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Literature Review

Promising Anthelmintic Properties of Papaya (Carica Papaya) Extract: A Literature Study

Studi Literatur Potensi Ekstrak Pepaya (*Carica papaya*) sebagai Antelmintik

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ABSTRACT

Helminthiasis is a lurking health issue worldwide. Currently, available anthelmintics focus on the benzimidazole group, despite their side effects and threats of anthelmintic resistance. Therefore, exploration of novel compounds with anthelmintic properties is crucial. Papaya (Carica papaya) contains active compounds with prospective anthelmintic properties. This literature review discusses the potential of papaya as an anthelmintic agent. We screened publications from indexed journals in English and Indonesian published between 2013–2023 covering topics of C. papaya active compounds and their anthelmintic properties. Seeds, leaves, bark, and stems of papaya showed various degrees of anthelmintic properties. Studies reported its efficacy against several helminth species with good safety profiles. C. papaya extract can be a promising anthelmintic candidate. Aside from its abundance, its effectiveness and safety yielded satisfactory results. Further research is needed to elicit the mechanism of C. papaya as a novel therapeutic modality for parasitic infections.

Keywords: *Active compounds, anthelmintic, Carica papaya, helminthiasis*

ABSTRAK

Kecacingan masih menjadi permasalahan kesehatan dunia. Antelmintik yang tersedia saat ini berfokus pada golongan benzimidazole, meski terdapat efek samping dan resistensi obat. Oleh karena itu, diperlukan eksplorasi bahan baru dengan potensi antelmintik. Ekstrak papaya (*Carica papaya*) diketahui memiliki kandungan aktif dengan potensi antelmintik. Studi lieratur ini membahas potensi pepaya sebagai agen antelmintik. Kami melakukan pencarian terhadap publikasi berbahasa Inggris dan Indonesia yang dipublikasikan antara tahun 2013–2023 yang mencakup topik mengenai bahan aktif *C. papaya* dan potensi antelmintiknya. Biji, daun, kulit batang, dan batang pepaya menunjukkan kemampuan antelmintik yang bervariasi. Efektivitas bahan-bahan aktif tersebut terhadap beberapa spesies helminth dengan profil keamanan yang baik telah dilaporkan. Ekstrak *C. papaya* dapat menjadi kandidat agen antelmintik yang menjanjikan. Selain mudah didapatkan, efektivitas dan keamanannya menunjukkan hasil yang memuaskan. Penelitian lebih lanjut diperlukan untuk mengetahui mekanisme *C. papaya* sebagai modalitas terapi baru untuk infeksi parasitik.

Kata Kunci: Antelmintik, bahan aktif, *Carica papaya,* helminthiasis*,*

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INTRODUCTION

Helminthiasis remains one of the most commonly found health issues in tropical countries. The World Health Organization (WHO) reported that more than 24% of the world population is infected by intestinal helminths (1). In Indonesia, the prevalence of soil-transmitted helminths (STH) reached up to 40-60% of the total population. The highest incidence in Indonesia includes STH species, especially *Ascaris lumbricoides* and *Trichuris trichiura*, and tapeworms (2). (2). As a result of its non-specific symptoms, worm infection is often overlooked and neglected. This situation results in increased risks of malnutrition and anemia, particularly in chronic helminthiasis in children. This, in turn, leads to disturbances in growth, intelligence, and productivity (3).

The most frequently used anthelmintic drug in the present involves the benzimidazole group, such as albendazole and mebendazole. Unfortunately, prolonged and inadequate use of these anthelmintics gives rise to drug resistance, which hinders proper helminth control programs (2). Furthermore, some anthelmintics displayed teratogenic effects if consumed by pregnant women in their first trimester. Therefore, it is important to explore compounds, including natural resources, to develop novel anthelmintic agents with better efficacy and safety.

