

A Systematic Review: Ethnomedicinal Uses And Pharmacological Activity Of Male Papaya Flower (*Carica papaya* L.)

Purwaningsih¹, Peni Indrayudha^{2*}

¹Magister of Pharmacy, Universitas Muhammadiyah Surakarta, Jl. A. Yani. 157 Pabelan, Sukoharjo, Indonesia

²Faculty of Pharmacy, Universitas Muhammadiyah Surakarta, Jl. A. Yani. 157 Pabelan, Sukoharjo, Indonesia

*E-mail: peni.indrayudha@ums.ac.id

Received: 23 January 2024; Accepted: 29 March 2024; Published: 31 March 2024

Abstract

An extensively utilized plant in traditional medicine is the papaya plant (*Carica papaya* L.). Papaya plants are useful in almost all parts, one part of (*Carica papaya* L.) that has potential is the papaya flowers. Papaya flowers are often used as a vegetable, but papaya flowers also have health benefits. The purpose of this review is to present thorough and current information on the ethnomedicinal usage and pharmacological activity of male papaya flowers. The search method was carried out using relevant keywords of the following databases: Google Scholar, ScienDirect, and NCBI. The results of the article search after going through the article selection process based on the database resulted in 22 relevant articles. Male papaya flowers contain many bioactive compounds known pharmacological activities, including antioxidant, anticancer, antibacterial, antidiabetic, analgesic, antihyperlipidemic, bioinsecticide, tyrosinase inhibition and sun protection activity. This pharmacological activity may be caused by the large number of bioactive compounds contained in male papaya flowers.

Keywords: male papaya flower, ethnomedicine, pharmacology activity

INTRODUCTION

Carica papaya known as the papaya plant is a plant that is often used in traditional medicine. Herbaceous in nature, the *Carica papaya* belongs to the *Caricaceae* family. Tropical and subtropical regions are home to the commonly growing plant *Carica papaya* Linn, which is native to Mexico and northern America. In many nations with tropical and subtropical climates, the papaya plant has been widely utilized in traditional medicine. (Ali et al., 2012).

Papaya plants grow in three different genders, namely male, female and hermaphrodite. This hermaphrodite has male and female reproductive organs which has flowers and can bear fruit (Wadekar et al., 2021). The flowers are trumpet-shaped, a distinctive bitter smell, rich in vitamins and a

good source of dietary fiber (Bergonio & Perez, 2016).

Papaya flowers have good potential for health that come from natural sources that are affordable and easy to obtain. Practically every component of the papaya plant has uses, one part of *Carica papaya* that has potential is the papaya flowers. Papaya flowers are often used as a vegetable, but papaya flowers also have health benefits. Traditionally, male papaya flowers are used to treat several diseases such as coughs, jaundice and to reduce fever (Vij & Prashar, 2015). For a long time, the plant *Carica papaya* has been used to cure a variety of infectious disorders, inflammation, dengue fever, and malaria (Dwivedi et al., 2020). This potential cannot be separated from the content of bioactive compounds in male papaya flowers. Research on the use of

papaya flowers has become increasingly popular in recent years, but there has been no research that comprehensively summarizes the benefits of male papaya flowers systematically. Therefore, this study or review includes the traditional or ethnomedicinal uses of male papaya flowers and pharmacological activity sourced from various literatures so that it can provide an overview of the health potential of male papaya flowers.

RESEARCH METHODOLOGY

This systematic review was prepared comprehensively by collecting published articles related to keywords. Online based search for study materials using scientific

databases including Google scholar, ScienDirect and NCBI involves using certain search terms, such as "Male Papaya flower", "Ethnomedicine", "Pharmacology activity", related keywords contained either in the complete text, the abstract, the title, or the keywords.

The following are the criteria used to determine inclusion in this review article:

1. Article of the ethnomedicine use of male papaya flowers and the pharmacological effects of male papaya flowers
2. Original research publication
3. Original research from 2015 to 2023
4. Original research publications in Indonesian and English.

