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REVIEW

Potential of frangipani flower (*Plumeria* sp.) as a source of antimicrobial and antioxidants and its application in the pharmacological activities: a short review

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Abstract. Frangipani *(Plumeria* spp.*)* was a flowering ornamental plant with several metabolites that can be used as traditional medicine for various diseases such as laxative, anti-itch, anti-inflammatory, diabetic, and malaria. The Frangipani flower showed antimicrobial activity against *E. coli, P. aeruginosa, S. aureus, C. albicans, S. pyogenes, S. typhi, B. pumilus, B. subtilis, S. dysenteriae, P. mirabilis, P. fluorescens, B. cereus, S. flexneri, A. flavus* and *M. furfur.* Frangipani flowers also have high antioxidant activity due to their significant phenol and flavonoid content, while saponin is one of the components responsible for antimicrobial activity. This study provided an overview of the application of Frangipani flowers for pharmaceutical purposes.

Keywords: antibacterial, antioxidant, pharmacology, Frangipani flower application, plumeria

INTRODUCTION

The use of natural materials today tends to increase along with the development of the concept of back to nature. Natural materials commonly used were mainly from plant species because they contain various complex and structurally diverse compounds, most of which were sources of medicinal compounds.

The factor that encourages the use of traditional medicine was the community's assessment that traditional medicine was considered safer to use than synthetic medicine. The side effects given by traditional medicine are relatively less than synthetic drugs. Traditional medicine in some remote areas was the primary source of health services. According to WHO [1], "traditional medicine is the total of knowledge, skill, and practices based on the theories, beliefs and experiences indigenous to different cultures". Traditional medicine has a long history of use in health maintenance and efforts to prevent and treat diseases, especially chronic diseases.

Various studies have been carried out to find medicinal plants that have the potential to cure different types of diseases. The Frangipani plant (*Plumeria* spp.) is one of the natural ingredients used since ancient times and is believed to have various properties in traditional medicine. *Plumeria* species were used in traditional medicine to treat leprosy, inflammation, diabetic mellitus, ulcers, wounds, itching, acne, toothache, earache, tongue cleaning, pain, asthma, constipation, antifertility, and malaria [2,3].

The frangipani extract contains several active compound components, which became an antibacterial and antioxidant source [4]. These compounds include phenols, tannins, steroids, saponins, flavonoids, volatile oil, alkaloids, and glycosides [5,6]. The antibacterial activity of frangipani includes against *B. pumilus, B. subtilis, E. coli, P. aeruginosa, S. aureus,* and *C. albicans* [5]. In addition, bioactive compounds of plants showing antibacterial activity can also function as antioxidants [4].

The ability of frangipani flower extract as an antibacterial has been shown to inhibit several bacterial strains and as an antioxidant that stabilizes or neutralizes free radicals. It needs to be developed for the benefit of humankind. This paper will examine the potential of frangipani flowers as antibacterial and antioxidants and their application in pharmacological activities, which have the potential for new drug discovery for several diseases. The application of frangipani plants in the food

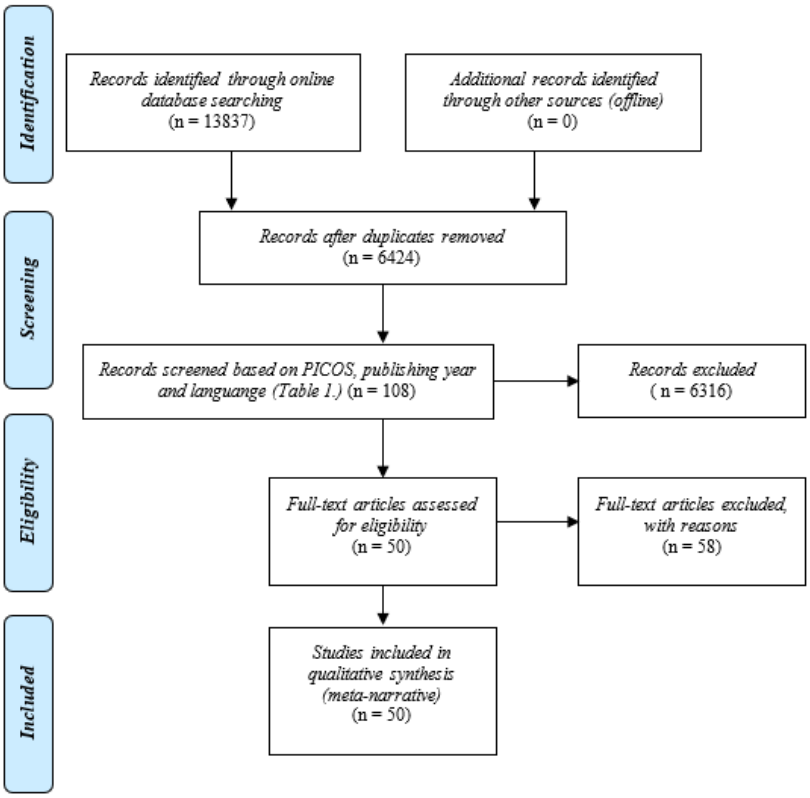

Figure 1. Flowchart of library screening using modified PRISMA method.

