Comparison of Bioactive Compound Content in *Carica papaya* and *Manihot esculenta* Leaf Extract Based on FTIR (Fourier Transform Infrared) Analysis in Traditional Dengue Hemorrhagic Fever (DHF) Therapy

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Abstract: Dengue Hemorrhagic Fever (DHF) is an infectious disease caused by the dengue virus transmitted by Aedes aegypti, often leading to thrombocytopenia. Herbal-based traditional therapies, such as papaya leaves (Carica papaya L.) and cassava leaves (Manihot esculenta Crantz), are considered potential supportive treatments. This study aims to compare the bioactive compounds of both plants through phytochemical screening and Fourier Transform Infrared (FTIR) analysis. The phytochemical results revealed that papaya leaves contain alkaloids, flavonoids, phenolics, tannins, saponins, steroids, and triterpenoids, while cassava leaves contain alkaloids, flavonoids, phenolics, tannins, and triterpenoids. FTIR analysis identified functional groups O–H, C=O, aromatic C=C, C–H, and C–O, indicating the presence of flavonoids, polyphenols, and glycosides. Pharmacologically, papaya leaf extract demonstrated greater potential as it has been clinically proven to increase platelet count through hematopoiesis stimulation and gene regulation. In contrast, cassava leaf extract exhibited antioxidant and hematopoietic potential but with limited clinical evidence. Therefore, papaya leaves are considered more effective as a traditional supportive therapy to aid platelet recovery in DHF patients.

1 INTRODUCTION

Dengue fever is caused by dengue virus infection transmitted through the bite of the Aedes aegypti mosquito. The disease can occur throughout the year and affects all age groups (Mahardika et al., 2023). Aedes aegypti mosquitoes have a habit of biting repeatedly (multiple biters), which is attacking several people in turn in a short time because they are very sensitive to stimuli and easily disturbed when sucking blood. This habit facilitates the transmission of dengue virus to many people at once, so that several family members in one house can be infected at almost the same time (Ustiawaty et al., 2020).

Dengue fever is widespread throughout the tropics with local variations in risk influenced by rainfall, temperature, and levels of urbanization (Kolondam et al., 2020). Until now, dengue treatment is still supportive. Supportive treatment is treatment by providing replacement fluids for the body (Azzahra et al., 2023). This condition encourages the search for supporting therapies that are safe, effective, and easily accessible. One potential alternative is the use of traditional medicinal plants that contain bioactive compounds with pharmacological activity.

Papaya leaves have long been utilized in traditional medicine practices in Indonesia for their health-supporting pharmacological properties. Recent studies have revealed that these leaves contain bioactive compounds such as flavonoids, alkaloids, and phenolics that exhibit antimicrobial activity, particularly antibacterial. The content is proven to be able to inhibit the growth of various pathogenic bacteria that have the potential to cause human infections, so papaya leaf extract has the opportunity to be developed as a natural antibacterial source (Zahrani et al., 2025).

Patil et al. (2013) stated that alkaloids in papaya leaves have a role in the bone marrow by increasing its ability to produce platelets. Therefore, the number of platelets in the blood is an important indicator in diagnosing this disease. Patients with dengue fever are categorized when the platelet count decreases to less than 100,000/mm³ of blood, while normal platelet levels range from 150,000-450,000/mm³. Thus, in patients who are confirmed positive for dengue hemorrhagic fever (DHF), various efforts need to be made to increase platelet counts in order to survive and recover (Susanti & Suharti, 2020).

Cassava (Manihot esculenta) leaves are a functional food source rich in protein, vitamins, minerals and antioxidants. The iron content in them plays an important role in the formation of hemoglobin, while vitamin C improves iron absorption, helping to prevent anemia. Folic acid and vitamin B complex support the synthesis of DNA and RNA, which are essential for blood cell production. In addition, flavonoids and polyphenols function as antioxidants that protect hematopoietic cells from damage. Research shows that cassava leaves can support blood health and have potential as a supportive therapy for dengue disease (Aisyah et al., 2021). Nutrients such as iron, folic acid, and vitamin B complex play an important role in blood cell formation by supporting the process of hemoglobin synthesis and proliferation of blood progenitor cells. With the availability of adequate nutrients, the production of red blood cells and platelets can increase, thus helping the therapy of dengue disease (Az-Zahra and Al Jihad, 2022). These compounds can be analyzed with FTIR (Fourier Transform Infrared) instruments.