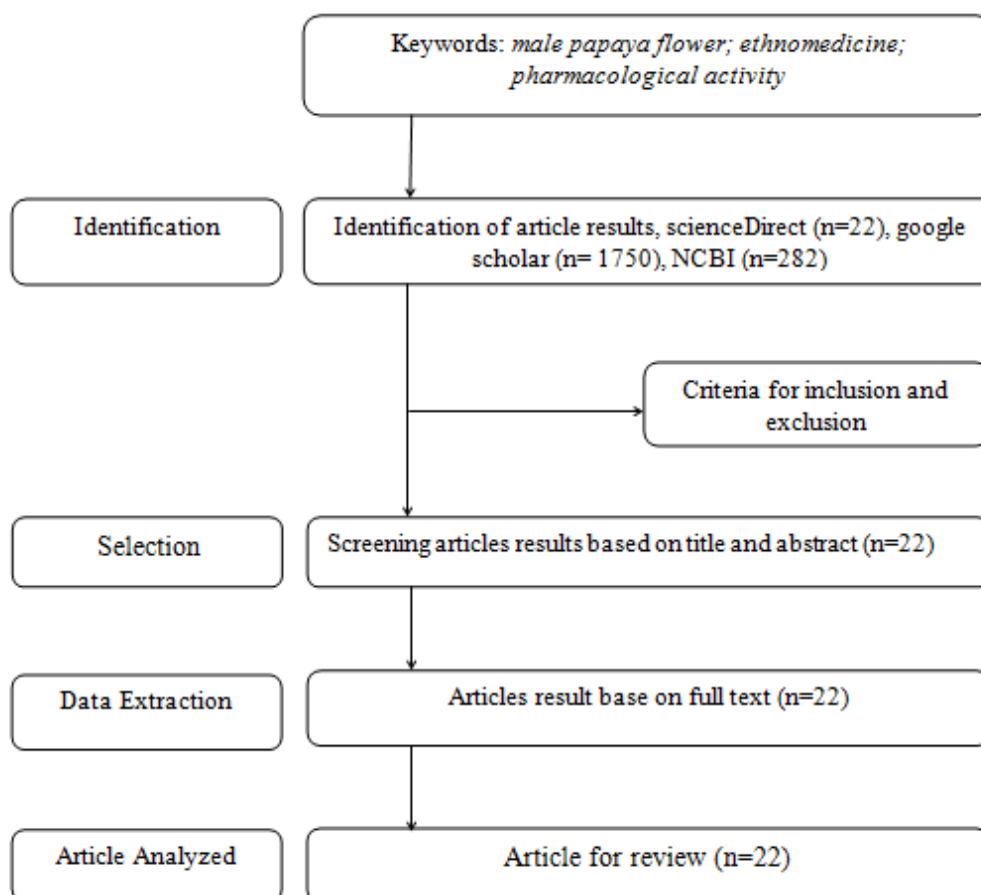


Figure 1. Flowchart of the selection process of materials to be reviewed

The following are the review's exclusion criteria:

1. Research articles in the formats of meta-analyses, systematic reviews, and literature reviews.
2. Research articles whose full texts are not available.

RESULT AND DISCUSSION

Chemical Content

Papain enzyme is a particular proteolytic enzyme produced by *Carica papaya*. Although plant sap makes up the majority of papain, the enzyme can be found throughout the entire plant (Hamid et al., 2022). Vitamins such as thiamine, riboflavin, niacin, and ascorbic acid are found in papaya flowers. Minerals such as calcium, magnesium, manganese, zinc, copper, cadmium, cobalt, lead, iron, potassium, and sodium are also said to be present in papaya flowers.

The study reports that the alkaloid components in male papaya flowers have a concentration of $0.53 \pm 0.01\%$, whereas flavonoids, saponins, tannins, terpenoids, steroids, and cardiac glycosides have different concentrations of $0.86 \pm 0.02\%$, $0.37 \pm 0.02\%$, and $2.06 \pm 0.01\%$, respectively (Okoye, 2017).

kaempferol 3-*O*- α -*L*-arabinopyranoside. (Van et al., 2020).

Alkaloid Compounds

Alkaloids that are bioactive include carpaine, pseudocarpaine, and dehydrocarpaine, which are found in papaya flowers (*Carica papaya* L). Research of Mukhaimin et al (2019), extracted the papaya flowers using the solid-liquid extraction method, liquid-liquid extraction and the microwave-assisted extraction (MAE) method. The highest total alkaloid content was 0.02981 mg/g (Mukhaimin et al., 2019).

Phenolic Compounds

Male papaya flowers contain phenolic compounds, along with eight additional compounds that were recovered from *Carica papaya* flowers and a novel phenolic compound called *Carica papaya* L. Through the use of NMR spectrum data, HR-ESI-MS analysis, and literature comparison, the structures of these substances were ascertained (Lien et al., 2019).

Proteins

Protein content in male papaya flowers was evaluated by Talukdar et al (2021). The Lowry method was used to determine the protein. The findings revealed that at 660 nm, the protein concentration was 300 μ g/mL (Talukdar et al., 2021).

Table 1. Ethnomedicinal Uses of Male Papaya Flower

Ethnomedicinal Uses	Type of uses	Result	Reference
Dietary supplement	Herbal tea	<i>Carica papaya</i> male flower tea has result about total protein 1,7%; sodium 3,5%; potassium 2,8%; carbohydrate 0,1%; vitamin A 0,02%	Bergonio & Perez, 2016
Antidiabetic	Infusion	2% concentration of papaya flower herbal tea can reduce blood sugar levels from 99.00 mg/dL to 83 mg/dL	Natalia et al., 2023

Flavonoid Compounds

Male papaya flowers contain flavonoids. Among the flavonoid types that are available are quercetin, quercitrin, quercetin 3-*O*- β -*D*-galactopyranoside, myricitrin, kaempferol, kaempferol 3-*O*- α -*L*-rhamnopyranoside, kaempferol 3-*O*- β -*D*-glucopyranoside, and

Ethnomedicinal Uses

Carica papaya has been widely utilized as a natural remedy for many diseases. The biological properties of papaya flowers have also been extensively researched (Table 1) Phytochemical test results showed that herbal flower tea contained bioactive

