the red intestine, producing the appearance of a barber's pole (Soulsby, 2006; Ferreira *et al*., 2013).

Life-cycle of *Haemonchus* species: The pre-parasitic development of *H. contortus* is very similar to that of any other strongyle (Srivastava *et al*., 1995; Ferreira *et al*., 2013). The eggs measure 70-85 μm by 41-48 μm and those passed in the faeces of the host contain an embryo divided into 16-32 cells. Egg hatches to the first stage larvae within 24 h (L_1). Under satisfactory environmental conditions infective larvae (L_3) are developed in four to six days. Optimal development takes place at 22-26°C. Low temperatures retard development and below 9°C little or no development takes place. The eggs and infective larvae of *H. contortus* are intolerant to desiccation and low temperatures (Soulsby, 2006; Ferreira *et al*., 2013).

The animals get infected by ingestion of free L_3 with infected grass. Larvae migrate into the gastric glands for two moults and then return to the lumen and become adult. Apparent clinical disease occurs in animals younger than two years of age, whereas, in older animals symptoms are less apparent or none (Kassai, 1999; Soulsby, 2006; Mohammed *et al*., 2013).

Pathogenesis: The developing larvae and adult worms, both may be pathogenic. Course of infection depends on the worm burden, age and nutritional status of the host (Soulsby, 2006; Ferreira *et al*., 2013). The principal feature of *Haemonchus* species infection is anaemia.

Dargie and Allonby (1975) and Soulsby (2006) have investigated the development of anaemia in sheep heavily infected with *H. contortus* with due emphasis on changes in the Packed Cell Volume (PCV) and serum iron. Infected animals lost large quantities of serum proteins into the gut with the mean faecal daily clearance of plasma being 210-340 mL day^{-1}. The adult and fourth larval stages suck blood and in addition move and leave wounds which cause haemorrhage in the abomasum. The average blood loss has been calculated at 0.05 mL/parasite/day and blood first appears in the faeces six to twelve days after infection (Soulsby, 2006; Mohammed *et al*., 2013).

Clinical signs: The clinical signs of haemonchosis may be divided into three syndromes as peracute, acute and chronic (Soulsby, 2006; Eguale *et al*., 2011). Peracute haemonchosis is uncommon but it may be seen when susceptible animals are exposed to a sudden massive infection (Mohammed *et al*., 2013). The extremely large number of parasites causes a rapidly developing anaemia, dark coloured faeces and sudden death from acute blood loss due to severe haemorrhagic gastritis (Soulsby, 2006; Hussain *et al*., 2011).

Acute haemonchosis is seen primarily when young susceptible animals become heavily infected. The anaemia is accompanied by hypoproteinaemia, oedema (bottle jaw) and death may occur (Srivastava *et al*., 1995; Mohammed *et al*., 2013). Faecal Egg Counts (FEC) are usually high (upto 100,000 EPG) and large number of parasites are present in the abomasum (1000-10,000) resulting in anaemia, dark coloured faeces, oedema, weakness and falling wool in sheep (Soulsby, 2006; Alemu *et al*., 2014).

Chronic haemonchosis is extremely common having considerable economic importance (Srivastava *et al*., 1995; Mini *et al*., 2013). The disease is due to chronic infection with a fairly low number of parasites (100-1000) showing 100% morbidity, but low mortality. Affected animals show inappetance, progressive weight loss, weakness and anaemia. Diarrhoea is seldom seen and animals may be even constipated (Soulsby, 2006; Ferreira *et al*., 2013).

PLANTS WITH ANTHELMINTIC ACTIVITY AGAINST *HAEMONCHUS* AND OTHER NEMATODES

***Calotropis*:** Garg and Atal (1963) reported remarkable vermicidal activity of calotropain (proteolytic enzyme isolated from the latex of *Calotropis procera*) and bromelain (an enzyme obtained as a by-product from pine apple industry) against *Oesophagostomum columbianum* and *Bunostomum trigonocephalum* of sheep origin compared to phenothiazine.

Anthelmintic property of *Calotropis procera* latex was investigated in experimentally induced *H. contortus* infection in Najdi sheep where there was reduction in the number of abomasal parasites. In the same study concentration dependant *in vitro* larvicidal activity was also demonstrated (Al-Qarawi *et al*., 2001).

Iqbal *et al.* (2005) studied the anthelmintic activity of *C. procera* flowers in comparison with levamisole through *in vivo* and *in vitro* methods and observed that, though the *in vitro* methods showed good anthelmintic activity, in *in vivo* only the aqueous extract and crude powder were effective which was also not significant compared to that of positive control, levamisole.

***Cucurbita*:** Sharma *et al.* (1971) reported on the significant *in vitro* effect of extracts of *Cucurbita pepo*, *Juglans regia*, *Momordica charantia*, *Musa paradisaca* and *Scindepsus officinalis* on the motility of adult *H. contortus* of goat origin. Therapeutic efficacy of *C. maxima* against clinical cases of nematodiasis in calves has been documented by Pradhan *et al.* (1992).

The anthelmintic effect of *C. maxima* seed powder was evaluated against *H. contortus* by Aswinikumar (1999) and found that it could cause effective reduction in EPG in sheep. The *in vitro* anthelmintic activity of *C. Mexicana* was analysed for its antiparasitic effect against *H. contortus* adult worms by Iqbal *et al.* (2001) in Pakistan and the results showed that *Cucurbita* possessed good wormicidal effect.

