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Ficus septica Burm. f.: A comprehensive review of its ethnomedicinal uses, phytochemistry, and pharmacological properties

Tazkiyatan Isria[1], Berna Elya[1], Roshamur Cahyan Forestrania[1], Muhammad Hanafi[2,3]

[1]*Department of Pharmacy, Faculty of Pharmacy, Universitas Indonesia, Depok, 16424, Indonesia*
[2]*Research Centre for Pharmaceutical Ingredients and Traditional Medicine, National Research and Innovation Agency (BRIN), Serpong, 15314, Indonesia*
[3]*Department of Phytochemistry, Faculty of Pharmacy, Pancasila University, Jakarta, 12640, Indonesia*

*Corresponding Author: berna.elya@farmasi.ui.ac.id

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ABSTRACT: *Ficus septica* Burm. f. is a significant medicinal plant within the Moraceae family, recognized for its extensive ethnomedicinal application throughout Southeast Asia, including Indonesia, the Philippines, and Papua New Guinea. It has been used to treat various conditions, from dermatological infections and fever to digestive disturbances. This review aimed to compile and critically evaluate the existing scientific literature on the botany, ethnomedicine, phytochemistry, and pharmacological potential of *F. septica*. A systematic literature search and selection process was conducted following the PRISMA guidelines to ensure transparency and reproducibility, supported by a narrative synthesis approach. Phytochemical investigations have consistently demonstrated that this species is abundant in diverse secondary metabolites, notably phenanthroindolizidine alkaloids (such as antofine, tylophorine, and ficuseptine), which serve as primary chemical markers. In conjunction with other flavonoids, terpenoids, and phenolic compounds, these compounds are responsible for many scientifically validated bioactivities. Pharmacological evidence highlights its anticancer capabilities, including apoptosis induction, cell cycle arrest, and anti-metastatic activity. Furthermore, it exhibits broad-spectrum antimicrobial activity, including antibacterial, antifungal, antiviral, and antiprotozoal effects. Its antioxidant, anti-inflammatory, and wound-healing properties have been extensively documented. This review affirms that contemporary scientific findings substantiate the traditional utilization of *F. septica* and underscores its potential as a valuable source for developing novel therapeutic agents, particularly in oncology and infectious disease management.

KEYWORDS: Anticancer; ethnomedicinal uses; *F. septica* Burm. f.; pharmacological properties; phytochemistry.

▪ INTRODUCTION

Ficus septica Burm. f., a species belonging to the Moraceae family, is typically observed as a shrub or deciduous tree, attaining heights of up to 25 m. Its natural distribution spans the Ryukyu Islands of Japan, the Malesian region (excluding the Malay Peninsula), the Solomon Islands, Vanuatu, and Queensland in Australia. Ecologically, *F. septica* exhibits high adaptability, thriving in lowland and montane forests, secondary growth areas, and proximal to rivers at elevations of up to 1800 m. Its rapid growth and fruiting facilitate its colonization of disturbed habitats, including urban environments in Indonesia [1]-[3]. Various parts of *F. septica* have been traditionally used in ethnomedicine systems across multiple countries, including Indonesia, the Philippines, Papua New Guinea, and Taiwan. These uses include treating skin infections, fever, and digestive disorders, as well as more serious ailments and conditions [4]–[12].

Although numerous studies have investigated the phytochemistry and biological activities of *F. septica*, the existing knowledge remains fragmented across ethnobotanical reports, isolated phytochemical studies, and pharmacological assays. Previous studies have generally focused on single

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domains, either ethnomedicinal uses or specific bioactivities, without providing an integrated synthesis that connects traditional knowledge with experimentally validated chemical constituents and biological mechanisms. In particular, the relationship between key secondary metabolites, such as phenanthroindolizidine alkaloids, and their pharmacological functions has not been comprehensively established within a unified framework.

To address this gap, this review systematically integrates evidence on the ethnomedicinal uses, phytochemical constituents, and pharmacological activities of *F. septica*. A structured literature search was conducted following the PRISMA guidelines, combined with a narrative synthesis approach based on Popay et al. (2006) to ensure transparency and methodological rigor. Unlike previous studies, this study provides a consolidated and critically organized overview that links traditional medicinal knowledge with experimental pharmacological findings. By mapping the relationships between bioactive compounds, plant parts, extraction methods, and reported biological activities, this review highlights the therapeutic potential of *F. septica* and identifies key research gaps, particularly in mechanism-based studies and bioactive compound isolation for future drug discovery.

▪ MATERIALS

A comprehensive literature search was conducted using the PubMed, Scopus, Google Scholar, and ScienceDirect databases. The search covered publications up to August 2025 to ensure the inclusion of the most recent studies. The primary keyword "*F. septica*" was used in combination with secondary terms related to ethnomedicine ("traditional use," "ethnobotany"), phytochemistry ("extract," "fraction" "isolation"), pharmacology ("bioactivity," "anticancer," "antimicrobial," "antioxidant," "anti-inflammatory"), and toxicology ("toxicity," "safety"). In addition, the reference lists of relevant articles were manually screened to identify further eligible studies for inclusion.

Methodology

This study employed a systematic narrative synthesis approach following the framework of Popay et al. (2006), with the review process guided by the PRISMA guidelines to ensure transparency and reproducibility. Eligible studies included full-text original research articles (in vitro, in vivo, and clinical studies), review articles, and ethnobotanical surveys focusing on *F. septica*, published in English or Indonesian languages. Studies on other Ficus species, non-research articles, and duplicate studies were excluded. A total of 166 records were initially identified, of which 141 remained after the screening. After full-text assessment, 95 studies met the inclusion criteria and were included in the final synthesis of the results. The selection process followed the PRISMA guidelines to minimize selection bias [13].

A narrative synthesis was conducted according to Popay et al. (2006), involving four stages: preliminary synthesis through tabulation and clustering of data into botanical characteristics, ethnomedicinal uses, phytochemical constituents, and pharmacological activities; exploration of relationships between phytochemical constituents and biological activities across in vitro and in vivo studies; assessment of robustness through critical evaluation of methodological heterogeneity and consistency of findings; and conceptual mapping to visualize relationships between plant parts used, extraction methods, and reported bioactivities. Due to high heterogeneity in study design, extraction methods, and outcome measures, no formal meta-analysis was performed, and a narrative synthesis was considered the most appropriate approach.

Botany and ecology

F. septica is a tree known for its yellow latex. The leaves are simple, ranging from elliptic to oblong in shape, and both surfaces are smooth and hairless. A distinctive feature of the Ficus genus is the syconium, a unique inflorescence that develops into false fruit. In *F. septica*, the syconium is a depressed

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globose or ellipsoid receptacle measuring 1.5–2 cm in diameter. To illustrate its main morphological features, Figure 1 shows a fresh specimen documented by the author. The sample was collected from Banyumas, Central Java, on July 26, 2025, and its identity was confirmed at the Herbarium Depokensis (UIDEP), Biota Collection Room, Department of Biology, Faculty of Mathematics and Natural Sciences, University of Indonesia, Indonesia.

An intriguing ecological aspect of this species is its pollination process. Contrary to the conventional belief that each Ficus species is pollinated solely by a specific wasp species, three potential pollinator species (*Ceratosolen* sp.) have been associated with *F. septica* in southern Taiwan. In Japan, this species is associated with the nematode Caenorhabditis inopinata, which resides within pollinated figs and is dispersed by pollinating wasps [1]–[3].

F. septica is widely distributed throughout the Indonesian archipelago, with its presence recorded across numerous islands and provinces. In Sumatra, it has been reported in Aceh [14]-[15], West Sumatra [16], and Bengkulu [10], [17] regions. The plant is also found extensively across Java, with documented occurrences in Banten [18], West Java [19]-[20], Central Java [9], [21]-[23], the Special Region of Yogyakarta [24]-[25], and East Java [25]-[28]. Its distribution extends to Borneo, specifically East Kalimantan [30], and throughout Sulawesi, including the provinces of South Sulawesi [31], Southeast Sulawesi [31]-[33], and Gorontalo [35]. Further east, it is found in Bali [4], [36]–[38], East Nusa Tenggara [39], and North Maluku [40]. This widespread presence is noted in diverse habitats, ranging from natural forests to disturbed areas, and it is also frequently found in urban settings and home gardens, where it may occur naturally or be cultivated in home gardens.

Ethnomedicinal

The uses of *F. septica* are extensive and well documented across multiple countries, reflecting its significant role in traditional healthcare systems. Papua New Guinea, its leaves and buds are prepared orally for headaches and gastroenteritis, or used as a heated, salt-moistened compress for body aches and wounds [6]-[8]. In the Philippines, a decoction of the stem or root is consumed to eliminate illnesses, and its leaves are used as an antidiabetic agent [5], [41]. The roots are also prominent in Malaysian traditional medicine for use during puerperal delivery and to treat headaches and stomach aches [12]. In Taiwan, its applications are broad, addressing fish and food poisoning, rheumatoid arthritis pain, dysentery, inflammation, and constipation [11].

Within Indonesia, this plant is ubiquitously used. It is widely applied for skin conditions such as boils in Bali and East Java [4], [42] and warts in West Java [20]. Its uses extend to treating fever in children in Central Java and West Sumatra [9], [16], appendicitis and asthma in East Java [26]-[27], and malaria in North Maluku [42]. In Sulawesi, local communities use it for diverse purposes, from eye drops and treating osteoarthritis in Central and South Sulawesi to addressing hemorrhoids and tuberculosis in Southeast Sulawesi [31]-[34], [43], [44]. Notably, in East Nusa Tenggara, the leaves are traditionally used for serious conditions such as stroke, fever, food poisoning, and HIV/AIDS, while in West Nusa Tenggara, the sap is applied directly to scorpion stings [39], [45]. Other specific uses include enhancing female fertility in Bengkulu by soaking the root and treating allergies and poisoning in Gorontalo by drinking water from boiled shoots [10], [35]. The ethnomedicinal applications of *F. septica* are summarized in Table 1 to provide a clear overview of the traditional uses of the plant across different regions.

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Table 1. Ethnomedicinal uses of *F. septica.*

Region/country	Local name	Part used	Ailment/use category	Specific use & preparation	Reference
Papua New Guinea	Omia, Bahuerueru, Manibwohebwahe	Dried buds, young leaves	Headache, Gastroenteritis	Taken orally.	[7]
		Fresh Leaves	Stomach Pain	Infusion in seawater was administered orally.	[6]
		Fresh Leaves	Pain Relief, Wound Care	Heated leaves moistened with salt were used as a hot compress for forehead and body aches and applied directly to wounds.	[8]
Philippines	Lagnob, hauili	Stem or Root	General Illness	A decoction of pounded stems or roots is administered daily.	[5], [41]
	Lagnob, hauili	Leaves	Diabetes	It is used as an antidiabetic agent.	
Malaysia	Ara, Litotobau, etc.	Root	Puerperal Care, Pain Relief	It is used during puerperal delivery and for headaches and stomachaches.	[12]
Taiwan	Leng guo rong	Root, Leaves, Fruit	Poisoning, Inflammation, Pain	It is used to treat fish and food poisoning, rheumatoid arthritis pain, dysentery, and inflammation.	[11]
		Leaf juice, Fruit	Digestive & Skin Issues	Leaf juice for constipation and dermatitis; fruit for constipation;	
Indonesia (Bengkulu)	Awar-awar	Root	Female Fertility	The root is soaked in water overnight and taken orally to enhance the fertility.	[10]
Indonesia (Bali)	Awar-awar	Leaves	Skin Conditions	Used to treat boils.	[4]
Indonesia (Central Java)	Awar-awar	Leaves	Fever, Parasites (Children)	It is used as an anthelmintic (anti-worm) and for treating fever in children.	[9]

