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Evaluation of Anthelmintic Activity of *Macaranga Peltata* Leaf Extract on Experimental Animals

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A B S T R A C T

Background: Helminth infections are one of the utmost health and economic problems in developing tropical countries. Synthetic anthelmintics are present and have some limitations, like inaccessibility and drug resistance, and so alternative anthelmintics become inevitable. Among medicinal plants, Macaranga peltata shows many bioactive compounds. Therefore, it can prove to be a drug, as well. Objectives: The anthelmintic activity of the extract of leaves of Macaranga peltata along with Albendazole compared between aqueous and alcoholic extracts. Methods: Macaranga peltata leaves were collected, authenticated, and processed for extract preparation. Phytochemical analysis revealed the presence of alkaloids, flavonoids, tannins, saponins, and terpenoids. Different concentrations of the prepared extracts (25 mg/ml and 50 mg/ml) were administered to Pheretima posthuma worms, and the efficacy was determined as measured by time to paralysis (P) and death (D). Statistical analysis was carried on the gathered data. Results: The anthelmintic activity was more significant from the ethanolic extract compared to the aqueous extract, with paralysis occurring after 18.91 ± 1.21 min and death after 35.14 ± 1.56 min at 50 mg/ml. It has been scientifically proven that phytochemicals present in the ethanolic extract, especially alkaloids and flavonoids, enhance the anthelmintic action. Conclusion: Macaranga peltata has promising anthelmintic activity and was found to be effective approximately similar to Albendazole in its ethanolic extract. These findings are promising for its potential as a natural anthelmintic, but further research is required in safety and optimal use.

Keywords: Anthelmintic activity; *Macaranga peltata;* Natural products; *Pheretima posthuma*; Phytochemical analysis.

1. INTRODUCTION

The infections by parasitic worms, especially helminths, form a highly dangerous menace not only to human beings but also to animals, primarily in the tropical and subtropical regions of the world (Hamid et al., 2023). The estimation is that 1.5 billion people are infected with soil-transmitted helminths spread over more than 150 countries and infect millions of children while causing morbidity and malnutrition (Aung et al., 2022). These infections from a variety of parasitic helminths such as roundworms, tapeworms, and flukes are harmful to the tissues of the host-the gastrointestinal tract-more commonly then subsequently bring about various serious health complications from being hindered in their development to anemia and even death in extreme cases (Hedley & Wani, 2015). Not only is it a severe health risk for humans but even enormous economic loss in terms of livestock productivity and expensive medications in the livestock industries (Kappes et al., 2023). The primary management of helminthiasis for centuries had been synthetic anthelmintic drugs that were expensive, and unavailable at some geographically distant locales, and increasing problems with drugs resistance made it crucial to search for more environment-friendly alternatives (Fissiha & Kinde, 2021). Such factors have drawn significant attention to the search for alternatives of anthelmintics from natural sources with an emphasis on the medicinal value of the plants that seems quite promising (Liu, Panda, & Luyten, 2020) and (Bhat & Shanbhag, 2023).

Plants have been in use for over a century for the conventional medicine practices meant to treat infections caused by parasites and there are plenty of bioactive compounds existing that seem to promise in developing anthelmintic compounds (Jayawardene, Palombo, & Boag, 2021). Apart from the traditional use in treating gastrointestinal disorders, some studies reported in that category of plants were due to scientific interest given to *Macaranga peltata* of family Euphorbiaceae. Phytochemical investigation of *Macaranga peltata* revealed the presence of alkaloids, flavonoids, tannins, saponins and terpenoids which are all associated with various kinds of biological activity (Magadula, 2014). These compounds are anthelmintic up to some extent and it is broadly ascribed to interference of the physiological functions with neuromuscular interference and inhibition of the enzymes besides the metabolic interference in parasitic worms.

The present study on the anthelmintic activity of *Macaranga peltata* leaf extract with special references to paralysis and mortality effects on experimental models infected with helminths shall focus on the evaluation of both aqueous as well as ethanolic extracts in order to find which extraction procedure would yield the maximum extraction of anthelmic potential from plant; synthetic control Albendazole has also been used. Another addition to the literature involving studies concerning the potential of plant-derived agents as anthelmintics, which just so happen to occur naturally in vastly less expensive costing than synthetic analogues; might serve as a foundation for future research in the pharmacological activity of *Macaranga peltata*. New knowledge generated by this study will be able to contribute to the knowledge bank on how plant-derived compounds interact with parasitic entities and may, in the long run, be used as an alternative means of antiparasitic management against helminths.