***Punica*:** The alcoholic extract of *Punica granatum* showed anthelmintic activity as revealed by a dose dependant inhibition of transformation of *H. contortus* eggs to larvae (Prakash *et al*., 1980). Therapeutic efficacy of *P. granatum* against clinical cases of nematodiasis in calves had been documented by Pradhan *et al*. (1992).

Aswinikumar (1999) conducted studies on the anthelmintic effect of *P. granatum* fruit rind, stem and root powders against *H. contortus* and found that all the components used were effective in reducing EPG in sheep. Mali and Mehta (2008) also reported on the efficacy of alcoholic extract of stem bark of *P. granatum* Linn in inhibiting transformation of eggs to larvae of *H. contortus* and also suggested that the stem bark contains an alkaloid pelletierine.

***Fumaria*:** Akhtar and Javed (1985) found *Fumaria parviflora* to have anthelmintic activity against *Trichostrongylus, Haemonchus* and *Trichuris* nematodes in sheep through their studies. Hordegen *et al*. (2003) conducted an *in vivo* study on the efficacy of *F. parviflora* in artificially infected lambs and observed a reduction in FEC.

The whole plant extract of *F. parviflora* was subjected to both *in vitro* and *in vivo* tests for anthelmintic activity against nematodes of sheep namely *Chabertia ovina*, *Haemonchus contortus* and *Strongyloides papillosus* by Al-Shaibani *et al.* (2009) and it was found that the plant extracts had anthelmintic activity.

***Artemisia*:** Hammond *et al.* (1997) reported that Jantana, a commercial ayurvedic anthelmintic preparation made from the plants, *Artemisia maritima*, *Brassica nigra*, *Cassia lanceolata*, *Vernonia anthelmintica*, *Cuprium sulphas* and *Embelia ribes* reduced FEC in cattle with mild to moderate mixed infections of *Haemonchus*, *Strongylus* and *Trichostongylus* from 300-1400 EPG, on the day of treatment to zero level, seven days after treatment.

Iqbal *et al*. (2004) carried out both *in vitro* and *in vivo* studies on the anthelmintic effect of whole plant of *A. brevifolia* against *Haemonchus contortus* and mixed species of GI nematodes in sheep and observed that the plant possessed anthelmintic activity against them. Tariq *et al.* (2009) evaluated the anthelmintic efficacy of aerial parts of *A. absinthium* against GI nematodes of sheep and found that the extracts produced results, which were comparable to albendazole both in *in vitro* and *in vivo* assays.

***Azadirachta*:** Hordegen *et al.* (2003) conducted an *in vivo* study on the efficacy of different plant products namely *Azadirachta indica, Ananas comosus, Vernonia anthelmintica, Embelia ribes* and *Caesalpinia crista* in lambs artificially infected with *H. contortus* and *T. colubriformis* and observed that none of these plants could cause reduction in FEC.

Dried, crushed leaves of *A. indica* fed along with concentrate feed was evaluated for its anthelmintic activity against *H. contortus* in sheep by Costa *et al.* (2006) and it was observed that none of the parameters evaluated such as EPG, worm burden, weight gain and haematocrit values of the treated group were significantly different from that of control group.

Six different plant species namely *A. indica*, *C. crista*, *V. anthelmintica*, *F. parviflora*, *E. ribes* and *A. comosus* were tested against exsheathed infective larvae of *H. contortus* using a modified methyl-thiazolyl-tetrazolium reduction assay by Hordegen *et al.* (2006) and proved that the plants had good anthelmintic activity *in vitro*. Maciel *et al.* (2006) conducted a study on the ovicidal and larvicidal activity of seeds and leaves of *Melia azadarach* extracts against *H. contortus* and reported that the ethanol extract of seed and leaf were very effective in inhibiting egg hatching and larval development respectively.

Chagas *et al*. (2008) tried to identify the anthelmintic efficacy of dried leaves of *A. indica* in Morada Nova sheep by feeding them orally. They observed that the treatment was not effective in controlling GI nematodes based on the EPG counts. *Azadirachia indica* extracts showed both *in vitro* ovicidal and larvicidal activity against *H. contortus* in the tests carried out by Costa *et al.* (2008). *In vitro* experiments were conducted to determine the anthelmintic effects of crude aqueous extracts of the leaves of *Azadrichta indica* on eggs and adults of *Haemonchus contortus.* Extracts of the leaves inhibited hatching of egg up to 100% at concentration of 1 mg mL^{-1} and very good activity against the adult worms of *H. contortus* at 4 mg mL^{-1} (Mohammed *et al*., 2013)

***Acacia*:** Dried leaves of two plants viz., *Acacia nilotica* (AN) and *Acacia karoo* (AK) were fed along with the basal diet to goats experimentally infected with *H. contortus* and the effect on FEC and worm burden were analysed by Kahiya *et al.* (2003) and they found that, though AK diets could cause significant decrease in the FEC and worm burden, the effect was non significant with AN.

Cenci *et al*. (2007) carried out a study to evaluate the effect of Condensed Tannins (CTs) present in the bark of *A. nigra* (*A. mearnsii*) on the natural worm infections of sheep on pasture and observed that there was a significant reduction in FEC and total worm count after eight weeks of feeding tannins. Another study conducted by Bachaya *et al.* (2009) on the fruit of *A. nilotica* showed that it was effective against *H. contortus* both *in vitro* and *in vivo*. Mohammed *et al*. (2013) reported i*n vitro* experiments to determine the anthelmintic effects of crude aqueous extracts of the stem bark of *Acacia tortilis* on eggs and adults of *Haemonchus contortus.* Extracts inhibited hatching of egg up to 100% at concentration of 1 mg mL^{-1} and showed very good activity against the adult worms of *H. contortus* at 4 mg mL^{-1}.