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Region/country	Local name	Part used	Ailment/use category	Specific use & preparation	Reference
Indonesia (East Java)	Awar-awar	Leaves, Roots, Sap, Fruits	Multiple Ailments	It is used to treat appendicitis, boils, urinary problems, constipation, vomiting, asthma, ear disorders, ulcers, and venomous snake bites.	[26], [27], [28], [46]
Indonesia (West Java)	Awar-awar	Leaves and Sap	Skin Conditions	It is used to treat skin diseases such as warts.	[20]
Indonesia (Central Sulawesi)	Lambonug	Leaves and Stem	Eye Conditions	Mashed plant parts are used as eye drops.	[43]
Indonesia (Southeast Sulawesi)	Tobo-tobo, Trahom	Leaves and Roots	Multiple Ailments	It is used for red eyes, hemorrhoids (the patient sits on heated leaves), and tuberculosis (TB) (the patient drinks water infused with peeled roots).	[32], [33], [34]
Indonesia (South Sulawesi)	-	Leaves and Stem	Pain Relief, Libido	Squeezed leaves in hot water are consumed for osteoarthritis and myalgia, and boiled stems are consumed to improve libido.	[31]
Indonesia (East Nusa Tenggara)	Kaboke	Leaves	Serious Illnesses, Maternal Care	The leaves were boiled and drunk for HIV/AIDS, boiled and eaten for stroke, headache, fever, and food poisoning, and chewed and applied to a pregnant woman's stomach.	[39]
Indonesia (West Nusa Tenggara)	Lembukik	Sap	Scorpion Stings	Sap from the trunk is applied to the wounds caused by scorpion stings.	[45]

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Region/country	Local name	Part used	Ailment/use category	Specific use & preparation	Reference
Indonesia (Gorontalo)	Bualo	Shoots	Poisoning, Allergies	Boiled shoots and the resulting water are consumed.	[35]
Indonesia (North Maluku)	Tagalolo	Leaves	Malaria	It is used as an antimalarial agent.	[42]
Indonesia (West Sumatra)	Batang lundang	Stem, Leaves, Roots	Fever	The boiled parts of the plant are consumed to treat fever.	[16]

Figure 1. *F. septica* Burm.f. showing a branch with leaves and cauliflorous syconia (figs).

Extraction

Various extraction methods have been employed to isolate bioactive compounds from different parts of *F. septica*, with maceration being the predominant technique. The choice of solvent and method has been tailored to target specific activities, including anticancer, anti-inflammatory, antioxidant, and antimicrobial activities.

For leaves, maceration with ethanol at different concentrations is the most common approach. For instance, 70% ethanol was used to obtain extracts for antiangiogenesis and anticancer (breast cancer) studies [40]–[42], with one study reporting a yield of 19.98% [50]. Maceration with 96% ethanol has been widely used to prepare extracts for evaluating anti-inflammatory, anticancer (hepatocellular and breast carcinoma), antibacterial, and wound healing activities [44]–[48]. Maceration with 95% ethanol was used to obtain extracts with broad-spectrum antimicrobial (antibacterial, antifungal, and antiprotozoal) activity [56]. Hot aqueous extraction (80 °C for 10 min) has also been utilized, specifically for preparing extracts for antioxidant assays [12].

For the stem bark, maceration with 80% methanol was used to obtain extracts for antiangiogenic studies [5], while 80% ethanol was used to assess antimitotic and antiproliferative activities [57]. Maceration with 96% ethanol yielded an extract for antioxidant evaluation, with a reported yield of 11.72% [58]. The fruit has also been extracted using maceration, with 96% ethanol (6.71% yield) [59] and 70% methanol [60] used to prepare extracts for antioxidant activity assessment. Maceration with methanol (13.62% yield) was used to obtain extracts for topical anti-inflammatory studies [61].

An optimization study focused on enhancing the alkaloid content of a 60% ethanolic leaf extract. Ultrasonic-assisted fractionation with *n*-hexane was optimized by varying the duration, extract-to-

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solvent ratio, and ultrasonic power levels. The optimal conditions, determined through a full factorial design, resulted in an alkaloid-rich fraction with 0.035% alkaloid content, nearly doubling the concentration from the initial extract. This demonstrates that advanced extraction and fractionation techniques can significantly improve the yield of the targeted bioactive compounds from *F. septica* [62].

Isolation and identification

Phenanthroindolizidine alkaloids are the hallmark constituents of this species. An early investigation of the roots and leaves using classical separation on Kieselgel G successfully isolated antofine and other minor bases of the same class (Herbert & Moody, 1972) [63]. Similarly, Russel (1963) identified key alkaloids, such as (−)tylophorine, (+)tylocrebrine, and the seco-alkaloid septicine [64]. More extensive work on stems by Damu et al. (2005) involved refluxing the plant material with methanol, followed by liquid-liquid partitioning with chloroform and *n*-butanol. The alkaloidal fractions were subjected to exhaustive purification using repeated silica gel column chromatography and HPLC, leading to the isolation of eight new and six known phenanthroindolizidine alkaloids. Their structures were elucidated through extensive spectroscopic analyses, including NMR, MS, and CD spectroscopy [65]. Leaves have also been a primary focus for alkaloid discovery. Ueda et al. (2009) performed a systematic study by extracting leaves with aqueous methanol, partitioning the extract across a polarity gradient (*n*-hexane, ethyl acetate, and butanol), and applying MPLC and HPLC to the basic fractions. This approach yielded known phenanthroindolizidine and seco-phenanthroindolizidine alkaloids and led to the discovery of new compound classes for this plant: aminocaprophenone-type (ficuseptamines A and B) and pyrrolidine-type alkaloids (ficuseptamine C) [66]. In a bioactivity-guided approach, Baumgartner et al. (1990) used a methanolic extract of the leaves, fractionated by silica gel and MPLC, to isolate the potent antifungal alkaloids antofine and a novel compound, ficuseptine [67], [68].

The non-alkaloidal content of *F. septica* is also diverse. Wu et al. (2002) investigated the non-alkaloidal fractions from the methanolic extract of the stem using silica gel chromatography and HPLC to isolate a variety of compounds, including seven triterpenes, two lignans, and simple phenolics [69].

This study reports the first natural isolation of a rare triterpene, 13,27-cycloursan-3β-yl acetate, with its structure unequivocally confirmed by single-crystal X-ray diffraction. Recently, Wang et al. (2024) explored the bark using a 95% methanol extract, fractionated on a silica column, and purified via reverse-phase HPLC, yielding seven sterols and three lignans previously unreported in this plant [70].

Various extraction solvents have been used to target less-polar constituents. Ragasa et al. (2016) used dichloromethane to extract twigs and leaves. Silica gel chromatography of the twig extract yielded β-sitosteryl-3β-glucopyranoside-6'-O-fatty acid esters, α-amyrin fatty acid esters, β-sitosterol, and stigmasterol, while the leaf extract produced β-amyrin and long-chain fatty alcohols [41]. Similarly, Su et al. (2022) studied a methanol extract of leaves, focusing on the ethyl acetate-soluble fraction. Purification via silica and reverse-phase HPLC led to the isolation of a diterpene (phytol), five sterols, and five triterpenoids, including uvaol and fernenol, which were novel for the species [11]. A unique study by Knothe et al. (2019) examined seeds extracted with hexane using a Soxhlet apparatus. GC-MS analysis of the oil revealed a profile rich in polyunsaturated fatty acids, as well as significant quantities of triterpenes (α-amyrin, β-amyrin, lupeol), sterols, and trace amounts of macrocyclic alkanes, which is rare for seed oils [71].

Throughout these studies, the standard methodology involves the extraction of compounds using a solvent of appropriate polarity (such as hexane, dichloromethane, or methanol), often followed by liquid-liquid partitioning for initial separation. The purification of individual compounds typically employs chromatographic techniques, including gravity column chromatography on silica gel, medium-pressure liquid chromatography (MPLC), and preparative normal- or reverse-phase HPLC.

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Thin-layer chromatography (TLC) is routinely used to assess the purity of the isolates, and their structures are elucidated using various spectroscopic methods, primarily 1D and 2D NMR spectroscopy, mass spectrometry (EIMS, HREIMS, FABMS), UV-Vis spectroscopy, and IR spectroscopy.

Phytochemistry

Phytochemical investigations of *F. septica* have revealed a rich and diverse array of secondary metabolites throughout the plant, including alkaloids, flavonoids, phenolics, terpenoids, and fatty acids. Quantitative analyses consistently highlight the leaves and fruits as being especially rich in phenolic and flavonoid compounds, which are often associated with the plant's antioxidant properties.

Quantitative screening of a 70% ethanolic leaf extract showed that the ethyl acetate-soluble fraction had the highest total phenolic content (TPC) at 35.53±1.79 mg GAE/100 mg of extract and the highest total flavonoid content (TFC) at 3.27±0.05 mg CAE/g [72]. An aqueous leaf extract also exhibited significant levels of phenolics (27.32±0.03 mg GAE/g) and flavonoids (12.65±0.00 mg CAE/g) [12]. Fruits have also been identified as a strong source of these compounds. The n-hexane fraction of a 70% methanolic fruit extract yielded a very high TPC of 105.16 mg GAE/g and TFC of 280.75 mg QE/g [60]. Similarly, the ethyl acetate fraction of a methanolic extract contained a TPC of 28±0.05 mg GAE/100 mg sample and a TFC of 43.08±0.48 mg QE/100 mg sample [60].

Bioactivity

Antioxidant activity

F. septica is a significant source of natural antioxidants. Various parts of the plant, including the leaves, stem bark, and fruits, demonstrate potent radical-scavenging capabilities, as shown by multiple in vitro assays. Studies have focused on evaluating the antioxidant potential of different extracts and fractions, correlating this activity with their total phenolic and flavonoid content.

A comprehensive re-evaluation of the antioxidant potential of *F. septica* underscores the complex relationship between its phytochemical composition and observed bioactivity, particularly in the leaves. Antioxidant potency was classified according to IC_{50} values as very strong (< 50 µg/mL), strong (50–100 µg/mL), moderate (100–200 µg/mL), and weak (> 200 µg/mL) [73]. The leaves demonstrated intriguing outcomes, revealing a significant discrepancy between the phytochemical content and antioxidant efficacy.

In particular, the aqueous extract exhibited exceptionally strong antioxidant activity (IC_{50} = 4.45 µg/mL). However, this high potency did not directly correlate with its total phenolic content (TPC: 27.32±0.03 mg GAE/g) and flavonoid content (TFC: 12.65±0.00 mg CAE/g), which were not among the highest reported values [12]. These observations imply that the remarkable activity of the aqueous extract is likely attributable to specific compounds with high intrinsic activity rather than the aggregate amounts of phenolic or flavonoid compounds.

Similarly, a 70% ethanolic extract also showed very strong activity (IC_{50} = 21.19 µg/mL) [74], further highlighting the high antioxidant potential of crude leaf extracts. In contrast, fractionation of the 70% ethanolic leaf extract resulted in fractions with only weak to very weak activity. The ethyl acetate-soluble, n-hexane, and ethyl acetate-insoluble fractions produced IC_{50} values of 400, 1,500, and 1,800 µg/mL, respectively. The low activity in these fractions corresponds with their generally low TPC and TFC levels [72], reinforcing the notion that phenolics and flavonoids are the primary active agents when present in sufficient amounts.

In contrast to the intricate findings observed in the leaves, the fruits consistently emerged as the most potent source of antioxidants, exhibiting a clear positive correlation between elevated

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phytochemical content and their bioactivity. In the ABTS, CUPRAC, and DPPH assays, various fruit fractions displayed markedly strong antioxidant activity, with IC_{50} values ranging from 6.33 to 17.69 µg/mL [59], [75]. This enhancement in activity is corroborated by significantly higher levels of total phenolic content (TPC) and total flavonoid content (TFC) in the fruit extracts [60], [75]. Concerning the stem bark, evaluation using the ABTS assay revealed moderate antioxidant activity, with a 96% ethanolic extract exhibiting an IC_{50} of 127.49±2.53 µg/mL [58]. As TPC and TFC data for the stem bark were not available, establishing direct correlations with phytochemical content was not feasible.