Table 2. Pharmacological activity of Male Papaya Flower

Effect	Host	Sample	Method and Result	Reference
Antioxidant	In vitro	Methanolic extract (500 µg/ml)	Enhancing scavenging activity using the Ferric Thiocyanate (FTC) testing method, which had the lowest IC ₅₀ of 17.47 µg/mL.	Halder et al., 2022
	In vitro	Hexane fraction	Using DPPH method, The result showed that IC ₅₀ was 100.81 ± 1.180 µg/mL.	Sianipar et al., 2018
	In vitro	Methanolic, chloroform, <i>n</i> -Hexan aqueous extract	Using the DPPH method which had the highest free radical was <i>n</i> -hexan extract that showed scavenging activity 64.07%	Dwivedi et al., 2020
	In vitro	ethanol extract (100 ppm)	Scavenging activity showed that the IC ₅₀ values of 4.8946 ppm were obtained when antioxidant activity was assessed using the ABTS technique.	Lusiyaningrum, 2021
Cytotoxic	WiDr cell	hexane fraction	Using the 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyl tetrazolium bromide test, cytotoxic activity revealed hexane fraction.	Sianipar et al., 2018
	WiDr cell	hexane fraction (8, 16, 24 and 32 µg/mL)	The (WiDr) colon adenocarcinoma cell cycle was blocked in the G0-G1, S, and G2-M phases using flow cytometer and combination index male papaya flowers.	Yusnita et al., 2018
	MCF-7 cell line	Ethanol extract, hexane, ethyl acetate water fraction (125 µg/mL)	Using the MTT assay, IC ₅₀ of the ethanol extract (55.875 µg/mL), the <i>n</i> -hexane fraction (101.282 µg/ml), the ethyl acetate fraction (148.692 µg/ml) and the water fraction (356.489 µg/mL)	Nainggolan & Kasmirul, 2015
	Hep-G2 cell	Ultrasound extract	The IC ₅₀ value of 56.63 ± 1.25 µg/mL	Le Thao My et al., 2020
Antibacterial	<i>E. coli</i> , <i>Bacillus subtilis</i>	Methanol, water, Chloroform, and Hexan extract	The antibacterial test of papaya flower extract showed the highest activity against methanol extract <i>Escherichia coli</i> (4.00 ± 0.08) and <i>Bacillus subtilis</i> (01.00 ± 0.05) using well diffusion method.	Dwivedi et al., 2020
	<i>E. coli</i> , <i>Staphylococcus aureus</i>	ethyl acetate fraction of ethanol extract (40, 10, 5, 2,5%)	According to the results of the MIC test, there was no inhibitory effect on <i>Escherichia coli</i> bacteria, however there was a minimum inhibitory power on <i>Staphylococcus aureus</i> bacteria at a concentration of 5%.	Santoso, 2020
	<i>E. coli</i> , <i>Staphylococcus aureus</i>	aqueous extract	Using disc diffusion method, zone inhibition of bacteria <i>Escherichia coli</i> and <i>Staphylococcus aureus</i> is 8 mm and 7 mm	Talukdar et al., 2021
	<i>E. coli</i>	ethanol extract (2; 1; 0,5; 0,25 mg/mL)	The MIC of 2 mg/mL. the time-kill test showed that was acquired between 0 and 24 hours, but the combination of the extract and tetracycline demonstrated antibacterial activity at 8 and 24 hours.	Anugraheni & Rini, 2023
	<i>E. coli</i>	ethanol extract (20, 30, and 40%)	The average diameter of the inhibition zone was 2.07, 2.03, and 2.6 cm.	Yuliasuti, 2021

Table 2. Continued...

Effect	Host	Sample	Method and Result	Reference
Antidiabetic	Male white rats	Ethanol extract (200, 400, 800 mg)	The results showed that ethanol extract of male papaya flowers decrease the blood glucose at a dose of 800 mg	Pongoh et al., 2020
	Male mice Balb/C	Ethanol extract (200, 400, 500 mg/KgBW)	Dose 400 and 500 mg/kgBW were better than control positive at decrease blood level	Wahyuni et al., 2018
	Male mice	Ethanol extract (200, 400, 500 mg/KgBW)	The result showed that three doses had antidiabetic effect.	Marpaung et al., 2021
	Wistar rats	Ethanol extract (150 and 260 mg/KgBW)	Dose 260 mg/kgBW of papaya flower extract could reduce blood glucose levels in mice with hyperglycemia.	Tangkumahat et al., 2017
Analgesic	Rats	Ethanol extract (75, 150, 300 mg/KgBW)	Doses 75, 150, and 300 mg/KgBW were shown to be efficient as an analgesic in rats for a duration of 12 minutes.	(Manengkey et al., 2019)
Antihyperlipidemic	Male rats Sprague dawley	Ethanol extract (31, 62, 125 mg/KgBW)	In the blood of mice, papaya flower extract significantly raised the average HDL and decreased the average LDL levels at doses of 31 mg/kgBW, 62 mg/kgBW, and 125 mg/kg BW.	Fitriani et al., 2019
Tyrosinkinase Inhibitory	L-tyrosine	Isolated compound (9 compound from <i>Carica papaya</i> flower)	Compounds (1, 2, and 4) showed tyrosinase inhibitory activity with IC ₅₀ values of (14.3 ± 2.7), (25.5 ± 1.9), and (19.8 ± 3.0) µM	Lien et al., 2019
Sun Protection	In vitro	Ethanol extract cream (5%, 10%, and 15%)	The SPF value of each formula respectively were 15.04; 18.75 and 22.12. SPF value indicates protection against UV rays	Antari et al., 2021
Bioinsecticide	flies	ethanol extract (25%, 50% and 75%)	The lowest fly mortality was 76.67%, namely 23 flies at a concentration of 25% and the highest was 97%, namely 28 flies at a concentration of 75%	Iskandar et al., 2020