Fourier Transform Infrared (FTIR) is an analytical method that can identify molecular functional groups based on the absorption of infrared radiation. This technique has the advantage of being fast, not damaging the sample, and providing qualitative information about chemical components in natural materials (Sjahfirdi et al., 2015). The application of FTIR in medicinal plant research can help reveal differences in the profiles of bioactive compounds from various sources. Therefore, this study aims to compare the content of bioactive compounds in papaya leaf and cassava leaf extracts through FTIR analysis as a basis for developing traditional therapies to support dengue treatment.

2 METHOD

Tools and Materials

The materials used were cassava leaves (Manibot esculenta), papaya leaves (Carica papaya) Ethanol, HCL 1%, concentrated HCL, magnesium, hot water, HCL ZN, FeC13 5%, distilled water, FeCl

1%, CHCI3 1%, acid, H2SO4. The tools used are blender, sieve, analytical balance, spoon, glass jar, rotary evaporator, beaker glass, stirrer, funnel, filter paper, dropper pipette, maksi tube, electric stove, pot, erlenmeyer, measuring cup, Fourier Transform Infra-Red (FTIR).

Research Procedure

- **Preparation of Cassava Leaf and Papaya Leaf Powder**

Extraction of papaya leaves (Carica papaya L.) and cassava (Manihot esculenta) was carried out using the maceration method with 70% ethanol solvent. The extraction process was carried out by first separating the leaves from the stems, then washing them with running water until clean. The leaves were cut into small pieces to speed up the drying process, either under the sun or using a drying oven. Once dry, the leaves were ground into a fine powder. A total of 250 grams of leaf powder was weighed and placed in a sealed glass container.

Next, 1,250 ml of distilled water was added, stirred until homogeneous, then left to stand for 2×24 hours with periodic stirring. The resulting maserate is filtered and squeezed using filter paper to obtain a liquid extract. The extraction process continues with the decoction of the leaf residue, which involves boiling the remaining extract solids using 70% ethanol solvent until boiling, with the aim of extracting any remaining compounds. The maserate is evaporated until only the pure leaf extract remains, which can then be used for phytochemical testing.

- **Phytochemical test**

a. Alkaloid test

A total of 0.5gram of cassava leaf extract sample was put in a test tube and added 1% HCL as much as 0.5ml, after which 1-2 drops of dragendorf were added. If it produces an orange color, it is positive for alkaloids.

b. Flavonoid test

A total of 200mg of leaf extract sample was put into a test tube. Then added 5ml. ethanol and heated for 5 minutes. After that, a few drops of concentrated HCI were added. Added magnesium as much as 0.2 grams. If a dark red (magenta) color appears, it shows positive flavonoids.

c. Phenolic test

A total of 0.5gram of leaf extract sample was put into an erlenmeyer and 10 ml of 70% ethanol was added. Taken 1 ml. of the solution formed and put into the reaction tank. After adding 5% FeC13 solution as much as 2 drops. If a green or bluish green color is formed, it is positive for phenol.

d. Tannin test

A total of 0.5gram of leaf extract sample was put into a test tube and added 2ml of distilled water. and added FeCD 1% as much as 2 drops. If it produces a bluish green color, it contains positive tannins.

e. Saponin test

A total of 0.5gram of leaf extract sample was put into a test tube. Then hot water is added and cooled. After the cold is shaken for 10 minutes. If foam is formed and added HCI 2. N the foam remains, it shows positive saponin.

f. Steroid and Triterpenoid test

A total of 0.5gram of cassava leaf extract sample was put into a test tube and 0.5mL of CHCI3 and 0.5mL of acetic acid were added. After that, 2ml of concentrated H2504 was added. Through the test tube wall. If positive, it contains triterpenoids when the color is formed. purple-red. While positive for steroids if it produces a green or blue color.