One of the potential resources as an anthelmintic candidate is the papaya plant or *Carica papaya*. *C. papaya* is easy to grow, abundant in tropical regions, and inexpensive, and its fruit and leaves are widely consumed in Indonesia. *C. papaya* contains bioactive components with important health roles, including anthelmintic properties. Thus, this literature review aims to explore the potential of *C. papaya* as an anthelmintic agent to support the development of therapeutic agents in the future that can support the management of helminthiasis by utilizing natural resources.

METHOD

We sought out published full-text articles related to the effectiveness of *C. papaya* against helminth infections in English or Indonesian, published between 2013 and 2023, in several public databases, including Google Scholar, PUBMED, ScienceDirect, ResearchGate, OneSearch, Cochrane, and JSTOR, as well as several publisher databases, including Nature, Wiley, and Hindawi. We used the keywords (“CARICA PAPAYA”) and (“WORM” or HELMINTH”) and (“CARICA PAPAYA”) and (INFEKSI CACING) for our search strategy. After identification and deduplication, 3355 articles were obtained. Accessible full texts comprised 30 articles, out of which, 13 were further selected due to their high relevance to the topic. The inclusion criteria and literature selection flow are summarized in Table 1 and Figure 1, respectively.

Table 1. Inclusion criteria

Criteria	Inclusion
Problems	Helminthiasis remains high prevalence in Indonesia
Intervention	*C. papaya* is a promising candidate as an anthelmintic agent
Comparison /control	The effectiveness of *C. papaya* compared to standardized anthelmintic drugs (albendazole, praziquantel, piperazine citrate, pyrantel pamoate, ivermectin)
Outcome	Efficacy parameters (egg count, worm death, worm burden, changes in worm morphology, interference of worm physiology, parasite findings in stool samples)
Study design	Experimental study

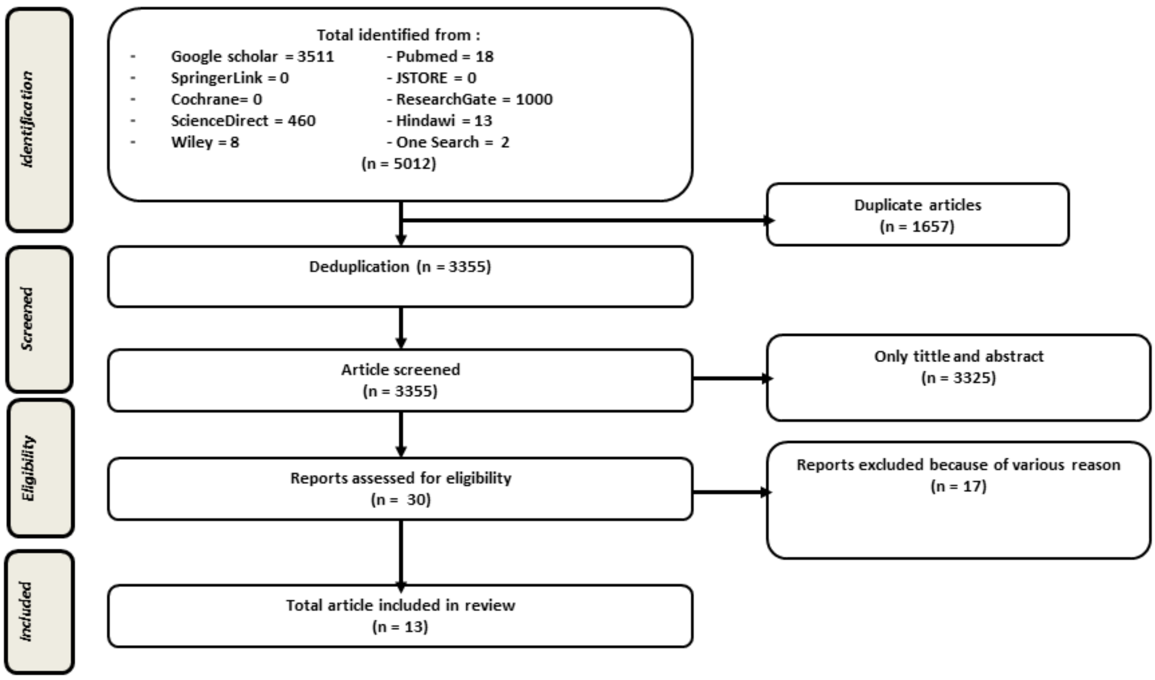

Figure 1. Literature search flow

Note: References in English and Indonesian on the topic of *Carica papaya* and helminths published in 2013-2023 were sought out from several scientific and publisher databases. After deduplication, articles with accessible full texts were further screened based on their high relevance and suitability, which resulted in 13 articles being selected.

