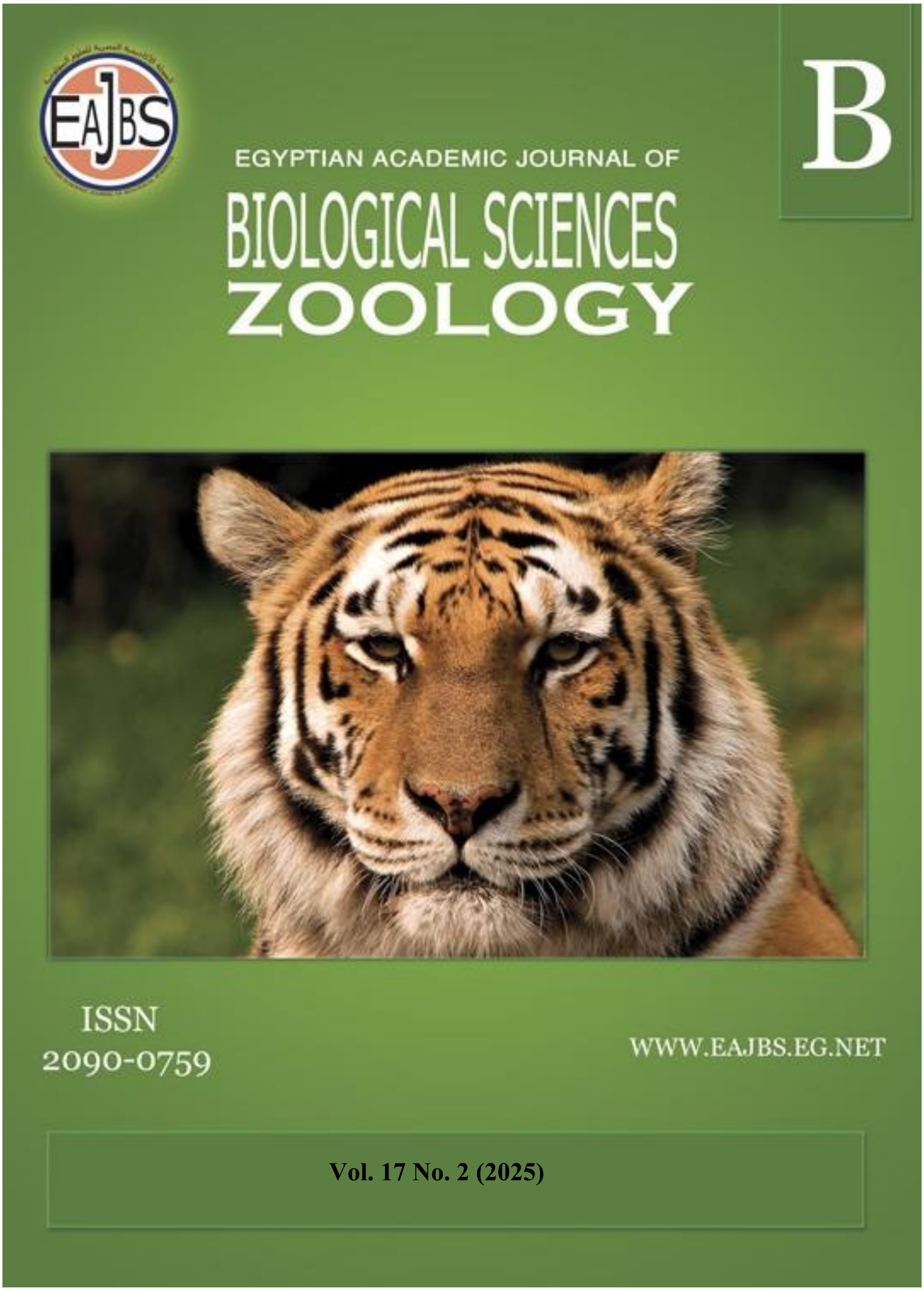

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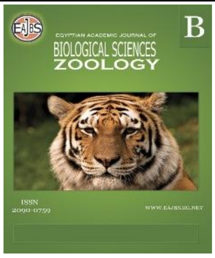

Critical Appraisal of Indian Medicinal Plants as Anthelmintic Agents: Emphasis on *In Vitro* vs. *In Vivo* Models in Ruminant Helminthiasis

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ABSTRACT

Gastrointestinal helminth infections in ruminants pose a serious threat to Indian livestock, with synthetic anthelmintics becoming increasingly ineffective due to resistance and cost barriers. This review systematically evaluates the anthelmintic potential of Indian medicinal plants as alternative therapies, emphasizing the distinction between in vitro and in vivo models. A total of 56 studies were included, predominantly in vitro, with only limited in vivo validation. The most frequently studied plant families include *Apiaceae*, *Euphorbiaceae*, and *Fabaceae*. While many plant extracts demonstrated promising effects against helminths in screening assays using free-living organisms (e.g., *Caenorhabditis elegans*, *Pheretima* spp.), these findings cannot be directly equated with clinical efficacy. Our analysis underscores the need for biologically relevant models and standardized evaluation protocols. We highlight critical gaps in methodological rigor, model relevance, and regional specificity in helminth susceptibility. This review advocates for future research prioritizing in vivo trials, phytochemical characterization, and pharmacodynamic profiling to transition from preliminary screening to validated therapeutic applications.

INTRODUCTION

Livestock including animal husbandry, dairy industry, and fishing industries plays a vital role in sustaining the livelihood of rural communities (poor farmers, consumers, dealers, and labourers) in developing countries (Upton, 2004). In India, small ruminants such as goats and sheep are indispensable to agricultural and allied sectors due to their high reproductive rates, low maintenance costs, and cultural acceptance of meat and milk products. These animals are often reared by landless and marginal farmers, especially women, for whom livestock provides not only nutritional security but also economic resilience. Enhanced small ruminant production is thus integral to sustainable rural development and improving the socio-economic status of disadvantaged populations. The Indian ruminant sector, which accounts for nearly 12% of the total value added by animal husbandry, is a critical component of the national economy (Kumar and Roy, 2013; Sharma, 2004).

However, gastrointestinal (GI) helminth infections represent a major challenge to ruminant productivity in India. Parasitic infestations, particularly by nematodes, significantly impair livestock health by causing weight loss, reduced feed conversion efficiency, anaemia, lowered milk yield, and in severe cases, death with substantial output declines in ruminants worldwide (FAO, 1992; Gall, 1981; Kuchai *et al*., 2011; Manikkavasagan *et al*., 2013; Singh *et al*., 2013). Hence, it is crucial to effectively manage and control helminth diseases by using anthelmintics for maximizing ruminant production yields (Fitzpatrick, 2013). Regional studies across the country including those from Ladakh, Kashmir, Tamil Nadu, and the sub-Himalayan zones consistently report high burdens of helminth infections (Bihaqi et al., 2020; Dixit et al., 2017; Kalkal et al., 2021; Rialch et al., 2013). Among them, *Haemonchus contortus* has emerged as the most prevalent and pathogenic species, particularly in sheep. The economic burden posed by these parasites is substantial, affecting both individual farmers and the broader agricultural economy.

For decades, control strategies have relied heavily on synthetic anthelmintics, including benzimidazoles, imidazothiazoles, and macrocyclic lactones. While initially effective, indiscriminate use has led to widespread anthelmintic resistance (AR), which has been documented in various Indian states such as Uttarakhand, Haryana, and Karnataka (Coffey *et al*., 2007). This resistance is exacerbated using single-drug regimens, under-dosing, and lack of rotation among drug classes. Moreover, commercial anthelmintics are expensive, often inaccessible to rural farmers, and pose risks of toxicity and environmental residues (Waller, 2003). As a result, the need to explore sustainable and cost-effective alternatives has gained momentum. Traditional phytotherapy, long embedded in Indian medical systems like Ayurveda and ethnoveterinary practices, offers a promising avenue (Athanasiadou *et al*., 2007; Singh *et al*., 2008). Many medicinal plants possess bioactive compounds that could serve as natural anthelmintics with distinct mechanisms of action, potentially reducing the likelihood of resistance. Thus, integrating these botanical approaches into modern parasitic control frameworks could be a viable solution for long-term livestock health and productivity.