- **FTIR test**

Testing using Fourier Transform Infrared (FTIR) is done by turning on the FTIR tool along with a computer connected to the analysis software. The sample is placed on the sample holder, then the FTIR tool is run until it produces an FTIR spectrum of the sample. The spectrum results obtained were then analyzed by comparing the spectrum data with the FTIR table to identify the functional groups contained in the sample.

- **Literature Review**

The method used in the research also uses literature review. Literature review is a literature review that is carried out in stages with steps: identifying themes, determining methods, determining journal criteria, searching and selecting articles, summarizing results, and presenting the review. The literature search was conducted through Google Scholar with the keywords papaya leaf, cassava leaf, FTIR, and dengue hemorrhagic fever (DBD). The criteria for journals in this study were journals published in 2013-2025; using Indonesian and English; and containing research on the content of bioactive compounds in papaya leaves and cassava leaves that have potential in traditional dengue therapy. The journal search was adjusted to the inclusion and exclusion criteria, then continued by reading the entire article to obtain relevant data.

3 RESULT AND DISCUSSION

The initial stage of analysis was carried out by phytochemical screening to detect secondary metabolite compounds contained in papaya leaf and cassava leaf extracts. The results obtained provide an overview of the variety of active compounds possessed by the two plants. A summary of the test results can be seen in Table 1.

Tabel 1. Results of Phytochemical Screening of Leaf Extracts

Compound	Result	
	Pepaya	Singkong
Alkaloid	+	+
Flavonoid	+	+
Phenolic	+	+
Tannin	+	+
Saponin	+	-
Steroid	+	-
Triterpenoid	+	-

The results of phytochemical analysis listed in table 1 show that papaya leaf extract contains compounds such as alkaloids, flavonoids, phenolics, tannins, saponins, steroids, and triterpenoids. This finding is in line with the statement from Undana (2021) which states that papaya (Carica papaya) leaf extract is rich in beneficial secondary metabolite compounds, including alkaloids, flavonoids, phenolics, tannins, saponins, steroids, and triterpenoids. Alkaloids, particularly carpaine, have been identified as major components with antimalarial, antioxidant, anti-inflammatory, and cardioprotective activities, which include blood pressure lowering and cardiac function protection. Flavonoids in papaya leaves, such as quercetin, kaempferol, and mirisetin, function as antioxidants, antibacterials, anti-inflammatories, and antidiabetics by inhibiting α-glucosidase enzyme (Jurnalhost, 2023). In addition, phenolic compounds and tannins were also detected, contributing to antioxidant activity and antibacterial effects (Undhirabali, 2022). Steroids and triterpenoids were also identified in the ethanol extract of papaya leaves, supporting the biological activity and therapeutic potential of this plant, which can be utilized in pharmacology (UINSGD, 2021).

The results of the cassava leaf phytochemical test contained in Table 1 show that the extract contains secondary metabolite compounds such as alkaloids, flavonoids, phenolics, tannins, and triterpenoids. This finding is supported by the research of Lin et al. (2018), which noted that cassava leaf extract contained some of these compounds, while steroids and saponins were not detected. The presence of alkaloids and flavonoids indicates potential pharmacological activities such as antimicrobial, anti-inflammatory, and antioxidant. Flavonoids and phenolic compounds can counteract free radicals through an electron donation mechanism, preventing oxidative damage to body cells. Cassava leaf extract also has high total phenolic value and antioxidant activity. Tannin and saponin compounds play an important role in antibacterial and antifungal activity.

Tannins help precipitate proteins and strengthen the mucosal layer, while saponins boost the immune system and disrupt microbial cell membranes. Based on research by Yulianti and Ferdinal (2024), ethanol extract of cassava leaves has a total phenolic value of 48.87 mg GAE/g and antioxidant activity with IC_{50} of 285.37 µg/mL, showing potential as a natural antioxidant. Although steroids and triterpenoids were not detected in this extract, modern studies suggest that other parts of the cassava plant, such as the stem and root bark, contain such compounds. A systematic review by Mohidin et al. (2023) explains that cassava leaves and stems contain flavonoids (such as rutin and kaempferol), phenolic acids, as well as triterpenoids and saponins that support pharmacological activities such as antidiabetes, antioxidants, and anti-inflammation.