Tannin containing plants: The urgent need to find alternative or complementary solutions to the use of synthetic anthelmintic to limit gastrointestinal parasitism had led to the use of CTs in small ruminants (Waller, 1999; Paolini *et al*., 2003a). The initial results obtained from the field studies conducted in New Zealand suggested that the consumption of tanniferous forages could affect the biology of the GI worms mainly by decreasing egg excretion and therefore could contribute to modulate the epidemiology of these parasitic diseases (Niezen *et al*., 1998).

In most studies on bioactive forages, it has been postulated that secondary metabolites of some plants and particularly CTs might possess anti parasitic properties and this hypothesis had been substantiated by several *in vivo* (Athanasiadou *et al*., 2000; 2001a, b) or *in vitro* results (Molan *et al*., 2000, 2003). Paolini *et al.* (2003b) studied the *in vivo* effect of quebracho extracts containing CTs against *H. contortus* in goats and found that the presence of tannins was associated with a significant decrease in egg excretion.

Forages of mimosa, papaya, leucaena, guava containing CTs have been reported to possess anthelmintic activity against *H. contortus* by Nguyen *et al.* (2005). Heckendorn *et al.* (2007) have investigated the direct anthelmintic effects associated with the feeding of fresh tanniferous forages (chicory, birdsfoot trefoil and sainfoin) against established populations of *H. contortus* and *C. curticei* in lambs. Administration of all tanniferous forages was found to be associated with significant reduction of total daily FEC specific to *H. contortus* but not against *C. curticei.*

Iqbal *et al.* (2007) studied the effect of CTs against *H. contortus* both *in vitro* and *in vivo* and showed that, though *in vivo* there was reduction in FEC, *in vitro* it was effective only in preventing the nematode eggs from hatching. Alonso-Diaz *et al.* (2008) through their studies on the *in vitro* larval migration and kinetics of exsheathment of *H. contortus* larvae exposed to extracts of four tropical tanniferous plants namely *Acacia pennatula, Lysiloma latisiliquum, Piscidia piscipula* and *Leucaena leucocephala* revealed that the Larval Migration Inhibition Assay (LMIA) showed a dose-dependent anthelmintic effect for all the three plants except *P. piscipula*, even though all plants interfered with the process of L_3 exsheathment.

The *in vitro* anthelmintic effect of *Acacia gaumeri* (AG), *Havardia albicans* (*HA*) and *Quebracho tannin* extracts was evaluated on a Mexican strain of *H. contortus*, L_3 larvae through LMIA by Orduno *et al.* (2008) and the results revealed that HA and *Quebracho* extracts had clear anthelmintic effects but not the AG extracts. The anthelmintic properties of eight plant extracts such as chestnut, pine tree, heather, genista, brambles, oak tree, hazel bush and ash tree which composed browse in the southern part of France have been examined on the three main nematode species of small ruminants using *in vitro* assays such as LMIA and adult worm's motility inhibition assay (AMIA) by Hoste *et al*. (2009). Overall, consistent results were found mostly with plant extracts that possessed the highest tannin content.

Martinez-Ortiz-de-Montellano *et al.* (2010) studied the effect of a tropical tannin-rich plant *L. latisiliquum* on adult populations of *H. contortus* in sheep and suggested that a short term consumption of this legume could modulate directly the biology of adult *H. contortus* affecting the worm size and female faecundity. Alonso-Diaz *et al.* (2011) conducted a study on the tropical tannin rich plant extracts of *A. gaumeri, Brosimum alicastrum, H. albicans and Leucaena leucocephala* against *H. contortus* infective larvae and their results showed that tannin rich plant extracts were more potent inhibitors of the exsheathment *of H. contortus* L_3 larvae than their motility. Alemu *et al*. (2014) reported *in vitro* inhibitory effects of tannin rich plant extracts of *Ficus sychomorus, Phyllanthus sepialis* and *Rhus glutinosa* on egg hatchability, larvae development and adult mortality of *Haemonchus contortus*.

Miscellaneous plants: Gadzhiev and Eminov (1986) reported that powdered *Heracleum sosnowskyi*, a common pasture plant in Azerbaijan cured 60% of sheep with natural nematode infections, when fed over a period of 10 days.

Javed and Akhtar (1986) concluded that treatment with aqueous and methanolic extract of *Psoralea corylifolia* seed powder could cause reduction in EPG of mixed GI nematodes in sheep.

Aqueous and methanolic extracts of powdered *Hyoscyamus niger* seeds and *Moringa oleifera* roots were shown to reduce EPG in sheep having mixed nematode infection by Akhtar and Ahmed (1990).

The *in vitro* anthelmintic activity of some commonly used plant materials like *Allium sativum, Zingiber officinale* and *Ficus religiosa* were analysed for their antiparasitic effects against *H. contortus* adult worms by Iqbal *et al.* (2001) in Pakistan. The results showed that all the materials possessed good wormicidal effect.

The anthelmintic effect of leaves and fruits of *Myrsine africana* and *Rapanea melanophloeos* were tested in sheep experimentally infected with the nematode, *H. contortus* by Githiori *et al.* (2002) and it was observed that there was no significant reduction in FEC with any of the concoctions, at any of the doses tested.