MATERIALS AND METHODS

A comprehensive literature review was conducted to evaluate the anthelmintic properties of medicinal plants reported from India between 2001 and 2023. Electronic databases including Web of Science, PubMed, and Scopus were systematically searched using combinations of keywords such as “anthelmintic,” “gastrointestinal helminths,” “ruminants,” “India,” “medicinal plants,” “in vitro anthelmintic,” and “in vivo anthelmintic.” Regional Indian journals and ethnoveterinary sources were also manually screened to capture local studies not indexed in global databases. The inclusion criteria were defined as original, peer-reviewed, full-text research articles that investigated the anthelmintic effects of plant-derived substances either in crude form or as isolated phytochemicals, against helminths affecting ruminants. Both *in vitro* and *in vivo* models were considered, including those using screening organisms like *Pheretima posthuma* and *Caenorhabditis elegans*, provided they demonstrated direct experimental outcomes such as parasite mortality, paralysis, or faecal egg count reduction. Studies were excluded if they focused on non-ruminant hosts, lacked experimental validation, or examined non-helminth organisms such as bacteria or ectoparasites. A total of 192 articles were initially retrieved; after removing duplicates and screening for relevance and methodological adequacy, 96 studies met all eligibility criteria and were included in the final synthesis. Data extracted from these studies included plant name, family, part used, solvent type, test species, helminth target, model system, and observed outcomes. The selection process is summarized in Figure 1, following the PRISMA 2020 guideline for systematic reviews (Matthew *et al.* 2021).

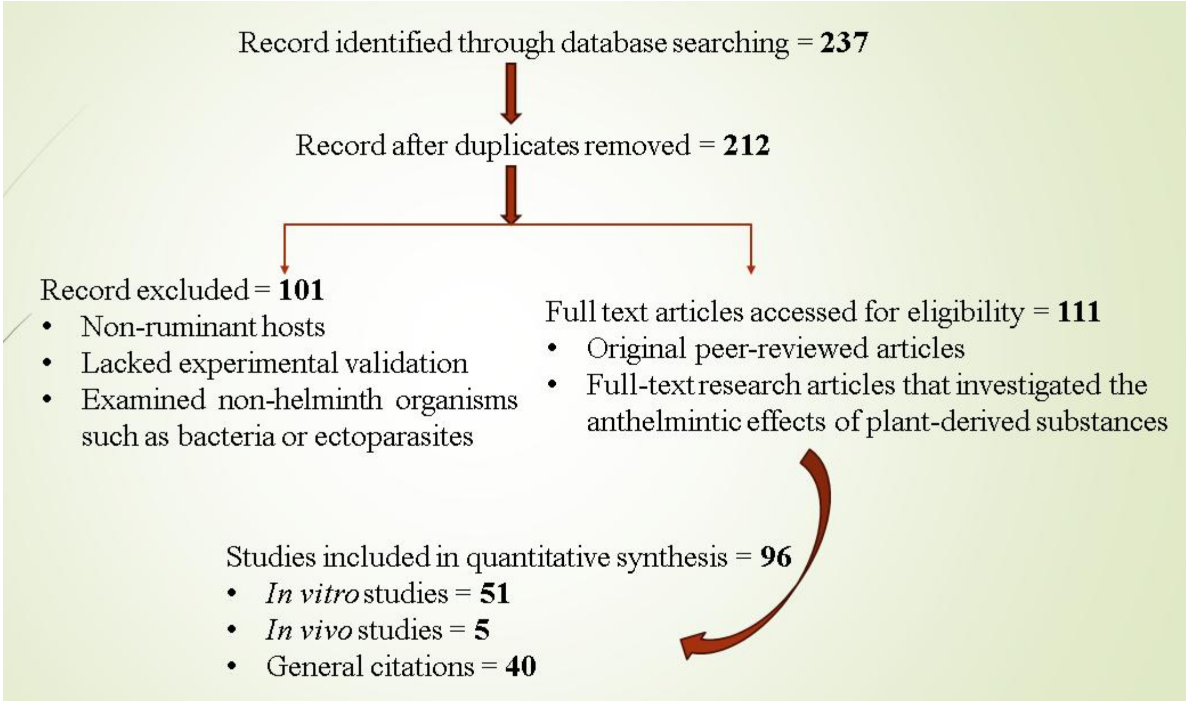

Fig. 1: PRISMA Flow Diagram of Study Selection Process.

RESULTS AND DISCUSSION

Results of Experimental Studies on Plant-Based Anthelmintics:

Anthelmintics have been the predominant method of managing helminth parasites in ruminants for several decades (Baloyi *et al*., 2012). Nonetheless, significant and continuous advancements have been achieved in recent years about the development of anthelmintic resistance in the parasitic worms that infect ruminants. Anthelmintic resistance (AR) is the term used to describe the heritable reduction in sensitivity of a population of parasites to a treatment that was previously successful against those parasites as compared to a normal population of the same species (Abbott *et al*., 2012). First, the genes that resist are not widespread in the population or come from rare mutations. However, as choice persists, both their frequency and the fraction of resistant parasites grow (Geary *et al*., 2012). The occurrence of AR was first documented in 1964 for *Haemonchus contortus*, a parasite that showed resistance to benzimidazole in sheep (Drudge *et al*., 1964). Regular reports of resistance in sheep parasites appeared within a decade of the first documentation of AR. Subsequently, resistance in equine and cattle nematodes was documented (Jackson *et al*., 2006). Despite the effectiveness and rapidity with which anthelmintics have been implemented, resistance has developed among nematodes in several sheep-producing nations, including Australia, South Africa, New Zeland, Switzerland, and Italy (Ahmed *et al*., 2010; Cringoli *et al*., 2007; Leathwick *et al*., 2001; Overend *et al*., 1994; Schnyder *et al*., 2005).

The initial documentation of AR to phenothiazine and benzimidazole (thiabendazole) drugs in organized sheep farms of Uttarakhand, India, was released in 1976 (Varshney and Singh, 1976). The significance of AR was marginalized until 1990 when reports of the condition began to circulate across India (Yadav, 1990). AR was primarily observed in sheep on a global scale until 1983 when Kettle *et al*. reported the initial instance of benzimidazole resistance in goats (Kettle *et al*., 1983). In South Africa Ivermectin, formerly hailed as a miraculous treatment in the 1980s, proved to be ineffective against GI nematodes (Carmichael *et al*., 1987). However, reliance on early reports without incorporating recent findings limits the contemporary relevance of this discussion. In recent years, numerous reports of AR have emerged from different agro-climatic zones of India, clearly highlighting regional disparities. In the sub-Himalayan region of northern India, Rialch *et al.* (2013) reported benzimidazole resistance in *Haemonchus contortus*. From central India, Dixit *et al.* (2017) documented ivermectin resistance in goats. In Kashmir, Bihaqi et al. (2020) also found reduced efficacy of benzimidazoles in sheep. From northwestern India, Kalkal et al. (2021) reported multi-drug resistance in Haryana. Similarly, in southern India, studies from Karnataka (Amulya *et al.,* 2016), Kerala, Das *et al.* (2023) and Tamil Nadu (Varadharajan and Vijayalakshmi, 2015) confirmed resistance to multiple anthelmintics. These findings reflect how variations in climate, grazing patterns, and treatment practices across India contribute to different AR patterns. The emergence of AR in ruminants is principally determined by four key factors: the frequency of treatment, the use of single-drug regimens, the targeting of treatments, and the failure to administer an adequate dose (Geerts *et al*., 2001).The use of plants for medicinal purposes in India may be traced back to the period of 3500-1800 B.C., as documented in the Rig-Veda, which highlights the therapeutic properties of numerous plants. Folklore also carries knowledge on the subject. Initially, anthelmintic plants have been studied using *Pheretima* and *Caenorhabditis* as test worms. In later years, helminth parasites from all three major groups such as nematodes (roundworms), cestodes (tapeworms), and trematodes (flukes), were used as experimental models to evaluate the efficacy of roots, tubers, stems, leaves, flowers, fruits, and seeds, whole plants as anthelmintics. Comparisons of their efficacy have been made with synthetic anthelmintics like praziquantel, albendazole, and piperazine citrate, etc. There have been reports of various flora in India possessing anthelmintic properties with some examples as follows:

A study was conducted to assess the effectiveness of crude *Millingtonia hortensis* extracts against Indian earthworms. The results indicated that at concentrations of 10, 20, 30, 40, and 50 mg/ml, conventional anthelmintics exhibited superior efficacy compared to the aqueous extract (Nagaraja *et al*., 2011). *Padina tetrastromatica* (Seaweed) extracts were tested for anthelmintic action, Raillietina tetragona finding that methanolic extract had greater anthelmintic action than usual medication, based on dose-dependent activity (Selvi *et al*., 2016). Another study used Indian earthworms to test the *in vitro* anthelmintic potency of ethanolic and carbon tetrachloride extracts of *Coriandrum sativum* Linn. at different concentrations by measuring worm paralysis and death. Ethanolic extract of *Coriandrum sativum* Linn. paralyzed earthworms faster than carbon tetrachloride extract (Chandan *et al*., 2011). It was revealed that both ethanolic and petroleum extracts of the aerial parts of *Ipomoea eriocarpa* show potent anthelmintic activity. Eleven phytoconstituents were identified in the petroleum ether extract and nine in the ethanol extract via GC-MS analysis; three of these phytoconstituents were shared by both extracts (Innovare 2014). *Pyrostegia venusta* extracts were evaluated at different concentrations for worm paralysis and death. Chloroform extract showed effective anthelmintic action against *Pheretima posthuma*, while methanolic extract showed significant paralysis and death times. Both extracts were less powerful than piperazine citrate (Nisha *et al*., 2012). Laboratory setting research was conducted to examine the anthelmintic activity of *Imperata cylindrica* against *Raillietina tetragona* and *Ascaridia galli.* Results showed that the plant extract, like albendazole, was dose-dependent and effective against both helminths, causing structural alterations like spine clumping, tegumental folds, lip collapse, and microtriches erosion in tapeworms (Lalthanpuii *et al*., 2020). Paralysis and worm death times of *Enicostemma littorale* were measured at 25, 50, 100, and 200 mg/ml of all extracts in presence of Albendazole as the reference and saline as control. All extracts showed dose-dependent action. Anthelmintic activity of *Corallocarpus epigaeus* roots and rhizomes was evaluated on adult earthworms *Lampito marutii*, *Eudrillus eugine*, and *Eisenla foetida* using piperazine citrate as the reference standard. Both alcoholic and aqueous extracts caused paralysis and death in worms at all dosage levels (Kirubha *et al*., 2011). The effectiveness of aqueous and ethanol extracts of the above-ground parts of *Artemisia absinthium* was assessed using tests measuring the inhibition of worm movement and a decrease in the number of eggs in the feces of sheep infected with nematodes. According to the research, ethanol extract was shown to be more effective in preventing worm movement and decreasing the number of eggs in the feces (Tariq *et al*., 2009). The research of Sujith *et al*. (2015) assessed the anthelmintic efficacy of leaf extracts from *Ocimum sanctum*, *Murraya koenigii*, and *Mallotus phillipensis* by an egg hatch test and evaluating the larvicidal activity. The phytochemical study revealed tannins and flavonoids in all extracts, with maximum ovicidal activity in Murraya's chloroform fraction. The extracts showed no adverse reactions and minimal larvicidal concentration (Sujith *et al*., 2015).

Jeyathilakan *et al*. (2010) investigated the *in vitro* impacts of Citronella and Neem oils on *Fasciola gigantica* with potential anthelmintic properties shown by 1% Citronella oil while Neem oil did not demonstrate such effects. The research further examined the morphology and histology of both treated and control fluke specimens (Jeyathilakan *et al*., 2010)**.** A study found that both aqueous and alcoholic extracts of *Citrullus colocynthis* fruit effectively killed *Cotylophoron cotylophorum*, with the alcoholic extract being more potent (Swarnakar *et al*., 2020)**.** Praziquantel (PZQ) and *Spilanthes acmella* were compared for anthelmintic action against *Raillietina echinobothrida*, an intestinal cestode. PZQ was more potent, causing significant tegument shrinkage, folds, sucker constriction, spine displacement, and microtriche erosion. The plant extract shrank and folded the body but not the scolex (Lalthanpuii *et al*., 2020). The research of Choudhary *et al*. (2018) assessed the *in vitro* anthelmintic efficiency of *Hedychium spicatum* extracts using an adult motility test. The methanolic extract showed the greatest effectiveness against *Haemonchus contortus* at doses of 2%, 4%, 6%, and 8%. Additionally, the methanolic extract demonstrated the shortest time for paralysis and death of the parasite compared to other extracts (Choudhary *et al*., 2018). β-sitosterol extracted from the rhizomes of *H. spicatum* showed strong anthelmintic properties against adult Indian earthworms, *Pheretima posthuma*. The findings demonstrated that β-sitosterol has a high affinity for the active pocket of tubulin, surpassing that of the conventional medication, Piperazine citrate. The duration of paralysis and mortality caused by β-sitosterol at a concentration of 40 mg/mL was like that of Piperazine citrate, as reported by Sravani *et al*. (2015). The aerial components of *Chenopodium album* were extracted from Indian adult earthworms *Eisenia foetida* using microwave-assisted extraction with petroleum ether, ethyl acetate, methanol, hydroalcoholic, and aqueous solvents (referred to as CAPE, CAEE, CAME, CAHE, and CAAE, respectively). Except for CAAE, all extracts immobilize and exterminate earthworms. The potency of CAEE extract surpassed that of piperazine citrate suspension since it induced paralysis and caused death at a concentration of 10 mg/ml. The anthelmintic action of CAEE is derived from two main constituents, NG and DG, which induce a state of flaccid, reversible paralysis in the body wall muscles (Choudhary *et al*., 2021). In sheep, *Calotropis procera* latex inhibits *H. contortus* infection with similar results against *Haemonchus contortus*. The same goes for *Osetertagia*, *Nematodirus*, *Dictyocaulus*, *Teania*, *Ascaris*, and *Fasciola* (Al-qarawi *et al*., 2001; Shivkar and Kumar, 2003). The leaf extracts of *Achyranthes aspera*, namely acetone, chloroform, ethyl acetate, hexane, and methanol, have been shown to induce death in the early fourth-instar larvae of *Aedes aegypti* and *Culex quinquefasciatus* within 24 hours. This confirms the anthelmintic function of the extracts (Bagavan *et al*., 2008). An *in vitro* study was conducted to evaluate the anthelmintic effectiveness of the methanolic extract of *Fumaria indica* against *Haemonchus contortus*, a kind of gastrointestinal worm found in sheep. After being exposed to various treatments for 30 minutes, the crude extract exhibited an average death rate of 94.44% (Khan *et al*., 2014). The *in vitro* study demonstrated that the crude methanolic extracts of *Nepeta cataria* caused paralysis and/or death in live *Haemonchus contortus* worms within 8 hours ($P > 0.05$). Sheep that were naturally infected with a combination of several species of gastrointestinal nematodes saw a 73.69% reduction in egg counts on day 15 when given methanolic extracts at a dosage of 2 g per kg of body weight (Bandh *et al*., 2011). *Euphorbia helioscopia*, a plant known for its gastrointestinal benefits, has been found to have dose-dependent anthelmintic effects on *Haemonchus contortus* worms, with its stem, leaves, and flowers inhibiting egg hatching less than levamisole in both aqueous and methanolic extracts (Lone *et al*., 2012). According to Swargiary *et al*. (2016), the methanolic extract of *Lippia javanica* showed effective anthelmintic action against *Paramphistomum* sp., resulting in paralysis (0.56±0.09 h) and death time (0.56±0.09 h) at 50 mg/ml.

