Systematic Review: The Antihelminthic Effect of Turmeric Rhizome Extract on Ascaris Parasitic Worm

Ratri Mauluti Larasati[1],
[1]Department of Physiology, Biochemistry and Biomolecular, Faculty of Medicine, Universitas Lampung, Bandar Lampung, Indonesia

*Corresponding Author: ratrilarasati717@gmail.com

ABSTRACT

Worm infections remain a significant health issue globally, including in Indonesia. The primary treatment for worms is the use of deworming medication, but this can have side effects. Turmeric produces various secondary metabolites that can be developed as drugs against pathogenic infections. Therefore, a literature review is needed to examine the anthelmintic activity of turmeric against Ascaris worms. A literature review methodology was applied, identifying primary data from journals worldwide and domestically over the previous ten years. The results indicate that turmeric rhizomes contain various active antihelminthic compounds that can treat Ascaris worm infections through various mechanisms, including inhibition of microtubulin proteins, muscle paralysis that inhibits motility, and disruption of worm digestion, leading to death. The active compounds in turmeric rhizomes have been shown to have a high affinity for beta-tubulin proteins, which play a key role in Ascaris worm motility.

Keywords: Turmeric plant extract, Ascaris worm, Protein Inhibition, Muscle paralysis

INTRODUCTION

Worm infections remain a significant health issue globally, including in Indonesia. Approximately 24% of the global population, equating to more than 1.5 billion individuals, is estimated to be affected by worm infections resulting from exposure to STH (Soil Transmitted Helminths) (Ghebreyesus, 2018). In Indonesia, STH infects 219 million people with a prevalence ranging from 1 to more than 50%.(Brauer *et al*, 2022).

The main treatment for worm problems is using worm medications such as Pyrantel Pamoate, Praziquantel, and the Benzimidazole group. (Elsheikha *et al*, 2011). Possible side effects of this medication include appetite loss, gastrointestinal upset, headaches, difficulty sleeping, and skin redness. Mebendazole (a benzimidazole) is known to have the side effect erratic migration. (Albonico *et al*, 2008). The use of deworming medication in pregnant women and children under 2 years of age is not recommended, and it is contraindicated in people with liver disease. Many cases of recurrent infections have been found despite antihelminthic therapy (Dharma, 2015). Therefore, a therapy is needed that has minimal side effects, and is expected to be consumed by all ages, one of which is herbal.

Turmeric species synthesize secondary metabolites that are not essential for primary physiological processes such as growth or reproduction. These metabolites—including alkaloids, flavonoids, tannins, and steroids—fulfill ecological roles as defense agents, antinutritional factors, attractants, and pheromonal signals, while also serving as promising candidates for drug development against pathogenic microorganisms. 40% of modern medicine today is derived from the development of secondary metabolites, including anthelmintics like ivermectin (Ridwan *et al*, 2020)

Research on the use of plants as a treatment for ascariasis has been carried out using several types of plants, such as bangle (*Zingiber purpureum*) (Murni *et al*, 2020). However, knowledge of plant extract compounds that have potential therapeutic effects for ascariasis or have anthelmintic effects against Ascaris worms is still limited. A comprehensive review of existing studies on the anthelmintic properties of plants against *Ascaris* is warranted, with the aim of shedding light on potential herbal therapies (Murni *et al*, 2020).