Anticancer

F. septica Burm. f., a plant employed in traditional medicine across Southeast Asia, has garnered considerable scientific interest due to its potential as a source of anticancer agents [76], [77]. Laboratory investigations have comprehensively documented its diverse bioactivities, including cytotoxicity, induction of apoptosis, cell cycle regulation, and anti-metastatic properties, making it a promising candidate for both monotherapy and combination cancer treatments.

The cytotoxic potential of *F. septica* has been demonstrated in a wide range of cancer cell lines. Ethanolic leaf extracts (EFS) and their fractions exhibited potent, dose-dependent growth inhibition. For example, EFS exhibited IC_{50} values of 6 and 13 µg/mL in MCF-7 and T47D breast cancer cells, respectively [78], [79]. Further fractionation enhanced this potency; alkaloid-rich fractions A and B showed high cytotoxicity against T47D cells with IC_{50} values of 2.57 µg/mL and 2.73 µg/mL, respectively [80], while the n-hexane insoluble fraction (HIF) displayed an IC_{50} of 9 µg/mL [81]. The activity extends to other types of cancer, including highly metastatic 4T1 breast cancer cells (IC_{50} = 15.2 µg/mL), WiDR colon cancer cells (IC_{50} = 75.9 µg/mL), and HepG2 hepatocarcinoma cells (IC_{50} = 50.9 µg/mL) [76]–[78]. Notably, these extracts exhibited high selectivity. Studies using Vero normal kidney cells revealed high selectivity indices (SI), such as 5.6 for HepG2 cells and over 3 for various other cancer lines, indicating that the extracts are significantly more toxic to cancer cells than to normal epithelial cells [81], [83], [84].

The primary mechanism underlying this cytotoxicity is the induction of apoptosis. In MCF-7 cells, the ethanolic extract induced apoptosis by downregulating the expression of the anti-apoptotic protein Bcl-2 [78]. In HepG2 cells, the cytotoxic effect is mediated by excessive generation of reactive oxygen species (ROS), resulting in oxidative stress and subsequent cell death [84]. In vivo studies using 7,12-dimethylbenz[a]anthracene (DMBA)-induced rat models further corroborated these findings, demonstrating that oral administration of the extract (750 mg/kgBW) induced apoptosis in both mammary and hepatic tumors. A significant finding from these investigations is that the apoptotic mechanism functions via a p53-independent pathway, suggesting its potential effectiveness in cancers with p53 mutations [49], [79].

In addition to inducing cell death, *F. septica* extracts modulate cell cycle progression to inhibit cell proliferation. The ethanolic extract induced cell cycle arrest at the G0/G1 phase in HepG2 cells and at the G2/M phase in HeLa cervical cancer cells [50], [84]. The hexane-insoluble fraction also induced G1 arrest in T47D cells [81].

The potential of this plant to counteract cancer metastasis has also been confirmed. In the highly metastatic 4T1 breast cancer cellular model, the ethanolic extract suppressed cell migration, an effect attributed to the downregulation of Matrix Metalloproteinase-9 (MMP-9) and Rac-1 protein expression, both of which are essential for cellular motility and invasion [85]. Moreover, *F. septica* exhibits notable antiangiogenic properties. In the ex ovo chorioallantoic membrane (CAM) assay, both the ethanolic extract and its n-hexane-insoluble fraction effectively impeded the formation of new blood vessels stimulated by basic fibroblast growth factor (bFGF) in a dose-dependent manner [47], [86]. At a concentration of 13.00 µg/mL, the extract achieved 62.30% inhibition of angiogenesis [47].

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A promising use of *F. septica* is as a co-chemotherapeutic agent, which enhances treatment effectiveness and reduces side effects. Numerous studies have documented a synergistic effect when its extracts are combined with agents such as doxorubicin or cisplatin. For instance, the combination of an ethanolic extract with doxorubicin and Curcuma xanthorrhiza extract on T47D cells yielded a synergistic outcome, as evidenced by a Combination Index (CI) value of 0.63 [87]. This combination modified the drug's impact on the cell cycle, transitioning doxorubicin-induced G2/M arrest to S-phase arrest. Similarly, the hexane-insoluble fraction enhanced doxorubicin cytotoxicity in T47D cells by shifting cell cycle arrest to the G1 phase and augmenting apoptosis through PARP cleavage [81]. Beyond its capacity to enhance cytotoxicity, the extract offers immunomodulatory advantages. In doxorubicin-treated rats, the hexane-insoluble fraction countered drug-induced immunosuppression by increasing lymphocyte proliferation, improving macrophage phagocytosis, and elevating CD8+ T cell levels, thereby safeguarding the immune system during chemotherapy [88].

The diverse anticancer activities of *F. septica* are predominantly ascribed to its abundant phenanthroindolizidine alkaloids [65], [69]. Compounds including tylophorine, antofine, ficuseptine, and tylocrebrine have been isolated from the stems, roots, and leaves and have exhibited potent cytotoxic effects against various cancer cell lines, such as nasopharyngeal (HONE-1) and gastric (NUGC) carcinomas [65], [89]. Among these, antofine was notably efficacious, with ED_{50} values of less than 0.1 µg/mL across multiple cell lines [89]. Although tylophorine is frequently recognized as the principal active compound, some studies indicate that other alkaloids may primarily account for the observed bioactivities, as chromatographic analyses occasionally do not detect significant quantities of tylophorine in bioactive extracts [47]. This suggests a complex phytochemical profile, in which multiple constituents likely contribute synergistically to the overall therapeutic efficacy.

In conclusion, *F. septica* offers a multifaceted approach to cancer therapy. Its extracts and constituents demonstrate selective cytotoxicity, apoptosis induction through various pathways, cell cycle arrest, and potent anti-metastatic and anti-angiogenic effects. Its synergistic relationship with conventional chemotherapeutics highlights its strong potential for development as an effective co-chemotherapy agent that can enhance treatment efficacy while reducing toxicity.

Antimicrobial

F. septica Burm.f., a member of the Moraceae family, has a longstanding tradition in traditional medicine, particularly in Papua New Guinea, for addressing infections and various other health conditions [6], [56]. Scientific investigations have substantiated these ethnobotanical assertions by revealing various antimicrobial activities, including antibacterial, antifungal, antiviral, and antiprotozoal effects of these plants. These activities are primarily attributed to its diverse phytochemical constituents, particularly indolizidine alkaloids.

Antibacterial

The antibacterial potential of *F. septica* has been consistently demonstrated in multiple studies using various plant parts and models. An early investigation by Baumgartner et al. (1990) on a methanolic leaf extract, utilizing a TLC bioautography assay, identified two key indolizidine alkaloids, ficuseptine and antofine, which exhibited significant antibacterial activity [90]. The minimum growth inhibition concentrations of ficuseptine were five µg against *Bacillus subtilis* and *Micrococcus luteus* and 10 µg against *Escherichia coli*. Antofine demonstrated similar potency against *B. subtilis* (5 µg) and *E. coli* (10 µg) but was more potent against *M. luteus* (1 µg). Subsequent in vitro studies employing ethanol extracts of leaves have reaffirmed this activity. Khusnuryani and Fuad (2015) utilized a disc diffusion assay and demonstrated moderate inhibition against *Staphylococcus aureus* ATCC 29523 and *E. coli* ATCC 35218, with inhibition zones ranging from 7.7 to 9.71 mm [54]. Similarly, Tuna et al. (2016) reported a potent dose-dependent inhibition by an ethanol leaf extract against *Staphylococcus aureus* and

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Escherichia coli, achieving inhibition zones of 27.5 mm and 24.8 mm, respectively, at 100 mg/ml. Furthermore, these studies observed that Gram-positive *Staphylococcus aureus* exhibited greater susceptibility than Gram-negative *Escherichia coli*, a phenomenon attributed to differences in their cell membranes [91]. Vital et al. (2010) supported these findings, showing that an ethanol leaf extract was as effective as ampicillin in inhibiting *S. aureus* and *E. coli* [56].

The clinical relevance of this antibacterial activity was explored in a cluster-randomized trial by Deli et al. (2022). This investigation examined *F. septica* exudate, a traditional remedy for treating small cutaneous ulcers in pediatric patients in Papua New Guinea. The exudate, which was found to be rich in ficuseptine (ranging from 23.3 to 53.9 mg/ml), exhibited bactericidal activity against known ulcer pathogens, including *S. aureus*, *Streptococcus pyogenes*, *Corynebacterium diphtheriae*, and *Fusobacterium ulcerans*. Its efficacy against *S. aureus* in a disc diffusion assay surpassed that of 0.2% *chlorhexidine*. Clinically, the topical application of the exudate was determined to be non-inferior in healing efficacy to *Savlon*® antiseptic cream and conventional soap-and-water treatment on day 14. Additionally, the study underscored the potent anti-inflammatory mechanism of the exudate, demonstrating its capacity to completely suppress the secretion of pro-inflammatory cytokines IL-6 and TNF-α from M1 macrophages and neutrophils at concentrations as low as 1.5 µg/ml, a critical action in promoting wound healing. Importantly, the exudate was confirmed to be non-mutagenic in the Ames test, affirming its safety for topical application [92].

Further investigation of the mechanism of action was conducted by Nurlailiyah et al. (2023), who examined the potential of bioactive compounds from *F. septica* leaves against Methicillin-resistant Staphylococcus aureus (MRSA) using an in silico study. Using molecular docking, several compounds, including coumarin, genistin, β-sitosterol, tylophorine, and stigmasterol, were identified as having strong potential to inhibit BlaR1 transducer protein, a key sensor in MRSA antibiotic resistance. Coumarin interacts with the critical active sites Lys526 and Thr527 of the BlaR1 protein, indicating a specific molecular mechanism for overcoming antibiotic resistance [93].

Antifungal

F. septica extracts also exhibited significant antifungal properties. The initial study by Baumgartner et al. (1989) reported strong activity of leaf extracts against Penicillium oxalicum. The isolated alkaloids, antofine and ficuseptine, were highly potent, with minimum inhibitory amounts of just three µg and one µg, respectively [67]. Vital et al. (2010) demonstrated that an ethanol leaf extract greatly inhibited the opportunistic yeast Candida albicans, with an inhibition zone of 17.67 mm, which was larger than that of the standard drug Nystatin® [56]. More recently, a methanolic leaf extract was tested against Aspergillus niger, and Julyeda et al. (2021) found a minimum inhibitory concentration (MIC) of 500 ppm. It produced an inhibition zone of 20.5 mm at 10,000 ppm, demonstrating its potential as a natural fungicide for preservation. The broad-spectrum antifungal activity is attributed to the synergistic effects of various phytochemicals, including flavonoids, tannins, and alkaloids [36].

Antiviral

The antiviral potential of *F. septica* was specifically examined against the *dengue virus* (*DENV*). Huang et al. (2017) evaluated crude extracts from various plant parts, including the fruit, heartwood, leaves, stem, and root bark. Using an immunofluorescence assay, methanol and acetone extracts from these parts demonstrated a significant inhibitory effect against enveloped *viruses DENV-1* and *DENV-2* in vitro across multiple human cell lines (A549, HepG2, and Huh7.5). The root bark acetone extract exhibited exceptional potency against *DENV-2*, with an IC_{50} of merely 3.05 ± 0.75 µg/ml. The proposed mechanism of action involves a direct interaction with viral particles. Experimental data demonstrated that pre-incubation of the virus with the leaf extract effectively inhibited infection, whereas the extract

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had no effect on the non-enveloped Aichi virus. These findings suggest that these active compounds may disrupt the envelope integrity of *DENV* or impair its capacity to bind to host cells [94].

Antiprotozoal

F. septica demonstrates efficacy against protozoan parasites, in addition to bacteria, fungi, and viruses. Vital et al. (2010) examined the activity of an ethanol leaf extract against *Trichomonas vaginalis* and *Entameba histolytica*, observing growth inhibition comparable to that of *metronidazole*. The extract induced apoptotic-like alterations in the trophozoites of the parasites, implying the involvement of a programmed cell death pathway [56].