Table 1. Inclusion and exclusion criteria with PICOS' format

Criteria	Inclusion	Exclusion
Problem	National and international journals from different databases and related to research variables, namely the potential of frangipani	National and international journals from different databases and not related to research variables
Intervention	Antibacterial and antioxidant testing	No intervention
Comparison	There is no comparison factor	There is no comparison factor
Outcome	The presence of antibacterial, antioxidant, and pharmacological activities	Absence of antibacterial, antioxidant, and pharmacological activities
Study design	Original research and review article in Journal / Proceeding	Report, Thesis, Dissertation, Presentation
Published year	2015 to 2021	< 2015
Language	Indonesian and English	Other than Indonesian and English

sector to create a functional food, rich in antioxidants or to lengthen food shelf life is also discussed.

METHODOLOGY

Writing Plans

This research was conducted up to October 2021 using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) method [7,8], which consists of 27 checklist items and a four-phase flow chart. The checklist aims to transparently report important items to be included in a systematic review. Flowchart items were then created to provide the number of records identified, articles excluded, and studies included. The step of this research was (1) setting the background and objectives; (2) identifying problems; (3) defining eligibility criteria; (4) data collection processing; (5) determining the risk of bias; (6) data extraction; and (7) synthesis of results.

Materials and Tools

The materials that will be used in the preparation of this literature study are libraries from national and international publications (journals) both in hardcopy

Table 2. Botanical of Frangipani Species

Frangipani Species	Character
 *Plumeria obtusa* L	1. The shape of the leaves and flower petals is rounded 2. The surface of the leaves is smooth and shiny 3. The leaves are dark green 4. The flowers are white with a yellow throat 5. The length of the pollen's polar axis is 56.52 m
 *Plumeria pudica* Jacq.	1. Leaf shape bends (fiddle) 2. Small rod diameter 3. Flowers form a bouquet (collection of flowers) at the top end of the stem 4. Flowers are white
 *Plumeria rubra* L.	1. The shape of the leaves and petals are tapered 2. Large green leaves arranged in groups at the ends of the branches 3. The amount of interest is more, 4. Flowers have three colors on one petal. 5. The length of the pollen's polar axis is 50.30 m
 *Plumeria acuminata*	1. The shape of the flower is rounded, and the ends are curled 2. The leaves are light green, elliptical with a pointed tip 3. The flowers are white to yellow
 *Plumeria alba* L.	1. The lanceolate leaves are oval and wavy 2. The flowers are white with a yellow tinge in the middle. 3. The length of the pollen's polar axis is 57.78 m

Sources: Ratnayani *et al.* [12]; Hariri *et al.* [10]; Sukarsa and Herawati [13]; Chamakuri *et al.* [14]; and www.pinterest.com.

and softcopy forms. Literature searches were carried out using various databases of Google Scholar, ScienceDirect, Neliti, Garuda, and DOAJ. Mendeley is used as a library management program (reference manager).

RESULTS

Frangipani plants in recent decades have been widely studied because they contain various metabolites. This was evidenced by the search for related literature totaling 13,837 articles, in the form of review articles and original research. The literature search and screening conducted in this study were presented in the form of a diagram in Figure 1.

The thing that underlies eligibility is an assessment of manuscript quality. Manuscript quality can be achieved by determining a library search strategy, to avoid the risk of bias. The library search strategy uses the PICOS framework (*Problem, Intervention, Comparison, Outcome, and Study design*) (Table 1).

According to Sanjaya *et al.* [15], the morphological character of pollen can be used as an identification tool in taxonomy to determine the type of frangipani plant. Genetic and environmental factors influence the diversity of morphological characters in the appearance of the phenotype.

Table 3. Components and phytochemicals of frangipani flower extract and their biological activity

Frangipani [Ref]	Extraction / Assay	Components	Phytochemicals	Biological activity
P. acuminata [22]	Ethanol 70% (flower yield 1.08%, leaf yield 1.17%); Ethanol 90% (flower yield 0.84%, leaf yield 0.86%)	Alkaloids, flavonoids, tannins, saponins		Antioxidant
P. acuminata [23]	Methanol	Saponin		Antifungal (Candida albicans); mild (inhibition zone 7.7 mm)
Adenium obesum [22]	Ethanol 70% (flower yield 0.73%, leaf yield 0.72%); Ethanol 90% (flower yield 0.64%, leaf yield 0.86%)	Alkaloids, flavonoids, tannins, saponins		Antioxidant
P. alba [5]	HCl 1%	Alkaloids		
	Water	Glycosides, tannin		
	Ethanol	Flavonoids, Phenolics		
	Hexane	Steroids		
*P. alba** [6]	Hexane	Saponin, steroids, volatile oil	Geranic acid	Antifungal
			Nerolidol 2	Antioxidant
			Hexadecenoic acid, methyl ester	Antioxidant
			Eicosane	Anticancer
			9-Octadecenoic acid, methyl ester	Anti-inflammatory, anticancer
			bis(2-ethylhexyl)phthalate	Anticancer
			Squalene	Antibacterial, antioxidant, antitumor, cancer preventive, immunostimulant, chemo preventive
	Dichloromethane	Saponin, steroids, volatile oil	2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one	Antifungal
			5-Hydroxymethylfurfural	Antioxidant, antiproliferative
			Benzofuran,2,3-dihydro-	Anticancer, antibacterial, antifungal
			Catechol	Antioxidant, antiseptic
			Hexadecanoic acid, methyl ester	Antioxidant
			Eicosane	Anticancer, antioxidant
			Squalene	Antibacterial, antioxidant, antitumor, cancer preventive, immunostimulant, chemo preventive
	Ethyl acetate	Flavonoids, phenolics, tannins	Benzofuran,2,3-dihydro-	Anticancer, antibacterial, antifungal
			bis(2-ethylhexyl)phthalate	Anticancer
	Butanol	Flavonoids, phenolics, saponins, tannins	Benzyl alcohol	Antibacterial
			L-α-terpinol	Antioxidant, anticancer
			5-Hydroxymethylfurfural	Antioxidant, anticancer
			Neric acid	Antibiotic, antifungal, antioxidant
	Aqueous	Flavonoids, phenolics, saponins, tannins	Furfural	Antimicrobial
			2-Furanmethanol	Antibacterial, antiviral
			Dihydroxyacetone	Antimicrobial
			Glycerin	Antimicrobial
			2,3-Dihydro-3,5-dihydroxy-6-methyl-4H-Pyran-4one	Antioxidant
			5-Hydroxymethylfurfural	Antioxidant, anticancer
	Methanol	Alkaloids, flavonoids, tannins, saponin		
P. obtusa [16]	Benzene	Alkaloids, steroids, triterpenoids, protein, amino acids, carbohydrates, volatile oils, fatty acids		
P. obtusa [17]	Histochemical assay	lignin, starch granules, tannins, volatile oils, and fat		