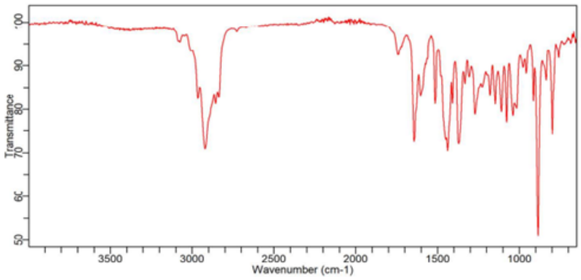
Papaya (Carica papaya) leaves contain more diverse bioactive compounds than cassava (Manihot esculenta) leaves. Apart from alkaloids, flavonoids, phenolics, and tannins which are also present in cassava, papaya leaves contain saponins, steroids, and triterpenoids which play an important role as antioxidants, anti-inflammatories, and immunomodulators (Setiawan et al., 2021). This content makes papaya leaves widely used in traditional medicine, especially to increase immunity and support the healing of infectious diseases (Arini et al., 2024).

In contrast, cassava leaves, although rich in flavonoids and phenolics, did not show positive results in simple tests for saponins, steroids and triterpenoids. However, cassava is characterized by the content of cyanogenic glycosides such as linamarin and lotaustralin which are not found in papaya. This compound can release cyanide so that it is toxic when consumed raw, although after proper processing cassava leaves remain useful as a source of natural antioxidants (Chukwuma et al., 2023). Therefore, the safety aspect of consumption is of particular concern in cassava leaves compared to papaya leaves.

The difference in phytochemical content is influenced by variations in secondary metabolic pathways in each plant. Papaya as a tropical fruit plant produces more proteolytic enzymes and triterpenoids for defense mechanisms against pathogens, while cassava as a tuber plant produces cyanogenic glycosides as a form of protection from herbivores (FAO, 2020). Environmental factors, extraction method, and type of solvent can also affect the detection of certain compounds.

Based on the results of the Fourier Transform Infra-Red (FTIR) spectroscopy test of cassava extract, the following data are shown

Gambar 1. Results of FTIR Testing of Cassava Extract



Tabel 2. Results of FTIR Testing of Cassava Extract

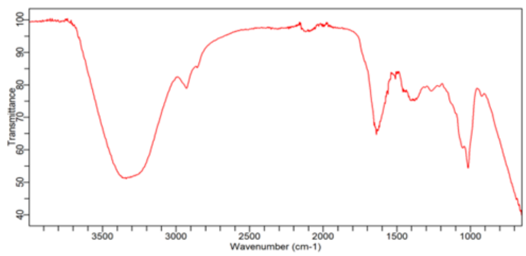
No	Wavelength	Function Group	Intensity
1	1045,51826	Alcohol, Ether, Carboxylic Acid, Ester (C-O)	Strong
2	1082,79164	Alcohol, Ether, Carboxylic Acid, Ester (C-O)	strong
3	1125,65603	Alcohol, Ether, Carboxylic Acid, Ester (C-O)	Strong
4	1313,88659	Aromatic ring (C=C)	Variable
5	1638,16498	Alkenes (C=C)	Variable
6	2107,80955	Alkenes (C=C)	Variable
7	3335,96736	Phenol, Alcohol Monomer, Hydrogen Bond Alcohol (O-H)	Variable

The results of the FTIR (Fourier Transform Infra-Red) test in table 2 can be analyzed that cassava leaves have various functional groups, including Alcohol, Ether, Carboxylic Acid, and Ester (C-O) at wave number 0.31393. Nitro (NO2) and Alkane (C-H) compounds were detected at wave number 0.56082, as well as Aromatic Ring (C=C) at wave number 0.65631 and 0.39097. Phenol, Alcohol Monomer, and Hydrogen Bonding Alcohol (O-H) were found at wave number 0.19140. According to Afriyani (2024), various compounds, such as potassium and flavonoids (with covalent bonds), can be found in the leaves of cassava. The presence of C=C, O-H, and C-H functional group bonds indicates that cassava leaf extract contains flavonoid compounds.