Pessoa *et al.* (2002) evaluated the ovicidal activity of the essential oil of *Ocimum gratissimum* Linn and its main component eugenol against *H. contortus* using Egg Hatch Assay (EHA) and put forth evidence that both the essential oil and eugenol inhibited egg hatch at 0.5% level.

Ovicidal and larvicidal activity of *Spigelia anthelmia* Linn extracts against *H. contortus* were tested *in vitro* by Assis *et al.* (2003) and the results suggested that *S. anthelmia* extracts may be useful in the control of GI nematodes of sheep and goats.

The anthelmintic efficacy of the plant, *Albizia anthelmintica* against the nematode parasites, *H. contortus* of sheep and *Heligmosomoides polygyrus* of mice was studied *in vivo* by Githiori *et al.* (2003). The efficacy levels noticed were well below 70% of the reduction required in FEC in lambs and no overall significant effects on FEC in mice.

Sharma *et al.* (2003) evaluated the efficacy of fresh juice of *Xanthium strumarium* leaves against benzimidazole resistant *H. contortus* strain using EHA and Larval Paralysis Assay (LPA) and suggested that the undiluted fresh juice corresponded with a significant inhibition of egg hatch and larval paralysis

Alcoholic extracts of four tropical plants *Zanthoxylum-zanthoxyloides*, *Newbouldia laevis*, *Morinda lucida* and *Carica papaya* were screened *in vitro* for potential antiparasitic effects against eggs, infective larvae and adult *H. contortus* by Hounzangbe-Adote *et al*. (2005) and they opined that these four plants traditionally used by small farmers in Western Africa, possessed antiparasitic properties.

Bizimenyera *et al*. (2006) revealed the inhibitory effect of *Peltophorum africanum* extracts on the egg hatching and larval development of the parasitic nematode, *Trichostrongylus colubriformis* through *in vitro* tests.

Extracts of *Swertia chirata* were subjected to both *in vitro* and *in vivo* studies against GI nematodes of sheep by Iqbal *et al.* (2006) and the results revealed that there was significant anti nematodal effect for the extracts.

The *in vitro* and *in vivo* anthelmintic activity of crude aqueous and hydro alcoholic extracts of *Coriandrum sativum* seeds against *H. contortus* was evaluated by Eguale *et al*. (2007b) and it was found that it was effective *in vitro* in preventing egg hatch as well as motility of adult *Haemonchus* and *in vivo* it reduced both FEC and total worm count.

Eguale *et al.* (2007b) through another study, analysed the *in vitro* and *in vivo* anthelmintic activity of aqueous and hydroalcoholic extracts of ripe fruits of *Hedera helix* against *Haemonchus* and stated that both the extracts possessed significant anthelmintic activity.

Jabbar *et al.* (2007) subjected *Chenopodium album* whole plant and *C. crista* seed kernel to *in vitro* and *in vivo* analysis for efficacy against *Trichostrongylid* nematodes of sheep and proved that *C. crista* was superior to *C. album* in anthelmintic activity.

A study was conducted to evaluate *Anogeissus leiocarpus* leaf and *Daniellia oliveri* stem bark as effective remedy against ova, larvae and adult worms of *H. contortus* by Adama *et al.* (2009) and they could identify that both the plants possessed significant anthelmintic activity and *D. oliveri* stem bark extract was superior to *A. leiocarpus* leaves.

Oliveira *et al.* (2009) analysed the *in vitro* and *in vivo* efficacy of *Cocos nucifera* (liquid of green coconut husk fibre) against *H. contortus* and observed that though *in vitro* assays showed significant effect, the *in vivo* studies failed to show relevant effect.

In vitro ovicidal and larvicidal activity of the leaves and fruits of the aqueous and hydroalcoholic extracts of *Maesa lanceolata* and aerial parts of *Plectranthus punctatus* were evaluated on the egg and larvae of *H. contortus* using EHA and Larval Development Assay (LDA) by Tadesse *et al.* (2009) and they have identified good anthelmintic activity of both the plants.

Ademola and Eloff (2010) ascertained the i*n vitro* anthelmintic activity of *Combretum molle* leaves against *Haemonchus contortus* ova and larvae through their experiment.

In vivo studies were conducted in both gerbils and sheep for evaluating anthelmintic activity of orange oil emulsion against *H. contortus* by Squires *et al.* (2010) and they pointed out that orange oil emulsion may potentially be useful in the control of ovine haemonchosis.

Carvalho *et al.* (2012) studied the anthelmintic effects of plant extracts from *Piper tuberculatum, Lippia sidoides, Mentha piperita, Hura crepitans* and *Carapa guianensis* through *in vitro* and *in vivo* methods and reported that the extracts of *P. tuberculatum*, *L. sidoides* and *M. piperita* were found to be effective *in vitro* against *H. contortus*.

The *in vitro* anthelmintic activity of crude extracts of five medicinal plants (*Senna occidentalis*, *Leonotis ocymifolia*, *Leucas martinicensis*, *Rumex abyssinicus* and *Albizia schmperiana*) were tested by Eguale *et al.* (2011) to determine the possible anthelmintic activity against *H. contortus* by *in vitro* means and it was opined that all the plants had potential activity.