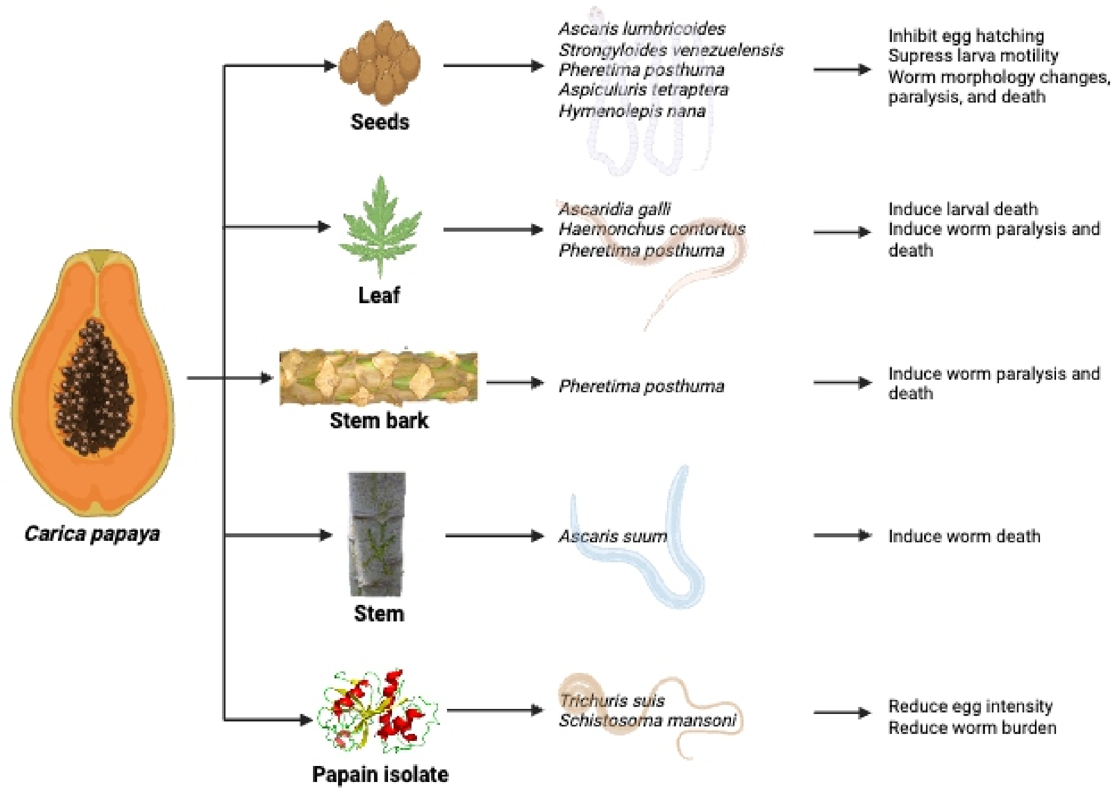

Figure 1. Proposed anthelmintic actions of *Carica papaya*

Note: Various parts of C. papaya, including the seed, leaf, stem bark, and stem, have been studied for their anthelmintic properties toward several nematodes, cestodes, and trematodes. Although the active compounds and their molecular pathways remain to be elucidated, the anthelmintic mechanism affected almost all helminthic life stages (egg, larva, and adult worm). Figure was created using BioRender.com.