*) Extraction was held following methanolic extraction (starting with *n*-hexane, dichloromethane, ethyl acetate and ended by *n*-butanol).

Table 3. Components and phytochemicals of frangipani flower extract and their biological activity (Cont.)

Frangipani [Ref]	Extraction / Assay	Components	Phytochemicals	Biological activity
P. pudica [14]	Hydro alcoholic	Alkaloids, carbohydrate, glycosides, fixed oils, saponin, flavonoids		
P. rubra [19]	Hexane	Phenolics, flavonoids		Xanthine oxidase inhibitory
	Chloroform	Phenolics, flavonoids		Xanthine oxidase inhibitory
	Methanol	Phenolics, flavonoids	3-*O*-Caffeoylquinic acid, 5-*O*-Caffeoylquinic acid, Chlorogenic acid, Citric acid, Kaemferol-3-*O*-glucoside, Kaemferol-3-rutinoside, Kaempferol, Quercetin 3-*O*-a-L-arabinopyranoside, Quercetin, Quinic acid, Rutin	Antioxidant, Xanthine oxidase inhibitory
	Water	Phenolics, flavonoids		Antioxidant
P. alba [24]	*n*-Hexane	Alkaloids, flavonoids, tannins, terpenoids		
	Ethyl acetate	Alkaloids, flavonoids, tannins, terpenoids		
	Methanol	Alkaloids, flavonoids, tannins, saponin		
P. obtusa [16]	Benzene	Alkaloids, steroids, triterpenoids, protein, amino acids, carbohydrates, volatile oils, fatty acids		
P. obtusa [17]	Histochemical assay	lignin, starch granules, tannins, volatile oils, and fat		
P. pudica [14]	Hydro alcoholic	Alkaloids, carbohydrate, glycosides, fixed oils, saponin, flavonoids		
P. rubra [19]	Hexane	Phenolics, flavonoids		Xanthine oxidase inhibitory
	Chloroform	Phenolics, flavonoids		Xanthine oxidase inhibitory
	Methanol	Phenolics, flavonoids	3-*O*-Caffeoylquinic acid, 5-*O*-Caffeoylquinic acid, Chlorogenic acid, Citric acid, Kaemferol-3-*O*-glucoside, Kaemferol-3-rutinoside, Kaempferol, Quercetin 3-*O*-a-L-arabinopyranoside, Quercetin, Quinic acid, Rutin	Antioxidant, Xanthine oxidase inhibitory
	Water	Phenolics, flavonoids		Antioxidant

*) Extraction was held following methanolic extraction (starting with *n*-hexane, dichloromethane, ethyl acetate and ended by *n*-butanol).

Phytochemical of Frangipani Flowers

Several chemical components of frangipani flower extracts have been isolated and identified, including essential oils, phenolics, flavonoids, steroids, saponin and tannins [6]. For example, the benzene extract of *P. obtusa* contains alkaloids, steroids, triterpenoids, proteins, amino acids, carbohydrates, and fatty acids [16]. On the other hand, Kamran *et al*. [17] found cardiac glycosides and tannins, but no alkaloids, saponins, or anthraquinones were found.

The content of essential oil, alcoholic compounds, and alkanes of frangipani hexane extract vary by the frangipani type, i.e., 4.457%, 2.908%, and 2.763% in yellow, white, and red frangipani, respectively [18]. The alcoholic chemical compounds such as geraniol, farnesol, and octadecanol are 2.64%; 8.61%; 3.87%, respectively. and alkanes such as octadecane in yellow frangipani by 21.24%, nonadecane in white and red frangipani by 7.54% and 7.84%, respectively.

Plumeria alba contains alkaloids, glycosides, flavonoids, phenolic compounds, tannins, and steroids. The phenolic value of the methanol extract was 67.73 µg GAE/mg [4]. Muhammad *et al.* [3] performed an analysis using GC-MS hexane (HEX), dichloromethane (DCM), ethyl acetate (EA), butanol (BuOH), and aqueous extract of the methanol extract of *P. alba* different from flavonoids, phenolics, saponin, tannins, steroids, and essential oils. Butanol extract was found to contain more phytochemical compounds compared to other extracts. However, steroids are not present in the butanol extract.