The study by Hernandez-Villegas *et al.* (2011) evaluated the leaf extracts derived from *Phytolacca icosandra* against infective L_3 larvae and eggs from *H. contortus* collected from sheep and the results revealed that the ethanolic and dichloromethane extracts possessed clear *in vitro* anthelmintic activity.

Hussain *et al.* (2011) conducted trials on the anthelmintic activity of *Trianthema portulacastrum* and *Musa paradisiaca* against GI nematodes of sheep and put forth evidence that both the plants possessed strong anthelmintic activity.

The traditional use of aqueous extracts of shoots and leaves of *Salvadora persica* and root bark of *Terminalia avicenoides* against strongyline nematodes in north eastern Nigeria was scientifically evaluated through *in vitro* anthelmintic assays and phytochemical screening by Reuben *et al.* (2011) and based on their findings the anthelmintic activity of these plants were validated.

Ombasa *et al.* (2012) studied the *Entada leptostachya* and *Rapanea rhododendroides* plants aqueous and solvent extracts for their *in vitro* antihelmintic activity against *Haemonchus contortus* adult worms. The results demonstrated 60-77% mortality by the plant extracts.

Ferreira *et al*. (2013) evaluated the *in vitro* anthelmintic effects of *A. muricata* aqueous leaf extract against eggs, infective larvae and adult of *H. contortus.* At higher doses, *Annona muricata* extract showed 84.91 and 89.08% of efficacy in Egg Hatch Test (EHT) and Larval Motility Test (LMT), respectively. In the adult motility test, worms were completely immobilized within the first 6-8 h of exposition to different dilutions of extract.

ANTHELMINTIC ACTIVITIES OF *ARISTOLOCHIA* PLANTS

General descriptions of *Aristolochia* plants: Two plants viz., *Aristolochia indica* and *Aristolochia bracteolata* which belong to the family 'Aristolochiaceae' are reported to have anthelmintic activity and are described in details below (Mini, 2012).

Arisiolochia indica A. bracteolata, Vernacular name, English Indian Birthwort, Tamil Thalaichuruli Aaduthinnapalai, Sanskrit Iswari Kitamari, Hindi Iswari Kitamar, Malayalam Iswaramooli Karalakam, Telugu Govilanalleswari Gadugagudupa.

Aristolochia indica is a perennial shrubby glabrous climber (Nair, 2007; Prajapathi *et al*., 2007; Mini, 2012). Stem colour is greenish or pale to dark purple and woody. The root is woody and grooved. Leaf is simple, alternate, broad form (12.5-7.5 cm) and narrow form (3.8-10cm) usually oblong, acuminate, short petioled leaves have a characteristic smell on crushing (Nair, 2007; Prajapathi *et al*., 2007). Flower is pale green or greenish white or light purplish in axillary cyme or fascicles with swollen or inflated basal part, contracted middle part and narrowly funnel shaped distal part. Fruits are oblong or globose, hexagonal. Seeds are flat, winged and brown in colour. The annual collection period for this plant is August-October. The plant grows throughout India (Nair, 2007; Prajapathi *et al*., 2007; Mini *et al*., 2013).

Folklore uses of *A. Indica*: The root of the plant is reported to have astringent, anodyne, antiperiodic, digestive, purgative, anthelmintic and anti-inflammatory properties (Nair, 2007; Mini *et al*., 2013). Traditionally the plant has been used in arthralgia, inflammation, leprosy, leucoderma, leprosy, skin diseases, colic, cough, catarrh, constipation, flatulence and dysmenorrhoea (Prajapathi *et al*., 2007). Additionally, Warrier *et al.* (1994) have mentioned two important specific uses against human intestinal round worms and all types of poisonous bites and stings.

Aristolochia bracteolata is a perennial prostrate herb with weak glabrous stems. Leaves are simple, alternate, reniform or broadly ovate and cordate at the base with a wide sinus upto 7.5 cm in diameter, finely reticulately veined (Nair, 2007; Prajapathi *et al*., 2007; Mini, 2012). Flowers are solitary with a large sessily, orbicular bract at the base, perianth tube cylindric with dark purple lip having revolute margins. Fruits are oblong-ellipsoid, 12-ribbed glabrous capsules. Seeds are deltoid with slightly cordate base. The plant is seen throughout India and annually it can be collected during December-January (Nair, 2007; Prajapathi *et al*., 2007; Mini *et al*., 2013).

Folklore uses of *A. Bracteolata*: The roots and leaves are bitter. Perusal of avaiable literature reveals that the plant is reported to have anti-inflammatory, appetizer and cathartic actions (Nair, 2007; Prajapathi *et al*., 2007; Mini *et al*., 2013). Traditionally used in conditions like kapha and vata, amenorrhoea, colic, ulcer, boils, syphilis arthralgia, eczema and other skin diseases. (Warrier *et al*., 1994; Kirtikar and Basu, 1998; Nair, 2007; Prajapathi *et al*., 2007; Bhutya, 2011). Mohamed *et al*. (2014) reported a bioassay-guided fractionation of methanol extract of *Aristolochia bracteolata* whole plant, its antimicrobial activity and identifed the active compounds in the extract.

INVITRO STUDY ON ANTHELMINTIC ACTIVITY OF *ARISTOLOCHIA* SPECIES OF PLANTS

The aqueous, ethanol and chloroform extracts of *A. indica* at 100 mg mL^{-1} produced 90, 70 and 64.69% inhibition respectively, in egg hatch assay of *H. contortus*. The aqueous, ethanolic and chloroform extracts of *A. bracteolata* at 100 mg mL^{-1} produced 80, 69 and 56% inhibition in egg hatch, respectively (Mini, 2012).