Wound healing activity

The potential of *F. septica* to promote wound healing has been examined, with research focusing on the topical application of its leaf extracts. Studies have utilized in vivo burn models to evaluate the effectiveness of formulations containing these plant extracts. In a particular study, a gel formulated with a 2.5% m/v concentration of a 96% ethanolic leaf extract was applied to burn wounds on rabbits, which were induced using hot metal. The treatment exhibited significant wound-healing activity, as demonstrated by a 1.50 cm reduction in the wound surface area over 12 days. Although the specific mechanism of action was not elaborated in this study, the results imply that the ethanolic extract of *F. septica* leaves comprises bioactive compounds that facilitate the repair of burn injuries [55].

Anti-inflammatory

F. septica has demonstrated significant anti-inflammatory properties in preclinical studies, with research primarily focusing on its leaves. The anti-inflammatory effects of this plant have been evaluated using in vivo models, suggesting its potential for mitigating inflammatory responses. A study investigating a 96% ethanolic leaf extract in a carrageenan-induced inflammation model in white rats showed significant activity. At a dose of 200 mg/kg body weight, the extract reduced the edema volume and diameter by 19% and 18%, respectively. The proposed mechanisms for this effect include the inhibition of neutrophil degranulation, cyclooxygenase (COX), and lipoxygenase enzyme activity, as well as the inhibition of histamine release [51]. In another study, a topical ointment containing a 2% concentration of 70% ethanolic leaf extract was tested on mice with λ-carrageenan-induced inflammation.

This formulation effectively reduced the back skin fold thickness by 38.79%, indicating strong topical anti-inflammatory activity [48]. These findings highlight the systemic and topical anti-inflammatory potential of F. septica leaf extracts, attributable to their ability to modulate key inflammatory mediators and pathways.

Immunomodulatory

F. septica has been studied for its immunomodulatory effects, particularly in reducing chemotherapy side effects. Research on doxorubicin-treated rats has shown that leaf extracts influence immune responses. The n-hexane insoluble fraction (HIF) at 1,500 mg/kgBW decreased immunosuppression by boosting macrophage activity, increasing lymphocyte density, and raising CD8+ T-cells in the blood [88]. It also reduced IL-10 expression in the spleen, indicating a shift to a more active immune state. Conversely, a 96% ethanolic leaf extract at 750 mg/kgBW decreased CD3+ and CD8+ lymphocytes, suggesting that the effects depend on the dose or extract type [95].

Toxicity

The toxicity of various extracts from *F. septica* was evaluated using the Brine Shrimp Lethality Test (BSLT), a preliminary assay to assess cytotoxic potential. The results indicate that toxicity varies depending on the plant part used and the type of extract. The root exhibited the highest toxicity, with

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an ethanolic extract showing a potent LC_{50} value of 1,16 ppm [96]. The fruits also demonstrated significant toxicity; a 96% ethanolic extract had an LC_{50} of 2,22 ppm, and its ethyl acetate fraction was slightly more potent with an LC_{50} of 2.18 ppm [59]. The stem showed moderate toxicity, with an 80% methanolic extract yielding an LC_{50} of 14.99 ppm [5]. In contrast, the leaves were found to be the least toxic among the parts tested, with a 70% ethanolic extract resulting in an LC_{50} of 39.71 ppm [97]. These findings suggest that the leaf extract is less toxic, whereas the root and fruit extracts possess strong cytotoxic activity.

▪ RESULT

F. septica Burm. f. is a resilient member of the Moraceae family, appearing as a shrub or tree reaching 25 m, characterized by its distinctive yellowish latex and smooth, elliptic to oblong leaves. Its ecological range is vast, spanning from Japan through the Malesian region to Australia, thriving in varied habitats from lowland forests to urban environments [1]-[3]. Within Indonesia, the species is widely distributed across Sumatra [10], [13]-[16], Java [9], [17]-[29], Borneo [29], Sulawesi, [30] - [34], and several other provinces [4], [35]-[39]. Ethnomedicinal records indicate its extensive use for treating dermatological conditions such as boils and warts [4], [25]-[27], [92]-[94], systemic issues such as fever and malaria, and serious conditions including stroke and HIV/AIDS [9], [16], [39]. Phytochemical profiling has identified a diverse array of secondary metabolites, most notably phenanthroindolizidine alkaloids, such as antofine [65], tylophorine [64], [65], [69], [99], and ficuseptine [69], [100], which serve as primary chemical markers. Additionally, the plant contains various flavonoids, terpenoids, lignans, and phenolics distributed across the leaves, bark, and seeds, as detailed in Table 2.

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Table 2. Phytochemical compounds in *F. septica*.

Plant part	Compound	Compound class	Reference
Bark	(+) Medioresinol (33), (+) Pinoresinol (34), Epipinoresinol (35)	Lignan	[70]
	Stigmast-5-ene-3β,7α-diol (46)	Steroid	[70]
	3β, 24S-3-(Acetyloxy) eupha-7,25-dien-24-ol (52), Oleana-9(11),12-dien-3β-yl acetate (57)	Triterpenoid	[70]
Leaves	(+)-Tylophorine N-oxide (1), 14α-Hydroxyisotylocrebrine N-oxide (9), Ficuline (13)	Alkaloid	[69]
	10S, 13aR-antofine N-oxide (4)	Alkaloid	[65]
	4,6-Bis-(4-methoxyphenyl)-1,2,3-trihydroindolizidinium chloride (10)	Alkaloid	[101]
	Ficuseptine A (14)	Alkaloid	[69], [100]
	Septicine (19)	Alkaloid	[64], [100]
	Phytol (22)	Diterpenoid	[11]
	Long chain saturated fatty alcohols (28)	Fatty alcohols	[41]
	Genistin (29), Kaempferitrin (30)	Flavonoid	[69]
	Pungenin (38)	Phenolic	[100]
	5-Acetyl-2-hydroxyphenyl-β-D-glucopyranoside (40)	Phenolic, Glycoside	[69], [90]
	Uracil (41)	Pirimidin	[69]
	3β-Hydroxystigmast-5-en-7-one (42), 7α-Hydroxysitosterol (43), 7β-Hydroxysitosterol (44)	Steroid	[11]
	Fernenol (55), Uvaol (60)	Triterpenoid	[11]
Seeds	Linoleic acid (24)	Fatty acid	[69], [41], [71]
	Oleic acid (25), Palmitic acid (26), Stearic acid (27)	Fatty acid	[71]
	Cycloalkane, Macrocyclic alkanes (C24 - C30)	Hydrocarbon	[71]
	Cholesterol (45), Sitosterol (51)	Steroid	[71]
	Squalene (59)	Triterpenoid	[69], [71]
	β-Sitosterol (64)	Triterpenoid	[71]
Stem	10R,13aR-tylocrebrine N-oxide (2), 10R,13aR-tylophorine N-oxide (3), 10S,13aR-isotylocrebrine N-oxide (5), 10S,13aR-S-tylocrebrine N-oxide (6), 10S,13aS-isotylocrebrine N-oxide (7), 10S,13aS-tylophorine N-oxide (8), Ficuseptine D (17)	Alkaloid	[65]

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Plant part	Compound	Compound class	Reference
	Lirioresinol A (36), Lirioresinol C (37)	Lignan	[102]
	(3β)-13,27-Cycloursan-3-yl acetate (53), Simiarenol (58)	Triterpenoid	[102]
Stem Latex	Ficin (23)	Enzim	[103]
Twigs	β-Sitosteryl-3β- glucopyranoside-6'-O-fatty acid esters (49)	Acylated Steroidal Saponin	[41]
	α-Amyrin fatty acid esters (62)	Triterpenoid	[41]
Bark, Leaves	24-Methylenecycloartanol (54)	Triterpenoid	[11], [70]
Leaves, Roots	Antofin (11)	Alkaloid	[63], [67], [69], [90], [100]
	β-sitosterol-D-glucoside (50)	Steroid, Glycoside	[69], [90], [99]
Leaves, Stem	Dehydrotylophorine (12)	Alkaloid	[65], [70]
	Ficuseptine B (15), Ficuseptine C (16)	Alkaloid	[65], [100]
	Isotylocrebrine (18)	Alkaloid	[65], [69]
	Tylocrebrine (20)	Alkaloid	[64], [65], [69]
	Vanillic acid (39)	Phenolic	[69], [102]
Leaves, Seeds, Stem	Tylophorine (21)	Alkaloid	[64], [65], [69], [99]
	Lupeol (56), α-Amyrin (61)	Triterpenoid	[11], [71], [102]
	β-Amyrin (63)	Triterpenoid	[11], [41], [71], [102]
Leaves, Root, Stem, Twigs	Stigmasterol (47)	Steroid	[41], [69], [102]
Bark, Leaves, Twigs, Root, Stem	β-Sitosterol (48	Steroid	[11], [41], [69], [102]

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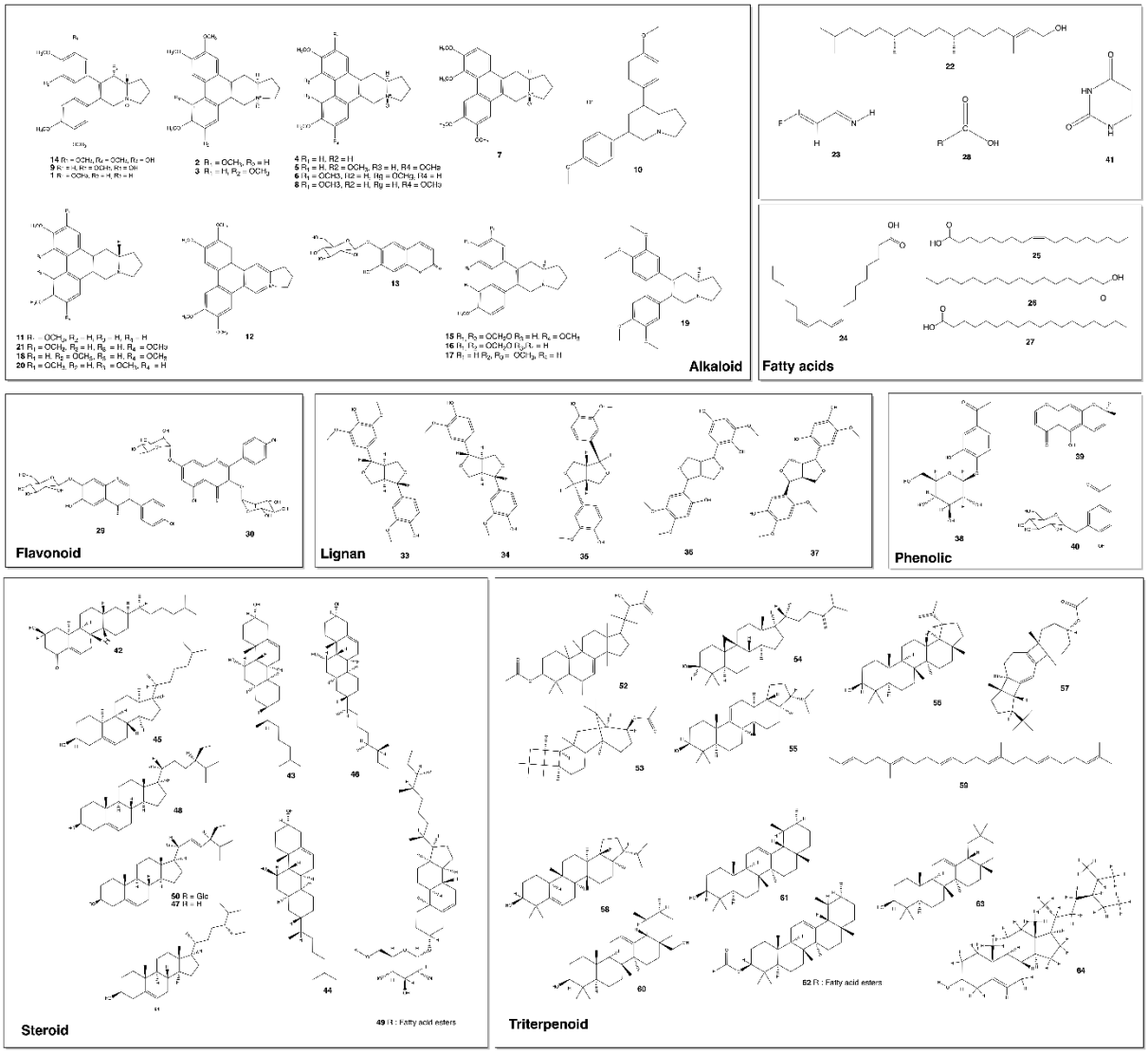

