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# Systematic Literature Review: Phytochemistry and Antimalarial Activity of Carrica Papaya Linn

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***Abstract***

Papaya leaves (*Carica papaya L.*) have been trusted and proven to antimalarial activity. Currently review information on morphology, phytochemical and pharmacology aspects of the papaya plant (*Carica papaya L*). Based on a literature study on papaya plants (*Carica papaya L.*) summarized from ScienceDirect, Google Scholar, Springer with search keys morphology, phytochemical, antimalarial, *Carica papaya L*, *plasmodium falciparum*, papaya leaf extract has antimalarial activity against *plasmodium falciparum*. Qualitative phytochemical analysis of papaya leaf extract (*Carica papaya L*) showed the presence of alkaloids, flavonoids, saponins, tannins, and glycosides. Flavonoids showed antimalarial activity against *P. falcifarum* which inhibited the entry of L-glutamine and myoinositol into infected erythrocytes during the intraerthrocytic phase of the *Plasmodium* life cycle.

Keywords*: Antimalarial activity, Carica papaya L, Phytochemical, Plasmodium falciparum*

## Introduction

The utilization of herbal plants as an alternative form of treatment has been extensively practiced within society. Historically, the Indonesian people have embraced traditional healing practices, one of which involves the use of medicinal plants, a cultural heritage that has been preserved and transmitted across generations. The accessibility of herbal plants to the general population has also contributed significantly to the increasing consumption of herbal remedies. Indonesia, renowned for its rich biodiversity, is home to approximately 40,000 plant species, with around 1,300 of them identified as having potential for use in traditional medicine (Muktiningsih et al., 2001). The development of herbal plants for therapeutic purposes continues to advance within the realm of scientific research, particularly in response to the growing issue of resistance to synthetic drugs. One such plant that has been extensively studied and recognized for its medicinal properties is the papaya plant (*Carica papaya* Linn). This plant has demonstrated wound-healing properties for various types of injuries, including abrasions, lacerations, burns, and puncture wounds. Furthermore, papaya leaves have been shown to possess pharmacological activities such as antibacterial, anti-inflammatory, pesticidal, and antimalarial effects.

Phytochemical investigations of the papaya plant have been widely conducted. According to (A'yun & Laily, 2015) papaya leaves contain several alkaloids, including carpaine, carpainine, and pseudocarpain, along with vitamins C and E, as well as colid and carposide. The leaves also contain a glucosinolate compound commonly known as benzyl isothiocyanate. Millin and Gurita further reported that papaya leaves contain alkaloids such as carpaine, along with other bioactive compounds including caricaxanthin, violaxanthin, papain, saponins, flavonoids, and tannins. A literature review conducted by (Farmasi et al., 2023) revealed that the ethyl acetate fraction of papaya leaf extract exhibited significant inhibition of parasitemia, thereby supporting its potential use as an active antimalarial agent. Medicina, (2025) elaborated that the presence of secondary metabolites in papaya serves as an inhibitory factor in the growth of *Plasmodium falciparum* and *Plasmodium berghei*, both of which are malaria-causing parasites transmitted by mosquitoes. This review aims to provide a comprehensive summary of the botanical morphology, phytochemical constituents, and antimalarial activity of the papaya plant. Phytochemical analysis serves as a crucial method for identifying the bioactive compounds present in *Carica papaya*, thereby supporting its application in traditional and modern medicinal contexts.

## Metode

This study is a literature review focusing on phytochemical and antimalarial activity of *Carica papaya*. Review was conducted from April to May 2025. The method employed was a descriptive qualitative literature review which is the authors collected and analyzed data from scientific articles relevant with topic of phytochemicals and antimalarial potential of *Carica papaya*. Selected articles were published within the last ten years and contain information related to the morphology, phytochemical constituents, and antimalarial activity of *Carica papaya*.

Literature searches were conducted through several reputable databases, including Google Scholar, ResearchGate, ScienceDirect, and SpringerLink. The key words used in the literature search included: Carica papaya morphology, phytochemical compounds, antimalarial activity, antiplasmodial, and secondary metabolites of papaya.