Table 4. Antimicrobial (antibacterial and antifungal) activity of frangipani flower extract by different methods

Frangipani Flower Type	Extraction	Methods	Microbes (diameter of inhibition zone)
P. acuminata [25]	Ethanol 1.25, 2.50, 25%	Disc diffusion	*E. coli* (weak, 6.1, 6.7, 8.2 mm)
P. acuminata [27]	Ethanol	Well diffusion Extract conc. 50% Extract conc. 90%	*S. dysenteriae* 9.27 mm 12.44 mm
P. acuminata [28]	Ethanol fraction, chloroform, and n-hexane	Well diffusion (Extract 60%)	*E. coli* (strong, 11.09 mm) *S. aureus* (strong, 10.61 mm)
P. acuminata [23]	Ethanol	Disc diffusion	*Candida albicans* (medium, 7.7 mm) Control + (ketoconazole) 4.2 mm Control – (methanol) 0.0 mm
P. alba [29]	Ethanol	Agar dilution (Extract 7.81 mg/mL)	*S. pyogenes* (strong, no bacterial colonies detected)
P. alba [5]	Methanol	Disc diffusion	*S. aureus, C. albicans* (weak)
	Ethyl acetate		*B. pumilus, B. subtilis, E. coli, P. aeruginosa, S. aureus, C. albicans* (strong)
	Ethanol		*P. aeruginosa* (medium) *B. subtilis, S. aureus, C. albicans, E. coli* (weak)
	Water		*B. subtilis*, *P. aeruginosa* (medium) *C. albicans*, *E. coli* (weak)
	Petroleum ether		-
P. alba [30]	Ethanol	Spectrophotometry Nylon plate dipped in Extract 100%	*C. albicans* (could inhibit 50% of fungal growth)
P. alba [4]	Ethanol	Disc diffusion Extract 3%	*S. aureus* Inhibition index is 1.27 Inhibition Index of Amoxycillin 2% is 1.85
P. alba [31]	Ethanol	Agar Dilution	*S. aureus, E. coli, S. typhi* (weak, 11 mm)
P. alba [32]	Deionized water	Disc diffusion Extract conc. 400 µg/mL	*E. coli* (medium, 16 mm)
P. alba [26]	Petroleum ether	Well diffusion	*E. coli* (9.6 mm) *B. cereus* (15.2 mm) *B. subtilis* (18.6 mm) *S. typhi* (18.6 mm) *S. aureus* (19.0 mm) *S. flexneri* (23.7 mm)
P. alba [33]	Methanol then fractionated using *n*-hexane, chloroform, and ethyl acetate	Well diffusion	*S. aureus* (9.77, 20.89, 19.44 mm) *S. typhi* (15.86, 27.69, 21.74 mm)
P. obtuse [34]	Ethanol 70%	Disc diffusion	*Aspergillus flavus* (17 m) *B. subtilis, C. albicans, S. aureus, S. typhi* (15 mm) *E. coli* (14 mm) *Micrococcus luteus* (10 mm) *Mallasezia furfur* (11 mm)
P. obtuse [35]	Chloroform, methanol, acetone, aqueous	Disc diffusion	*S. typhi* (15, 19, 10, 14 mm) *S. aureus* (14,17,10, 16 mm) *P. aeruginosa* (14, 18, 14, 14 mm) Control positive (Amoxycillin) (31-32 mm)
P. rubra [36]	Methanol	Disc diffusion	*E. coli* Flower (8.33 mm) Leaf (4.33 mm) Control + (Chloramphenicol) (22.00 mm)
P. rubra [37]	Ethanol Extract 100%, 50%, 25%	Well diffusion	*Shigella dysenteriae* (7.92, 4.37, 2.10 mm)
P. rubra [38]	Methanol, Water	Disc diffusion (Disc size 6 mm, Sample conc. 4 mg/mL)	*B. subtilis* (18.64, 9,21mm) *S. aureus* (19.58, 8.61 mm) *P. aeruginosa* (22.08, 7.01 mm) *E. coli* (23.17, 7.51 mm) *C. albicans* (10.41, 8.07 mm)

Table 4. Antimicrobial (antibacterial and antifungal) activity of frangipani flower extract by different methods (cont.)

Frangipani Flower Type	Extraction	Methods	Microbes (diameter of inhibition zone)
P. rubra [37]	Ethanol Extract 100%, 50%, 25%	Well diffusion	*Shigella dysenteriae* (7.92, 4.37, 2.10 mm)
P. rubra [38]	Methanol, Water	Disc diffusion (Disc size 6 mm, Sample conc. 4 mg/mL)	*B. subtilis* (18.64, 9,21mm) *S. aureus* (19.58, 8.61 mm) *P. aeruginosa* (22.08, 7.01 mm) *E. coli* (23.17, 7.51 mm) *C. albicans* (10.41, 8.07 mm)