2. MATERIALS AND METHODS

2.1 Plant Material

2.1.1. Collection and Authentication of Plant Material:

The leaves of *Macaranga peltata* were collected from the local areas of Puttur, Karnataka during July 2024. Dr. Siddaraju M. N., Assistant Professor and Research Guide, Dept of Botany, University College Mangalore on 16/07/2024 authenticated the plant material. The leaves were thoroughly washed with water to remove the dust and dried in the air at room temperature in the shade for a couple of weeks until it became moisture-free. Crushed finely with a mechanical grinder, leaves were kept in an airtight container for the sake of preservation of identity.

2.1.2 Extract Preparation

The leaves were shade-dried at 25 ± 2°C with a relative humidity of 60 ± 5%. The dried leaves were then reduced into a fine powder of 40 mesh size with the help of a mechanical grinder. Further extraction was done with distilled water at a 1:10 (w/v) ratio after a 24-hour maceration process, followed by 70% ethanol with the help of a Soxhlet apparatus for 48 hours. The extracts were concentrated using the rotary evaporator at 40°C, after which the percentage yield of each extract was calculated (Shanbhag et al., 2022).

2.1.3 Phytochemical Analysis

The detection of phytochemicals was based on standard protocols used in the detection of alkaloids, flavonoids, tannins, saponins, and terpenoids (Bhat et al., 2024).

2.2 Experimental Animals

The research was carried out with the *Pheretima posthuma* adult worms, 8-10 cm long, collected from Pilikula Nisargadhama and authenticated by H.S. Shenoy Principal Scientist and Head of Botany division, Pilikula development authority, Mangalore.

The worms were acclimatized to the laboratory at a temperature of 25 ± 2°C and relative humidity of 60 ± 5% for 24 hours before the experiment. The experiment was divided into six groups having six worms in every group (n=6 worms/group). Group I was assumed as control by administering normal saline. The Albendazole was given to the Group II at a concentration of 20 mg/ml. Group III and Group IV were administered aqueous extract at concentrations of 25 mg/ml and 50 mg/ml, respectively. Group V and Group VI were treated with ethanolic extract at 25 mg/ml and 50 mg/ml, respectively (McDonough, Guo, & Guo, 2021).

2.3 Ethical Statement

The experimental procedures of *Pheretima posthuma* were carried out with respect to the code of ethics of the treatment of invertebrate animals in experiments. All possible care was taken to not cause any suffering of the worms; thus, acclimatization was done cautiously before experimentation to ensure a healthy condition of the worms before experimentation. It also conformed to the law regarding the humane treatment of laboratory animals.

2.3 Anthelmintic Activity Assessment

The anthelmintic activity of the treatments was evaluated by measuring two important parameters, namely Time to Paralysis (P) and Time to Death (D) in *Pheretima posthuma* worms. Time to paralysis would be determined by the period for the worms to lose their motility without being revived on placing them in normal saline indicating the onset of paralysis. The worms were touched or otherwise mechanically stimulated to ensure that they had reached a total stop in movement as confirmation of death. The readings for both variables were taken at intervals of every 5 minutes to derive more detailed estimates of the effects of treatments throughout the experiment (Bhardwaj, Anand, Chandrul, & Patil, 2012).

2.4 Statistical Analysis

The data were analyzed with GraphPad Prism 9.0 software. The results are expressed as mean ± SEM. For the comparison of more than two groups, one-way ANOVA analysis was applied along with Dunnett's post-hoc test. A p-value of less than 0.05 was taken to be significant.

3. RESULTS

3.1 Extract Yield

The percent yield of extracts obtained from aqueous and ethanolic extracts was; it was 15.2% in aqueous extract while at 22.5% in ethanolic extract. Hence, ethanolic extraction was better compared to the aqueous extraction of bioactive compounds from the leaves of *Macaranga peltata*.

3.1 Phytochemical Analysis

Qualitative phytochemical screening of the leaf extracts of *Macaranga peltata* showed the presence of a number of bioactive compounds. The ethanolic extract generally possessed a higher concentration of most phytoconstituents compared to the aqueous extract except for saponins which were more abundant in the aqueous extract as shown in Table 1.

Table 1: Phytochemical Screening Results of *Macaranga peltata* Leaf Extracts

Phytoconstituents	*Test*	*Aqueous Extract*	*Ethanolic Extract*
Alkaloids	Mayer's	+	++
	Wagner's	+	++
	Dragendorff's	+	++
Flavonoids	Alkaline reagent	++	+++
	Lead acetate	++	+++
	Shinoda	+	++
Tannins	Ferric chloride	++	++
	Lead acetate	++	++
	Gelatin	+	++
Saponins	Foam	+++	++
	Hemolysis	++	+
Terpenoids	Salkowski	+	++
	Liebermann-Burchard	+	++

+: Present in small amount; ++: Present in moderate amount; +++: Present in large amount

3.2 Anthelmintic Activity

Pheretima posthuma was used to study the anthelmintic activity of extracts, paralysis time and death time. Both the extracts proved to be concentration dependent and showed significant anthelmintic activity though ethanol extract was more potent than aqueous extract as shown in Table 2.