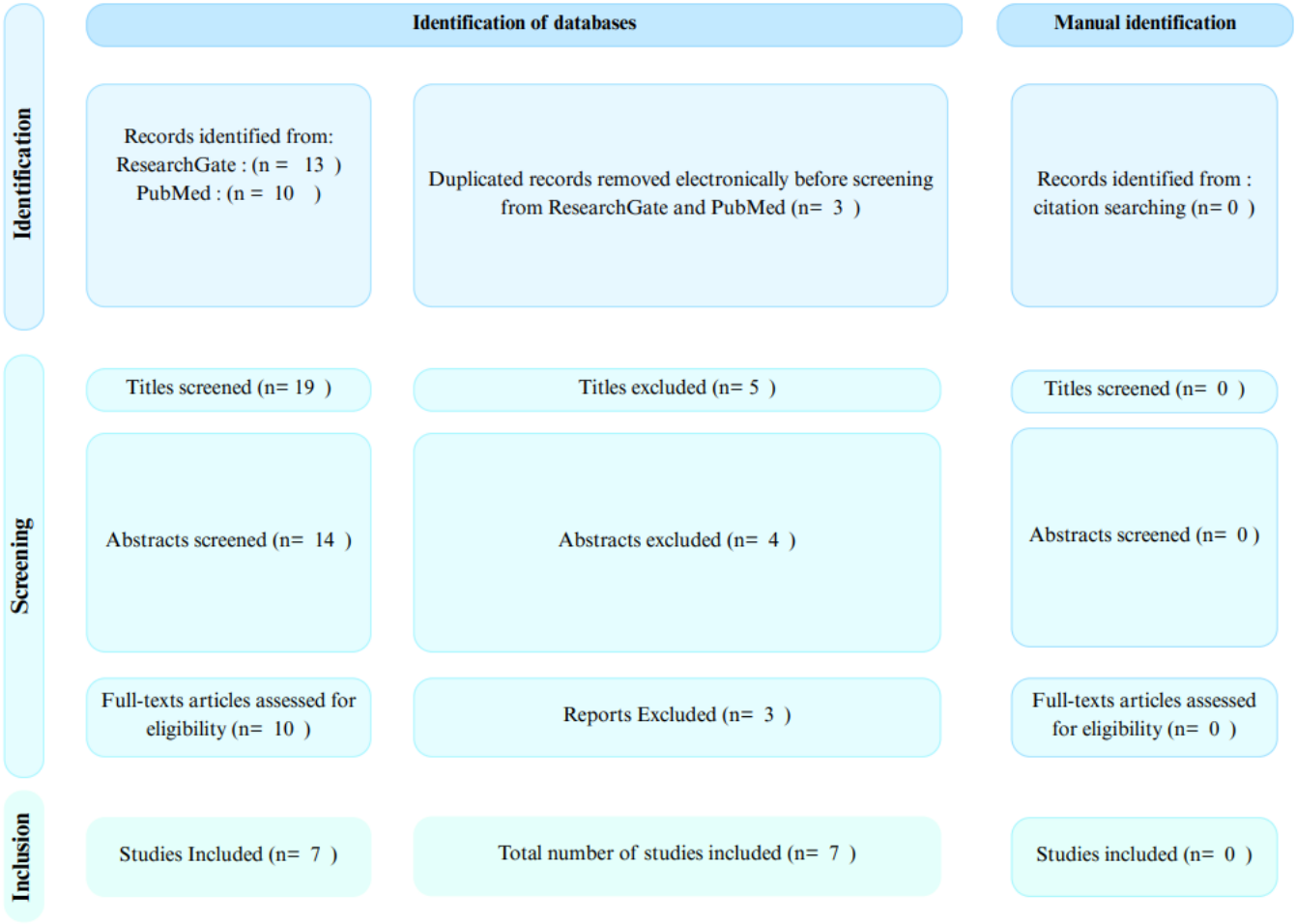

Figure 1. PRISMA Diagram

METHODS

This review was prepared using a literature study approach, which entailed gathering primary sources from national and international journals published within the past decade. The data collection process was carried out through online platforms, including Google and journal databases such as NCBI and PubMed (NCBI, PubMed, etc.)

RESULTS AND DISCUSSION

Pathogenic microorganisms such as bacteria, viruses, parasites, and fungi are responsible for causing infectious diseases. Parasites include protozoa, worms, and ectoparasites. (Ghebreyesus, 2019). Turmeric rhizomes contain chemical compounds consisting of 2 groups, namely curcuminoids and essential oils. (Kiso, 1983).

The active substances contained in turmeric are used as traditional medicines such as hepato- and cardioprotective, antihyperglycemic, antifungal, antioxidant, antiparasitic and antibacterial (Verma *et al.*, 2018). Turmeric is a herb containing saponins, flavonoids, and tannins. Exposure to saponins leads to disruptions In the ability of the worm's cell membrane to allow substances to pass through. This leads to vacuolization and disintegration of the worm's tegument. This causes the worm to experience flaccid paralysis and death. Flavonoids cause worm death by degenerating neurons and denaturing proteins in the worm's body tissue. Tannins cause protein clumping in the worm's walls, disrupting its metabolism and homeostasis. This disruption leads to nutrient deficiencies, leading to its death (Ulya *et al*, 2014).