had total protein 1,7%; sodium 3,5%; potassium 2,8%; carbohydrate 0,1%; vitamin A 0,02% for a single serving (2 gram/tea bag). Analysis of the composition of bioactive compounds showed that food

nutrients were good for the body and even had higher amounts compared to tea sold in general. Papaya flowers have good potential use as an ingredient in making herbal tea and for commercial production. The nutritional

value and potential health benefits of male papaya flower herbal tea are very good. The results of the sensory evaluation papaya flower herbal tea values on color, aroma and overall taste attributes were observed to be lower than the two commercial teas. The potential for using male papaya flowers as an ingredient in dietary supplements or herbal tea was great. (Bergonio & Perez, 2016).

Herbal tea of male papaya flower was tested for its effect on decreasing blood glucose levels. A group of test animals were given male papaya flower tea every morning and evening, after 7 days of steeping papaya flower tea with a concentration of 2%, it was able to reduce blood sugar levels from 99 mg/dL to 83 mg/dL. The research results showed that brewing male papaya flower herbal tea had the potential to reduce sugar levels blood against White Rats (*Rattus norvegicus*) induced by fructose and fat. (Natalia et al., 2023). Male papaya flowers contain secondary metabolite compound had potential as an antihyperglycemia. Flavonoid compounds which could reduce blood glucose levels because they were able to stimulate insulin secretion, regulates glucose in the liver and improves hyperglycemia (Wahyuni et al., 2018).

Pharmacological Activity

The summary of the pharmacological activity of male papaya flowers as demonstrated in **Table 2**. Every part of the *Carica papaya* plant had potential, including the male papaya flowers. The pharmacological activity of male papaya flowers contained the phytochemical compounds. Among the many pharmacological activities of male papaya flowers, antioxidant, antibacterial, anticancer and antidiabetic activities were the most frequently found. Apart from that, papaya flowers also had pharmacological activities such as antihyperlipidemia, analgesic, tyrosinkinase inhibitor, protection against UV rays and bioinsecticide. This activity was thought to originate from the compounds contained in male papaya flowers.

The antioxidant activity test of male papaya flower was studied using the Ferric Thiocyanate (FTC) testing method, which had the lowest IC₅₀ of 17.47 µg/mL. Antioxidant activity was based on its facilitating redox properties as a reducing agent, hydrogen donor and metal chelator. Phenolic and polyphenolic compounds were antioxidant agents in papaya flowers (Halder et al., 2022). The hexan fraction of male papaya flower was evaluated using α,α -diphenyl- β -picrylhydrazyl method, The result of the radical scavenging showed that male papaya flower had an antioxidant activity with IC₅₀ was 100.81 ± 1.180 µg/mL. The potential antioxidant from hexan fraction papaya male flower was came from the phytochemical contain that had strong value of triterpenoid and steroid compound (Sianipar et al., 2018). The antioxidant activity from methanol, chloroform, *n*-Hexan and aqueous extract was examination. Using the α,α -diphenyl- β -picrylhydrazyl (DPPH) method which had the highest free radical was *n*-hexan extract that showed scavenging activity 64.07% and the chloroform extract was the lowest antioxidant activity. The *n*-Hexan extract phytochemical screening had flavonoids, tannin, saponin and steroid compound who responsible to scavenging free radical (Dwivedi et al., 2020). The antioxidant activity was assessed using the ABTS technique. The male papaya flower had an antioxidant activity with IC₅₀ values of 4.8946 ppm were obtained. The flavonoid compound from ethanol extract of *Carica papaya* male flower was the reason male papaya flowers can be used as an antioxidant (Lusiyaningrum, 2021).

Carica papaya male flower also had cytotoxic activity, the hexan fraction of papaya male flower was evaluated in colon cancer cell (WiDr cell) and normal cell (Vero cell). The anticancer potential activity of hexan fraction of male papaya flower was studied using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide method. The result showed that hexan fraction had