Figure 2. Chemical structures of the compounds identified in *F. septica.*

Pharmacological evaluations have consistently validated these traditional uses of the plant. The plant exhibits potent anticancer activity, with leaf extracts showing significant cytotoxicity against breast cancer (MCF-7 and T47D) [46], [72]-[76], [81], [97], colon cancer (WiDR) [105], and hepatocarcinoma (HepG2) cells [84]. These mechanisms include p53-independent apoptosis induction and cell cycle arrest at the G0/G1 or G2/M phases [42], [72]-[75]. Antimicrobial studies have demonstrated broad-spectrum efficacy against bacteria (e.g., S. aureus [54], [56], [92], [106], E. coli [54], [56]), fungi (*C. albicans*, *A. niger*), and viruses such as dengue (DENV-1 and DENV-2) [94]. Furthermore, the leaves possess both systemic and topical anti-inflammatory properties [48], [51], while the fruits have been identified as the most potent source of antioxidants [59], [75]. Toxicity assessments via Brine Shrimp Lethality Tests revealed that while the roots [96] and fruits [59] are highly toxic, the leaves are comparatively safer for medicinal application [97]. The data compiled in Table 3 are further organized based on compounds or extracts, enabling direct comparison of phytochemical composition, pharmacological activity categories, experimental models, and observed biological effects across studies.

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Table 3. Biological Activities and Phytochemistry of *F. septica.*

Compound / extract	Major metabolite	Biological activity	Experimental model	Potency	Mechanism of action	Ref.
70% Ethanolic Leaf Extract (Crude)	Phenolics, Flavonoids	Antioxidant; Toxicity	In vitro (Antioxidant); Brine Shrimp Lethality Test (Toxicity)	IC_{50} = 21.19 µg/mL (Antioxidant); LC_{50} = 39.71 ppm (Toxicity)	-	[74], [97]
70% Ethanolic Leaf Extract (Ethyl Acetate Fraction)	Phenolics, Flavonoids; TPC: 35.53±1.79 mg GAE/100 mg, TFC: 3.27±0.05 mg CAE/g	Antioxidant	In vitro	IC_{50} = 400 µg/mL	-	[72]
70% Ethanolic Leaf Extract (n-Hexane Fraction)	TPC : 0.33±0.55 mg of GA/100 mg of extract and TFC : 0.0486±0.0005 mg of CAE/g	Antioxidant	In vitro	IC_{50} = 1.500 µg/mL	-	[72]
70% Ethanolic Leaf Extract (Ethyl Acetate-Insoluble Fraction)	TPC: 7.59±1.79 mg of GA/100 mg of extract and TFC: 0.81±0.012 mg of CAE/g	Antioxidant	In vitro	IC_{50} = 1.800 µg/mL	-	[72]
Aqueous Leaf Extract	TPC: 27.32±0.03 mg GAE/g, TFC: 12.65± 0.00 mg CAE/g	Antioxidant	In vitro	IC_{50} = 4.45 µg/mL	Attributable to specific compounds with high intrinsic activity	[12]

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Compound / extract	Major metabolite	Biological activity	Experimental model	Potency	Mechanism of action	Ref.
Fruit Fractions from methanolic extract	Ethyl acetate fraction TPC : 28±0.05 mg GAE/100 mg sample TFC : 43.08±0.48 mg QE/100 mg sample; n-Hexan fraction TPC : 105.16 mg GAE/g TFC : 280.75 mg QE/g	Antioxidant	ABTS, CUPRAC, DPPH assays	IC_{50} = 6.33 to 17.69 µg/mL	Positive correlation with elevated phytochemical content	[59], [60], [75]
96% Ethanolic Stem Bark Extract	-	Antioxidant (Moderate)	ABTS assay	IC_{50} = 127.49±2.53 µg/mL	-	[58]
Ethanolic Leaf Extracts (EFS) & Fractions	Alkaloids	Anticancer (Cytotoxicity), Co-chemotherapeutic, Anti-angiogenic	MCF-7, T47D, 4T1, WiDR, HepG2, HeLa cancer cells; Vero normal cells; CAM assay; DMBA-induced rat models	IC_{50} = 6–75.9 µg/mL (various cell lines); SI > 3	Apoptosis induction (Bcl-2 downregulation, ROS generation), G0/G1 & G2/M cell cycle arrest, p53-independent pathway, suppresses MMP-9 and Rac-1, transition to S-phase arrest	[47], [50], [78], [79], [82], [83], [84], [85], [87], [107]
EFS Alkaloid-rich Fractions A and B	Alkaloids	Anticancer (Cytotoxicity)	T47D breast cancer cells	IC_{50} = 2.57 µg/mL (Frac A), 2.73 µg/mL (Frac B)	-	[80]

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Compound / extract	Major metabolite	Biological activity	Experimental model	Potency	Mechanism of action	Ref.
EFS n-Hexane Insoluble Fraction (HIF)	-	Anticancer (Cytotoxicity, Anti-angiogenic, Co-chemotherapeutic), Immunomodulatory	T47D cells, CAM assay, Doxorubicin-treated rats	IC_{50} = 9 µg/mL (T47D); 1,500 mg/kgBW (in vivo)	G1 cell cycle arrest, PARP cleavage, impedes new blood vessel formation, increases lymphocyte proliferation and CD8+ T-cells, lowers spleen IL-10	[81], [86], [88]
Isolated Alkaloids (Tylophorin, Antofine, Ficuseptine, Tylocrebrin)	Phenanthroindolizidine and indolizidine alkaloids	Anticancer, Antibacterial, Antifungal	HONE-1, NUGC cells; B. subtilis, M. luteus, E. coli, P. oxalicum	ED_{50} < 0.1 µg/mL (Antofine, anticancer); MIC = 1–10 µg (Antibacterial); MIC = 1–3 µg (Antifungal)	-	[65], [67], [68], [89]
F. septica Exudate	Ficuseptine (23.3 to 53.9 mg/ml)	Antibacterial, Anti-inflammatory, Clinical Wound Healing	Pediatric cutaneous ulcers, Macrophages/ Neutrophils	Suppressed IL-6 and TNF-α at 1.5 µg/ml	Bactericidal, completely suppresses pro-inflammatory cytokine secretion	[92]
Leaf Bioactive Compounds (Coumarin, Genistin, β-sitosterol, Tylophorine, Stigmastero)	-	Antibacterial (MRSA resistance inhibition)	In silico (MRSA)	-	Inhibits BlaR1 transducer protein; coumarin interacts with Lys526 and Thr527	[93]

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Compound / extract	Major metabolite	Biological activity	Experimental model	Potency	Mechanism of action	Ref.
Root Bark Acetone Extract	-	Antiviral (Dengue virus)	Immunofluorescence assay (A549, HepG2, Huh7.5 cells)	IC_{50} = 3.05±0.75 µg/ml (against DENV-2)	Disruption of envelope integrity or impaired host cell binding	[94]
Ethanolic Leaf Extract	-	Antibacterial, Antifungal, Antiprotozoal	Disc diffusion assay (S. aureus, E. coli, C. albicans, T. vaginalis, E. histolytica)	Inhibition zones: 7.7–27.5 mm (Antibacterial), 17.67 mm (Antifungal)	Apoptotic-like alterations in trophozoites	[54], [56], [106]
96% Ethanolic Leaf Extract	-	Wound Healing, Anti-inflammatory, Immunomodulatory	Burn wounds (rabbits), Carrageenan-induced inflammation (rats), Doxorubicin-treated rats	1.50 cm wound reduction in 12 days; 19% edema reduction at 200 mg/kgBW; decreased CD3+ and CD8+ at 750 mg/kgBW	Inhibits neutrophil degranulation, COX, lipoxygenase, and histamine release	[51], [55], [95]
70% Ethanolic Leaf Extract (Ointment)	-	Anti-inflammatory (Topical)	λ-carrageenan-induced inflammation (mice)	Reduced back skin fold thickness by 38.79% (2% ointment)	-	[48]
Ethanolic Root Extract	-	Toxicity	Brine Shrimp Lethality Test (BSLT)	LC_{50} = 1.16 ppm	-	[96]
96% Ethanolic Fruit Extract & Ethyl Acetate Fraction	-	Toxicity	Brine Shrimp Lethality Test (BSLT)	LC_{50} = 2.22 ppm (Ethanol), 2.18 ppm (Ethyl Acetate)	-	[59]

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Compound / extract	Major metabolite	Biological activity	Experimental model	Potency	Mechanism of action	Ref.
80% Methanolic Stem Extract	-	Toxicity	Brine Shrimp Lethality Test (BSLT)	LC_{50} = 14.99 ppm	-	[5]

DISCUSSION

The correspondence between the ethnomedicinal use of *F. septica* and findings from modern studies provides a useful basis for further investigation into its therapeutic potential. For example, the traditional use of plant exudates for cutaneous ulcers in Papua New Guinea has been supported by studies reporting comparable outcomes to conventional antiseptics, potentially related to the modulation of pro-inflammatory cytokines, such as IL-6 and TNF-α [92]. This observation highlights the role of traditional knowledge in guiding pharmacological investigations.

However, variability in the reported antioxidant activity, particularly in leaf extracts, suggests that bioactivity does not always correlate directly with the total phenolic or flavonoid content [12]. This may indicate the involvement of specific active compounds or synergistic interactions, rather than the overall phytochemical abundance. In contrast, fruit extracts appear to show a more consistent relationship between phytochemical content and antioxidant activity [59], [75]. These differences may also reflect variations in extraction methods and experimental conditions across studies.

The anticancer potential of *F. septica* has been widely reported, with studies indicating cytotoxic [79], [80], [84], [89], anti-metastatic [85], and anti-angiogenic effects [47], [86], which are primarily attributed to its phenanthroindolizidine alkaloids [89]. Some studies have also reported synergistic effects between plant extracts and chemotherapeutic agents, such as doxorubicin [52], [53], [81], [83]. However, it is important to note that most of these findings are derived from in vitro and limited in vivo models, and their clinical relevance remains to be established in vivo.

Additionally, reports of toxicity in certain plant parts, particularly roots [96] and fruits [59], highlight the importance of careful selection of plant material and the need for standardized extraction protocols. Overall, while the existing evidence indicates promising pharmacological properties, further studies, including well-designed in vivo and clinical investigations, are necessary to better evaluate the safety, efficacy, and therapeutic applicability of *F. septica*.

CONCLUSION

F. septica Burm. f. is a medicinal plant with a range of reported biological activities, supported by ethnomedicinal use and preclinical studies. This review highlights its potential pharmacological properties, including anticancer, antimicrobial, anti-inflammatory, and antioxidant effects, which are associated with its phytochemical constituents, particularly phenanthroindolizidine alkaloids, such as antofine and tylophorine. Although these findings indicate promising therapeutic potential, most of the evidence remains at the preclinical level. Further studies focusing on extract standardization, mechanistic understanding, and well-designed clinical investigations are needed to better evaluate the safety and efficacy of this approach. Overall, *F. septica* is a promising candidate for future research in natural product-based drug discovery.

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REFERENCES

[1] C. C. Berg, E. Corner, and H. P. Nooteboom, "Flora Malesiana. Series I, Seed plants. Volume 17, Part 2: Moraceae (Ficus).," 2005.