In addition, the relationship between flavonoid compounds and aromatic ring groups is due to the fact that flavonoid compounds are part of polyphenolic compounds that have 15 carbon atoms, consisting of C6-C3-C6. This indicates that the carbon skeleton of the compound consists of two C6 groups (substituted aromatic rings) joined by a C3 aliphatic chain or three carbons (Tian-yang et al., 2018). Based on the results table, it is known that cassava leaves contain C-O or ester groups, where esters can bind to O-H which helps connect fatty acids with glycerol in lipids. Therefore, cassava leaves can be identified as containing lipid compounds, namely fatty acids. Research by Pereira et al (2016) proved that after analyzing fatty acids through lipids, cassava leaves have 10 kinds of fatty acids in mg/100g.

Based on the results of the Fourier Transform Infra-Red (FTIR) spectroscopy test of papaya extract shows the following data:

Gambar 2. Results of FTIR Testing of Papaya Extract



Tabel 3. Results of FTIR Testing of Papaya Extract

No	Wavelength	Function Group	Intensity
1	1015,69956 (C-O)	Alcohols, ether, carboxylie acids, esters	Strong
2	1051,10927 (C-O)	Alcohols, ether, carboxylie acids, esters	Strong
3	1399,61536 (C-H)	Alkanes/alkana	Strong
4	1638,16498 (C=C)	Alkenes/alkena	Variable
5	2927,82387 (C-H)	Alkanes/alkana	Strong
6	3337,83103 (N-H, O-H)	Amines, amides Hydrogen-bonded alcohol, phenols	Medium Variable sometimes broad
7	1015,69956 (C-O)	Alcohols, ether, carboxylie acids, esters	Variable
	1051,10927 (C-O)	Alcohols, ether, carboxylie acids, esters	

Based on the results table 3, it can be analyzed that papaya leaf extract has various functional groups including Alcohol, Ether, Carboxylic Acid, Ester (C-O) at wave numbers 1015.69956 and 1051.10927, Alkane (C-H) at wave numbers 1399.61536 and 2927.82387, Alkenes (C=C) at wave numbers 1638.16498, and Amines, Amides (N-H) at wave numbers 3337.83103. The presence of Alcohol, Ether, Carboxylic Acid, Ester (C-O) groups in papaya leaf extract indicates that papaya leaves contain flavonoid compounds, but the presence of these compounds is also characterized by the presence of aromatic rings that bind to hydroxyl groups (alcohol). This is supported by the statement of Bangun and Rahman (2021) which states that papaya leaf extract has high flavonoid levels. In addition, the presence of Alcohol, Ether, Carboxylic Acid, Ester (C-O) groups can also indicate the presence of terpenoid compounds that contain hydroxyl groups (alcohol) and can form ethers.

The presence of Amine, Amide (N-H) functional groups in the results table can indicate the content of amino acid and alkaloid compounds. Amino acids have amine functional groups (NH_2) and carboxyl groups (COOH), this also occurs in alkaloids which have N-H amine functional group bonds. The presence of this compound in papaya leaves is supported by research by Haris et al (2023) which states that the high mortality of pests caused by several extracts such as papaya leaves, tobacco leaves and taro leaves is due to the large content of Alkaloid substances 9.65%, Flavonoids 0.42%, Amino acids 10.71%, Nicotine 31, 26%, Oxalic acid 46.78% and Tannin 4.47%. Based on the results of the analysis of functional groups in papaya leaf extract, Alkane (C-H) groups were also obtained, where this group is part of terpenoids, this compound has a carbon skeleton consisting of C-H (Alkane) bonds. In the research of Sudarwati and Fernanda (2018) stated that one part of papaya, precisely the leaves, contains tannins, flavonoids, terpenoids, saponins, and carpain alkaloids which act as antibacterial compounds.