## Result and Discussion

### Morphology and Botany

*Carica papaya* is classified as a semi-woody plant characterized by a single, erect, and hollow stem. This species typically exhibits a lifespan ranging from 5 to 10 years and is known for its unbranched, monopodial growth habit. Originally native to North America, papaya has since been widely cultivated across almost all tropical regions and parts of subtropical zones (Morton, 1987).

In Indonesia, the distribution of papaya is extensive and evenly spread across various regions. Each locality often attributes a distinct vernacular name to the plant, such as *kates* in Java, *gedang* in Sulawesi, *kapaya* in Sulawesi, and *papas* in Ambon. The papaya tree typically reaches a height between 2.5 and 10 meters and comprises several principal morphological structures as follows:

**Leaf**

The leaves of Carica papaya exhibit a rounded morphological structure and are green in color, with diameters typically ranging from 60 to 90 cm. The leaves are arranged spirally in terminal clusters and are classified as simple leaves, each borne on a petiole measuring approximately 30 to 70 cm in length (Wadekar et al., 2021). These leaves are palmatifid, characterized by their single, deeply lobed structure resembling fingers radiating from a central point. The leaf texture is membranous and radiately lobed. Morphologically, each leaf comprises a petiole (petiolus) and a lamina (lamina), forming the principal structural components of the leaf.

Figure 1. Papaya Leaves

**Flowers**

C. papaya Linn are polygamous species which can be classified based on the flowers. There are three categories, namely male papaya (stamina), female papaya (pistil) and hermaphrodite papaya (bisexual).


Figure 2. Classification of papaya

Flower of the female papaya plant (figure 1a) has sharp tip and produced by female papaya plant. It has ovaries so it can receive pollen from male flowers, therefore female papaya plants can produce fruit. In contrast to female papaya flowers, hermaphrodite papaya flowers (figure 1b) not only have ovaries but also have stamens. These stamens have pollen so that hermaphrodite papaya plants do not need pollen from male papaya plants to produce fruit. Meanwhile, the male papaya flowers (figure 1c) are smaller, tubular in shape and more numerous. Male papaya flowers do not have ovaries so they cannot produce fruit.

**Fruit**

Papaya fruit is round and oval which is green and turns yellow-orange when ripe. Papaya fruit length ranges from 15-50 cm with a thickness between 10-20 cm and weighs up to 9 kg.

Hermaphrodite papaya fruit tends to be oval and cylindrical (figure 2a) while female papaya fruit tends to be round (figure 2b). Papaya fruit is only produced by female papaya and hermaphrodite papaya.

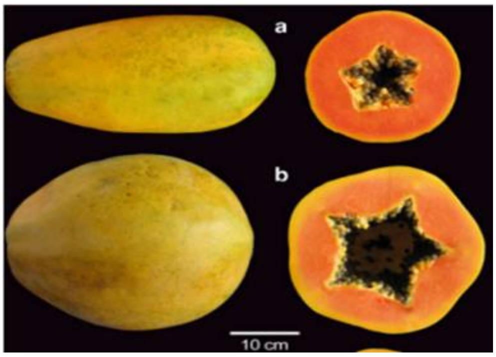


Figure 3. Papaya fruit (a) hermaphrodite papaya (b) female papaya.

**Seeds**

Papaya seeds are ovules composed of seed coat, endosperm and embryo. These seeds are ovoid, dark brown with size 4-6 mm. In papaya plants, seeds are formed in the papaya fruit cavity which is covered by yellow juicy flesh.

Figure 4. Papaya seeds

**Botany Description**

Papaya plant is a single-stemmed herbal plant with a height among 20-30 feet. This plant is crowned by green leaves that are arranged in a spiral with a length over to 1 m. In tropical climates this plant will bear fruit throughout the year. When immature, papaya fruit is identical by the color that change from green turn into yellow

Table 1. Botanical classification of papaya plants

| **Domain** | **Flowering Plant** |
|---|---|
| Kingdom | *plantae* |
| Sub-kingdom | *tracheobionta* |
| Class | *mangnoliopsida* |
| Subclass | *dilleniidae* |
| Superdivision | *spermatophyta* |
| Phylum | *steptophyta* |
| Order | *brassicales* |
| Family | *caricaceae* |
| Ethnic group | *Caricaceae* |
| Clan | *Carica* |
| Botani name | *Carica Papaya L* |

**Phytochemicals Carica Papaya L**

The activity of plants as herbal medicines in accordance with content of active chemical compounds. *C. Papaya Linn* contain active chemical compounds with different structures in each part. Both of them are glucosinolates and benzylisothiocyanate (BIT) (Williams et. al., 2013). Ripe and unripe papaya fruit, papaya seeds and leaves contain alkaloids, terpenoids, vitamin C, vitamin E, papain, and others. (Mannaa, et. al., 2014). Papaya plants also contain phenolics (phenolic acids and flavonoids) and carotenoids.