Isa *et al.* [19] showed that the methanolic extract of *P. rubra* contains high amounts of phenolic (184.63 mg GAE/g) and flavonoid (203.20 mg QE/g) content. In addition, it also contains chlorogenic acid, neochlorogenic acid, citric acid, astragalin, nicotiflorin, kaempferol, avicularin, quercetin, quinic acid, and rutin. On the hand, Chen *et al*. [20] show that flower-free *P. rubra* L phenolic components detected by Ultra Performance Liquid Chromatography (UPLC) technique are gallic acid 42.65 µg/g, protocatechuic acid 105.24 µg/g, catechins 453.35 µg/g, vanillic acid 13.15 µg/g, caffeic acid 64.86 µg/g, syric acid 26.87 µg/g, epicatechin 152.62 µg/g, p-coumaric acid 12.38 µg/g, ferulic acid 536.58 µg/g, rutin 506.40 µg/g, isoquercetin 337.11 µg/g, querticin 646.86 µg/g, and quercetin 68 µg/g.

Zheng *et al.* [21] reported that the phenolic and flavonoid content of *P. rubra* Linn flowers is higher than in *P. rubra* Acutifolia, i.e., 56.02 mg GAE/g and 15.69 mg QE/g respectively in *P. rubra* L, while only 20.6 mg GAE/g and 3.83 mg QE/g in *P. rubra* Acutifolia.

Chamakuri *et al.* [14] explained that hydro-alcoholic extracts of *P. pudica* flowers contained alkaloids, carbohydrates, glycosides, oils, saponin, and flavonoids. However, the tannin, steroid, mucilage, and triterpenoid tests did not give positive results.

Identification of compounds carried out by Shofi *et al.* [22] against *P. acuminata* using ethanol solvent with a concentration of 70% and 96% proved the presence of alkaloid compounds, flavonoids, tannins and saponin. However, steroid compounds were not found because they did not show a color change in the solution that should have turned blackish green. Components, phytochemicals and biological activity of frangipani are presented in Table 3.

Antimicrobial (Antibacterial and Antifungal) Potential of Frangipani Flower Extract

Antimicrobial/Antifungal Compound

Alkaloids, flavonoids, terpenoids, and tannins are phytochemical compounds in frangipani flowers showing antibacterial properties. In addition, frangipani flowers also contain essential oils and fulvoplumierin compounds. According to Prihardini and Kristianingsih [25], essential oils and fulvoplumierin are chemical compounds that prevent the growth of *E. coli* bacteria. The volatile oil contained in frangipani flowers causes an increase in ion permeability and impairs bacterial enzyme systems.

Alkaloids are a group of secondary metabolites with various pharmacological activities. Results of GC-MS analysis on *P. alba* flower extract revealed that 11 alkaloid compounds were matched with the alkaloid mass spectrum in the *National Institute of Standards and Technology* (NIST) database [26]. Based on this research, alkaloids act as antibacterial compounds such as *B. cereus, B. subtilis, S. aureus, E. coli, S. typhi, and S. flexneri*, which are pathogenic food bacteria.

Flavonoids and terpenoids are phytochemical compounds with antibacterial activity [25]. These compounds attack cell membranes and cause the permeability of the bacterial cell membrane to be disturbed and decreased, resulting in the bacterial cell being deprived of nutrients and dying. In addition, the tannin content in Frangipani flowers can inhibit protein synthesis from bacterial cells, so bacterial growth is inhibited.

According to Win *et al.* [5], the antibacterial activity of *P. alba* flowers was low due to the presence of phenolic compounds, which was evidenced by carrying out the test using petroleum ether, methanol, ethanol, and water extracts of *P. alba* flowers. The petroleum ether extract sample did not show activity on six organisms, while the methanol extract sample had an inhibition zone of 10-14 mm, the ethanol and aqueous extracts had an inhibition zone of 10-19 mm, and the largest inhibition zone was in the ethyl acetate extract >20mm.

Antibacterial/Antifungal Activity

The methods used in testing the antibacterial activity include the disk diffusion method, well diffusion, and agar dilution. This method was used in *testing frangipani flower extract* and showed antibacterial activity against *E. coli, P. aeruginosa, S. aureus, C. albicans, S. pyogenes, S. typhi, B. pumilus, B. subtilis, S. dysenteriae, P. mirabilis, P. fluorescens, B. cereus, S. flexneri* and *M. furfur*. Antifungal activity against *Candida albicans* has been also reported. The data that has been collected regarding the potential antibacterial activity of Frangipani flowers can be seen in Table 4.

Disc diffusion or *Kirby-Bauer* is one method to evaluate plant extracts' antibacterial activity against certain microorganisms' growth. The *Kirby-Bauer* method was carried out with 6 mm paper discs, then placed on agar media planted with microorganisms. The antimicrobial

agent diffuses into the agar and inhibits the growth of the test microorganism. The test results are based on the diameter of the inhibition zone (inhibition zone) through the formation of a clear zone in the area around the paper disc. The clear zone indicates the inhibition of microorganisms' growth on the surface of the agar medium as an antimicrobial gene [39].

Prihardini and Kristianingsih [25] tested the antibacterial activity by disc diffusion method of ethanol extract and *P. acuminata* flower essential oil against *E. coli* bacteria. The concentration of 1.25% extract formed an inhibitory zone of 6.1 mm, and a 10% concentration of essential oils indicated the presence of antibacterial activity, which created an inhibition zone of 9.66 mm. The greater the concentration of extracts and essential oils, the wider the diameter of the inhibition area.