RESULTS

Upon selection of articles according to inclusion and exclusion criteria, 13 full-text articles were selected to be included in this review. The studies were then classified based on the parts of *C. papaya* used (seed, leaf, stem bark, stem, or active compound). Each part will be further classified based on their experimental study design (in vitro, in vivo, or clinical study) and type of extract preparations. The anthelmintic potencies of the extracts were summarized based on their outcomes and compared to the control drug (if available). The summary is presented in Figure 1 and Table 2.

Table 2. Summary of literature search results

Author, Year	Worms Species and Study Design	Plant Part	Extract	Extract Activity	Comparison/Control
Cabral *et al*., (4)	*Strongyloides venezuelensis* (in vitro)	Seed	Hexane	Egg hatching inhibition : 95.74% (56.6mg/mL) and 92.16% (5.66mg/mL) Larval motility suppression: 100% (566mg/mL) and 97.32% (56.6mg/mL) The lethal dose of egg hatching and larval motility: 78.14mg/mL and 20.02mg/mL at 24 h (respectively)	Egg hatching inhibition : 90% (albendazole 0.025mg/mL) Larval motility suppression: 100% (ivermectin 0.316mg/mL)
Goku *et al*., (5)	*Pheretima posthuma* (in vitro)	Seed	Ethanol (SE) and Hydroethanol (SHE)	Worm paralysis (m ins): 7.210±0.01 (5mg/mL SE) and 8.310±0.01 (5mg/mL SHE) Worm death (min s): 9.150±0.00 (5mg/mL SE) and 10.210±0.00 (5mg/mL SHE)	Worm paralysis (mi ns): 16.030±0.03 (5mg/mL albendazole) Worm death (min s): 27.210±0.00 (5mg/mL albendazole)

Table 2. Summary of literature search results (Cont.)

Author, Year	Worms Species and Study Design	Plant Part	Extract	Extract Activity	Comparison/Control
Mahdy *et al*., (6)	*Aspiculuris tetraptera* (in vivo)	Seed	Powder	Changes in morphology, edema, swelling, cuticular vacuolization in various areas, and worm alae shrinkage: 1.2g/kg BW in 3 days	-
Shady *et al*., (7)	*Hymenolepis nana* (in vivo)	Seed	*Aqueous*	Worm burden: 11.67±4.84 (first 2 H) and 9±4.34 (3rd day) Total of eggs: 59.17±21.85 (first 2 h) and 18±9.4 (3rd day) Viability of eggs: 23.17±8.08 (first 2 h) and 8.17±5.12 (3rd day)	*Worm burden*: 5.33±6.44 (first 2 h) and 0±0 (3rd day) Total of eggs: 11.83±9.6 (first 2 h) and 1.33±3.27 (3rd day) Viability of eggs: 0 .67±1.63 (first 2 h) and 0.33±0.82 (3rd day) (Praziquantel)
Ambarwati (8)	*Ascaris lumbricoides* (clinical study)	Seed	Powder	Worm eggs: all negative after 7 days	-
Saeni *et al*., (9)	STH (in vivo)	Seed	Flour	Infection status: 100% negative after 1 week	-
Rahmasari dan Wibowo (10)	*Ascaridia galli* (clinical study)	Leaf	Ethanol	Worm death: 2.75 (5%), 4.5 (10%), and 5 (20%, 40%, 60%, 80%) after 12 h LC90: 14.42%	Worm death: 5 (pyrantel pamoate 0.5%) after 12 h
Widiastuti *et al*., (11)	*Ascaridia galli* Schrank (in vitro)	Leaf	Ethanol	Worm death (h): 22.13 (5%), 20.27 (10%), and 18.67 (15%) LC50: 4.42% LC90: 7.68%	Worm death (h): 7,73 (piperazine citrate 0.4%) LC50: 0.4%
Ekawasti *et al*., (12)	*Haemonchus contortus* (in vitro)	Leaf	Ethanol	Larval death: 55% (after 24 h) and 65% (after 48 h) Worm death: 5 (at 5th h)	Larval death: 75% (albendazole after 24 h) and 85% (albendazole after 48 h) Worm death: 5 (at 6th h)
Goku *et al*. (5)	*Pheretima posthuma* (in vitro)	Leaf	Ethanol (LE) and Hydro ethanol (LHE)	Worm paralysis (minute): 9.120±0.02 (5mg/mL SE) and 8.510±0.00 (5mg/mL SHE) Worm death (minute): 11.480±0.26 (5mg/mL SE) and 12.250±0.00 (5mg/mL SHE)	Worm paralysis (minute): 16.030±0.03 (5mg/mL albendazole) Worm death (minute): 27.210±0.00 (5mg/mL albendazole)
Goku *et al.* (5)	*Pheretima posthuma* (in vitro)	Stem Bark	Ethanol (STE) and Hydro ethanol (STHE)	Worm paralysis (minute): 10.420±0.29 (5mg/mL SE) and 9.280±0.02 (5mg/mL SHE) Worm death (minute): 14.220±0.00 (5mg/mL SE) and 16.350±0.02 (5mg/mL SHE)	Worm paralysis (minute): 16.030±0.03 (5mg/mL albendazole) Worm death (minute): 27.210±0.00 (5mg/mL albendazole)
Obeng *et al*., (13)	*Pheretima posthuma* (in vitro)	Stem Bark	Ethanol	Worm paralysis (minute): 71.88±0.62 Worm death (minute): 231.62±0.42 Combination of extract 0.5mg/mL and albendazole 2.5mg/mL = Worm paralysis (minute): 153.54±0.62 Worm death (minute): 254.96±0.99	Worm paralysis (minute): 165.23±1.78 (albendazole 10mg/ml) Worm death (minute): 324.70±2.85 (albendazole 10mg/ml)
Bestari *et al*., (14)	*Ascaris suum* (in vitro)	Stem	Ethanol	Worm death: 1.46h after therapy (0.4g/mL)	Worm death: 7 h after therapy (pyrantel pamoate 0.5g/mL)