[2] R. C. Lin, C. K. L. Yeung, J. J. Fong, H. Y. Tzeng, and S. H. Li, "The lack of pollinator specificity in a dioecious fig tree: sympatric fig-pollinating wasps of *Ficus septica* in Southern Taiwan," *Biotropica*, vol. 43, no. 2, pp. 200–207, Mar. 2011, doi: 10.1111/J.1744-7429.2010.00686.X.

[3] G. C. Woodruff and P. C. Phillips, "Field studies reveal a close relative of C. elegans thrives in the fresh figs of Ficus septica and disperses on its Ceratosolen pollinating wasps," *BMC Ecology 2018 18:1*, vol. 18, no. 1, pp. 1–16, Aug. 2018, doi: 10.1186/S12898-018-0182-Z.

[4] P. Y. G. Artha, "Studi etnobotani kawasan masyarakat lokal Desa Trunyan Provinsi Bali sebagai buku ajar pada matakuliah etnobotani di perguruan tinggi / PT Mulyana Grisnawati Artha," Universitas Negeri malang, 2016.

[5] P. M. J. Gamallo and G. Rovelyn, "Evaluation of Antiangiogenic Property and Toxicity of *Ficus septica* Burm. f. Stem Extracts," in *RF-ISERD International Conference*, Singapore, Mar. 2017. [Online]. Available: https://www.researchgate.net/publication/318784006

[6] D. Holdsworth, "Traditional medicinal plants of the North Solomons Province Papua New Guinea.," *Quarterly Journal of Crude Drug Research*, vol. 18, pp. 33–44, 1980.

[7] D. Holdsworth, "High altitude medicinal plants of Papua New Guinea," *Pharmaceutical Biology*, vol. 27, no. 2, pp. 95–100, 1989, doi: 10.3109/13880208909053944/ASSET//CMS/ASSET/8F041847-0F5C-49FB-B3FC-9B8738431AC6/13880208909053944.FP.PNG.

[8] D. Holdsworth, "Medicinal plants of the Gazelle Peninsula, New Britain Island, Papua New Guinea," *International Journal of Pharmacognosy*, vol. 30, pp. 85–190, 1992.

[9] W. Mulyanah, "Etnobotani tumbuhan yang dimanfaatkan sebagai obat penyakit pada anak-anak Di Desa Colo Kecamatan Dawe Kabupaten Kudus Jawa Tengah," Universitas Islam Negeri Walisongo, Semarang, 2019.

[10] S. E. Rahayu, R. Oktapianti, and I. Matondang, "Ethnobotany survey of medicinal plants used for traditional maternal healthcare by Serawai tribe, Seluma district, Bengkulu - Indonesia," *Journal of Current Medical Research and Opinion*, vol. 3, no. 04, pp. 441–448, Apr. 2020, doi: 10.15520/jcmro.v3i04.275.

[11] Y. C. Su, M. J. Cheng, W. Y. Lin, and J. R. Weng, "Natural Products from Littoral Plants of Ficus septica," *Chemistry of Natural Compounds*, vol. 58, no. 6, pp. 1170–1172, Nov. 2022, doi: 10.1007/s10600-022-03897-2.

[12] S. Vun-Sang and M. Iqbal, "Phytochemical Analysis and Antioxidant Activity of Aqueous Extract of Ficus septica Leaves from Sabah, Malaysia," *Borneo Journal of Resource Science and Technology*, vol. 13, no. 2, pp. 67–78, Dec. 2023, doi: 10.33736/bjrst.5591.2023.

[13] J. Popay *et al.*, *Guidance on the Conduct of Narrative Synthesis in Systematic Reviews A Product from the ESRC Methods Programme*. Lancaster University, 2006. [Online]. Available: 10.13140/2.1.1018.4643

[14] D. Djufri, H. Hasanuddin, A. Abdullah, and V. R. Puspa, "Vegetation analysis of the Forest Park of Pocut Meurah Intan (THRPMI), Seulawah Subdistrict, Aceh Besar, Aceh Province," in *IOP Conference Series: Earth and Environmental Science*, IOP Publishing Ltd, Jan. 2022. doi: 10.1088/1755-1315/956/1/012010.

[15] Djufri and Samingan, "Flora of tripa peat swamp forest in west Aceh Distric," *Jurnal EduBio Tropika*, vol. 1, no. 1, Oct. 2013.

[16] S. Rahmayenti, . N., and. Z., "Tumbuhan Obat yang Ditemukan di Dataran Tinggi Kabupaten Solok," *Jurnal Pendidikan, Sains Dan Teknologi*, vol. 3, no. 2, pp. 254–264, May 2024, doi: 10.47233/jpst.v3i2.1635.

[17] G. Anwar and A. Susatya, "Abundance and Distribution of Medicinal Plants in Madapi Forest Kerinci Seblat National Park (KSNP) Rejang Lebong, Bengkulu," in *Proceedings of the International Seminar on Promoting Local Resources for Sustainable Agriculture and Development 2020*, Bengkulu: Atlantis Press, Oct. 2021.

[18] U. Izzati, H. S. Hasibuan, and T. L. Indra, "Riparian Landscape Design Based on Urban Forest at Cisadane River, South Tangerang City, Indonesia," in *The 4th ISS-2017*, Bogor, Oct. 2017, pp. 102–108.

[19] Peniwidiyanti, I. Qayim, and T. Chikmawati, "A Study on Diversity and Distribution of Figs (Ficus, Moraceae) in Bogor City, West Java, Indonesia," *Journal of Tropical Biodiversity and Biotechnology*, vol. 7, no. 2, Aug. 2022, doi: 10.22146/jtbb.68516.

[20] I. Rahmiyani, R. Mardiana, and P. Farmasi STIKes Bakti Tunas Husada Tasikmalaya, "Inventarisasi Dan Skrining Fitokimia Tumbuhan Obat Berkhasiat Antiinflamasi Yang Digunakan Oleh Masyarakat Kampung Naga," *Jurnal Kesehatan Bakti Tunas Husada: Jurnal Ilmu-ilmu Keperawatan, Analis Kesehatan dan Farmasi*, vol. 13, no. 1, May 2015, doi: 10.36465/JKBTH.V13I1.11.

[21] F. Haqqin *et al.*, "Diversity, composition, and role of woody Non-Timber Forest Products in Tawangmangu, Central Java, Indonesia," *Asian Journal of Ethnobiology*, vol. 7, no. 1, Jun. 2024, doi: 10.13057/asianjethnobiol/y070108.

[22] A. A. Metananda, W. F. Afrianto, L. N. Hasanah, Y. S. Aini, and A. S. Noorfajria, "Ethnobotanical study on plant leaves for food wrapping in traditional markets of Wonosobo District, Central Java, Indonesia," *Biodiversitas*, vol. 24, no. 7, pp. 3804–3814, 2023, doi: 10.13057/biodiv/d240718.

[23] Siswo, C. W. Yun, and S. Abdiyani, "Assessing vegetation composition and the indicator species around water source areas in a pine forest plantation: A case study from Watujali and Silengkong Catchments, Kebumen, Indonesia," *Forests*, vol. 10, no. 10, Oct. 2019, doi: 10.3390/f10100825.

[24] T. Handayani, Alpendi, and Nugroho, "The Diversity of Tree Strata Vegetation in Ancient Volcano Mujil Kulon Progo Region as A Learning Source for Biology Subject in the First Grade of Senior High School," in *Proceedings of the 5th Progressive and Fun Education International Conference*, Atlantis Press, Aug. 2020.

[25] A. Suyanto, "Flora fauna characteristic of Winong Lake in Gunungkidul, Indonesia," in *AIP Conference Proceedings*, American Institute of Physics Inc., Jun. 2016. doi: 10.1063/1.4953476.

[26] J. Batoro and D. Siswanto, "Ethnomedicinal survey of plants used by local society in Poncokusumo district, Malang, East Java Province, Indonesia," *Asian Journal of Medical and Biological Research*, vol. 3, no. 2, pp. 158–167, Aug. 2017, doi: 10.3329/ajmbr.v3i2.33563.

[27] I. H. Nurrosyidah, M. A. Riya, and A. F. Ma'ruf, "Ethnobotanic Study Of Local Knowledge-Based Medicine Plant in Seloliman Village, Kecamatan Trawas, Mojokerto District East Java," *Jurnal Riset Kefarmasian Indonesia*, vol. 2, no. 3, 2020.

[28] F. Rohman, Y. Juma, D. Hari Utomo, S. Rahayu Lestari, S. Nur Arifah, and W. Eka Putra, "Plants diversity as a medicinal plants by the Tengger Tribe, Bromo Tengger Semeru National Park, East Java, Indonesia," 2019.

[29] A. Septiasari, M. Balgis, M. N. Lathifah, P. D. Hanugroho, and A. D. Setyawan, "Identification and potential of vascular plants in the karst ecosystem of Somopuro Cave, Pacitan, East Java, Indonesia," *International Journal of Tropical Drylands*, vol. 5, no. 2, Dec. 2021, doi: 10.13057/tropdrylands/t050204.

[30] R. Amirta *et al.*, "Plant diversity and energy potency of community forestin East Kalimantan, Indonesia: Searching for fast growing wood species for energy production," *Nusantara Bioscience*, vol. 8, no. 1, May 2016, doi: 10.13057/nusbiosci/n080106.

[31] S. Azis, S. Zubaidah, S. Mahanal, J. Batoro, and S. B. Sumitro, "Local knowledge of traditional medicinal plants use and education system on their young of ammatoa kajang tribe in south sulawesi, indonesia," *Biodiversitas*, vol. 21, no. 9, pp. 3989–4002, Sep. 2020, doi: 10.13057/biodiv/d210909.

[32] W. Ode Jumiarni and O. Komalasari, "Inventory of medicinal plants as Utilized By Muna Tribe In Kota Wuna Settlement," *Traditional Medicine Journal*, vol. 22, no. 1, p. 2017, 2017.

[33] A. Slamet, S. H. Andarias, D. P. I. Ardiyati, Y. B., and W. D. F. Inang, "Potential of Local Plants from Buton Island as a Source of Learning Biology," *Bioedusiana: Jurnal Pendidikan Biologi*, vol. 5, no. 1, p. 26, Jul. 2020, doi: 10.34289/bioed.v5i1.1555.

[34] S. S. Tahoangako, D. Santosa, and N. Fakhrudin, "Study on the Utilization of Medicinal Plants by the Community of Uelawu Village, Konawe District, Southeast Sulawesi," *Majalah Farmaseutik*, vol. 19, no. 3, Jun. 2023.

[35] N. Y. Kandowangko, M. Latief, and R. Yusuf, "Short communication: Inventory of traditional medicinal plants and their uses from Atinggola, North Gorontalo District, Gorontalo Province, Indonesia," *Biodiversitas*, vol. 19, no. 6, pp. 2294–2301, Nov. 2018, doi: 10.13057/biodiv/d190637.

[36] N. K. D. Julyeda, I. B. G. Darmayasa, and J. Hardini, "Potential of Awar-awar Leaf Methanol Extract (*Ficus septica Burm.* f.) Against Aspergillus niger on Balinese Lontar," *Metamorfosa: Journal of Biological Sciences*, vol. 8, no. 2, p. 268, Sep. 2021, doi: 10.24843/metamorfosa.2021.v08.i02.p10.

[37] R. I. Putri, J. Supriatna, and E. B. Walujo, "Ethnobotanical Study of Plant Resources in Serangan Island, Bali," *Asian Journal of Conservation Biology*, vol. 3, no. 2, p. 44, 2014.

[38] I. M. S. Wijaya and M. R. Defiani, "Diversity and distribution of figs (Ficus: Moraceae) in Gianyar district, Bali, Indonesia," *Biodiversitas*, vol. 22, no. 1, pp. 233–246, Jan. 2021, doi: 10.13057/biodiv/d220129.