good anticancer activity on breast cancer. It caused triterpenoids and steroids compound in hexan fraction (Sianipar et al., 2018). Anticancer activity of papaya flower ultrasound extract against the Hep-G2 cell line, the result showed that IC_{50} value of $56.63 \pm 1.25 \mu\text{g/mL}$, male papaya flower could inhibit the growth of cancer cells. The flavonoid compound composition evaluated by LC-MS to isolate and purificate of flavonoid. The flavonoid extracted showed medicinal properties for anticancer (Le Thao My et al., 2020). The papaya male flower had cytotoxic activity on (WiDr) colon adenocarcinoma cell cycle was blocked in the G0-G1, S, and G2-M phases using flow cytometer and combination index male papaya flowers and had strong synergistic effect with doxorubicin at $8 \mu\text{g/ml}$ was optimum concentration (Yusnita et al., 2018). The anticancer activity of male papaya flowers were due to the secondary metabolite compounds. Male papaya flowers contain secondary metabolite compounds including flavonoids, saponins, tannins, steroids and terpenoids (Okoye, 2017). Flavonoids had a mechanism to inhibit cancer cell proliferation by inhibiting oxidative processes that could trigger cancer. Saponin could bind cholesterol to cancer cells because cancer cells contain compounds such as cholesterol, so saponin interfere with membrane permeability. Saponin was able to reduce the occurrence of reactive oxygen such as hydrogen peroxide and inhibit the phosphatidyl inositol-3 kinase signaling pathway. Steroid and terpenoid compounds also had proliferation, apoptosis, invasion and metastasis and angiogenesis activities so they showed good potential as anticancer (Nainggolan & Kasmirul, 2015).

Male papaya flowers contained secondary metabolites which were responsible for inhibiting bacterial growth. The antimicrobial effect of male papaya flower was determination from different solvent. It was methanol, chloroform, *n*-Hexan and aqueous extract to different

bacterial target. The metanol extract of male papaya flower had the biggest inhibition zone at *Escherichia coli* and *Bacillus subtilis*. The methanol extract phytochemical screening of papaya flower had flavonoids, alkaloid, tanin, saponin and steroid compound who responsible to inhibit bacterial growth (Dwivedi et al., 2020). According to the results of the MIC test of ethanol extract and ethyl acetate fraction of male papaya flower was determination, there was no inhibitory effect on *Escherichia coli* bacteria, however there was a minimum inhibitory power on *Staphylococcus aureus* bacteria at a concentration of 5%. Linalool compound was one of them essential oil components that were able to inhibit bacteria. Class of compounds contained in the ethyl acetate fraction and ethanol extract of male papaya flowers were E-Citral which had a similarity percentage of 49%, Linalool compound 87% and 2-Methoxy-4-vinylphenol 87 (Santoso, 2021). Antimicrobial activity also determined of aqueous extract of male papaya flower. The aqueous extract male papaya flower could give zone inhibition against *Escherichia coli* and *Staphylococcus aureus* bacteria. The inhibition of growth bacteria showed by metabolite secondary profiling from aqueous extract such as flavonoid, phenol, saponin and tanin (Talukdar et al., 2021). The antimicrobial test of ethanol extract of papaya flower was evaluated on *Escherichia coli* bacteria, the result showed 20%, 30% and 40% concentration gave average diameter of the inhibition zone was 2.07, 2.03, and 2.6 cm (Yulastuti, 2021). The study to evaluation effect of male papaya flower, ethanol extract had a minimum inhibitory concentration (MIC) of 2 mg/mL. The results of the time-kill test indicated that the antibacterial activity was acquired between 0 and 24 hours, but the combination of the extract and tetracycline demonstrated antibacterial activity at 8 and 24 hours (Anugraheni & Rini, 2023). The antibacterial activity of male papaya flowers involved the compound

quercetin which was a derivative of flavonoid compound which had an antibacterial effect. The hydroxy groups in flavonoids would form protein complexes which could cause the bacterial membrane to be damaged (Hidayati et al., 2020).

The antidiabetic activity of male papaya flower had also been extensively researched. The 70% ethanol extract was determined with 200 mg, 400 mg and 800 mg dose against male white rats (*Rattus novergicus*) alloxan induced, the results showed that ethanol extract of male papaya flowers decrease the blood glucose at a dose of 800 mg. The content of flavonoid compounds of papaya flower could be one of the causes of this pharmacological activity. Flavonoids had ability in inhibiting the glucosidase enzyme and alpha amylase broke down carbohydrates into monosaccharides so there was no glucose that could be absorbed and could decrease in levels glucose in the blood (Pongoh et al., 2020). The antidiabetic of 96% ethanol extract papaya flower was determined 150 and 260 mg/KgBW against Wistar rats (*Rattus novergicus* L.) induced by alloxan. The administration of 260 mg/kgBW of papaya flower extract could reduce blood glucose levels in mice with hyperglycemia. Papaya flower extract in dosage 260 mg/KgBW decrease effective blood glucose levels against percentage reduction in blood glucose levels on the day 12, it was 18.37% compared to papaya flower extract with a dose of 150 mg/Kg BW (Tangkumahat et al., 2017). The 96% ethanol extract of papaya flower also determined antidiabetic activity on mice induced alloxan used dose 200, 400 and 500 mg/KgBW. The result all of dose had antidiabetic effect (Marpaung et al., 2021). The ethanol extract of male papaya flower also had effects of antidiabetic activity. The studied male papaya flower extract against male mice Balb/C induced by streptozotoin with three doses 200, 400 and 500 mg/kgBW. The result showed that dose 400 and 500 mg/kgBW were better than control positive

at decrease blood level. The phytochemical screening of male papaya flower was indicated had flavonoid, tanin, steroid and terpenoid. The flavonoids compound in papaya flower was responsible to reduce blood sugar level. Flavonoids could stimulate insulin secretion, regulate glucose metabolism in the liver so that it could improve hyperglycemia (Wahyuni et al., 2018).