Table 2. Summary of literature search results (Cont.)

Author, Year	Worms Species and Study Design	Plant Part	Extract	Extract Activity	Comparison/Control
Tallima *et al.*, (15)	*Schistosoma mansoni* (in vivo)	Active compound	Papain isolate	Worm burden: decreased to >60%	-
Levecke *et al.*, (2)	*Trichuris suis* (in vivo)	Active compound	Papain isolate	Eggs at high-intensity infection: 98.9% (450µM) Mature worms at high - intensity infection: 97.4% (450µM)	Eggs at high-intensity infection: 64.4% (400mg albendazole) Mature worms at high - intensity infection 59.0% (400mg albendazole)

Note: h: hour, kgBW: kilogram body weight, LE: ethanolic extract from leaves, LHE: hydroethanolic extract from leaves, SE: ethanolic extract from seeds, SHE: hydroethanolic extract from seeds, STH: soil-transmitted helminths, STHE: hydroethanolic extract from stem

DISCUSSION

Anthelmintic Activity of Papaya Seed Extract

Various parts of the papaya were used in numerous trials, including the seeds, leaves, stalks, latex, and stems. Based on previous studies, the most studied part is the seed. According to Saeni *et al.*, (9), *C. papaya* seeds contain carpaine, an alkaloid that can inhibit bacterial growth, and ringed lactonic alkaloid with 7 groups of methylene chain, which is potent in inhibiting the growth of several organisms, including helminths. Hexane extract of *C. papaya* seeds showed significant ovicidal and larvicidal activity in in vitro studies against *Strongyloides venezuelensis*. Concentrations 56.6mg/mL and 5.66mg/mL were found to have the greatest inhibitory effects on egg hatching numbers with inhibition values of 95.74% and 92.16%, respectively. This activity was more effective than albendazole 0.025mg/mL which only inhibited 90% of egg hatching. In addition, a high concentration of 566mg/mL lysed *S. venezuelensis* specimens is better than other solutions. Papaya seed extract with a concentration of 566mg/mL and 56.6mg/mL was also effective in suppressing larval motility by 97%-100%. These results were as effective as ivermectin 0.316mg/mL. The same study also reported that *C. papaya* seed extract had a lethal dose for worm egg hatching and larval motility of 78.14mg/mL and 20.02mg/ml, respectively, at the 24^{th} hour of treatment (4).