The Well diffusion method is like disc diffusion, except that a well is made to test for antibacterial activity. Wells are made with a diameter of 6-8 mm using a sterilized blue tip. Before making the wells, the test bacteria were evenly inoculated on the media and then allowed to stand for 5 minutes. Plant extracts and controls were added to the wells as much as 20-100 µL, then incubated for 24 hours at 37ºC. The antimicrobial agent will diffuse in the agar medium and inhibit the growth of the tested microbial strain. The diameter of the inhibition zone is observed and measured using a caliper [39].

The antibacterial activity of petroleum ether extract from P. alba flower was evaluated using a Well diffusion test and minimum inhibitory concentration value. Raw plant extracts are more active against pathogens. The antibacterial activity of *P. alba* flower extract against *S. flexneri* was the most sensitive organism with an inhibition zone of 23.7 mm, then *S. aureus* at 19.0 mm. *B. cereus, B. subtilis, and S. typhi* were sensitive with an inhibition zone range of 15.2-18.6 mm. *E. coli* was inhibited with a zone diameter of 9.6 mm [26]. Mindasari [37] showed that frangipani flower extract (*P. rubra* L.) has antibacterial activity against *Shigella dysenteriae* bacteria with an inhibition area of 100%, 50%, and 25% resulting in an average of 7.92 mm, 4.37 mm, and 2.1 mm, respectively.

The dilution method is used to determine the potential of a compound for microbial activity by selecting the Minimum Inhibitory Concentration (MIC) and Minimum Kill Concentration (KBM). The principle of dilution carries out the dilution method. Observations of the dilution method were analyzed descriptively and can be assessed visually. Jiwantono *et al.* [29] tested the antibacterial activity of *P. alba* flower extract against *S. pyogenes* bacteria by liquid dilution, showing that KBM was at 7.81 mg/mL.

Antioxidant Potential of Frangipani Flower Extract

Antioxidant compounds

Antioxidant compounds are compounds that function to protect cells from the effects of free radicals. Phytochemical compounds that have the potential as a source of natural Antioxidants are phenols, especially flavonoids. Phenol is a plant compound with a hydroxyl group in response to environmental stress and exhibits significant biological functions such as protection against oxidative stress and degenerative diseases [5].

Flavonoids have antioxidant activity that can increase self-defense from diseases induced by free radicals by donating hydrogen atoms. Flavonoids are also known to prevent the accumulation of fat because of its ability as a metal chelating agent, which is a catalyst for lipid peroxidation so that it can overcome the problem of obesity which is the cause of diabetes mellitus [40]. Rahman *et al*. [41] reported that flavonoids play a role in anti-inflammatory because they can inhibit several enzymes such as aldose reductase, xanthine oxidase, phosphodiesterase, Ca^{2+} ATPase, lipoxygenase, and cyclooxygenase.

Antioxidant Activity

The DPPH method (2,2-diphenyl-1-picrylhydrazyl) is the first to evaluate a material's antioxidant compounds. The extracted material is mixed with a DPPH solution, and the absorbance value is recorded for a certain period [42]. The DPPH radical is stable in an aqueous solution and has a strong absorption at a wavelength of 517 nm in the oxidized form. A dark purple color change indicates antioxidant activity from DPPH to pink or pale yellow [43].

Antioxidant activity is expressed in terms of IC_{50} values and terms of percentage inhibition of DPPH. The IC_{50} value is the concentration that causes a 50% loss of DPPH activity. Molyneux [44] stated that a compound is said to have very high antioxidant activity if the value of IC_{50} < 50 µg/mL, strong if the value of IC_{50} revolves around 50-100 µg/mL, medium if the value of IC_{50} revolves around 101-150 µg/mL, and weak if the value of IC_{50} > 150 µg/mL. Antioxidant activity will be related to the bioactive compounds contained in a sample. Data on the antioxidant activity of frangipani flowers can be seen in Table 5.

DPPH testing conducted by Mohammad Isa *et al.* [19] showed the antioxidant activity of *P. rubra* due to the presence of phytochemicals that can inhibit xanthine oxidase (XO). XO inhibitory activity in vitro test had the highest inhibitory effect on IC_{50} = 23,91 µg/mL. According to Win *et al.,* [5] on methanol extract *P. alba* value IC_{50} = 0,87 µg/mL was found to have higher antioxidant activity than ethanol extract IC_{50} = 0,99 µg/mL and extract the sample water which only IC_{50} = 3,61µg/mL. The rich phenol fraction of *P. alba* flower shows the potential source of natural antioxidants, as evidenced by the value IC_{50}.