Table 1. Antihelminthic Effect of Turmeric Rhizome Extract on *Ascaris sp* Parasitic Worm article reviews

No	Title	Method	Result
1	An in-silico study of active compounds from turmeric rhizomes (*Curcuma domestica*) on the inhibition of acetylcholinesterase, microtubulin (beta tubulin), and calcium channel activation as an anthelmintic therapy (Arfi *et al*, 2020)	Computational evaluation was performed to examine how active compounds bind to Acetylcholinesterase, Microtubulin (β-Tubulin), and Calcium Channels.	Cyclocurcumin shows a strong tendency to inhibit the β-tubulin protein in *Ascaris lumbricoides* worms.
2	Turmeric rhizome ethanol extract caused muscle paralysis and death of Ascaris suum Goeze in vitro. (Khoirunnisa *et al*, 2020)	An in vitro experiment was conducted using *Ascaris suum* Goeze, categorized into five treatment groups exposed to turmeric rhizome ethanolic extract at concentrations of 0.5%, 1%, 2%, 4%, and 8%.	A linear relationship was observed between the concentration of turmeric rhizome ethanolic extract and its anthelmintic activity. The extract demonstrated a PC value (Paralysis Concentration) PC50 value of 2.05% and an Lethal Concentration (LC50) value of 3.96%.
3	Anthelmintic Activity of Galangal, Turmeric, and Ginger in Single and Combination (Azhari *et al.*, 2024)	The analysis of anthelmintic activity involved measuring paralysis duration, mortality time, Inhibitory Concentration (IC50), and the combination index.	Galangal, turmeric, and ginger ethanol extracts exhibited anthelmintic activity with IC50 values of 7.66, 22, and 13.14 mg/mL. The blends of galangal–turmeric, galangal–ginger, and turmeric–ginger showed IC50 values of 10.22, 3.92, and 34.93 mg/mL, respectively.
4	Effects of curcumin on *Toxocara vitulorum* adult worms and eggs under ex vivo conditions(Dahab *et al*, 2021)	In an ex vivo setup, adult *Toxocara vitulorum* and eggs were incubated at 37°C for 4 hours with curcumin concentrations ranging from 0 to 500 μM, using RPMI 1640 medium supplemented with 2% DMSO.	Curcumin reduced the viability and motility of about 30% of worms in a dose-dependent fashion. At higher concentrations, scanning electron microscopy showed cuticular alterations along the entire length of the roundworms. Additionally, curcumin exposure led to a marked rise in egg mortality and inhibited progression to the infective stage occurred in a manner dependent on both dose and exposure time.
5	Comparison of the anthelmintic efficacy of large white ginger (*Zingiber* var. Roscoe) and turmeric (*Curcuma longa* L.) extracts against Ascaris Suum worms in vitro (Jusran *et al.*, 2023)	This experimental study evaluated the lethal effects of ginger and turmeric on *Ascaris suum*, considering both concentration and exposure time. For each extract, the collected samples were categorized into four separate groups.: a control group (0.9% NaCl) and treatment groups at 2%, 4%,	The lethal effects of ginger and turmeric differed significantly across concentrations ($p < 0.000$) compared with the negative control. Both extracts exhibited anthelmintic activity against *Ascaris suum*, which was dependent on concentration and exposure duration.
6	In vitro assessment of the anthelmintic properties of *Curcuma longa* (Linn.) rhizome extracts (Pandey et al, 2018)	Different extract concentrations (1, 2.5, 5, and 10 mg/mL) in PBS were evaluated, with outcomes reported as paralysis time and mortality rate.	Both methanolic and aqueous extracts of *Curcuma longa* rhizome demonstrated significant efficacy ($p \leq 0.05$) in inducing paralysis and mortality of worms at all concentrations examined, effects were observed within 12 hours

			versus the negative control. Extracts obtained from the rhizome also exhibited dose-dependent activity in producing worm paralysis.
7	Effects of ethanol extract of a combination of turmeric rhizome (*Curcuma domestica*) and ginger rhizome (*Zingiber officinale* var. Amarum) on the paralysis and mortality of adult Ascaris suum goeze worm in vitro (Sahara *et al*, 2020)	Ethanol extracts of turmeric and ginger were tested at 0.81%, 1.62%, 3.25%, 6.50%, and 13.00%. Controls consisted of 0.9% NaCl (negative) and pyrantel pamoate 5 mg/mL (positive).	The findings indicated that higher concentrations of the combined ethanol extract of turmeric and ginger produced proportionally greater anthelmintic activity. The extract exhibited a PC50 of 2.33% and an LC50 of 2%.

The saponin compounds in this herb have the same mechanism of action as pyrantel pamoate. This drug can cause muscle paralysis by inhibiting the enzyme acetylcholinesterase. The anthelmintic properties of saponins are known to be due to their sapogenin or triperpenoid group, pentose, hexose, and uronic acid groups. The sapogenin group works by inhibiting the enzyme acetylcholinesterase. (Kuntari, 2008).