An in vitro study on the effect of ethanol extract of *C. papaya* seeds against *Pheretima posthuma* showed worm paralysis and worm death at 7.210±0.01 minutes and 9.150±0.00 minutes, respectively, after administration of 5mg/mL extract. *C. papaya* seed extracted using hydro ethanol also showed anthelmintic activities, including worm paralysis and worm death at 8.310±0.01 minutes and 10.210±0.00 minutes, respectively, after administration of 5mg/mL extract. The control drug, albendazole at a concentration of 5mg/mL, showed worm paralysis and death at 16.030±0.03 minutes and 27.210±0.00 minutes, respectively, after administration. These results indicated that *C. papaya* seed extract showed a superior anthelmintic activity compared to albendazole at the same dose (5).

In vivo study of *C. papaya* seed extract at a dose of 1.2g/kg for 3 days against the nematode *Aspiculuris tetraptera* in mice showed changes in morphology, edema, swelling, cuticle vacuolization in various areas, and shrinkage of the worm alae. In addition, a focus area containing leukocytes was found on histopathological examination which indicated the anthelmintic activity of the alkaloid component (benzyl isothiocyanate) of *C. papaya* seeds (6). Another in vivo study by Shady et al. reported that *C. papaya* seed extract was effective in reducing the number of adult worms (worm burden) and eggs in albino rats infected with *Hymenolepis nana*. In this study, rats given *C. papaya* seed extract showed significant changes in decreasing the worm burden, egg number, and egg viability on the third day of treatment. On the other hand, there was no significant difference in the number of cysticercoids in the small intestine among groups on the fourth day after infection (7).

The anthelmintic effect of *C. papaya* seed extract had also been tested in humans in a quasi-experimental study of elementary school students aged 7–12 years who were infected with *A. lumbricoides*. In this study, the subjects who received *C. papaya* seed powder showed satisfactory results with no helminth eggs found after 7 days of treatment (8). Another clinical study by Saeni *et al.*, (9) also showed a positive effect of *C. papaya* on anthelmintics. In this study, surveillance was conducted on the STH status of elementary school students in Taduy Village, West Sulawesi. A total of 35 elementary school students who were involved in the study had positive infection of STH before the administration of *C. papaya* seed flour, which was dried for 2, 3, or 4 hours at 50°C. After 1 week of treatment, 100% of the subjects were negative for STH infection. The drying time of *C. papaya* seeds did not show a significant difference in their effectiveness.

Anthelmintic Activity of Papaya Leaf Extract

Another commonly used *C. papaya* part is the leaves. The leaves contain high levels of saponins and papain. Saponins act by damaging the cell membranes and cell proteins of the helminths, while papain inhibits the supply of the worms' nutrients by destroying their body proteins. An in vitro study by Rahmasari and Wibowo (10) using an infusion extract of *C. papaya* L. leaves at concentrations of 5%, 10%, 20%, 40%, 60%, and 80% against *Ascaridia galli* showed anthelmintic effectiveness after 12 hours of administration. The results showed that a concentration of 14.42% was needed to kill 90% of the worm population. They also reported a dose-dependent anthelmintic activity. The infusion method displayed different results compared to ethanol extraction since the latter was able to produce a higher amount of active ingredients, to provide maximum results. This was demonstrated in another in vitro study by Widiastuti *et al.,* (11) who reported that the ethanol extract of papaya leaves with increased concentrations of 5%, 10%, and 15% accelerated the death time of *A. galli Schrank*, starting at 16 hours after treatment. The lethal concentration of 50% (LC50) of papaya leaf ethanol extract was 4.42%, with an LC90 of 7.68%. Thus, it was concluded that the LC50 of the ethanol extract of *C. papaya* leaves was lower than that of the infusion extract, indicating its higher anthelmintic potential, despite still being below the LC50 of piperazine citrate (0.4%) as the control drug.