Aqueous and ethanolic extracts of *A. indica* were most effective, which produced larval development inhibition of 60.20 and 50.83% at 100 mg mL^{-1} dose and was found to be higher than that of fenbendazole at 1 µg mL^{-1}. However, aqueous extract of *A. bracteolata* was more effective compared to its other extracts (Mini *et al*., 2013).

Mini (2012) showed that the L_3 paralytic activity on *Haemonchus contortus* was consistently above 90% in aqueous, ethanol and chloroform extracts of *A. indica* at 100 mg mL^{-1}. On the other hand chloroform extract of *A. bracteolata* produced maximum larval paralytic activity (96%), whereas, aqueous, acetone and ethanol extracts maintained consistency with 80% efficacy.

Mini *et al*. (2013) showed that motility of adult worms was first suppressed by *A. indica* acetone extract followed by its chloroform extract. However, other extracts caused paralysis variably in the range of 120-175 min (*A. indica* aqueous and ethanol extracts, *A. bracteolata* chloroform and aqueous extracts).

Mini (2012) has used scanning electron microscopy after subjecting the adult *Haemonchus contortus* worms to 100 mg mL^{-1} concentration of the aqueous, ethanolic, acetone and chloroform extracts of *A. indica, A. bracteolata* and it was found that the extracts induced cuticular damages similar to the standard drugs.

CONSTITUENTS OF PLANTS WITH ANTHELMINTHIC ACTIVITY

Plant chemicals can be classified as primary and secondary constituents. Primary constituents include the common sugars, the proteins, amino acids, purines and pyrimidines of nucleic acids and chlorophyll which are essential for the plant metabolism (Prajapathi *et al*., 2007; Mini *et al*., 2013). Secondary constituents comprise of alkaloids, terpenoids, acetogenins and phenolics. They have a role in protecting the plant from environmental pressures or in controlling plant growth. Major classes of the plant chemicals include the terpenoids or isoprenoids, alkaloids and other nitrogen-containing metabolites, phenolic metabolites (Walton and Brown, 1999; Nair, 2007; Prajapathi *et al*., 2007).

Tannins: These are water soluble phenolic natural products that can precipitate proteins from aqueous solution. Molecular weight ranges from 500-20,000. Depending on the structure, they can be categorized into two major groups, the hydrolysable tannins and the condensed tannins (Nair, 2007; Alonso-Diaz *et al*., 2008).

Hydrolyzable tannins: Hydrolyzable tannins (HTs) are polymers esterified to a core molecule, commonly glucose or a polyphenol such as catechin. They are gallic or ellagic acid esters of sugars. These tannins can be easily hydrolysed with acid, alkali, hot water or enzymes (Prajapathi *et al*., 2007).

Condensed tannins (CTs): They are polyphenols of high molecular weight that consist mainly of oligomers or polymers of monomeric units of flavan-3-ols (catechin, epicatechin). They are also described as proanthocyanidins (Prajapathi *et al*., 2007). Depending on the chemical structure of the monomeric unit, particularly the number of hydroxyl groups they are classified into four groups; of which the commonest are procyanidins and prodelphinidins (Nair, 2007; Alonso-Diaz *et al*., 2008). Tannins form soluble and insoluble complexes with macromolecules such as protein, fibre and starch. Proanthocyanidins (CTs) are relatively stable in the digestive tract of the animal and rarely have toxic effects (Reed, 1995; Prajapathi *et al*., 2007).

Considerable research has shown that some plants not only affect the nutrition of animals, but also have antiparasitic effects (Waghorn and McNabb, 2003). For example, plants that contain CTs have these effects. The vast majority of studies investigating the effects of CTs on GI nematode parasites, either in experimental or in grazing conditions have been conducted using sheep (Niezen *et al*., 1996; Niezen *et al*., 1998; Molan *et al*., 2000; Athanasiadou *et al*., 2001a; Waghorn and McNabb, 2003).

Studies have also shown that CTs had an effect on GI parasite infections in goats (Kabasa *et al*., 2000; Kahiya *et al*., 2003; Paolini *et al*., 2003b). Investigations were conducted on tropical forages such as *Acacia karoo,* which was fed to goats infected with *H. contortus* leading to significant reductions of FEC and the number of parasites in the abomasum (Kahiya *et al*., 2003). The possible modes of action of CTs against GI nematodes have been reviewed by Kahn and Diaz Hernandez (2000) and Min *et al.* (2003).

Niezen *et al.* (1995) found that the performance of parasitized lambs could vary markedly depending on the forage species being grazed. They found that lambs grazing on *Hedysarum coronarium*, which contains CTs had lower FEC and lower worm burdens of *Trichostrongylus* species at slaughter than those grazing on *Medicago sativa*, which does not contain CTs. As per the observations of Asquith and Butler (1986) CTs affect abomasal nematode numbers and react and form complexes with protein. Binding can be highly specific for different tannins as well as different proteins. Plants containing CTs such as *Lotus pedunculatus* significantly increased growth of parasitized lambs (Niezen *et al*., 1998).