Swargiary *et al*. (2021) investigated the mortality rate of trematode parasites when exposed to different amounts of extracts from *A. scholaris*, *C. halicacabum*, *H. sibthorpioides*, and *H. japonicum*. *H. japonicum* showed the highest parasite death rate, followed by *H. sibthorpioides*, *C. halicacabum*, and *A. scholaris*. The alcoholic extract of *Alpinia nigra* resulted in significant damage and disruption of the outer covering of *Fasciolopsis buski*, known as the tegument. This produced structural alterations, such as the reduction of the inner tissue and the detachment of connecting tubules (Roy *et al*., 2009). *Ascaridia galli*, when exposed to a methanol extract of *Acacia oxyphylla* at concentrations of 5-20 mg/ml, experienced burst ovaries, malformed egg membranes, disconnected cuticles, disintegrating muscle layers, and ultimately perished (Lalchhandama, 2008). Banerjee *et al*. (2019) isolated andrographolide from *Andrographis paniculata*, an Indian botanical species often used in traditional Indian medicine for its vermifugal properties. The chemical had significant ovicidal and larvicidal actions at doses of 0.125 µg/mL and 19 µg/mL, respectively. The study tested the anthelmintic activity of *Cleome viscosa* and *Cleome burmanni* extracts against *Pheritima posthuma*, an Indian earthworm. The extracts were tested at doses ranging from 50-2000 µg/ml, with worm paralysis and death time as the primary outcomes. The methanol extract of *Cleome viscosa* showed the most effective therapy (Pillai *et al*., 2011). The methanolic extract of *Mimusops elengi* showed effective anthelmintic activity against *Pheretima posthuma* at a concentration of 5 mg/mL. It caused paralysis and death of the worms at 163.3 and 223.2 minutes, respectively (Jana *et al*., 2010). The extracts derived from the shell of *Anacardium occidentale*, the fruit of *Illicium verum*, and the seed of *Artocarpus heterophyllus* exhibited anthelmintic effects that depended on the dosage. These effects included the prevention of egg hatching, paralysis of larvae, and death of worms. The shell of *Anacardium occidentale* exhibited the highest level of activity, causing paralysis in 100% of L_3 larvae and reducing egg hatch, larval paralysis, and adult worm mortality at lower concentrations compared to extracts from *I. verum* fruit and *A. heterophyllus* seeds. All samples markedly inhibited lactate dehydrogenase (LDH) activity in adult *H. contortus* (Davuluri *et al*., 2020). The ethanolic and aqueous extracts of *Trachyspermum khasianum* demonstrated a dose-dependent anthelmintic action at 10, 20, and 40 mg/ml compared to the standard medication (Sutnga *et al*., 2020). The study investigated the effects of *Trachyspermum ammi* leaf extracts on Indian earthworms. The extracts and Albendazole were administered at different concentrations, and the paralysis and death times decreased dose-dependently. The extracts were found to be anthelmintic, with paralysis times of 2.07, 4.65, and 9.47 minutes and death times of 6.17, 9.8, and 9.8 minutes. The study supports the use of *T. ammi* leaf for helminthoses treatment (Tambe and Mahadik, 2020).

The anthelmintic activity of *Punica granatum* fruit peel methanolic extract was observed to be the highest among all the extracts in a dose-dependent manner (Mahajan *et al*., 2014). The research examined by Singh *et al*. (2013) showed the anthelmintic properties of extracts derived from the leaf, stem, and fruits of *Cyamposis tetragonoloba* against *Pheretima* *posthuma* test worms. Results showed a decrease in paralyzing and death time with different concentrations. The ethanol and aqueous extracts of fruit and leaves showed significant activity, while stem part extracts were not effective. The results support the use of fruits and leave of *Cyamposis tetragonoloba* as an anthelmintic agent (Singh *et al*., 2013). In another study, it was highlighted that crude leaf neem powder has anthelmintic activity as it showed a significant decrease in eggs per gram (EPG) after the post-treatment with crude extract of neem (Jamra *et al*., 2015). *Allium sativum* and *Cucurbita maxima* showed good anthelmintic activity in dose and time-dependent manner (Masanta *et al*., 2019). The methanolic and aqueous extracts of *Curcuma longa* showed notable anthelmintic activity against *Haemonchus* spp, a gastrointestinal parasite in goats. The extracts induced paralysis and mortality within 12 hours at all doses, as compared to the negative control. The effectiveness of the rhizome extracts increased in a dose-dependent manner (Pandey *et al*., 2018). Vinav *et al*. (2016) investigated the impact of the fruit of *Momordica charantia* on *E. foetida*, findings that aqueous and methanolic extracts containing 10 mg/ml exhibited paralysis and death times of 117 and 100 minutes and 151 and 140 minutes, respectively. Different research conducted a comparison of the anthelmintic properties of aqueous and ethanolic extracts derived from the seeds of *Apium leptophyllum* and *Apium graveolens*, employing adult earthworms from India. The findings indicated that the ethanolic extracts exhibited significant efficacy in comparison to the conventional Albendazole, although the aqueous extract also showed anthelmintic action (Shiba *et al*., 2020). The methanolic and aqueous extracts of *Euphorbia* were tested for their anthelmintic activity. The effects of *Thymifolia* were examined on *Pheretima posthuma* and *Ascaridia galli*. The extracts at different concentrations exhibited substantial anthelmintic action, which increased proportionally with the dosage (Kane *et al*., 2009). One of the studies investigated the anthelmintic activity of *Carum carvi* seeds' aqueous and ethanolic extracts on Indian adult earthworms. The extracts showed significant activity compared to standard Albendazole, with ethanolic extracts showing more effectiveness. However, aqueous extract also showed anthelmintic activity (Morris *et al*., 2016). The anthelmintic activity of *Euphorbia milii* leaves was investigated in adult *Pheretima posthuma*, using albendazole as a reference standard and it was found that varying methanolic concentrations, as a potential treatment for nematodiasis (Nazmi *et al*., 2023). The list of some anthelmintic plants that are used in India, along with their common names and potential mechanism of action are provided in Table 1. Figure 2 illustrates that about 46 plant groups exhibit anthelmintic action. The family *Apiaceae*, followed by *Euphorbiaceae* and *Fabaceae*, has the highest number of plants with anthelmintic potential.

Table 1: List of some anthelmintic plants from the Indian Medicinal Data Base with their potential mechanism of action

Common Name	Botanical Name	Family	Parts Used	Potential mechanism of action
Tamarind	*Tamarindus indica*	Fabaceae	Leaves nd Bark	Tannins in tamarind inhibit the egg hatching and motility of L_1 and L_2 stage larvae
Palash	*Butea monosperma*	Fabaceae	Seeds	Alkaloids in Palash cause starvation in helminth parasites
Khimp	*Leptadenia pyrotechnica*	Apocynaceae	Whole plant	Leading to paralysis of worms
Apple of Sodom	*Calotropis procera*	Apocynaceae	Aerial parts	Killing the parasite worms by eosinophils, attacks on the structural protein of parasite nematodes.
Ashwagandh a	*Withania Somnifera*	Solanaceae	Roots and Leaves	Causing paralysis of infected parasitic worms or death.
Marigold	*Calendula Officinalis*	Asteraceae	Leaves and	Causing flaccid paralysis of the worms followed by death just like Albendazole

			Flowers	
Cork Tree	*Millingtonia hortensis*	Bignoniaceae	Stem bark	Causing paralysis of worms
Marine seaweed	*Padina tetrastromatica*	Dictyotaceae	Whole plant	Having adulticidal and egg hatch inhibitory effects
Coriander	*Coriandum sativum*	Apiaceae	Aerial parts	Decrease the number of worm eggs in feces and also prevent the hatching of these eggs
Eriocarpa morning glory	*Ipomoea eriocarpa*	Convolvulaceae	Whole plant	Causing death of worms
Flamevine	*Pyrostegia venusta*	Bignoniaceae	Stem and Leaves	Causing paralysis and death of worms
Cogon grass	*Imperata cylindrica*	Poaceae	Rhizomes and Roots	The cuticular shrinking causes the lips to collapse and leads to the creation of a warty surface throughout the whole body
Whitehead plant	*Ericostemma littorale*	Gentianaceae	Whole plant	Tannins act on worm cuticles to toughen the skin and paralyze and kill them
Grand wormwood	*Artemisia absinthium*	Asteraceae	Aerial parts	Causing paralysis, inanimation, lipid congregation, and a decrease in the EPG worm
Redfruit Creeper	*Corallocarpus epigaeus*	Cucurbitaceae	Rhizome	Causing paralysis followed by death of the worms
Tulsi	*Ocimum sanctum*	Lamiaceae	Leaves	Impact the growth and maturation of the parasite during the egg and larval phases
Curry tree	*Murraya koenigii*	Rutaceae	Leaves	Resulting in paralysis and death of worms
Kamala tree	*Mollotus phillipensis*	Euohorbiaceae	Leaves	-
Curry leaf tree	*Cymbopogan nardus*	Rutaceae	Stem and Leaves	Having a flukicidal effect similar to that of oxyclozanide
Bitter melon	*Citrullus colocynthis*	Cucurbitaceae	Fruits	Causes of inhibition of egg hatching
Toothache plant	*Spilanthes acmella*	Asteraceae	Aerial parts	Causing shrinkage and folds on the main body
Spiked Ginger Lily	*Hedychium spicatum*	Zingiberaceae	Rhizomes	Causing paralysis followed by death of the worms
Wild Spinach	*Chenopodium album*	Amaranthaceae	Aerial parts	Inducing worm death and preventing eggs from developing
Prickly Chaff Flower	*Achyranthes aspera*	Amaranthaceae	Stem	Causing paralysis in worms
Indian Fumitory Plant	*Fumaria indica*	Papaveraceae	Stem and leaves	Causing loss of mortality
Catnip	*Nepeta cataria*	Lamiaceae	Aerial parts	Leading to paralysis and reduction in fecal egg count
Sun spurge or Madwoman's milk	*Euphorbia heliscopa*	Euphorbiaceae	Aerial parts	Causing paralysis and egg hatch inhibition
Fever tea	*Lippia javanica*	Verbenaceae	Aerial parts	Leading to paralysis of worms
Matted- st. johnswort	*Hypercium japonicum*	Hypericaceae	Leaves	Causing worm paralysis
Lawn Pennywort	*Hydrocotyle sibthorpiodious*	Apiaceae	Leaves	This leads to worm mortality
Balloon plant	*Cardiospermum halicacebum*	Sapindaceae	Leaves	Causing worm paralysis