Table 2: Anthelmintic Activity of *Macaranga peltata* Leaf Extracts Against *Pheretima posthuma*

Treatment	*Concentration (mg/ml)*	*Time to Paralysis (min)*	*Time to Death (min)*
Control	-	-	-
Albendazole	20	15.24 ± 1.05***	30.36 ± 1.28***
Aqueous Extract	25	25.76 ± 1.48**	50.42 ± 1.98**
Aqueous Extract	50	22.34 ± 1.12***	45.28 ± 2.06***
Ethanolic Extract	25	20.64 ± 1.39**	40.18 ± 1.74**
Ethanolic Extract	50	18.91 ± 1.21***	35.14 ± 1.56***

*Values represent mean ± SEM (n=6). Statistical significance: **p < 0.01, ***p < 0.001 compared to Albendazole-treated group.*

The activity of the ethanolic extract at 50 mg/ml was the most prominent and emerged as the most potent among all test extracts that worked upon with a paralysis time of 18.91 ± 1.21 minutes and death time of 35.14 ± 1.56 minutes. Although it was less potent than the standard drug albendazole (20 mg/ml) having shown a paralysis time of 15.24 ± 1.05 min and death time of 30.36 ± 1.28 min, yet it showed an amazing anthelmintic activity ($p < 0.001$).

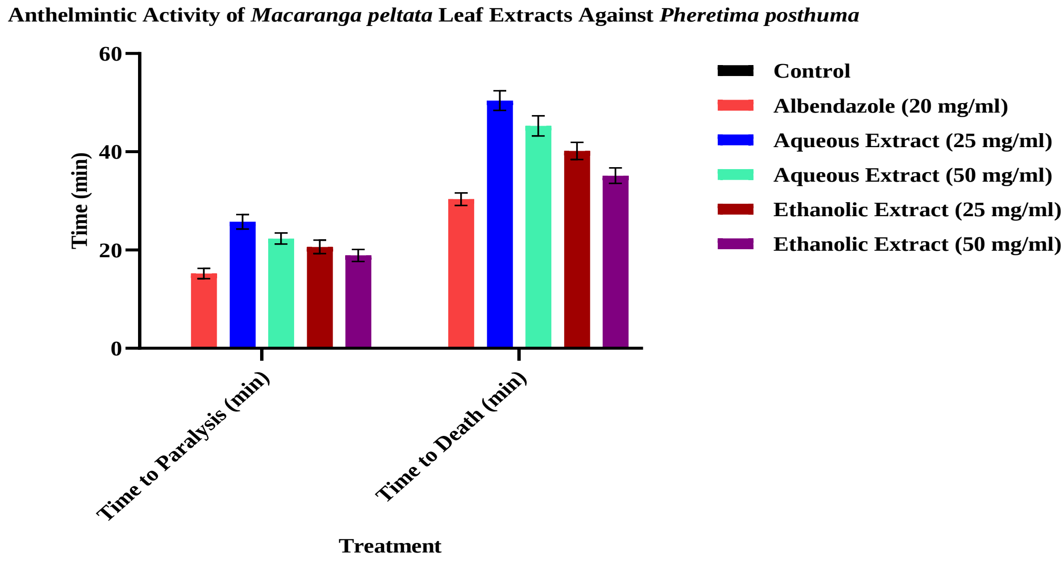

Fig. 1: Anthelmintic Activity of *Macaranga peltata* Leaf Extracts Against *Pheretima posthuman*

4. DISCUSSION

One of the most significant challenges for global health throughout these years is disease burden, in a very broad spectrum including infectious diseases, chronic disorders, and lifestyle-related conditions (Bhat, Uday, Palakki, Bhandary, & Karicheri, 2024), (Pradeep & Bhat, 2024). Much scientific progress has been achieved in modern medicine, but still, the effective access to health care at affordable prices remains an outstanding problem, especially for developing countries. From the early days of human history, individuals used natural resources, especially medicinal plants, as therapeutic agents, and it is still estimated that 80% of the world's population today utilizes plant-derived medicines for the majority of its healthcare needs (Noronha, Fathima, Bhat, & Shabaraya, 2022).