Table 2. Total phenolic compounds, flavonoids, vitamin E, vitamin C and carotenoids in papaya plants

| *Plant parts* | *Component bioactive* | *Rate* | *Reference* |
|---|---|---|---|
| Papaya leaf | Total phenolic | 4.24 mg GAE/g | (Maisarah et. al., 2014) |
| | Vitamin E | 0.003 mg/g | |
| | Vitamin C | 0.85 mg/g | |
| | Total -carotene | 38.60 g/g | |
| | Vitamin C | 0.25-0.38 mg/g | (Nwofia et. al., 2012) |
| | Total -carotene | 6.44-6.66 IU/g | |
| | Total flavonoids | 8.36 mg CE/g | (Vuong et. al., 2013) |
| | Total phenolic | 28.61 mg CE/g | |
| | Proanthocyanin | 3.02 mg CE/g | |
| | Vitamin C | 0.08–0.13 mg/g | (Nwofia et. al., 2012) |
| | Total-carotene | 0.54–0.73 IU/g | |

| *Plant parts* | *Component bioactive* | *Rate* | *Reference* |
|---|---|---|---|
| Papaya seeds | Total phenolic | 0.3032mg GAE/g | (Maisarah et. al., 2014) |
| | Vitamin E | 0.04 mg/g | |
| | Vitamin C | 0.14 mg/g | |
| | Total -carotene | 1.2 g/g | |
| | Total phenolic | 2.66–3.01 mg/g | (Santos et. al., 2014) |
| | Vitamin C | 2.96–3.37 mg/g | |
| Papaya skin | Total phenolic | 9.9 mg/g | (Calvache, et.al.,2016) |
| | Vitamin C | 0.14 mg/g | |
| | Total carotenoids | 0.081 mg/g | |
| | Total phenolic | 5.53–5.75 mg/g | (Santos et. al., 2014) |
| | Vitamin C | 0.12–0.15 mg/g | |
| Papaya fruit (ripe) | Total phenolic (Aqueous extract/ethanol) | 75.7 mg GAE/g/65.0 mg GAE/g | (Annegodwa et. all., 2014) |
| | Total tannins (Aqueous extract/ethanol) | 3.10 mg CE/g/2.86 mg CE/g | |
| | Total flavonoids (Aqueous extract/ethanol) | 3.36 mg/g/3.75 mg/g | |
| Papaya fruit (raw) | Total phenolic (Aqueous extract/ethanol) | 37.9 mg GAE/g/44.8 mg GAE/g | (Annegodwa et. all., 2014) |
| | Total tannins (Aqueous extract/ethanol) | 2.24 mg CE/g/1.48 mg CE/g | |
| | Total flavonoids (Aqueous extract/ethanol) | 2.30 mg/g/1.25 mg/g | |

The total phenolic content in papaya fruit varies according to the level of maturity. Based on the analysis conducted by Annegodwa, et. al., (2014) in unripe and ripe papaya using aqueous and ethanol extracts, the total phenolic compounds obtained ranged from 37.9-75.7 mg GAE/g, the total flavonoids obtained ranged from 2.24-3.10 mg GAE/g and tannins ranged from 2.30-3.36 mg GAE/g. Meanwhile, it has also been reported by Saaed, et. al., (2014) that papaya peel has a decreased phenolic content during the ripening process. The total content of phenolics, flavonoids, vitamin E, vitamin C and carotenoids of papaya plants can be seen in Table 2.

Isolation of chemical compounds contained in papaya plants has been carried out by various methods. El-Messallamy, et. al., (2015) found the content of phenolic compounds in the ethanolic extract of papaya leaves by using chromatography and mass spectroscopic analysis to determine the structure of the isolated compounds. Another isolation result was reported by

Anjum, et. al., (2017) using ultra-performance liquid chromatography-quadruple orthogonal acceleration time of flight tandem mass spectrometer (UPLC-qTOF/MS) showed the presence of kaemprefol, trans- ferulic acid, caffeic acid and mirycetin compounds in papaya leaf extract. Several methods have been used in the analysis of chemical compounds in papaya plants, which are summarized in table 3.