Another in vitro study conducted by Ekaswati *et al.*, (12) used the maceration method with 96% ethanol solvent for *C. papaya* leaves. *C. papaya* leaf extract was given to eggs from fecal samples, cultured larvae, and the adult stage of *Haemonchus contortus*. The study showed that *C. papaya* leaf extract at a concentration of 1% was able to inhibit the nematode spawn egg and death. Fifty-five percent of larval mortality occurred in the first 24 hours and increased to 65% at 48 hours. In addition, 5% of worms died 5 hours after therapy. These results were in line with an in vitro study by Goku et al[5] showing that the ethanol extract (98%) and hydroethanolic extract of *C. papaya* leaves at concentrations of 1, 2.5, and 5.0mg/mL accelerated the paralysis and death of *P. posthuma* in a dose-dependent manner. The efficacy of the extract was also better than albendazole at the same concentration.

Anthelmintic Activity of Papaya Stem Bark Extract

A study by Goku *et al.,* found that the bark of *C. papaya* stems influenced the paralysis and death of *P. posthuma* (5). The ethanol and hydroethanol extracts of papaya stem bark surpassed the efficacy of albendazole in inducing worm paralysis. Another study with similar subjects and parameters also showed satisfactory results, where the anthelmintic activity of ethanol extract (70%) of *C. papaya* stem bark was more effective than albendazole according to paralysis time and worm death parameters. Albendazole at a concentration of 10mg/mL significantly immobilized and killed the worms 1.78- and 2.85-minutes post-treatment ($p<0.00001$). Compared to albendazole, the ethanol extract of *C. papaya* stem bark at 10mg/mL significantly caused worm paralysis at 0.62 minutes and death at 0.42 minutes after therapy ($p<0.00001$). In addition, the ethanol extract of *C. papaya* stem bark could increase the anthelmintic activity of albendazole through combination therapy of *C. papaya* stem bark extract 0.5mg/mL and albendazole 2.5mg/mL, which significantly accelerated the paralysis and death of worms to 0.62- and 0.99-minutes post-treatment ($p<0.00001$), respectively (13).

Anthelmintic Activity of Papaya Stem Extract

An in vitro study on 96% ethanol extract from papaya stems against *Ascaris suum* showed satisfactory results as an anthelmintic. A concentration of 0.4g/mL resulted in worm death within 1.46 hours after therapy. This was significant when compared to the positive control group using pyrantel pamoate 0.5%, which showed worm death at 7 hours after therapy (14).

Anthelmintic Activity of Papain Isolate from Papaya

Utilization of papain as the active compound from *C. papaya* has also been studied by Tallima *et al.,* (15) who observed *Schistosoma mansoni* in immunocompetent and athymic heterogeneous mice. Papain extract significantly reduced more than 60% of the worm burden. The absence of the cysteine peptidase enzyme did not show a different effect because both of them were able to increase egg death in the intestine and decreased the number and diameter of granulomas in the liver. An in vivo study in pigs with high-intensity *Trichuris suis* infection reported satisfactory anthelmintic activity of papain. The group receiving papain experienced a more significant reduction in the number of eggs and adult worms compared to the group receiving albendazole. In addition, this study also supported the dose-dependent activity of papain in reducing eggs and adult worm numbers. Administration of a single dose of 450µM papain reduced the number of eggs and caused the death of adult worms for more than 97%. In addition, papain was also superior in decreasing the eggs compared to other anthelmintics, such as single doses of albendazole (64.5%) and mebendazole (62.7%), multiple doses of albendazole (94.8%) and mebendazole (90.3%), as well as administering several doses of other anthelmintics (2).