Wild Ginger	*Alpinia nigra*	Zingiberaceae	Shoot	Degrades tegument surface architecture, inhibits energy metabolism enzymes and inhibits neuromuscular coordination enzymes
Sticky leaved Wattle	*Acacia oxyphylla*	Fabaceae	Stem bark	This leads to cuticle wrinkling, blistering, and slow digestion by nematode parasites
Green Chireta	*Andrographis paniculata*	Acanthaceae	Leaves	This leads to paralysis and death of worms
Asian spider flower or Tick weed	*Cleome viscosa*	Cleomaceae	Stem and leaves	Causing paralysis followed by death
Spider plant	*Cleome burmanni*	Cleomaceae	Stem and leaves	Causing paralysis followed by death
Spanish Cherry plant	*Mimusops elengi*	Sapotaceae	Stem bark	Damage to reactive oxygen species (ROS), denaturation of proteins, and defence mechanism production.
Cashew tree	*Anacardium occidentale*	Anacardiaceae	Stem bark	Causing paralysis and death of worms
Star anise plant	*Illicium verum*	Schisandraceae	Fruit	Paralyzing and killing worms
Jack tree	*Artocarpus heterophyllus*	Moraceae	Leaves	The effectiveness of the anthelmintic treatment on *H. contortus* eggs, L3 larvae, and adult worms varies according to the dosage administered
Ajwain	*Trachyspermum ammi*	Apiaceae	Leaves	Inducing paralysis in parasitic worms or resulting in their demise
Wild Carom	*Trachyspermum khasianum*	Apiaceae	Aerial parts	Leading paralysis and death of worms
Pomegranate	*Punica granatum*	Lythraceae	Fruit	Trigger inflammation in epithelial cells via peroxisome proliferator-activated receptor-γ and δ-dependent pathways, and inhibit the metamorphosis of larvae from eggs
Cluster bean	*Cyamposis tetragonoloba*	Fabaceae	Stem, Leaves, and Fruit	Resulting in paralysis and death of parasite worms
Bitter gourd	*Momordica charantia*	Cucurbitaceae	Fruit	Anti-helminthic activity, the potential to reduce worm burden
Turmeric	*Curcuma longa*	Zingiberaceae	Rhizome	Curcumin content may have anti-parasitic properties
Neem tree	*Azadiracta indica*	Meliaceae	Leaves	Disruption of larval development, antifeedant effects
Garlic	*Allium sativum*	Amaryllidaceae	Blubs	Allicin content may interfere with parasite metabolism
Ajmuda	*Apium leptophyllum*	Apiaceae	Seeds	The mortality is caused by the adherence of the parasite worm to either free protein compounds in the gastrointestinal tract of the host or glycoproteins on the cuticle of the worm
Asthma plant	*Euphorbia. thymifolia*	Euphorbiaceae	Stem and Leaves	Possibly causes parasite or host animal mortality by binding to proteins in the GI tract or cuticle.
Caraway/Persian cumin	*Carum carvi*	Apiaceae	Seeds	The antioxidant activity of *Carum carvi* extract reduces nitrate formation, disrupting local homeostasis and helminths mortality.
Christ-plant	*Euphorbia milii*	Euphorbiaceae	Leaves	Causing paralysis and death of worms

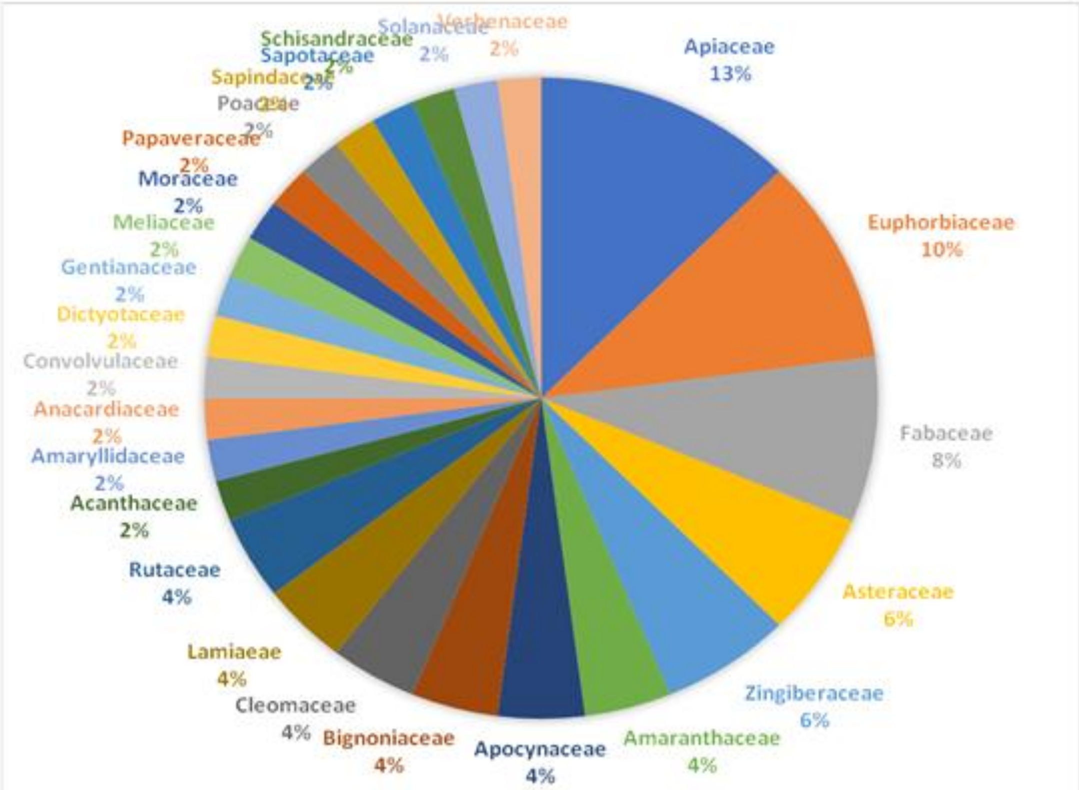

Fig. 2: Percentage availability of 46 families of plants that possess anthelmintic activity.

Pattern Summary of *In Vitro* and *In Vivo* Evidence:

The research articles on anthelmintic activity of medicinal plants incorporated in this review, revealed that most of the studies have used free living annelids including *Pheretima* (earthworm), *Tubifex* (sludge worm) and nematodes including *Caenorhabditis elegans* (roundworm) as an experimental model based on their death and/or paralysis to validate the anthelmintic effect of tested medicinal plants in Indian context, thus providing wrong evidence. However, to confirm the anthelmintic potential of any plant-based product or chemical or an extract, it should be evident that the anthelmintic efficacy is visible against true parasitic gastrointestinal helminths of animals such as *Haemonchus contortus*, *Fasciola gigantica*, or *Trichuris* spp., either under in vitro or in vivo conditions. Subsequent research should concentrate on these parasitic species utilizing validated host models (e.g., small ruminants or rats) that more completely replicate natural host-parasite interactions, hence facilitating a significant evaluation of efficacy. Therefore, the biological activity claimed against free living earthworms, sludge worms and roundworms cannot be considered as anthelmintic effect as the studies claim but are only a source of illegitimate scientific proof. Therefore, the protocols used to claim anthelmintic effects against free living animals cannot be considered authentic, as the anatomical, physiological and other biological attributes of parasitic and free-living worms are entirely different. Further, the internal milieu and the microhabitat conditions of the hosts also play a significant role while evaluating the anthelmintic potential of any biological or plant-based product under in-vivo conditions. It may be alternatively termed as anti-earthworm (anti-annelid) and anti *c. elegans* activity or any related term which may be of some other biological significance in literature, and their use can't be claimed as experimental anthelmintic parasitic models.