Athanasiadou *et al*. (2000) found that feeding *Quebracho* containing CT reduced FEC and worm burden in sheep infected with L_3 of *H. contortus* and *T. colubriformis*. The same team of authors in 2001 reviewed the effect of the same tannins through *in vitro* method and ascertained that the tannins decreased the viability of L_3 of the above said worms in the culture also. Molan *et al.* (2000) demonstrated that the CT extracted from *L.pedunculatus*, *L.corniculatus, H. coronarium* reduced the rate of both egg hatching, larval development and decreased the mobility of L_3 larvae.

In vitro studies have demonstrated that CTs extracted from forage legumes have direct inhibitory activity against L_1 and L_3 stages of deer origin lung worm larva and L_3 of deer and sheep origin GI nematode larvae as measured using a larval migration inhibition assay. Administration of *Quebracho* extracts containing high levels of CTs to goats experimentally infected with *H. contortus* was associated with a significant decrease in egg excretion (Paolini *et al*., 2003a). The study that was conducted by Cenci *et al*. (2007) to evaluate the effect of CT from *Acacia mearnsii* on sheep infected naturally with GI helminths proved that CT had an antiparasitic effect decreasing the FEC.

Four tropical tanniniferous plants namely *Acacia pennatula, Lysiloma latisiliquum, Piscidia piscipula* and *Leucaena leucocephala* were evaluated using LMIA against *H. contortus* L_3 larvae (Alonso-Diaz *et al*., 2008). The results have shown that the plant extracts with the highest levels of total phenol, tannins and CTs inhibited the migration of *H. contortus* in a dose dependant manner whereas *P. piscipula* which had the lowest levels of the various biochemical compounds did not affect migration (Alonso-Diaz *et al*., 2008, 2011).

Two native plants widely browsed by goats and sheep in Yucatan, Mexico possessing high content of CTs namely *H. albicans* and *A. gaumeri* were subjected to anthelmintic activity test against *H. contortus* through LMIA by Orduno *et al.* (2008). Anthelmintic effects obtained were consistent with the high content of CT and the high biological activity of its extracts, whereas *A. Gaumeri* in spite of its high CT content showed a low biological activity responsible for its lack of anthelmintic activity. The same study also evaluated the effect of commercial tannin preparation (*Schinopsis* species *quebracho*) through LMIA of *H. contortus* and found that it could produce a significant reduction in larval migration.

Hoste *et al.* (2009) compared *in vitro* anthelmintic effects of eight tannin-rich plants browsed by goats in the Southern part of France and found that the most consistent results were obtained with plant extracts possessing the highest tannin content, which supports the hypothesis that tannin content is one modulating factor in the anthelmintic activity of plants. Martinez-Ortiz-de-Montellano *et al.* (2010) evaluated the direct and indirect effects of consumption of a tannin rich plant, *L. latisiliquum* on adult *H. contortus* in sheep and suggested that the short term consumption of this fodder can adversely affect the adult worm population in sheep and could reduce the pasture contamination with nematode eggs (Alonso-Diaz *et al*., 2008, 2011).

Terpenoids: The terpenoids are characterized by their biosynthetic origin from isopentenyl and dimethylallyl pyrophosphates and their highly lipophilic properties (Nair, 2007; Prajapathi *et al*., 2007). They are present in leaves, glandular trichomes in bud exudates and bark resins. Chemically they are cyclic unsaturated hydrocarbons with varying degrees of oxygenation in the substituent groups attached to basic carbon skeleton (Nair, 2007). Terpenoid class comprises of monoterpenoids (volatile essential oil constituents), iridoids, sesquiterpenoids (higher boiling essential oil constituents), sesquiterpene lactones, diterpenoids, triterpenoid saponins, steroid saponins, cardenolides, phytosterols and cucurbitacins (Nair, 2007; Prajapathi *et al*., 2007).

Eugenol one of the main constituent of the essential oil of *Ocimum sanctum*, produced inhibition of egg hatch of *H. contortus* comparable to that of thiabendazole the positive control (Pessoa *et al*., 2002; Prajapathi *et al*., 2007). The anthelmintic activity of C*roton zehntneri* and *Lippia sidoides* essential oils and their major constituents, anethole and thymol were evaluated using *in vitro* assays with the eggs and larvae of *H. contortus* by Camurca-Vasconcelos *et al.* (2007) and they have reported that all the constituents were effective in preventing egg hatching and larval development.

The essential oil and its chief constituent eugenol showed potent *in vitro* anthelmintic activity against the nematode *Caenorhabditis elegans*. Eugenol has been suggested as the putative anthelmintic principle. The other important constituents reported are beta caryophyllene, sesquiterpene and monoterpenes (Mali and Mehta, 2008). Squires *et al.* (2010) attributed the anthelmintic activity of orange oil emulsion against *H.contortus* to an orange terpene and orange Valencia oil, the major component of which is d-limonene.

The sesquiterpene lactones (8-deoxy lactucin-DOL, lactucin-LAC) isolated from forage chicory were evaluated through EHA against *H. contortus* by Foster *et al.* (2011) and the results predicted that LAC had minimal effect on egg hatch whereas DOL was highly inhibitory for egg hatch. Typical monodesmoside saponin which destabilizes membrane and increases cell permeability by combining with membrane bound sterols have been shown to be associated with the anthelmintic activity of *C. molle* against *H. contortus* (Ademola and Eloff, 2010).