The analgesic effect was evaluated from ethanol extract male papaya flower against white rats (*Rattus novergicus*). Treatment was given to rats that had been induced by heat using a water bath with a temperature of 53.5°C for approximately 1 minute. Male papaya flower extract at doses of 75, 150, and 300 mg/KgBW were shown to be efficient as an analgesic in rats for a duration of 12 minutes. The effectiveness of analgesic effect showed with the presence decreased stories in rats. The best reduction was shown by the extract of male papaya flower at a dose of 300 mg/kgBW. Flavonoids and tanins compound of male papaya flower also had function as an inhibitor of cyclooxygenase activity, preventing prostaglandin formation and thereby mitigating pain (Manengkey et al., 2019). The analgesic effect could be caused by the tannin content in male papaya flowers. Tannin compounds showed activity as an analgesic (Nirmala et al., 2012).

Papaya flowers had activity as a tyrosinase inhibitor. The new phenolic compound under investigation from *Carica papaya* flower. The phenolic compound, namely carica papayol(1) and 8 others compound (2-9) were isolated from papaya flower. compounds 1 until 9 were then determined their effects on the activity of mushroom tyrosinase using L-tyrosine as a substrate. Tyrosinase inhibitors could prevent the formation of o-quinone from phenolics substrate, suppressing the browning process. Compounds 1, 2, and 4 showed tyrosinase inhibitory activity with IC₅₀ values of (14.3 ± 2.7), (25.5 ± 1.9), and

(19.8 ± 3.0) μM comparison with positive control kojic acid. The browning process may be stopped by this tyrosinase inhibitor by preventing the synthesis of e-quinone from phenolic substrates (Lien et al., 2019).

Male papaya flower cream has been studied for its protective effect against UV rays. Several secondary metabolite compounds such as flavonoids contained in male papaya flowers were thought to work as active sun protection. the SPF value of extract ethanol cream each formula respectively were 15.04; 18.75 and 22.12. ethanol extract cream of male papaya flower with a concentration of 10% had the most effective absorption of UV B rays compared to cream preparations with concentrations of 5% and 7.5%. SPF value indicates protection against UV rays. Flavonoids were strong antioxidants and were also metal binders which were thought to be able to prevent the harmful effects of UV rays or to reduce skin damage (Antari et al., 2021). The bioinsecticide activity of ethanol extract papaya flower was evaluated. Ethanol extract of papaya flower with 25%, 50% and 75% concentration gave result with the lowest fly mortality was 76.67%, namely 23 flies at a concentration of 25% and the highest was 97%, namely 28 flies at a concentration of 75%. The most effective concentration of male papaya flower extract as a bioinsecticide on flies was 75%, with the resulting average death as many as 28 individuals. It can be concluded that papaya flower extract is effective as a bioinsecticide for flies. Death in flies during administration with papaya flower extract occurs because

the secondary metabolite compounds contained therein have activities that can affect flies. Due to the presence of substances such tannins, flavonoids, steroids, and terpenoids, papaya flower extract exhibits bioinsecticide activity. The metabolite secondary compounds in male papaya flowers could act as antifeedant, repellents and disrupt development and reproduction and cause death in insects so they could interrupt metamorphosis in flies (Iskandar et al., 2020).

CONCLUSION

Carica papaya is a plant with extraordinary pharmaceutical uses, almost all parts of this plant can be used for food and medicine. One part that is beneficial for health is the flower part. This review is one of many that offer a wealth of knowledge about the traditional medicinal uses and pharmacological activity of male papaya flowers in both vitro and in vivo. Papaya flowers have been used to treat various diseases, ethnomedicinally male papaya flowers are used to reduce blood sugar levels and as a herbal tea and herbal dietary supplement. Studies reveal that papaya flowers have antioxidant, anticancer, antibacterial, antidiabetic, analgesic, antihyperlipidemic, tyrosinkinase inhibition, bioinsecticide and sun protection activity.

ACKNOWLEDGMENT

The authors are grateful that Faculty of Pharmacy Muhammadiyah University of Surakarta has provided the necessary space for this review to be completed successfully.

References

- Ali, A., Devarajan, S., Waly, M. I., Essa, M. M., & Rahman, M. S., 2012. Nutritional and Medicinal Values of Papaya (*Carica papaya* L.). Natural Products and Their Active Compounds on Disease Prevention. August, 8, 307–324. <https://doi.org/10.20959/wjpps20178-9947>
- Antari, E. D., Purwaningsih, Septiarini, Dwi, A., Wardani, & Siska, T., 2021. Analysis of SPF (*Sun Protection Factor*) Value for Sunscreen Cream of Ethanol Extract of Male Papaya (*Carica papaya* L.) Flowers using Spectrophotometric UV-Vis Method. Ester.