Out of the total reported plant species, 51 plant species were evaluated in-vitro against different helminth parasites and only 5 plant species were tested under in-vivo against helminth infection. Thus, in-vitro studies were almost 10 times greater than in-vivo studies. Although these in-vitro studies provide a kick point for researchers to gather insight or preliminary investigations into how an experimental model for a plant extract/compound in a controlled and isolated environment can behave under laboratory conditions they overlook complicated pharmacokinetic and pharmacodynamic factors including absorption, metabolism, host immunity, and parasite location. These biological variables are crucial in figuring out true efficacy in a clinical or veterinary setting. Therefore, these in-vitro results are extremely difficult to extrapolate on a clinical scale as these studies are not performed in an intact living organism where entirely different far more biological variables of both parasite and its host are in play. So, the plant-based extracts and products should be evaluated under in-vivo conditions either in the same host animal or in some experimental model animal to standardize the anthelmintic efficacies and to advance the drug development studies.

This review also highlighted several plant extracts show significant anthelmintic activity, often comparable to or exceeding that of conventional synthetic drugs like methanolic extract of *Hedychium spicatum,* aqueous and fresh extracts of latex of *Calotropis procera,* ethanolic and aqueous extracts of leaves and bark of *Tamarindus indica,* methanolic extract of *Leptadenia pyrotechnica* and aaqueous extracts of *Withania somnifera* and *Calendula officinalis.* Few plants exhibited moderate to minor anthelmintic activities like *Millingtonia hortensis*, *Padina tetrastromatica*, *Ipomoea eriocarpa*, *Nepeta cataria, Curcuma longa, Momordica charantia* and *Euphorbia helioscopia.* To provide a comparative overview of key findings, a summary table (Table 2) has been compiled. It presents detailed characteristics of select Indian medicinal plants with reported anthelmintic properties, including plant parts used, extraction solvents, helminth targets, model systems, observed outcomes, and reference sources. This allows for a clearer visualization of trends in in vitro and in vivo efficacy across different species.

Table 2: Comparative summary of selected Indian medicinal plants with anthelmintic activity against gastrointestinal helminths

Plant Species	Family	Plant Part Used	Extract Type	Target Helminth(s)	Test Species	Model Type	Outcome	Reference
Fumaria indica	Papaveraceae	Whole plant	Methanol	*H. contortus, Pheretima*	Earthworm	In vitro	Paralysis at 20 min	Author *et al.,* 2020
Withania somnifera	Solanaceae	Root	Ethanol	*H. contortus*	Sheep	In vivo	70% reduction in EPG	Sharma et al., 2019
Spilanthes acmella	Asteraceae	Leaves	Aqueous	*Raillietina spp.*	Chick intestine	In vitro	Spine and sucker degeneration	Patel et al., 2021
Lippia javanica	Verbenaceae	Leaves	Crude	*H. contortus*	Goat	In vivo	80% EPG reduction, better weight gain	Swargiary *et al.,* 2018
Imperata cylindrica	Poaceae	Whole plant	Methanol	*Raillietina echinobothrida*	Hen intestine	In vitro	Scolex and tegument disruption	Devi *et al.,* 2022
Alpinia nigra	Zingiberaceae	Rhizome	Essential oil	*Paramphistomum spp.*	Fluke culture	In vitro	Surface erosion, flaccid paralysis	Rajkhowa *et al.,* 2020
Euphorbia helioscopia	Euphorbiaceae	Leaves	Ethanol	*Ascaridia galli*	Poultry	In vitro	Worm expulsion in < 30 min	Khan *et al.,* 2016
Hedychium spicatum	Zingiberaceae	Rhizome	Methanol	*Fasciola gigantica*	Fluke ex vivo	In vitro	Tegumental collapse at 1% concentration	Dutta *et al.,* 2021

Current scenario in India:

Table 3 provides a summary of the most often used strategies for detecting AR in the helminths of ruminants. These strategies may be used either alone or together to provide a thorough comprehension of AR in the helminths of ruminants. The selection of the method often relies on variables such as expenses, resource accessibility, and the distinct characteristics of the parasite population being examined. The possible anthelmintic qualities of plant-based control methods are considered as an alternative or complementary approach to synthetic medications and have the potential to be utilized as a part of integrated parasite management programs. Still a major question, though, is whether these AR detection methods are possible and accepted in rural Indian conditions with minimal resources. Although advanced methods include molecular diagnostics and genomic approaches which provide more accuracy, they are rarely available to field-level veterinarians or small diagnostic labs due to cost, equipment, and training restrictions. Though simpler methods like Fecal Egg Count Reduction Test (FECRT) and Egg Hatch Assay (EHA) may lack the sensitivity or specificity of molecular techniques but are more practical for regular use in rural regions. Therefore, context-specific evaluation is required when applying AR detection techniques in the several agro-climatic and socioeconomic conditions of India. In Indian rural field environments, technical talent availability, infrastructure, and cost typically restrict the viability of implementing AR detection techniques. Thus, field-adapted techniques such as FECRT and EHA are first-line diagnostic tools; molecular and genomic assays are better suited for centralized surveillance programs or research environments. One could balance real-world practicalities with diagnostic accuracy via a tired approach.

Table 3: Methods for detecting drug resistance in livestock helminths.

Technique	Description	Advantages	Limitations
Egg Hatch Assay (EHA)	Measures the drug-induced suppression of egg hatching	Easy and widely used	Laborious and require skilled personnel
Larval Development Assay (LDA)	Assesses how drugs affect larval development	Mimics *in vivo* conditions are better than EHA	Slow and laborious
Fecal Egg Count Reduction Test (FECRT)	Compare egg counts in a herd before and after treatment	Measures population medication efficacy	Resistance is not the only element affecting the results
Molecular Techniques (PCR, RT-qPCR)	Identify resistance-associated genetic markers	High sensitivity and specificity	Requires specialized equipment and training
Genomic Approaches (Next Generation sequencing)	Genomes are sequenced for resistance markers	Allows complete mechanism analysis	Costly and may generate large datasets for study
Anthelmintic Field Trials	Tests on drug efficacy naturally	Provides practical effectiveness insights	Beyond resistance, other factors may affect the results
Pharmacokinetic Studies	Temporal drug concentrations in host tissues	Examines medication levels and efficacy	Needs intrusive sampling and analysis
In vitro Culture systems	Expose cultured helminths to medications for evaluation	Allows controlled drug susceptibility testing	Challenging *in vitro* culture maintenance limits
Biochemical Assays	Measures resistance-related enzymes	Resistance may alter metabolic pathways	Limited by marker availability

Exploring Botanicals as Bio-Compatible Therapeutics:

The anthelmintic activity of ethanolic and aqueous extracts derived from the leaves and bark of *Tamarindus indica* Linn. was evaluated against *Pheretima posthuma* and *Tubifex tubifex*. In contrast to piperazine citrate, the paralysis and mortality time of the alcoholic and aqueous extracts were diminished (Das *et al*., 2011). An additional investigation assessed the anthelmintic activity of *Butea monosperma* seeds against *Caenorhabditis elegans*. The seeds of *B. monosperma* were extracted with methanol and demonstrated potent anthelmintic activity (Prashanth *et al*., 2001). The anthelmintic activity of unrefined latex derived from *Calotropis procera* was assessed using adult earthworms in a separate investigation. Aqueous and fresh extracts of desiccated latex induced pin-prick responses and inhibited spontaneous motility (paralysis). Shivkar and Kumar (2003) found that the impact of higher concentrations (100 mg/ml of aqueous extract and 100% fresh latex) was like that of 3% piperazine. The anthelmintic activity of a methanolic extract derived from the entire plant of *Leptadenia pyrotechnica* against *Pheretima posthuma* was investigated at two concentrations (50 and 100 mg/ml), with the worm's immobilization and mortality duration being recorded (Kumar *et al*., 2011). *Corallocarpus epigaeus* extract showed anthelmintic activity against *Pheritima posthuma* at four concentrations. The extract showed the best action, with a MIC value of 12.5 mg/ml. It contained alkaloids, flavonoids, saponin, phenol, tannins, and steroids. The extract also contained six HPTLC bands and six GC-MS bands (Ishnava *et al*., 2020). The anthelmintic activity of pure extracts of *Withania somnifera* (L.) and *Calendula officinalis* (L.) against *Pheretima posthuma* was investigated. At concentrations of 2, 4, 6, and 8 mg/ml, all four aqueous extracts of the roots and leaves of *W. somnifera* and desiccated flowers and leaves of *C. officinalis* exhibited significant anthelmintic activity (Purwal *et al*., 2010).