Phenolic metabolites: Phenolic compounds are aromatic structures bearing one or more hydroxyl groups (Prajapathi *et al*., 2007). Most of them are polyphenols (e.g., flavanoids) having several hydroxyl groups substituted with methyl and glycosyl groups. Biosynthetic origins of these are from phenylalanine. P-hydroxycinnamic acid formed from phenylalanine occupies a central role in the formation of various classes of plant phenol (Nair, 2007; Adama *et al*., 2009). The biosynthesis of flavanoids follows from the condensation of p-hydroxycinnamic acid with malonyl co-enzyme A to give chalcones. Phenolic constituents include anthocyanins, coumarins, flavanoids, flavones, flavonols, isoflavonoids and tannins (Prajapathi *et al*., 2007; Adama *et al*., 2009).

In vitro anthelmintic activity of *P. africanum* extracts on the egg hatching and larval development of the parasitic nematode *T. colubriformis* has been attributed to the presence of poly phenols in the leaves, bark and root of the particular plant with which the extracts were made (Bizimenyera *et al*., 2006). According to Adama *et al.* (2009) flavanoids, saponin and tannin present in two plants namely *A. leiocarpus* and *D. oliveri* were responsible for their *in vitro* anthelmintic effect against the eggs, L_1 larvae and adult stages of *H. contortus* and the traditional use of these plants by farmers in and around Burkino Faso seems to be justified.

The aqueous and hydro-alcoholic extracts of *Coriandrum sativum* were tested for its inhibitory effects on egg hatch and the motility of adult *H. contortus* and further its affects *in vivo* were analysed by Eguale *et al.* (2007, 2011).The anthelmintic efficacy of the extracts have been suggested to be due to the presence of secondary metabolites like flavanoids and alkaloids. Flavones namely yuankanin and amentoflavone were isolated from *Struthiola argentea*, tested to ascertain anthelmintic activity against *H. contortus* by *in vitro* means and was found to be potent in inhibiting larval motility (Ayers *et al*., 2008).

Alkaloids and other nitrogen containing metabolites: Nitrogen containing metabolites of plants with organic bases are usually linked into a five or six carbon cyclic system. Different alkaloids are indole, quinoline, isoquinoline, quinolizidine, pyrrolidine and pyrrolizidine and tropane. Soetan *et al.* (2011) attributed the *in vitro* anthelmintic activity of the seeds and leaves of African locust bean, *P. biglobosa* against bovine nematode eggs to alkaloids, cardenolides, saponins and tannins.

Ascariasis in cattle and buffalo being very common in Pakistan and of considerable economic importance, Akhtar (1984) evaluated the efficacy of santonin against *Toxocara vitulorum* in buffalo calves which were naturally infected. Santonin was synthesized from *Artemisia maritima* flower heads and was available commercially in Pakistan as a broad spectrum anthelmintic. Glycosides extracted from roots of *Saussurea lappa* resulted in reduction of EPG in sheep and in buffalo calves infected with mixed species of nematodes (Akhtar and Makhdoom, 1988).

An active principle (D-3-o-methyl chiroinositol) isolated from the methanolic extract of stem bark of the plant, *Piliostigma thonningii* has been reported to cause paralysis of third stage larvae of *Haemonchus contortus* (Asuzu *et al*., 1999). The anthelmintic activity of the fresh juice of *Xanthium strumarium* leaves against *H. contortus* has been attributed to the alkaloids and sesquiterpene lactones (Xanthinin, xanthumin and xanthatin) isohexacosane, chlorobutanol, stearyl alcohol, α and β sitosterol, palmitic acid and xanthanolides (Sharma *et al*., 2003).

Phytochemical analysis of the extracts of *Melia azedarach* which possessed ovicidal and larvicidal activity against *H. contortus* revealed the presence of triterpenes, alkaloids and condensed tannins (Maciel *et al*., 2006). The anthelmintic activity of *S. persica* and *T. avicenna* against strongyle nematode of small ruminants was reported to be due to the collective action of different phytochemical constituents of these plants namely terpenes, sterols, flavonoids, saponins, tannin, reducing sugars, antracenocides, flavone aglycone and some alkaloids (Reuben *et al*., 2011).

CONCLUSION AND FUTURE RESEARCH NEEDS

Small ruminants represent a major asset among resource-poor small holder farmers. Haemonchosis is highly pathogenic nematode parasite of small ruminants causing haemorrhagic anaemia, mortality and heavy loss in production. Development of resistance to the currently used anthelmintics has resulted in the failure of treatment for haemonchosis. Hence, as an alternative solution to this problem, many anthelmintic principles with different modes of action have been isolated from plants which could be of value in the treatment of resistant nematodes. Anthelmintics with different modes of action are the necessity of the hour, which has changed the focus to other sources like plants. Screening of medicinal plants for their anthelmintic activity has become great scientific interest. Ethnopharmacological surveys provide the rationale for selection and scientific investigation of medicinal plants. Herbal drugs were extensively used as anthelmintics in the developed world before the era of broad spectrum drugs. Many currently available therapeutic compounds are plant derived or synthetic analogues derived from those compounds.

Large numbers of studies have shown that the various plants have promising anthelmintic activity against haemonchosis through the *in vitro* tests. However, the effects produced needs further confirmation in the biological system using *in vivo* trials. Pilot scale *in vitro* and *in vivo* studies need to be conducted for confirmation of different plant extracts for practical use in the long run. Electron microscopic studies need to be conducted more extensively to understand mode of action of the different active principles. Quality control and safety pharmacology studies need to be conducted *in vivo* for any side effects of the phytocheicals. Moreover, the active phytochemicals present in the extracts need to be isolated in the pure form and studies should also be conducted on the anthelmintic activity of these components in the future.

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