[39] Y. J. A. Mela, E. J. Bria, and I. M. Y. Tnunay, "Ethnobotany of semi-arid medicinal plants used by Bunaq Tribe in Lamaknen, Belu District, East Nusa Tenggara, Indonesia," *International Journal of Tropical Drylands*, vol. 6, no. 1, Jun. 2022, doi: 10.13057/tropdrylands/t060103.

[40] T. R. Soeprobowati, J. Jumari, T. R. Saraswati, H. C. Suhry, and P. Gell, "Land-use changes concerning the riparian vegetation in Galela Lake, North Maluku, Indonesia," *Ecological Engineering*, vol. 170, Nov. 2021, doi: 10.1016/j.ecoleng.2021.106368.

[41] C. Y. Ragasa, M. R. Macuha, M. M. De Los Reyes, E. H. Mandia, and I. A. Van Altena, "Chemical constituents of Ficus septica Burm. F," *International Journal of Pharmaceutical and Clinical Research*, no. 11, pp. 1464–1469, Nov. 2016.

[42] M. Nasir, Bahtiar, and Suparman, "Prospect of Making Anti-Malaria Development Based on Ethnomedicine Kesultanan Jailolo Community," in *Biology Education Conference*, Solo: Universitas Sebelas maret, Oct. 2018.

[43] D. F. Tabeo, N. Ibrahim, and A. W. Nugrahani, "Etnobotani Suku Togian Di Pulau Malenge Kecamatan Talatako, Kabupaten Tojo Una-Una, Sulawesi Tengah," *Biocelebes*, vol. 13, no. 1, Jun. 2019, Accessed: Dec. 27, 2024. [Online]. Available: https://bestjournal.untad.ac.id/index.php/Biocelebes/article/view/12868

[44] H. Andarias, "Studi Etnobotani dan Identifikasi Tumbuhan Berkhasiat ObatMasyarakat Sub Etnis Wolio Kota Baubau Sulawesi Tenggara," *Proceeding Biology Education Conference: Biology, Science, Enviromental, and Learning*, Oct. 2018, Accessed: Dec. 27, 2024. [Online]. Available: https://www.academia.edu/110677667/Studi_Etnobotani_dan_Identifikasi_Tumbuhan_Berkhasiat_ObatMasyarakat_Sub_Etnis_Wolio_Kota_Baubau_Sulawesi_Tenggara

[45] S. Riswan and D. D. Andayaningsih, "Keanekaragaman Tumbuhan Obat Yang Digunakan Dalam Pengobatan Tradisional Masyarakat Sasak Lombok Barat," 2008.

https://doi.org/10.35814/jifi.v24i1.2033
JIFI 2026; 24(1): 174-201

[46] Moh. Q. Zaman, "Etnobotani Tumbuhan Obat di Kabupaten Pamekasan-Madura Provinsi Jawa Timur," Tesis, Universitas Islam Negeri Maulana Malik Ibrahim Malang, Malang, 2009.

[47] L. Garna Nurhidayati, A. Endro Nugroho, B. Retnoaji, and N. Fakhrudin, "Antiangiogenesis Activity of Awar-Awar Leaf Extract (Ficus Septica Burm. F.) In Chorioallantoic Membrane Assay," *Indonesian Journal of Pharmacy*, vol. 32, no. 1, pp. 1–9, 2021.

[48] R. Arief and Z. Thahir, "Uji Aktivitas Antiinflamasi Sediaan Salep Ekstrak Daun Awar-Awar (Ficus Septica Burm. F) Terhadap Udema Kulit Punggung Mencit (Mus musculus)," *Jurnal Kesehatan Yamasi Makassar*, vol. 2, 2018.

[49] A. Pra Darma, I. Nurzijah, D. Brenna Septhea, and A. Endro Nugroho, "Ficus septica Burm. f. Leaves Ethanolic Extract Triggered Apoptosis on 7,12-Dimethylbenz[a]anthracene-Induced Rat Mammary Carcinogenesis Qualitatively," *Indonesian Journal of Cancer Chemoprevention*, 2012, [Online]. Available: http://ccrc.farmasi.ugm.ac.id

[50] R. A. Santoso, A. S. Lienaningrum, E. D. Bangun, H. G. Reformatika, R. A. Susidarti, and E. Meiyanto, "Black cumin (Nigella sativa L.) and awar-awar (Ficus septica burm. F.) combination extract inhibits proliferation and modulates cell cycle on HeLa cell," in *AIP Conference Proceedings*, American Institute of Physics Inc., Apr. 2019. doi: 10.1063/1.5098428.

[51] A. Syafirah Rahmadani, I. Asmaliani, I. Santi, R. Kosman, and H. Herman, "Antiinflammatory Effect Test of Ethanol Extract Awar-Awar Leaves (Ficus septica Burm L.) on White Rats (Rattus norvegicus) Induced with Carrageenan)," *As-Syifaa Jurnal Farmasi*, vol. 16, no. 1, pp. 2085–4714, Jul. 2024.

[52] S. Haryanti, U. M. Zulfin, I. A. Salsabila, F. Wulandari, and E. Meiyanto, "The Cytotoxic and Anti-Migratory Properties of Caesalpinia sappan and Ficus septica, in Combination with Doxorubicin on 4T1 TNBC Cells with Nephroprotective Potential," *Asian Pacific Journal of Cancer Prevention*, vol. 23, no. 2, pp. 743–753, 2022, doi: 10.31557/APJCP.2022.23.2.743.

[53] S. Haryanti, S. Pramono, R. Murwanti, E. Meiyanto, B. Besar Penelitian dan Pengembangan Tanaman Obat dan Obat Tradisional, and K. Kesehatan Republik Indonesia, "The Synergistic Effect of Doxorubicin and Ethanolic Extracts of Caesalpinia sappan L. Wood and Ficus septica Burm. f. Leaves on Viability, Cell Cycle Progression, and Apoptosis Induction of MCF-7 Cells," 2016.

[54] A. Khusnuryani and Z. Fuad, "Antibacterial Activity of Awar-awar Leaves (Ficus septica Burn f) AgainstStaphylococcus aureus ATCC 29523 and Escherichia coli ATCC 35218," in *International Conference Green technology 6th*, Malang, Sep. 2015, pp. 14–19.

[55] D. Isnaeni and A. Ulfah Magefirah Rasyid, "Awar-Awar Leaf Ethanol Extract Gel Effectiveness (Ficus septica Burm. F) On Healing Burn Burn (Oryctolagus cuniculus)," *Jurnal Kesehatan Pharmasi (JKPharm*, no. 1, 2022.

[56] P. G. Vital, R. N. Velasco, J. M. Demigillo, and W. L. Rivera, "Antimicrobial activity, cytotoxicity and phytochemical screening of Ficus septica Burm and Sterculia foetida L. leaf extracts," *Journal of Medicinal Plants Research*, vol. 4, no. 1, pp. 58–63, 2010, doi: 10.5897/JMPR09.400.

[57] D. C. P. Luceñara, L. A. Ombat, and M. E. Q. Won, "Antimitotic and Antiproliferative Action of Ficus septica Burm. F. Stem Bark Ethanolic Extract," *Cytologia*, vol. 87, no. 4, Jul. 2022.

[58] N. Alim, S. Fauziah Noer, W. Daniati, A. Irfayanti, and P. S. Farmasi, "Antioxidant Activity of Klika Awar-awar (Ficus septica Burm. F) Origin of South Buton Land using ABTS Method," *Novem Medika Farmasi*, vol. 1, no. 3, Aug. 2023.

[59] Z. D. Palar, D. G. Katja, V. S. Kamu, and M. Kumaunang, "Aktivitas Antioksidan dan Toksisitas dari Ekstrak dan Fraksi Daging Buah Awar-Awar (Ficus septica BURM.)," *Chemistry Progress*, vol. 16, no. 2, pp. 153–162, Dec. 2023, doi: 10.35799/cp.16.2.2023.48139.

https://doi.org/10.35814/jifi.v24i1.2033
JIFI 2026; 24(1): 174-201

[60] N. Hikmah *et al.*, "Chemometric Evaluation of Antioxidant Activity in Libo Fruit Extracts: Correlation with Phenolic and Flavonoid Content," *Indonesian Journal of Pharmaceutical Education*, vol. 5, no. 2, pp. 213–229, May 2025, doi: 10.37311/ijpe.v5i2.31234.

[61] N. Trinovitasari, I. Anwar, R. Malina, N. Hikmah, S. Raodah Nurul Jannah, and S. Aprilia Paramita, "Ativitas antiinflamasi ekstrak buah libo (*Ficus septica Burm*. F) serta korelasinya dengan total flavonoid," 2025.

[62] M. H. Ridho, A. P. Gani, S. Wahyuono, and N. Fakhrudin, "Application of Ultrasonic-Assisted Fractionation with Full-Factorial Design for the Production of Alkaloid-Rich Fraction from Ficus septica Leaves," *Journal of Food Pharmaceutical Sciences*, vol. 8, no. 3, pp. 294–305, 2020.

[63] R. B. Herbert and C. J. Moody, "Alkaloids of Ficus septica," *Phytochemistry*, vol. 11, p. 1184, 1972.

[64] J. H. Russel, "Alkaloids of Ficus species. Occurence of Indolizidine Alkaloids in Ficus septica," *Naturwissenschaften*, Jan. 1963, Accessed: Dec. 26, 2024. [Online]. Available: 10.1007/BF00601596

[65] A. G. Damu *et al.*, "Phenanthroindolizidine alkaloids from the stems of Ficus septica," *Journal of Natural Products*, vol. 68, no. 7, pp. 1071–1075, Jul. 2005, doi: 10.1021/np050095o.

[66] J. Y. Ueda, M. Takagi, and K. Shin-ya, "Aminocaprophenone- and pyrrolidine-type alkaloids from the leaves of Ficus septica," *Journal of Natural Products*, vol. 72, no. 12, pp. 2181–2183, Dec. 2009, doi: 10.1021/np900580f.

[67] B. Baumgartner, C. A. Erdelmeier, A. D. Wright, T. Rali, and O. Sticher, "Antofine, a Strong Antifungal Alkaloid from Ficus septica Leaves," *Planta Medica*, vol. 55, 1989.

[68] B. Baumgartner, C. A. J. Erdelmeier, A. D. Wright, T. Rali, and O. Sticher, "An Antimicrobial Alkaloid From Ficus septica," *Phytochemistry*, vol. 29, no. 10, pp. 3327–3330, Feb. 1990.

[69] P. L. Wu, K. V. Rao, C. H. Su, C. S. Kuoh, and T. S. Wu, "Phenanthroindolizidine alkaloids and their cytotoxicity from the leaves of Ficus septica," *Heterocycles*, vol. 57, no. 12, pp. 2401–2408, Dec. 2002, doi: 10.3987/COM-02-9615.

[70] H. C. Wang, M. J. Cheng, W. Y. Lin, and J. R. Weng, "Chemical Constituents Isolated from the Bark of Ficus septica," *Chemistry of Natural Compounds*, vol. 60, no. 3, pp. 579–581, May 2024, doi: 10.1007/s10600-024-04386-4.

[71] G. Knothe, L. F. Razon, and M. E. G. de Castro, "Fatty acids, triterpenes and cycloalkanes in ficus seed oils," *Plant Physiology and Biochemistry*, vol. 135, pp. 127–131, Feb. 2019, doi: 10.1016/j.plaphy.2018.11.030.

[72] K. Nastiti, Sudarsono, and A. E. Nugroho, "Evaluation of in vitro immunomodulatory effect of fractions of Ficus septica Burm. f. and their total flavonoid and phenolic contents," *International Food Research Journal*, vol. 21, no. 5, 2014.