Acetylcholinesterase functions to hydrolyze acetylcholine. Acetylcholine itself is a substance released from motor nerve endings to activate receptors, which initiate a series of contractions. Inhibiting the acetylcholinesterase enzyme will increase inhibition of neuromuscular impulse transmission, resulting in increased acetylcholine production and sustained contractions. This will cause muscle paralysis in Ascaris suum worms. (Syarif and Elysabeth, 2011).

Most of the anthelmintic test studies used alcohol extracts in the form of ethanol or methanol, namely eight studies, with different concentrations, namely 70% and 96%. According to (Zhang *et al*, 2018), The active compounds contained in medicinal plants are always low. Therefore, precise extraction is necessary to achieve the desired results. One method is to use solvents, which is currently the most widely used extraction method.

Another approach employed was in silico molecular docking, a technique commonly used to predict how small-molecule drug candidates interact with protein targets by estimating their activity and binding affinity (Mukesh and Rakesh, 2011). This approach yields the free binding energy (ΔG), inhibition constant (Ki), surface interactions, and the amino acid residues involved in the interaction between the active compound and the target receptor.

The binding of the active compounds of Turmeric Rhizome to Beta Tubulin that were identified showed that the free binding energy value of the Cyclocurcumin compound was lower than the value of the Mebendazole control of -7.39 kcal/mol. For the inhibition constant, the results showed that only the Cyclocurcumin compound had an inhibition constant value below the Mebendazole control value, which was 3.81 μM. The turmeric rhizome compounds with the greatest surface interaction values, exceeding Mebendazole, were Monodemethylcurcumin (864.165 Å), Dihydrocurcumin (806.416 Å), and Cyclocurcumin (802.705 Å). The amino acid residue similarity to the Beta Tubulin protein was greatest for Dihydrocurcumin with 16 amino acid residues. (Arfi *et al*, 2020). These results indicate that the key active substance found in turmeric rhizome which is predicted to have strong potential to bind to the target protein Beta Tubulin of the worm *Ascaris lumbricoides*, the free binding energy of Cyclocurcumin was –7.39 kcal/mol.

Molecular docking results showed that the ligand affinity for the microtubule protein (beta-tubulin) cyclocurcumin had the lowest ΔG value of -7.39 kcal/mol, with 81% similarity in amino acid residues to the control.(Arfi *et al* 2020). According to (Yuliana and Dewi, 2013) The lower the free binding energy, the higher the stability and spontaneity of ligand binding to the target protein.

Cyclocurcumin, a curcuminoid compound, is predicted to have potential as an anthelmintic therapy due to its high affinity for the beta-tubulin target protein in *Ascaris lumbricoides* worms.

Meanwhile, the control compound, mebendazole, is predicted to have strong potential in inhibiting the beta-tubulin target protein.

CONCLUSION

Turmeric rhizomes contain various active antihelminthic compounds that can treat Ascaris worm infections through various mechanisms, including inhibition of microtubulin proteins, muscle paralysis that inhibits motility, and disruption of worm digestion, leading to death. The active compounds in turmeric rhizomes have been shown to have a strong tendency to bind β-tubulin proteins, which are vital for the movement of *Ascaris* worms.

ACKNOWLEDGEMENTS

The author gratefully acknowledges the support and assistance of all parties who contributed to the completion of this article.

REFERENCES

Albonico, A., Allen, H. and Chitsulo, L. (2008) 'Controlling Soil-Transmitted Helminthiasis in Pre-School-Age Children through Preventive Chemotherapy', *PLoS Negl Trop Dis*, 2(3).

Arfi, A.., Lestari, R.. and Damayanti, D.. (2020) 'Studi In Silico Senyawa Aktif Rimpang Kunyit (Curcuma Domestica) Terhadap Penghambatan Acetylcholinesterase, Microtubulin (Beta Tubulin), Dan Aktivasi Calcium Channel Sebagai Terapi Antelmintik', *Jurnal Ilmiah Mahasiswa Unisma*, pp. 36–47.

Azhari, M. *et al.* (2024) 'Anthelmintic Activity of Galangal, Turmeric, and Ginger in Single and Combination', *Indonesian Journal of Pharmaceutical Science and Technology*, 11(3), pp. 294–304.

Brauer, M *et al* (2022) 'Distribution of soil transmitted helminth survey data in Indonesia', *Global Atlas of Helminth Infections.*, 11(1), pp. 78–92.

Dahab, M.., Sayed, A. and Mahana, N. (2021) 'Curcumin Impact on Ex Vivo Toxocara vitulorum Adult Worms and Eggs', *International Journal of Veterinary Science*, 11(3), pp. 280–288.