- Nber Working Papers, 5, 89. <http://www.nber.org/papers/w16019>
- Anugraheni, A., & Rini, C. S., 2023. Effect of Papaya Flower Ethanolic Extract (*Carica papaya*) on the time kill of tetracyclin against *Escherichia Coli*. *Pharmaciana*, 13(2), 246. <https://doi.org/10.12928/pharmaciana.v13i2.2471>
- Bergonio, K. B., & Perez, M. A., 2016. The Potential of Male Papaya (*Carica papaya* L.) Flower as a Functional Ingredient for Herbal Tea Production. *Indian Journal of Traditional Knowledge*, 15(1), 41–49.
- Dwivedi, M. K., Sonter, S., Mishra, S., Patel, D. K., & Singh, P. K., 2020. Phytochemical Characterization of *Carica papaya* Flowers. *Beni-Suef University Journal of Basic and Applied Sciences*, 9, pp.1-11.
- Fitriani, D., Rusmini, H., & Marek, Y. W., 2019. The Influence of Papaya Flower Extract (*Carica papaya* L) on High Density Lipoprotein (HDL) and Low Density Lipoprotein (LDL) Blood Male Rats (*Rattus norvegicus*) var. *Sprague dawley* Given a High-Fat Diet. *Jurnal Ilmu Kedokteran Dan Kesehatan*, 6(4), 247–256. <https://doi.org/10.33024/jikk.v6i4.2293>
- Halder, S., Dutta, S., & Khaled, K. L., 2022. Evaluation of Phytochemical Content and In vitro Antioxidant Properties of Methanol Extract of *Allium cepa*, *Carica papaya* and *Cucurbita maxima* Blossoms. *Food Chemistry Advances*, 1(September), 100104. <https://doi.org/10.1016/j.focha.2022.100104>
- Hamid, N. K. A., Somdare, P. O., Md Harashid, K. A., Othman, N. A., Kari, Z. A., Wei, L. S., & Dawood, M. A. O., 2022. Effect of Papaya (*Carica papaya*) Leaf Extract as Dietary Growth Promoter Supplement in Red Hybrid Tilapia (*Oreochromis mossambicus* x *Oreochromis niloticus*) diet. *Saudi Journal of Biological Sciences*, 29(5), 3911–3917. <https://doi.org/10.1016/j.sjbs.2022.03.004>
- Hidayati, T. K., Susilawati, Y., & Muhtadi, A., 2020. Pharmacological Activities Of Various Parts *Carica papaya* Linn. Extract: Fruit, Leaf, Seed, Steam, Bark And Root. *Jurnal Riset Kefarmasian Indonesia*, 2(3), 211–226. <https://doi.org/10.33759/jrki.v2i3.97>
- Iskandar, I., Horiza, H., & Bahri, S., 2020. Effect of Papaya Flower Extract (*Carica papaya*) as a Bioinsecticide on Fly Deaths at TPA Ganet, Tanjungpinang. *Sanitasi: Jurnal Kesehatan Lingkungan*, 11(1), 14–19. <https://doi.org/10.29238/sanitasi.v11i1.932>
- Le Thao My, P., Van Luc, T., Do Dat, T., Hoai Thanh, V., Khanh Duy, H., Thanh Phong, M., Minh Nam, H., & Huu Hieu, N., 2020. Optimization of Flavonoids Extraction from Vietnamese Male Papaya (*Carica papaya* L.) Flowers by Ultrasound-Assisted Method and Testing Bioactivities of the Extract. *ChemistrySelect*, 5(42), 13407–13416. <https://doi.org/10.1002/slct.202002723>
- Lien, G. T. K., Van, D. T. T., Cuong, D. H., Yen, P. H., Tai, B. H., & Van Kiem, P., 2019. A New Phenolic Constituent from *Carica papaya* Flowers and Its Tyrosinase Inhibitory Activity. *Natural Product Communications*, 14(7). <https://doi.org/10.1177/1934578X19850987>
- Lusiyaningrum, T. A., 2021. The Antioxidant Activity Test Of Papaya Flower *Carica papaya* L Ethanolic Extract Using Abts Method (2,2 Azinobis (3-Etilbenzotiazolin)-6-Asam Sulfonat). In *Paper Knowledge. Toward a Media History of Documents* (Vol. 3, Issue 2).
- Manengkey, S.F., Karauwan, F.A., Ginting, A.R. and Tumbel, S.L., 2019. The Effectiveness