[73] P. Molyneux and M. Associates, "The use of the stable radical Diphenylpicrylhydrazyl (DPPH) for estimating antioxidant activity," vol. 26, no. 2, 2004, [Online]. Available: https://www.researchgate.net/publication/237620105

[74] D. Sahyuni Putri Koto, M. Ahda, and A. Guntarti, "Determination of Polifenol Content and Antioxidant Activity Test of Ethanol Extract 70% Awar-Awar (Ficus septica Burm. F) Leaf using DPPH Method (1,1-Difenil-2-Pikrilhidrazil) Kadar Polifenol dan Aktivitas Antioksidan Ekstrak Etanol 70% Daun Awar-Awar (Ficus septica Burm. F) dengan Metode DPPH (1,1-Difenil-2-Pikrilhidrazil)," 2019. [Online]. Available: www.journal.ugm.ac.id/v3/JFPS

[75] Y. Yamin, A. Rina, S. Sabarudin, H. Nur, and K. Henny, "Antioxidant activity assay and determination of phenolic and flavonoid content of Libho (Ficus Septica Burm. F) fruits," *Open Journal of Chemistry*, vol. 8, no. 1, pp. 008–013, Oct. 2022, doi: 10.17352/ojc.000029.

[76] K. L. Cabanlit, M. A. J. Torres, and C. G. Demayo, "Ficus spp. (Figs) and their anticancer potential: A systematic review of laboratory studies and traditional uses in the Philippines," *Journal of HerbMed*

Pharmacology, vol. 14, no. 2. Shahrekord University of Medical Sciences, pp. 133–152, 2025. doi: 10.34172/jhp.2025.52854.

[77] E. P. Lansky, H. M. Paavilainen, A. D. Pawlus, and R. A. Newman, "Ficus spp. (fig): Ethnobotany and potential as anticancer and anti-inflammatory agents," *Journal of Ethnopharmacology*, vol. 119, no. 2. pp. 195–213, Sep. 2008. doi: 10.1016/j.jep.2008.06.025.

[78] D. A. Sekti, M. F. Mubarok, I. Armandani, S. Junedy, and D. E. Meiyanto, "Awar-Awar (*Ficus Septica* Burm. F.) leaves ethanolic extract induced apoptosis of MCF-7 Cells by Downregulation of Bcl-2," *Majalah Obat Tradisional*, vol. 15, no. 3, pp. 100–104, 2010.

[79] D. B. Septhea, Anindyajati, A. Pra Darma, I. Nurzijah, A. Endro Nugroho, and E. Meiyanto, "*Ficus septica* Burm. F. leaves ethanolic extract induces apoptosis in 7, 12-dimethylbenz nthracene-induced rat liver cancer quatitavely," *Indonesian Journal of Cancer Chemoprevention*, vol. 2, no. 2, 2011, Accessed: Dec. 20, 2024. [Online]. Available: https://www.ijcc.chemoprev.org/index.php/ijcc/article/view/39

[80] A. E. Nugroho, F. F. Akbar, A. Wiyani, and Sudarsono, "cytotoxic effect and constituent profile of alkaloid fractions from ethanolic extract of *ficus septica* Burm. f. leaves on T47D breast cancer cells," *Asian Pacific Journal of Cancer Prevention*, vol. 16, no. 16, pp. 7337–7342, 2015, doi: 10.7314/APJCP.2015.16.16.7337.

[81] A. E. Nugroho, A. Hermawan, D. D. P. Putri, A. Novika, and E. Meiyanto, "Combinational effects of hexane insoluble fraction of *Ficus septica* Burm. F. and doxorubicin chemotherapy on T47D breast cancer cells," *Asian Pacific Journal of Tropical Biomedicine*, vol. 3, no. 4, pp. 297–302, 2013, doi: 10.1016/S2221-1691(13)60066-0.

[82] I. R. Sutejo, H. Putri, S. Handayani, R. I. Jenie, and E. Meiyanto, "In vitro study of the combination of doxorubicin, curcuma xanthorrhiza, brucea javanica, and *Ficus septica* as a potential novel therapy for metastatic breast cancer," *Indonesian Journal of Pharmacy*, vol. 30, no. 1, pp. 15–24, 2019, doi: 10.14499/indonesianjpharm30iss1pp15.

[83] I. R. Sutejo and H. Putri, "Synergistic combination of curcuma xanthorrhiza, *Ficus Septica* and doxorubicin inhibits metastasis of breast cancer through inhibition MMP-9 Activity," in *International Conference on Medicine and Health Sciences*, Jember, Aug. 2016.

[84] S. Haryanti, N. Rahmawati, I. Y. M. Sholikhah, and Y. Widiyastuti, "*Ficus septica*, an ecosystem keystone species induced ROS-mediated cytotoxicity in HepG2 hepatocarcinoma cells," in *IOP Conference Series: Earth and Environmental Science*, IOP Publishing Ltd, Nov. 2021. doi: 10.1088/1755-1315/905/1/012101.

[85] S. Haryanti *et al.*, "Different 4T1 Cells Migration under Caesalpinia sappan L. and *Ficus septica* Burm.f ethanolic extracts," *Indonesian Journal of Cancer Chemoprevention*, 2017.

[86] D. Nurhasanah, N. Fakhrudin, B. Retnoaji, and A. E. Nugroho, "antiangiogenic activity of n-hexane insoluble fraction and its tylophorine component from *Ficus septica* Leaves in chicken chorioallantoic membrane induced by bFGF," *Asian Pacific Journal of Cancer Prevention*, vol. 24, no. 1, pp. 75–80, 2023, doi: 10.31557/APJCP.2023.24.1.75.

[87] L. N. Muna and R. I. Jenie, "Combination of curcuma (*Curcuma xanthorriza Roxb*) and awar-awar (*Ficus septica Burm*.F.) ethanolic extracts enhance doxorubicin to modulate Cell Cycle Progression of T47D Cells," *Indonesian Journal of Cancer Chemoprevention*, 2018.

[88] A. E. Nugroho *et al.*, "Immunomodulatory effects of hexane insoluble fraction of *Ficus septica Burm*.F. in doxorubicin-treated rats," *Asian Pacific Journal of Cancer Prevention*, vol. 13, no. 11, pp. 5785–5790, 2012, doi: 10.7314/APJCP.2012.13.11.5785.

[89] A. G. Damu, P. C. Kuo, L. S. Shi, C. Y. Li, C. R. Su, and T. S. Wu, "Cytotoxic phenanthroindolizidine alkaloids from the roots of *ficus septica*," *Planta Medica*, vol. 75, no. 10, pp. 1152–1156, 2009, doi: 10.1055/s-0029-1185483.

[90] B. Baumgartner, C. A. J. Erdelmeier, A. D. Wright, T. Rali, and O. Sticher, "An antimicrobial alkaloid from *Ficus septica*," *Phytochemistry*, vol. 29, no. 10, pp. 3327–3330, Jan. 1990, doi: 10.1016/0031-9422(90)80209-Y.

[91] I. D. A. Tuna, P. M. Wowor, and H. Awaloei, "Uji daya hambat ekstrak daun awar-awar (*ficus septica burm*.f) terhadap pertumbuhan bakteri staphylococcus aureus dan eschericia coli," *eBiomedik*, vol. 4, no. 2, 2016, doi: 10.35790/EBM.V4I2.14656.

[92] J. Deli *et al.*, "*Ficus septica* exudate, a traditional medicine used in Papua New Guinea for treating infected cutaneous ulcers: in vitro evaluation and clinical efficacy assessment by cluster randomised trial," *Phytomedicine*, vol. 99, May 2022, doi: 10.1016/j.phymed.2022.154026.

[93] F. A. Nurlailiyah *et al.*, "inhibition of antibacterial bioactive compounds from awar-awar (*Ficus septica Burm*, F.) leaves for Methicillin Resistant Staphylococcus aureus (MRSA) Infection: an in silico study," *JSMARTech Journal of Smart Bioprospecting and Technology*, 2023, doi: 10.21776/ub.jsmartech.2023.004.01.32.

[94] N. C. Huang *et al.*, "Ficus septica plant extracts for treating Dengue virus in vitro," *PeerJ*, vol. 2017, no. 6, 2017, doi: 10.7717/peerj.3448.

[95] D. I. Sari, A. H. Yazin, R. A. Anovia, U. Ismayani, and E. Darmawan, "Effect of combination immune system enhancement awar-awar (*Ficus Septica Burm*. F) leaf ethanol extract and moringa (*Moringa Oleifera*) leaf ethanol extract as co-chemotherapy cancer in rats female sprague dawley strain induced by doxorubicin," *Pharmaciana*, vol. 5, no. 2, Nov. 2015.

[96] Suryanita, "Uji efek toksisitas ekstrak etanol akar awar-awar (*Ficus Septica Burm*.F) dengan metode Brine Shrimp Lethality Test (BSLT)," *Jurnal Farmasi UIN Alauddin Makassar*, vol. 5, no. 1, 2017.

[97] J. Aritan, J. Mongie, S. Untu, and D. Pareta, "Uji toksisitas akut ekstrak etanol daun tagalolo *ficus septica* burm f terhadap larva artemia salina leach dengan metode Brine Shrimp Lethality Test (BSLT)," *The Tropical Journal of Biopharmaceutical*, vol. 2, no. 1, pp. 85–90, 2019.

[98] Mardiana, "Laporan Praktikum Biokimia Karbohidrat," Universitas Hasanuddin, Makassar, 2011.

[99] C. W. Yang, W. L. Chen, P. L. Wu, H. Y. Tseng, and S. J. Lee, "Anti-inflammatory mechanisms of phenanthroindolizidine alkaloids," *Molecular pharmacology*, vol. 69, no. 3, pp. 749–758, Mar. 2006, doi: 10.1124/MOL.105.017764.

[100] J. Y. Ueda, M. Takagi, and K. Shin-ya, "Aminocaprophenone- and pyrrolidine-type alkaloids from the leaves of *Ficus septica*," *Journal of Natural Products*, vol. 72, no. 12, pp. 2181–2183, Dec. 2009, doi: 10.1021/np900580f.

[101] B. Baumgartner, C. A. J. Erdelmeier, A. D. Wright, T. Rali, and O. Sticher, "An antimicrobial alkaloid from *Ficus septica*," *Phytochemistry*, vol. 29, no. 10, pp. 3327–3330, Feb. 1990.

[102] P.-C. Kuo *et al.*, "Non-alkaloidal constituents from the stem of *Ficus septica*," *Journal of the Chinese Chemical Society,* vol. 49, pp. 113–116, 2002.

[103] S. Wahyuni, R. Susanti, and R. Sri Iswari, "Isolation and caracterization of ficin enzyme from *Ficus septica Burm* F stem latex," *Wahyuni et al. Indonesian Journal of Biotechnology*, vol. 20, no. 2, pp. 161–166, Dec. 2015.

[104] D. N. Hidayati, R. I. Jenie, and E. Meiyanto, "Combination of curcuma (*Curcuma xanthorriza Roxb*) rhizome ethanolic extract and awar-awar (*Ficus septica Burm*.F) leaves ethanolic extract increases cisplatin cytotoxicity on t47d breast cancer cells through cell cycle modulation," *Indonesian Journal of Cancer Chemoprevention*, 2017.

[105] I. R. Sutedjo, H. Putri, and E. Meiyanto, "Ethanolic leaves extract of awar-awar (*Ficus Septica*) as Selective chemopreventive agent on various cancer cells," *NurseLine Journal*, vol. 1, no. 2, Nov. 2016.

[106] I. D. A. Tuna, P. M. Wowor, and H. Awaloei, "Uji daya hambat ekstrak daun awar-awar (*ficus septica* burm.f) terhadap pertumbuhan bakteri staphylococcus aureus dan eschericia coli," 2016.

[107] Anindyajati, A. Pra Darma, I. Nurzijah, D. B. Septhea, and A. Endro Nugroho, "*Ficus septica* Burm. f. Leaves ethanolic extract triggered apoptosis on 7,12-dimethylbenz[a]anthracene-induced rat mammary carcinogenesis qualitatively," *Indonesian Journal of Cancer Chemoprevention*, vol. 3, no. 1, 2012, Accessed: Dec. 20, 2024. [Online]. Available: https://www.ijcc.chemoprev.org/index.php/ijcc/article/view/39.

https://doi.org/10.35814/jifi.v24i1.2033
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