Secondary Metabolites in Plants: Key Player:

Small chemical compounds called secondary metabolites are produced by plants that are not vital for their regular growth but play crucial roles in reproduction and defence against various threats such as bacteria, fungi, viruses, and vertebrates. These compounds possess significant potential for serving as medicinal drugs (Boy *et al*., 2018; Mawalagedera *et al*., 2019) and represent a diverse array of naturally occurring compounds with therapeutic properties, offering valuable applications in the treatment of various diseases (Leicach *et al*., 2014). Plant-derived compounds, found in natural extracts, exhibit a remarkable chemical diversity in comparison to their synthetic counterparts. This diversity frequently translates into distinct and specific biological activities (Newman *et al*., 2008). Regarding parasites, several regions of the world continue to use medicinal herbs that have been used for generations to fight these infections (Newman *et al*., 2007). Finding novel anthelmintics in plant extracts is an emerging field of study. Extensive research on secondary metabolites has been carried out since the 1850s (Kabera *et al*., 2014). Figure 3, illustrates the chemical structures of representative secondary metabolites with known or potential anthelmintic activity, aiding in understanding the diversity and mechanistic differences among the various classes of compound. Phytochemicals and secondary metabolites, including alkaloids, flavonoids, tannins, glycosides, terpenes, and saponins, make up the bulk of plant-derived compounds (Mukherjee *et al*., 2016; Overend *et al*., 2012; Symeonidou *et al*., 2012). Table 4, summarizes the major phytochemical classes identified across selected medicinal plants, the corresponding species in which they occur, and the proposed mechanisms by which these compounds exert anthelmintic effects.

Terpenes:

Terpenes are made up of various isoprene units combined (C5H8) (Chanda *et al*., 2019). Terpenoids cause worms to quickly become paralyzed. By binding to the critical locomotor receptors - the Levamisole sensitive nicotinic receptor (L-AChR) and the GABA (A) (UNC-49) receptor - it demonstrates anthelmintic activity, quickly paralyzing worms. In a study conducted by Hernandez *et al*. (2019), it was found that carvacrol, thymol, and eugenol inhibited the egg-hatching process of *Caenorhabditis elegans*.

Saponins:

Saponins are hydrophilic compounds consisting of triterpene or steroid aglycons attached to sugar chains (Osbourn *et al*., 2011). Saponins demonstrate their anthelmintic effect by inhibiting acetylcholinesterase, leading to the paralysis and death of worms (Manjusa *et al*., 2023). They are known to have lethal effects on *Pheretima posthuma* (Lipi *et al*., 2010).

Compared to the usual medicines, piperazine citrate, β-sitosterol has a superior binding affinity to the active pocket of tubulin (Sravani *et al*., 2015).

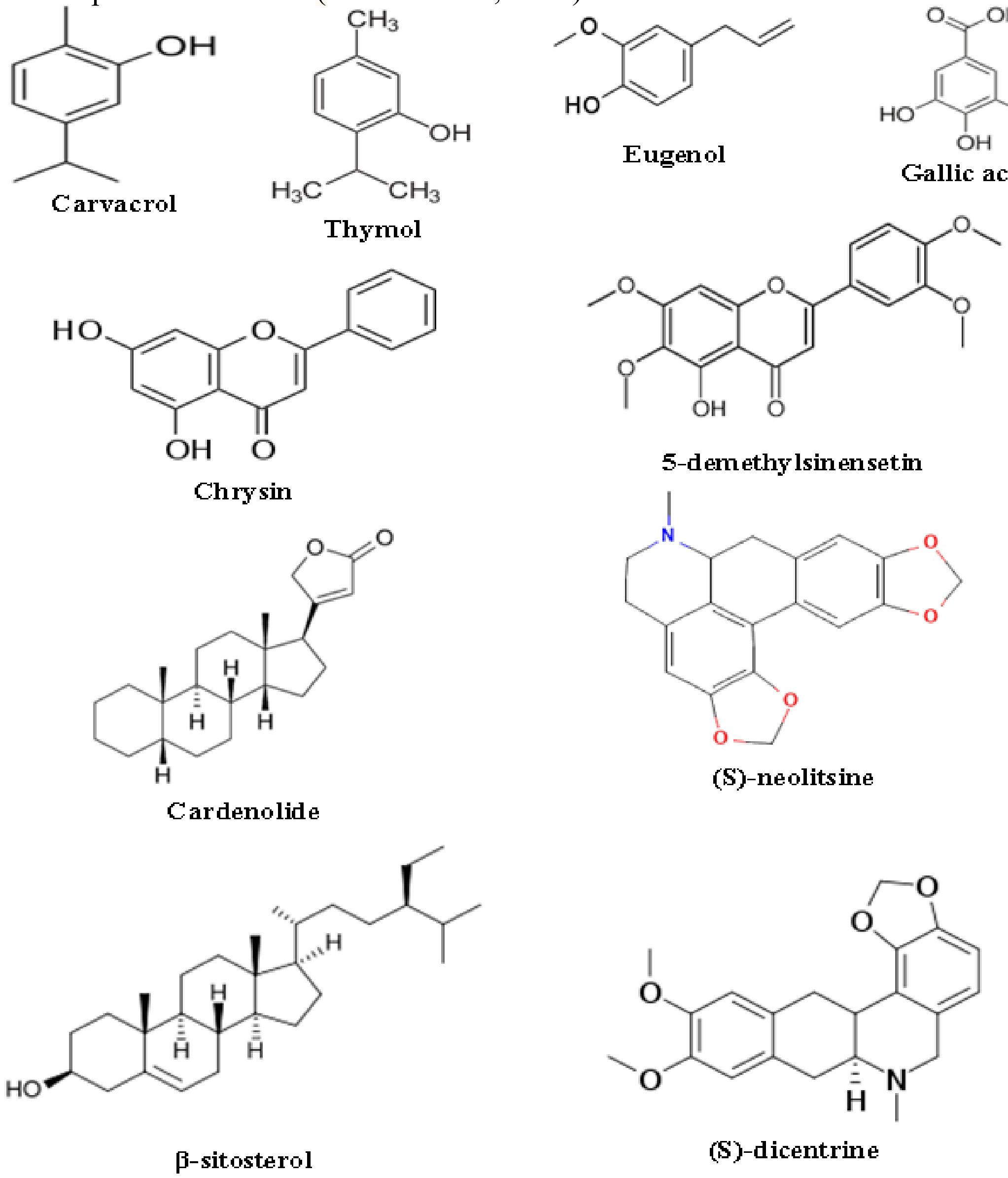

Fig. 3: The structure of the chemical compounds that possess anthelmintic activity.

Tannins:

Tannins are a group of compounds that facilitate the destruction of nematodes by impeding the worms' capacity to assimilate nutrients from their host cells. The larvae's digestive tissues and cuticle suffered significant injury from condensed tannins. Condensed tannins have a direct influence on *Ascaris suum*, causing a decrease in the capacity of newly hatched third-stage larvae to move and reducing the movement and survival of fourth-stage larvae in pigs. Condensed tannins have a direct suppressive effect on *A. suum* by decreasing the migratory capacity of recently hatched third-stage larvae and impairing the movement and viability of fourth-stage larvae originating from pigs (Williams *et al*., 2014).

Glycosides:

Glycosides have notable efficacy in combating certain helminths (Overend, 2012). Cardenolide inhibits Na+/K+-ATPase pumps in parasite cells, disrupting osmotic balance and leading to cellular dysfunction and nematode death (Wang *et al*., 2009).