- Test of Male Papaya Flower Extract *Carica papaya* L. as Analgesics Against White Rats *Rattus norvegicus*. The Tropical Journal of Biopharmaceutical, 2(2), 158–169.
- Marpaung, F. S., Tampubolon, E. J. br, Andika, M. I., Lubis, Y. E. P., & Mutia, M. S., 2021. The Effectiveness Test of Papaya (*Carica papaya* L.) Flower Extract on Blood Sugar Level of the Sucrose induced Male Mice (*Mus musculus* L.). Biospecies, 14(1), 24–31.
- Mukhaimin, I., Saraswati, E. A., Ajizah, R., & Triyastuti, M. S., 2019. Product Quality of Quercetin Extract From *Carica papaya* L Flower by Microwave-Assisted Extraction (MAE). Jurnal Rekayasa Kimia & Lingkungan, 14(2), 139–146. <https://doi.org/10.23955/rkl.v14i2.14598>
- Nainggolan, M., & Kasmirul., 2015. Cytotoxicity Activity of Male *Carica papaya* L . Flowers on MCF-7 Breast Cancer Cells. Journal of Chemical and Pharmaceutical Research, 7(5), 772–775.
- Natalia, E., Potensi, B., Teh, S., Bunga, H., Jantan, P., Barung, E. N., Aditia, O., Sasue, A., Kalonio, D. E., Politeknik, J. F., Kementerian, K., & Manado, K., 2023. Potential of Brewing Male Papaya Flower Herbal Tea (*Carica papaya* L) In Reducing Blood Sugar Levels in White Rats Fructose and Fat Induced. Prosiding Seminar Nasional Dies Natalis Poltekkes Kemenkes Manado XXII Tahun 2023 Dalam Menu. 2, 304–308.
- Nirmala, S., Arun, S., & Sivanagamoorthi, M., 2012. Antioxidant [In vitro] and Analgesic Activity [In vivo] of Tannin Fraction of Stem Bark of *Ficus Racemosa* Linn. Research Journal of Pharmaceutical, Biological and Chemical Sciences, 3(1), 597–603.
- Okoye, E. I., 2017. Preliminary Pharmaceutical Constituents of Crude Solvent Extracts of Flower and Stalk of Male *Carica papaya*. Chemistry Research Journal, 2017(1), 20–26. www.chemrj.org
- Pongoh, A. F., Queljoe, E. De, & Rotinsulu, H., 2020. Antidiabetic Test Of Ethanol Extract Of Papaya Flowers (*Carica papaya* L.) Against Male White Rats (*Rattus norvegicus*) Induced by Alloxan. Pharmacoin, 9(1), 160. <https://doi.org/10.35799/pha.9.2020.27423>
- Santoso, D. S. P., Septianingrum, N.M.A.N. and Yuliastuti, F., 2021.. Antibiotic Potential Of Ethyl Acetate Fraction Of Ethanol Extract Male Papaya Flowers (*Carica papaya* L). Borobudur Pharmacy Review, 1(2), pp.34-39.
- Sianipar, M. P., Suwarso, E., & Rosidah, R., 2018. Antioxidant and Anticancer Activities of Hexane Fraction from *Carica papaya* L. Male Flower. Asian Journal of Pharmaceutical and Clinical Research, 11(3), 81–83. <https://doi.org/10.22159/ajpcr.2018.v11i3.22382>
- Talukdar, N., Barchung, S., & Barman, I., 2021. Phytochemical Screening and Study of Total Protein Content, Antimicrobial Activity of the Male Flower of *Carica papaya* L . Nayan Talukdar, Sutula Barchung and Phytochemical Screening and Study of Total Protein Content, Antimicrobial Activity of the Mal. September, 12 (5), 1540–1542.
- Tangkumahat, F. G., Rorong, J. A., & Ftimah, F., 2017. Effect Of Flower And Papaya Leaf Extract (*Carica papaya* L.) On Wistar Rats Blood Glucose Level (*Rattus norvegicus* L.) Which Hyperglycemic. Jurnal Ilmiah Sains, 17(2), 143. <https://doi.org/10.35799/jis.17.2.2017.17681>
- Van, D. T. T., Cuong, D. H., Lien, G. T. K., & Yen, P. H., 2020. Phytochemical Study of the Ethyl Acetate Extract of Male *Carica papaya* Flowers from Quang Nam – Da Nang. Vietnam Journal of Chemistry, 58(2), 145–150. <https://doi.org/10.1002/vjch.201900029>

- Vij, T., & Prashar, Y., 2015. A review on Medicinal Properties of *Carica papaya* Linn. Asian Pacific Journal of Tropical Disease, 5(1), 1–6. [https://doi.org/10.1016/S2222-1808\(14\)60617-4](https://doi.org/10.1016/S2222-1808(14)60617-4)
- Wadekar, A.B., Nimbawar, M.G., Panchale, W.A., Gudalwar, B.R., Manwar, J.V. and Bakal, R.L., 2021. Morphology, Phytochemistry and Pharmacological Aspects of *Carica papaya*, an review. GSC Biological and Pharmaceutical Sciences, 14(03), 234–248. <https://doi.org/10.30574/gscbps.2021.14.3.0073>
- Wahyuni, W., Ilyas, M. and Agusraeni, R., 2018. The Antidiabetic Potential Test Of Papaya Flower Extract (*Carica papaya* L.) On Male Balb/C Mice Induced Streptozocin (Stz). Jurnal Insan Farmasi Indonesia, 1(1), 130–144.
- Yuliasuti, F. yuliasuti., 2021. Test Activity Of Male Papaya Flower Extract As Antidiarrheal Against *Eschericia coli*. Jurnal Jamu Kusuma, 1(1), 15–20. <https://doi.org/10.37341/jurnaljamukusuma.v1i1.1>
- Yusnita, Y., Masfria, M., Rosidah, R., & Iksen, I., 2018. Effect of Hexane Fraction from Papaya (*Carica papaya* L.) Male Flower on Cell Cycle of Colon Adenocarcinoma (widr) Cell and Its Combination Index with Doxorubicin. Asian Journal of Pharmaceutical and Clinical Research, 11(7), 138–140. <https://doi.org/10.22159/ajpcr.2018.v11i7.25023>