Table 3**.** Isolation of papaya plant compounds

| **Compounds** | **Plant parts** | **Methods** | **Reference** |
|---|---|---|---|
| Hexahydro-1-aH-naphtho [1,8a-b] oxiren-2(3H)-one, 3, 7-dimethyloct-7- en-1-ol, 3-methyl-4- (phenylthio)-2- enyl - 2.5-dihydrothiophene-1,1 dioxide,cyclopentaneundecanoic acid methyl ester, 3, 7, 11, 15-tetramethyl- 2-hexadecen-1-ol and 9-octadecenamide | Papaya leaf | GCMS | (Igwe, 2015) |
| Quercetin and b-sitosterol | Papaya fruit | HPLC | (Oloyede et al., 2016) |
| Lycopene, -carotene and -cryptoxanthin | Papaya fruit | HPLC | (Sangsoy et. al., 2017) |
| Octadecanoic acid, hexadecenoic acid, Z-11 and hexadecanoic acid and methyl ester | Unripe papaya | GC-MS | (Ezekwe and Chikezie, 2017) |
| Oleic acid | Papaya seeds | GC-MS, FTIR, HNMR and CNMR | (Ghosh et al.,2017) |
| Carpain | Papaya leaf | HPLC | (Vien and Loc.,2017) |
| Equisetin, 5'-epiequisetin and tenuazonic acid | Papaya leaf | HPLC | (Eze et al.,2019) |
| p-hydroxybenzoic acid, hyperoxide, salicylic acid, genteel alcohol, triallyl glucose and kaemferolhexoside | Papaya seeds | LC-MS | (Singh at ai. 2020a, 2020b, 2020c) |
| Carpaine | Papaya leaf | HPTLC | (Haldar et al.,2020) |

| | | | |
|---|---|---|---|
| Stigmast-4-ene-3-one,β-sitosterol3-O- β-D-glucopyranoside,3-O-(6-O-tetradecanoyl-β-D-glucopyranosyl)-β-sitosterol,benzyl D-glucopyranoside , uracil and palmitic acid | Papaya flower and leaf stalk | Extraction, chromatography and spectroscopic methods | (Nga et.al.,2020) |

**Antimalarial Activity**

*C. Papaya Linn* contain a variety of secondary metabolites such as alkaloids, flavonoids, tannins and others. Based on the results of tests conducted by Teng et. all., (2019) reported antimalarial activity against strains of Plasmodium falciparum 3D7 and Dd2. It was found that carpain, one of the alkloid compounds in dichloromethane leaf extract, showed good activity against the inhibition of both Plasmodium falciparum with IC50 of 2.01 ± 0.18 g/mL (4.21 M) and 2.19 ± 0.60 g/mL (4.57 M). Further analysis was reported by Zeleke, et.al., (2017) by *in vivo* test with methanol extract, chloroform and petroleum ether of papaya peel and root against Plasmodium berghei. The highest antiplasmodial activity was obtained by peroleum ether extract of papaya peel with maximum parasite suppression of 6, 78% in the highest dose (400 mg/kg/day). Papaya root petroleum ether extract had a maximum suppression of 48.11%. Konvedan et. all., (2012) also reported promising inhibition of plasmodium falciparum strain of papaya leaf ethanol extract by administering four different concentrations of ethanol extract (20, 50, 100, 150 g/Ml) with IC50 of 40.75%, 36.54%, 25.30%, 18.0% respectively.

## Conclusions

From the research study, *C. Papaya Linn* is one of the most versatile plants which has been used as a medicinal. Total phenolic compounds, flavonoids, vitamin E, vitamin C and carotenoids in papaya plants. All parts of *C.* Papaya Linn had been used for treatment of various diseases. Phytoconstituents that obtained on *C. Papaya Linn* are the best alternative to combact the diseases specificly for antimalarial. Secondary metabolism such as alkaloids, flvaonoids, tanins and others showed antimalarial activity against strains of plasmodium falciarum 3D7 and 3D2.

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