Frangipani Flower Extract Application

Frangipani plants have various pharmacological activities. Pharmacological activity is the application of

Table 5. Antioxidant activity of frangipani flower extract using different solvents

Frangipani type [ref]	Solvent extraction	Methods	Activity
Adenium obesum [22]	Ethanol 70% (Ascorbic acid)	DPPH (IC_{50})	Flower 358.85 ppm Leaf 224.48 ppm (48.66 ppm)
	Ethanol 96% (Ascorbic acid)		Flower 379.52 ppm Leaf 478.65 ppm (48.66 ppm)
P. acuminata [22]	Ethanol 70% (Ascorbic acid)	DPPH (IC_{50})	Flower 98.41 ppm leaf 366.82 ppm (48.66 ppm)
	Ethanol 96% (Ascorbic acid)		Flower 533.13 ppm Leaf 416.09 ppm (48.66 ppm)
P. alba [5]	Ethanol Methanol Water (Ascorbic acid)	DPPH (IC_{50})	0.99 µg/mL 0.87 µg/mL 3.61 µg/mL (1.17 µg/mL)
P. alba [4]	Ethanol	DPPH	57.5%
P. alba [45]	Ethyl acetate	DPPH	±60%
P. alba [24]	n-Hexane Ethyl acetate Methanol	DPPH	72.44 ppm 2.96 ppm 116.93 ppm
P. obtuse [46]	Methanol (Ascorbic acid)	DPPH	76.19 mg/mL (65.06 mg/mL)
P. rubra [20]	Methanol:acetone:water (7:7:6, v/v/v)	DPPH	88.08 µmole TE/g DW
P. rubra [46]	Methanol (Ascorbic acid)	DPPH	70.58 mg/mL (65.06 mg/ml)
P. rubra Acutifolia [21]	Acetone, water, and acetic acid (70:29.5:0.5, v/v/v)	DPPH	28.59 µmole TE/g
P. rubra L. [21]	Acetone, water, and acetate acid (70:29.5:0.5, v/v/v)	DPPH	153.33 µmole TE/g
P. rubra [19]	Methanol Water (Ascorbic acid)	DPPH (IC_{50})	59.39 µg/mL 231.06 µg/mL (29.60 µg/mL)

antibacterial and antioxidant compounds that have potential in the pharmaceutical field. Pharmacological activities (Table 6.) include anti-inflammatory, antifungal, hypolipidemic, anti-arthritis, anti-anaphylactic, antipyretic, antidiabetic, and anticancer activities.

Ahaotu *et al.* [40] investigated the anti-inflammatory effect of ethanol extract of white frangipani flowers on the soles of white male rats induced by λ-carrageenan as much as 1%. This test is carried out using a digital plethismometer based on the principle of Archimedes' law. The anti-inflammatory effect on rats was at a dose of 250 mg/kg (wb) because it was comparable to the positive control, sodium diclofenac 9 mg/kg (wb).

Frangipani flowers have antifungal activity. Nuraini *et al.* [58] reported that ethanol extract of white frangipani flower (*P. acuminata*) at various concentrations of 80, 85, and 90% could inhibit the growth of the fungus *Candida albicans*. The higher the concentration used, the greater the antifungal activity limits the development of the *Candida albicans* fungus. Oktaviana *et al.* [48] also proved that an extract of frangipani flowers at a concentration of 0.9 g/mL could inhibit the growth of *Aspergillus clavatus*, which has the same inhibitory using ketoconazole at 0.02 g/mL. *Aspergillus clavatus* can produce mycotoxin compounds that cause disease in animals and humans.

Several studies explain that *Plumeria* species contain high phenolic compounds and show good antioxidant activity, so a hypolipidemic test was carried out. The ethanolic extracts of frangipani flowers of *P. alba* and *P. rubra* had hypolipidemic activity [59]. *P. rubra* had higher hypolipidemic activity than *P. alba*, 60%, and 52%, respectively.

Choudhary *et al.* [60] showed that in Sprague-Dawley rats, ethyl acetate and n-butanol P. alba had anti-arthritis activity. This protective activity against arthritis supports the traditional use of *P. alba* for rheumatism.

P. rubra has the potential to be used as an antidiabetic disease. Zhang *et al.* [40] showed the inhibitory activity (IC_{50}) of α-glucosidase and protein tyrosine phosphatase of 19.45 µM and 0.21 µM, respectively. In addition, *P. rubra* flower decoction has traditionally been used in China and Mexico to treat diabetes.

Table 6. Application of frangipani flower extract in the pharmaceutical field

Frangipani type	Method	Application	Ref
Plumeria sp.	-	Biolarvicides	[47]
P. acuminata	Solid dilution	Antifungal	[48]
P. alba	Experimental Animals	Anti-inflammatory	[49]
P. alba	-	Pharmacology	[50]
P. alba	-	Malaria, cancer, and tumors	[51]
P. alba	Spectrophotometry	*Denture cleanser*	[30]
P. alba	-	Molecular medicine	[2]
P. alba	Disc diffusion	Antifungal on *C. albicans*	[23]
P. alba	Experimental	Anti-hepatotoxicity	[42]
P. alba	Methanol	Antiproliferative	[43]
P. alba	-	Pharmacology	[11]
P. alba	Ethanol	Analgesic	[52]
P. alba	Methanol	Drug therapy	[6]
P. alba	Disc diffusion	Natural disinfectant	[53]
P. alba	-	Pharmacology	[54]
P. obtusa	Phytochemical analysis	Pharmacology	[17]
P. pudica	-	Pharmacology	[14]
P. pudica and *P. rubra*	Denaturation of egg protein and albumin	Anti-arthritis	[55]
P. rubra	In vitro assay In vivo assay (hyperuricemic mice)	Xanthine oxidase inhibitor Anti-hyperuricemic	[19]
P. rubra	In vitro assay (spectrophotometry)	Antidiabetic	[40]
P. rubra	In vivo assay (hind paw oedema in albino mice)	Anti-inflammatory Anti-anthelmintic	[38]
P. rubra	-	Pharmacology	[56]
P. rubra	-	Pharmacology	[3]
P. rubra	-	Analgesic	[57]

Cytotoxicity of the ethyl acetate extract of *P. rubra* was tested against the human breast cancer cell line MDA-MB. Jeyarani *et al.* [61] showed that incubating MCF-7 cells with ZW inhibited cancer growth and proliferation. In addition, the ethyl acetate extract of *P. rubra* showed intense MDA-MB-231 activity against the clinical activity of triple-negative breast cancer cells.