Flavonoids:

Flavonoids disrupt phosphorylation reactions preventing parasitic worms from producing energy and killing them (Adak *et al*., 2022; Panche *et al*., 2016). Chrysin was most vermicidal at 40 mg/ml. They also hinder mitochondrial oxidative phosphorylation pathways and could bind to tubulin, therefore blocking microtubule polymerization vital for parasite proliferation (Cho et al., 2020; Gupta et al., 2002).

Alkaloids:

Alkaloids hinder glucose uptake and target acetylcholine receptors, making them effective anthelmintics. Malnutrition kills helminths (Badarina *et al*., 2017). Two aporphine alkaloids, (S)-dicentrine and (S)-neolitsine, had anthelmintic activity with EC90 values of 6.3 and 6.4 microg/ml.

Table 4: Representative phytochemical classes found in Indian medicinal plants, associated plant species, and their proposed anthelmintic mechanisms.

Phytochemical Class	Representative Plant Species	Proposed Mechanism of Action	References
Tannins	*Acacia nilotica*, *Terminalia chebula*	Protein binding on cuticle surface, reduced nutrient uptake	Kamaraj et al. (2011); Roy et al. (2019)
Saponins	*Calotropis procera*, *Achyranthes aspera*	Membrane disruption, neuromuscular paralysis	Pathak et al. (2013); Yadav et al. (2020)
Alkaloids	*Justicia adhatoda*, *Piper longum*	Interference with neurotransmission, acetylcholinesterase inhibition	Gupta & Dixit (2014); Bano et al. (2021)
Flavonoids	*Ocimum sanctum*, *Azadirachta indica*	Reactive oxygen species generation, metabolic stress	Tandon et al. (2012); Kumar et al. (2022)
Terpenoids	*Artemisia maritima*, *Mentha piperita*	Cuticle shedding, inhibition of larval development	Singh & Kaur (2017); Alam et al. (2020)
Phenolics	*Phyllanthus emblica*, *Punica granatum*	Enzyme inhibition, oxidative stress induction	Verma et al. (2016); Sharma et al. (2018)

Though plant secondary metabolites exhibit encouraging anthelmintic action, but their extraction, purification, and commercial formulation create major challenges. Many plant-derived compounds are rare and require large volumes of plant material, which may not be economically feasible. On the other hand, applying gene technology from this angle seems exciting. Additionally, the extraction and purification processes can be technically demanding, time-consuming, and expensive. Moving from lab research to making anthelmintic phytopharmaceuticals that can be sold is made harder by issues with scaling up production, differences in manufacturing batches, and regulatory hurdles. To enhance mechanistic clarity and visualize how phytochemical classes contribute to helminth control, a conceptual framework was developed (Fig. 4). This diagram illustrates the pathways by which major plant-derived secondary metabolites exert anthelmintic effects either through direct damage to the helminth cuticle, disruption of neuromuscular function, or interference with metabolic and oxidative processes. These mechanisms ultimately lead to reduced parasite motility, survival, and fecundity.

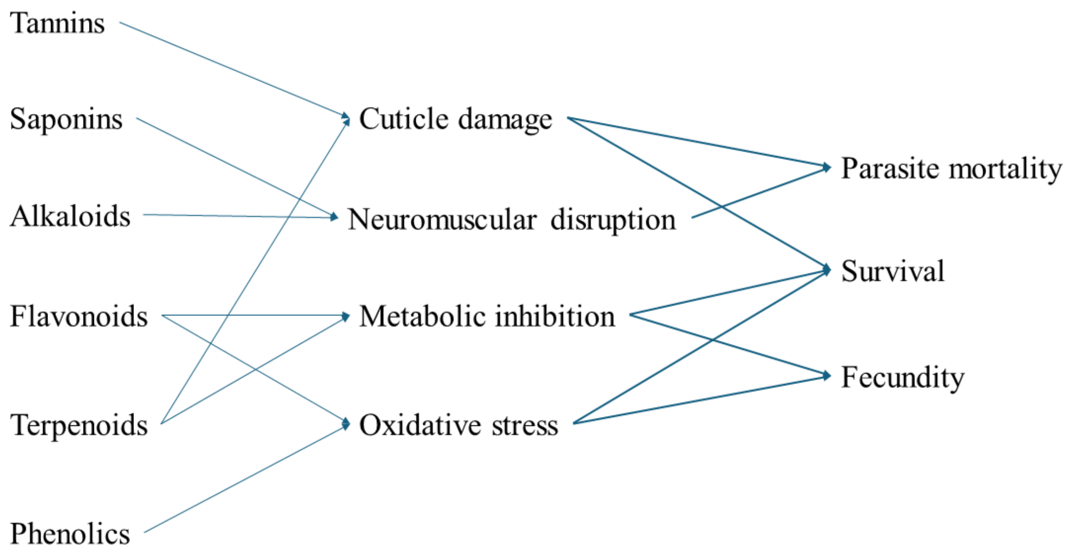

Fig. 4: Proposed anthelmintic mechanisms of phytochemical classes.

Limitations of Current Methodologies:

Despite the growing interest in plant-derived anthelmintics, a critical gap exists in the methodological rigor of many published studies. A substantial number of investigations evaluate the anthelmintic activity of plant extracts using non-parasitic free-living organisms such as *Pheretima posthuma* (earthworms) and *Caenorhabditis elegans*. While these bioactivity screening models offer logistical convenience and cost efficiency, they lack clinical relevance to gastrointestinal parasitic helminths affecting livestock. The physiological and anatomical differences particularly in neuromuscular receptors, digestive structures, and host immune interactions make it scientifically inappropriate to extrapolate findings from these organisms to pathogenic parasites like *Haemonchus contortus* or *Fasciola gigantica*. Furthermore, such studies often omit validation through in vivo experimentation in ruminant hosts, leading to potentially misleading claims of efficacy. Without appropriate models that mimic the parasite's natural habitat and host interactions, the therapeutic potential of plant-based compounds remains speculative. To advance this field meaningfully, future research must prioritize biologically relevant helminth species and standardized protocols that include both in vitro and in vivo validation phases. Emphasizing methodological appropriateness from the outset is essential to ensure translational impact and scientific integrity in anthelmintic drug discovery.

Conclusion and Future Prospects:

The emergence of anthelmintic resistance (AR) is a worldwide concern and a challenge for the scientific community and a concern for a pastoralist as the conventional anthelmintics are becoming either ineffective or less effective. Therefore, this problem demands urgent and concerted attention. Moreover, the cost of synthetic drugs not only exacerbates the AR problem but also increases their level of toxicity. This kind of scenario has sensitized the research community to explore the alternatives. Among these alternatives, herbal or plant-based products have shown promising potential as effective and viable options against helminth infections. This review paper provides a thorough examination of the use of unrefined plant extracts to study anthelmintic properties, with a focus on a variety of *in vitro* experiments in light of the limited *in vivo* investigation protocols and techniques. Development and application of frameworks for clinical trials and standardized testing procedures should be the main goals of the next research projects. Measures will cover improving funding and fostering cooperation among academic institutions, governmental agencies, and industry players to help plant-based anthelmintics move from laboratory research to practical usage. These steps will help plant-based anthelmintics go from lab to clinical use. Additionally, detailed investigations on the phytochemical, clinical efficacy, toxicological and molecular mechanisms of action of the anthelmintic plants/extracts are strongly recommended. There is also a need to either refine existing anthelmintic drugs or identify novel molecular targets that can lead to the development of next generation anthelmintics. This can be accomplished using a multidisciplinary strategy that integrates natural product chemistry with the synthetic synthesis of structural variants to boost activity and mitigate resistance. The integration of ancient knowledge with contemporary scientific approaches is equally essential, encompassing community involvement, acknowledgment of indigenous practices, and respect for intellectual property rights. These inclusive methodologies enhance study outcomes while guaranteeing the ethical and sustainable use of natural resources. Moreover, investigations into combinatorial strategies such as the integration of phytochemicals with synthetic pharmaceuticals may yield synergistic advantages that enhance efficacy while postponing the emergence of resistance. Finally, initiatives must be undertaken to standardize potent plant extracts, facilitating the creation of reliable and high-quality herbal formulations that may boost or substitute current synthetic anthelmintics. These integrated tactics will be essential for attaining sustainable and effective parasite control in the future.

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