Papaya leaf extract (Carica papaya) has been scientifically proven to increase platelet count in patients with dengue hemorrhagic fever (DHF). The main mechanism is through stimulation of platelet formation (thrombopoiesis) by increasing the expression of genes related to megakaryocyte differentiation, such as ALOX12 and PTAFR, so that platelet production from the bone marrow increases (Ahmad et al., 2021). In addition, the flavonoids and papain content in papaya leaves have anti-inflammatory and antioxidant activities that help protect platelets from damage due to oxidative stress and reduce platelet degradation by the immune system (Gowda et al., 2020). Research conducted by Subenthiran et al., 2013 showed that DHF patients who were given papaya leaf extract experienced a faster platelet increase than the control group so that this extract was widely studied as a therapy for increasing platelets in patients with DHF.

Unlike papaya, cassava leaf extract (Manihot esculenta) does not yet have strong clinical evidence related to increasing platelet counts in DHF patients. Phytochemical studies show that cassava leaves contain flavonoids, phenolics, and saponins that have potential as antioxidants and anti-inflammatory (Chukwuma et al., 2023). These compounds can support the process of hematopoiesis and protect blood cells from oxidative damage. However, several in vitro studies have actually found anticoagulant and thrombolytic activity from cassava extract, so it is not in line with the mechanism of increasing platelet count (Uddin et al., 2015). Thus, although the bioactive content of cassava leaves has the potential to support the hematological system, research to increase platelets in DHF is still not available.

This difference may be explained by variations in the secondary metabolite pathways of each plant. Papaya leaves produce triterpenoids, flavonoids and proteolytic enzymes that work synergistically in increasing platelet production and stability. In contrast, cassava leaves tend to produce phenolics and cyanogenic glycosides that function as a defense against herbivores, but are not directly related to the stimulation of thrombopoiesis (Tijjani et al., 2022). Therefore, in the context of adjunctive therapy for DHF, papaya leaves have been shown to be more potent as a platelet-enhancing agent while cassava leaves are still limited in their potential, which requires further research.

4 CONCLUSIONS

Based on the results of the analysis, papaya leaf and cassava leaf extracts both contain secondary metabolites such as flavonoids, alkaloids, phenolics, tannins, and triterpenoids that act as antioxidants, anti-inflammatory, and immunomodulators. Both have the potential to increase platelet count in patients with dengue hemorrhagic fever (DHF). However, papaya leaf extract is considered superior because it has been clinically proven to be effective in increasing platelets through clear mechanisms, namely stimulation of hematopoiesis and regulation of genes that play a role in platelet formation. Meanwhile, cassava leaf extract also shows potential with flavonoids, phenolics, and essential fatty acids that support blood cell regeneration, but clinical evidence is still limited. Thus, papaya leaves are more effective than cassava leaves as a natural supportive therapy in helping platelet recovery in DHF patients.

5 REFERENCES

Afriyani, R. (2024). Kandungan Fitokimia Daun Singkong (*Manihot esculenta*) dan Potensinya Sebagai Sumber Antioksidan. *Jurnal Biologi Tropis*, 22(1), 45–53.

Ahmad, N., Fazal, H., Ayaz, M., Abbasi, B. H., Mohammad, I., & Fazal, L. (2020). Dengue fever treatment with *Carica papaya* leaves extracts. *Asian Pacific Journal of Tropical Biomedicine*, 10(5), 201–210.

Ahmad, N., Fazal, H., Ayaz, M., Abbasi, B. H., Mohammad, I., & Fazal, L. (2021). Carica papaya leaf extract promotes thrombopoiesis via upregulation of *ALOX12* and *PTAFR* genes. *Journal of Ethnopharmacology*, *271*, 113890.

Aisyah, A. N., Setyowati, D. N. A., & Astriana, B. H. (2021). Potensi Pemanfaatan Daun Singkong (*Manihot utilissima*) Terfermentasi Sebagai Bahan Pakan untuk Meningkatkan Pertumbuhan Ikan Mas (*Cyprinus carpio*). *Jurnal Perikanan Unram*, 11(1), 13-25.

Arini, R., Lestari, I., & Nugraha, R. (2024). *Comparison of phytochemical content in papaya leaf extracts using different ethanol concentrations*. *Majalah Farmaseutik, 20*(1), 45–55.

Az-Zahra, A. J., & Al Jihad, M. N. (2022). Peningkatan Kadar Trombosit pada Pasien Anak Demam Berdarah Dengue (DBD) dengan Mengonsumsi Jus Jambu Biji Merah. *Ners Muda*, 3(2), 187-192.