Frangipani flowers also have the potential to be applied to the cosmetic and food fields. Mata *et al.* [32] reported that *P. alba* has antibacterial and catalytic activity as nanoparticles against *E. coli*. Antimicrobial activity depends on particle size. The smaller the size, induces more significant the activity is. The best antibacterial activity was PAGNPs2 (*P. Alba* gold nanoparticles synthesized 5% flower extract) with a nanoparticle concentration of 400 g/mL, showing an inhibition zone of 16 mm.

Furthermore, PAGNPs2 samples showed more pronounced catalytic activity than PAGNPs1 after analyzing six harmful dyes. The mechanism of catalysis is described as the electron transfer process from a $NaBH_4$ donor to an acceptor. The smooth green synthesis of eco-friendly nanoparticles demonstrates this method's potential for industrial applications [32].

Another application of Frangipani flowers is in the cosmetic field as body scrubs and soaps. Dewi and Megasari [62] reported that *P. alba* flower extract and soybean flour with a ratio of 7 g : 3 g can potentially be used as traditional scrub products. On the other hand, Nurzaman *et al.* [63] added that saponin extracted from *P. rubra* could lower the surface tension to formulate cleansing cosmetics. The aqueous extract of the flowers, leaves, and stems of *P. rubra* had the highest saponin content compared to other solvent extracts, with a Critical Micelle Concentration (CMC) value of the flower part of 8.61%.

Frangipani can also be applied in the food sector as a coagulant [64], an alternative source of proteases [12], and a control of food pathogenic bacteria [26]. The presence of active phytoconstituents in *P. alba* flowers is not only suitable for use as medicine for human health but also in food preparations [5].

Frangipani has been used as a source of cheese-making enzymes. *Peuhl* cheese in the local language is commonly called *waragashi, warangachi, wagashi,* and *wara*. *Waragashi* cheese is a soft and nutritious cheese. Generally made using *calotropin* enzyme from the plant *Calotropis procera* as milk coagulant. Bankole *et al.* [65]

showed that *P. alba* latex is an alternative enzyme source for waragashi cheese production. Waragashi cheese produced using *P. alba* showed texture properties comparable to those made using *C. procera*, and maximum milk-clotting activity (MCA) at temperatures close to 80°C. However, the texture or hardness of waragashi cheese varies, indicating that the function of each plant coagulant is different. The resulting waragashi cheese has a yellow color character.

Ratnayani *et al.* [12] reported that frangipani has the potential as an alternative protease source. The protease enzyme is one of the enzymes that has been isolated from frangipani plant latex. The protease enzyme (plumerin) plays a role in the protein degradation process, e.g., in the food industry (bread, milk, protein hydrolysate), the detergent industry, and is traditionally used as a meat tenderizer.

In control of foodborne pathogens, antimicrobials derived from plants are more potent and effective. The antimicrobial activity of *P. alba* flower extract might correlate with the presence of alkaloids that justify this plant for various diseases. Control of foodborne pathogens such as *B. cereus, B. subtilis, S. aureus, E. coli, S. typhi, and S. flexneri.* Therefore, an antimicrobial drug formulation containing *P. alba* flower extract to control foodborne pathogens is feasible [26].

The use of frangipani flowers in the food sector that can affect the product's sensory properties has not been found in the appropriate literature. The frangipani flowers are traditionally directly consumed as herbs, not as a mixture of food ingredients. In addition, there is still limited literature that reports the use of other parts of the frangipani plant, such as roots, stems, leaves, and latex.

The latex from the frangipani plant can affect the sensory properties of food, e.g., cheese, on texture parameters in cheese products [24]. The latex of the frangipani plant is rich in protein and minerals. The coagulation activity of *P. alba* and *P. rubra* latex on milk is optimum at 70ºC, which means that the protease in frangipani latex is a thermostable enzyme, which is useful as a biocatalyst in the dairy industry [64]. However, compared with the papaya latex, the latex of frangipani has not been commercialized.

CONCLUSION

Compounds isolated from different frangipani flowers (*P. obtusa, P. pudica, P. rubra, P. acuminata,* and *P. alba*) showed antimicrobial and antioxidant activity. The antimicrobial activity of the frangipani flowers is against *E. coli, P. aeruginosa, S. aureus, C. albicans, S. pyogenes, S. typhi, B. pumilus, B. subtilis, S. dysenteriae, P. mirabilis, P. fluorescens, B. cereus, S. flexneri, A. flavus,* and *M. furfur.* The high antioxidant activity of frangipani flowers is due to the content of phenols and flavonoids, while one of the antimicrobial components is saponin. Frangipani flower extract has a broad application in pharmaceutical fields, i.e., anti-hyperuricemia, anti-inflammatory, antifungal, antidiabetic, anti-proliferative, analgesic, denture, malaria, cancer, tumor, and bio larvicide, as well as in cosmetics field as cleanser agent.

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