Active Compounds with Anthelmintic Activities in C. papaya

Table 3. Active compounds of *Carica papaya* with anthelmintic properties

Extract	Papaya Parts	Active Compounds
Ethanol	Seed	Alkaloids, saponin, glycoside, fixed oil5
	Leaf	Alkaloids (5,9,11–13), saponin (5,9,11,13), glycoside (10,13), tannin (5,9,11,12), triterpenoids (13), flavonoid (10,12)
	Stem	Saponin, alkaloids, tannin, papain (14)
	Stem Bark	Alkaloids, saponin, glycoside, triterpenoid (5)
Hydroethanol	Leaf	Alkaloids, tannin, saponin, glycoside (5)
	Seed	Alkaloids, saponin, glycoside, fixed oil (5)
	Stem Bark	Alkaloids, saponin, glycoside (5)
Hexane	Seed	Glycoside, alkaloids, benzyl isothiocyanate (4)
Powder	Seed	Alkaloids (9)
Aqueous	Seeds	Alkaloids (7)
Papain isolate	Latex	Papain (2)

The active compounds in various parts of *C. papaya* that exert anthelmintic activity are summarized in Table 3. Alkaloids acted by damaging the cell walls of worms composed of proteins and lipids which caused the death of worms (16). In addition, alkaloids exhibited neurotoxic anthelmintic properties and were able to damage the worm DNA (17). Saponins increased calcium flow which causes increased worm muscle activity leading to paralysis (16). Moreover, it was reported that after the administration of saponins, an increase in pro-apoptotic calcium-dependent proteins caused membrane instability. In addition, saponins also reduced the absorption and transport of glucose in the intestinal worms (17).

In helminths, the cuticle is an easy target for macromolecules, such as tannins. The activity of tannins decreased worm motility due to reduced cuticle flexibility and a direct effect on components of the extracellular matrix and muscles (18). In addition, tannins caused lysis of the worm membrane due to the destruction of membrane proteins (16). Tannins also showed a unique property that increased the uptake of amino acids in the host intestine, which was useful in increasing immunity against worms. Thus, tannins were useful in utilizing nutrients and improving the immune system against worms (19).

Flavonoids acted by inhibiting the catabolic enzyme nicotinamide adenine dinucleotide (NAD+), a coenzyme that regulated calcium, which affected worm motility (20). Flavonoids also inhibited larval growth and arachidonic acid metabolism, leading to neuron degeneration in worms. *C. papaya* also contains papain which could damage the protein of the worms to hamper the worm's nutritional intake (10). Moreover, papain had been shown to effectively induce the hatching of helminth eggs (15). Fixed oil extracted from *C. papaya* seeds contained myristic, palmitic, stearic, arachidic, behenic, and unsaturated fat. These ingredients exhibited the ability to lyse and kill worms (5).

Triterpenoids in *C. papaya* are a secondary metabolite with anthelmintic activity. Papaya seeds contain triterpenoids which could overstimulate the worm's nervous system, resulting in paralysis (21). Furthermore, triterpenoids reduced the permeability of the worm membrane (17). Damage to worm membranes was caused by free radicals that were involved in the apoptosis and death of worms (19).

C. papaya also contains benzyl isothiocyanate which is the product of enzymatic hydrolysis of benzyl glucosinolate. The process of extracting papaya seeds caused damage to the seeds and allowed contact between the myrosinase enzyme and its substrate, which facilitated the metabolism of glucosinolates, producing benzyl isothiocyanate. The compound was able to cause worm death by interfering with the worm's intake of glucose for energy (22).

In conclusion, this literature review summarized that extracts from various parts of *C. papaya* exert positive efficacies as anthelmintic. *C. papaya* can become one of the promising anthelmintic agent candidates to overcome the current anthelmintic drug resistance and undesirable side effects. Furthermore, the use of *C. papaya* can optimize the utilization of the abundant natural resources in Indonesia. In the future, further research regarding the efficacy and safety of *C. papaya* as an anthelmintic agent is needed.

AUTHOR DECLARATION

All authors have agreed with the contents of the manuscript and declare no conflict of interest. We certify that the submission is an original work and is currently not under review at any other publication.

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