Azzahra, J., Narsa, A. C., & Gama, N. I. (2023). Analisis Karakteristik dan Profil Pengobatan Pasien Demam Berdarah Dengue Anak di Instalasi Rawat Inap Rumah Sakit Samarinda Medika Citra Tahun 2020-2021. *Jurnal Sains dan Kesehatan*, 5(SE-1), 10-18.

Bangun, P. P. A., & Rahman, A. P. (2021). Analisis Kadar Total Flavonoid Pada Daun Dan Biji Pepaya (*Carica Papaya* L.) Menggunakan Metode Spektrofotometer Uv-Vis. *Jurnal Ilmiah Farmasi Attamru*, 2(1), 1-5.

Chukwuma, C. I., Mashele, S. S., & Ibrahim, M. A. (2023). Phytochemical profile and pharmacological properties of cassava (*Manihot esculenta*) leaves: A systematic review. *Frontiers in Pharmacology*, *14*, 1158492.

Food and Agriculture Organization of the United Nations (FAO). (2020). *Cassava safety and processing guidelines*. FAO.

Gowda, A., Jagadish, K. S., & Shariff, R. (2020). Clinical efficacy and safety of *Carica papaya* leaf extract in dengue patients: A randomized trial. *BMC Complementary Medicine and Therapies, 20*(1), 350.

Haris, A., Suherah, S., & Dewa, A. S. (2023). Pengaruh Pemberian Ekstrak Daun Pepaya, Daun Tembakau Dan Daun Talas Terhadap Mortalitas Hama Ulat Grayak (*Spodoptera Liturafabriciu* Je Smith). *Agrotek: Jurnal Ilmiah Ilmu Pertanian*, 7(2), 118-123.

Jurnalhost. (2023). Identifikasi Flavonoid Daun Pepaya (*Carica papaya* L.) Serta Aktivitas Penghambatan α-glukosidase. *Jurnal Ilmu Kefarmasian*, 15(2), 55–63.

Lin, K. Z., Phyu, P., Phyu, C., & Myint, P. P. (2018). Estimation of Nutritive Value, Total Phenolic Content and in Vitro Antioxidant Activity of *Manihot esculenta* Crantz. *Journal of Medicinal Plants Studies*, 6, 73–78.

Mahardika, I. G. W. K., Rismawan, M., & Adiana, I. N. (2023). Hubungan Pengetahuan Ibu dengan Perilaku Pencegahan DBD pada Anak Usia Sekolah di Desa Tegallinggah. *Jurnal Riset Kesehatan Nasional*, 7(1), 51-57.

Mohidin, S. R. N. S. P., Moshawih, S., Hermansyah, A., Asmuni, M. I., Shafqat, N., & Ming, L. C. (2023). Cassava (Manihot esculenta Crantz): A Systematic Review for the Pharmacological Activities, Traditional Uses, Nutritional Values, and Phytochemistry. *Journal of Evidence-based integrative Medicine*, 28, 2515690X231206227.

Patil, S., Shetty, S., Bhide, R., & Narayanan, S. (2013). Evaluation of Platelet Augmentation Activity of *Carica Papaya* Leaf Aqueous Extract in Rats. *Journal of Pharmacognosy and Phytochemistry*, 1(5), 57-60.

Pereira, I. G., Vagula, J. M., Marchi, D. F., Barão, C. E., Almeida, G. R., Visentainer, J. V., ... & Santos, O. O. (2016). Easy Method For Removal of Cyanogens from Cassava Leaves with Retention of Vitamins and Omega-3 Fatty Acids. *Journal of the Brazilian Chemical Society*, 27(7), 1290-1296.

Setiawan, A., Nurmalasari, & Widodo, A. (2021). Phytochemical composition and antioxidant activity of *Carica papaya* leaves. *Journal of Applied Pharmaceutical Science*, *11*(6), 120–126.

Sjahfirdi, L., Aldi, N., Maheshwari, H., & Astuti, P. (2015). Aplikasi Fourier Transform Infrared (FTIR) dan Pengamatan Pembengkakan Genital pada Spesies Primata, Lutung Jawa (*Trachypithecus Auratus*) untuk Mendeteksi Masa Subur. *Jurnal Kedokteran Hewan-Indonesian Journal of Veterinary Sciences*, 9(2).