In modern drug discovery, these natural sources have significantly been implicated because most pharmaceutical compounds were directly isolated from plants or modeled after templates derived from them (Shanbhag, Bhat, Prabhu, & Shabaraya, 2022). Plant-based bioactive compounds are amazingly diverse, including alkaloids, flavonoids, terpenoids, and tannins. These compounds have represented some of the most exciting leads in the treatment of many diseases and disorders, from infections by infectious agents to chronic conditions such as diabetes, cancer, and cardiovascular disorders (Bhat, Hemalatha, & Shabaraya, 2023). Among them, helminthic infections continue to infect nearly 1.5 billion people worldwide, especially those with minimal access to health care and proper sanitation. Such infections can cause serious morbidity in the nutritional status, cognitive development, and loss of productivity in the work environment (Aung et al., 2022). The conventional drugs used for treatment include albendazole, mebendazole, and ivermectin, among others (Echevarria et al., 2016). However, their widespread use has caused drug resistance issues to become increasingly relevant. In addition, many branded products are highly expensive and, therefore, are hardly accessible in resource-limited settings (Varshini, Himasvi, Bhat, & Shabaraya, 2023). Helminthic infections have been treated with several medicinal plants by the traditional medicine systems in question, mainly Ayurveda. Some plants listed under 'krimighna' properties in ancient Ayurvedic texts are Vidanga (*Embelia ribes*), Palasha (*Butea monosperma*), and numerous others that have been in successful use for thousands of years in traditional healing practices (Soni et al., 2017), (Bhat et al., 2022).

This study provides significant evidence for the anthelmintic activity of *Macaranga peltata* leaf extracts. Aqueous and ethanolic preparations have both been shown active against *Pheretima posthuma*, especially the ethanolic preparation. At high concentrations, they provide paralysis times and death times virtually identical to the standard drug albendazole. The better performance of the ethanolic extract at a yield of 22.5% compared to the aqueous extract of 15.2% suggests that compounds responsible for anthelmintic activity have better solubility in ethanol than in water. Interestingly, this result is in line with research findings in plant-based anthelmintics that indicate ethanol as an effective solvent in extracting active compounds from other organisms.

Both the extracts exhibited marked dose-dependent activity where the concentration at 50 mg/ml showed a much higher anthelmintic activity as compared to that at 25 mg/ml. Paralyzing and killing times presented by the ethanolic extract, at 50 mg/ml, took 18.91 ± 1.21 min and 35.14 ± 1.56 min respectively, while at 25 mg/ml they prolonged to 20.64 ± 1.39 and 40.18 ± 1.74 min, respectively. The activity of the aqueous extract was dose-dependent, although less pronounced than that of the ethanolic extract. Concentration dependence in this case indicates a direct correlation between the amount of bioactive constituents extracted and their anthelmintic effects, hence predictive and reliable therapeutic potential.

The phytochemical analysis of the leaf extracts of *M. peltata* revealed the complicated nature of its bioactive compounds, ethanolic extract particularly had high levels of flavonoids combined with moderate quantities of alkaloids, tannins, and terpenoids, which, according to literature, are also recognized for anthelmintic activities. The rapid onset of paralysis followed by death of the test organisms suggests interference with multiple pathways. Alkaloids probably interfere with neuromuscular functions while flavonoids may interfere with the energy metabolism within the parasites. The presence of tannins and saponins, known to disrupt cellular membranes and bind with proteins, probably contributes toward the general anthelmintic action through direct disruption of surface integrity of the parasite.

The difference in the amount of active compounds within the aqueous and ethanolic extracts explains the difference in their anthelmintic potency. The superior performance of the ethanolic extract is consistent with higher levels of essential phytochemicals such as alkaloids and flavonoids. It therefore relates chemical composition to biological activity, which in turn substantiates traditional knowledge about the medicinal attributes of *M. peltata* and proposes mechanisms for its observed therapeutic effects. The time-dependent response of the parasites to treatment, from paralysis to death, reflects a systemic impairment in vital functions possibly due to the synergistic action of many bioactive compounds.

Such studies are particularly relevant in this context because concern over anthelmintic resistance towards traditional pharmacological drugs is growing. The evidence that *M. Peltata* extracts would therefore provide alternative or adjunct therapy at locations where conventional anthelmintics are still not available. However, further research is necessary to fully elucidate the contributions of each identified compound and its mechanism of action. In vivo studies would prove useful in validating these findings under physiological conditions and would thereby expose potential toxicity. Further, standardization of the extract and interaction potential with other drugs would be necessary for the progress of this plant as a medicinal reagent.

5. CONCLUSION

The results of this study will indicate that the leaf extract of *Macaranga peltata* shows a highly significant level of anthelmintic activity, and the ethanolic is significantly more effective than the aqueous extract in a dose-dependent manner. Bioactive compounds like alkaloids, flavonoids, tannins, and saponins present in it seemed to cause its anthelmintic properties due to possible mechanisms of action. The ethanolic extract at 50 mg/ml revealed equal effectiveness compared to the standard drug albendazole and suggested its potential as a natural alternative for helminth control. Not only do these results validate the traditional use of *M. peltata* to treat parasitic infections but also indicate a scientific basis for its development into a therapeutic product. Still, further in vivo studies are needed to determine its safety profile and optimize its therapeutic potential.

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Conflicts of Interest

The authors declare no conflict of interest.

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