Dharma, Y.. (2015) *Resistensi Anti Helminth pada Infeksi Soil Transmitted Helminth*. University of Lampung.

Elsheikha, H.., McOrist, S. and Geary, T.. (2011) 'Antiparasitic Drugs: Mechanisms of Action and Resistance', in *Essential of Veterinary Parasitology*. Caisher Academic Press, p. 194.

Ghebreyesus, TA (2018) *Soil-transmitted helminth infections*. Available at: https://www.who.int/news-room/fact-sheets/detail/soiltransmitted-helminth-infections.

Ghebreyesus, TA (2019) *Soiltransmitted helminth infections*, *Who.int*. Available at: https://www.who.int/news-room/factsheets/detail/soil-transmitted-helminthinfections.

Jusran, A.. *et al.* (2023) 'Perbandingan Efektivitas Antelmintik Ekstrak Jahe Putih Besar (Zingiber Officinale Var. Roscoe) Dan Kunyit (Curcuma Longa L.) Terhadap Cacing Ascaris Suum Secara In Vitro', *Biomedika*, 15(2), pp. 149–155.

Khoirunnisa, S., Falyani, S.. and Damayanti, D.. (2020) 'Efek Ekstrak Etanol Rimpang Kunyit Terhadap Paralisis Dan Kematian Cacing Dewasa Ascaris Suum Goeze Secara In Vitro', *Jurnal Ilmiah Mahasiswa Unisma*, pp. 48–58.

Kiso, Y. (1983) 'Anti-hepatotoxic Principles of Curcuma longa Rhizomes', *Planta Medica*, 49, pp. 185–187.

Kuntari (2008) 'Daya Antihelmintik Air Rebusan Daun Ketepeng (Cassia Alata L) Terhadap Cacing Tambang Anjing In vitro', *Fakultas Kedokteran Universitas Islam Indonesia* [Preprint].

Mukesh, B. and Rakesh, K. (2011) 'Molecular Docking : A Review', *International Journal of Research in Ayurveda & Pharmacy*, 2(6), pp.

1746–51.

Murni, M., Isnawati, R. and Lobo, L.T. (2020) 'Aktivitas Anthelmintik Ekstrak Murni Bangle (Zingiber purpureum) terhadap Cacing Gelang (Ascaris suum. L) Secara In Vitro', in *Seminar Nasional Biologi*, pp. 1–8. Available at: http://103.76.50.195/semnasbio/article/view/15431.

Pandey, J., Mishra, S. and Jaiswal, K. (2018) 'In Vitro Evaluation Of The Anthelmintic Activity Of Rhizome Extracts Of Curcuma Longa (Linn.)', *Asian Journal of Pharmaceutical and Clinical Researches*, 11(12), pp. 425–428.

Ridwan, Y., Satrija, F. and Handharyani, E. (2020) 'Aktivitas Anticestoda In Vitro Metabolit Sekunder Daun Miana (Coleus blumei. Benth) terhadap Cacing Hymenolepis microstoma', *Jurnal Medik Veteriner*, 3(1), p. 31.

Sahara, S., Herbani, M. and Damayanti, D.. (2020) 'Efek Ekstrak Etanol Kombinasi Rimpang Kunyit (Curcuma Domestica) Dan Rimpang Jahe Emprit (Zingiber Officinale Var.Amarum) Terhadap Paralisis Dan Kematian Cacing Dewasa Ascaris Suum Goeze Secara In Vitro', *Jurnal Ilmiah Mahasiswa Unisma* [Preprint].

Syarif, A. and Elysabeth (2011) *Farmakologi dan Terapi Edisi 5*.

Ulya, N., Endharti, A.. and Setyohadi, R. (2014) 'Uji daya anthelmintik ekstrak etanol daun kumis kucing (Orthosiphon aristatus) sebagai anthelmintik terhadap Ascaris suum Goeze secara In Vitro', *Majalah kesehatan FKUB*, 1(3), pp. 130–136.

Verma, R.. *et al.* (2018) 'Medicinal properties of turmeric (curcuma longa l.): a review', *International Journal of Chemical Studies*, 6(4), pp. 1354–1357.

Yuliana and Dewi (2013) 'In Silico Screening of Chemical Compounds from Roselle (Hibiscus Sabdariffa) as Angiotensin-I Converting Enzyme Inhibitor Used PyRx Program', *Journal of Science and Technology* [Preprint].

Zhang, Q.W., Lin, L.G. and Ye, W.C. (2018) 'Techniques for Extraction and Isolation of Natural Products: A comprehensive review', *Chinese Medicine*, 13(20), pp. 1–26.