Subenthiran, S., Choon, T. C., Cheong, K. C., Thayan, R., Teck, M. B., Muniandy, P. K., & Ismail, Z. (2013). *Carica papaya* Leaves Juice Significantly Accelerates the Rate of Increase in Platelet Count Among Patients with Dengue Fever and Dengue Haemorrhagic Fever. *Evidence-Based Complementary and Alternative Medicine*, 2013, 616737.

Subenthiran, S., Choon, T. C., Cheong, K. C., Thayan, R., Teck, M. B., Muniandy, P. K., Afzan, A., Abdullah, N. R., & Ismail, Z. (2013). *Carica papaya* leaves juice significantly accelerates the rate of increase in platelet count among patients with dengue fever. *Evidence-Based Complementary and Alternative Medicine, 2013*, 616737.

Sudarwati, T. P. L., & Fernanda, M. A. (2018). Aktivitas Antibakteri Daun Pepaya (*Carica Papaya*) Menggunakan Pelarut Etanol Terhadap Bakteri Bacillus Subtilis. *Journal Of Pharmacy and Science*, 3(2).

Susanti, A., & Suharti, P. (2020). Pengaruh Pemberian Air Seduhan Daun Pepaya (Carica Papaya) Dan Air Seduhan Kayu Secang (*Caesalpina Sappan*) Terhadap Jumlah Sel Trombosit Darah Mencit (*Mus Muscullus*). *Pedago Biologi: Jurnal Pendidikan dan Pembelajaran Biologi*, 8(1), 24-29.

Tian-Yang., Wang., Qing Li., Kai-Shun Bi. (2018). Flavonoid Bioaktif Dalam Obat Tumbuhan: Struktur, Aktivitas dan Biologi Fateasian. *Jurnal Farmasi Sains*, 13, 12–23.

Tijjani, H., Bello, A. M., & Musa, M. (2022). Bioactive compounds in cassava (*Manihot esculenta*) leaves and their pharmacological significance. *Journal of Ethnopharmacology, 293*, 115350.

Uddin, M. N., Saha, M. R., Hossain, M. S., Hasan, M., & Islam, M. M. (2015). Anticoagulant and thrombolytic activity of *Manihot esculenta* leaf extract in vitro. *International Journal of Pharmaceutical Sciences and Research, 6*(2), 729–735.

UIN Sunan Gunung Djati. (2021). Skrining Fitokimia Ekstrak Daun Pepaya (*Carica papaya* L.) Asal Manokwari. Proceedings of the Green Development Conference Series, 4(1), 231–237.

Undana. (2021). Identifikasi Senyawa Carpaine dari Daun Pepaya Lokal Kupang dan Uji Aktivitas Antioksidan. *Chemistry Nature*, 9(1), 34–40.

Undhirabali. (2022). Perbedaan Kandungan Metabolit Sekunder Daun Pepaya (*Carica papaya* L.) pada Dataran Rendah dan Tinggi. *Jurnal Medisains*, 6(2), 145–152.

Ustiawaty, J., Pertiwi, A. D., & Aini, A. (2020). Upaya Pencegahan Penyakit Demam Berdarah Melalui Pemberantasan Nyamuk Aedes aegypti. *Jurnal Pengabdian Magister Pendidikan IPA*, 3(2), 200-204.

Yulianti, E., & Ferdinal, F. (2024). Uji Fenolik Total dan Kapasitas Antioksidan DPPH Ekstrak Daun Singkong (*Manihot esculenta*). *Jurnal Sehat Indonesia (JUSINDO),* 7(2).

Zahrani, U. T., Rahayu, I. D., Ulandari, A. S., & Triyandi, R. (2025). Kandungan Senyawa Fitokimia dan Aktivitas Antibakteri Ekstrak Daun Pepaya (*Carica Papaya* L.): Narrative Review. *Jurnal Riset Ilmu Kesehatan Umum dan Farmasi (JRIKUF*), 3(2), 40-51.