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Antifungal Activity the Active Fraction of Orange Jasmine (*Murraya paniculata* (Linn) Jack) Leaves and Stem Bark Against *Malassezia furfur*

Aktivitas Antifungi Fraksi Aktif Daun dan Kulit Batang Kemuning (*Murraya paniculata* (Linn) Jack) terhadap *Malassezia furfur*

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ABSTRACT

Leaves and stem bark of orange jasmine have bioactive compounds such as phenol and flavonoids, which these compounds could be extracted by organic solvent and have antifungal activity against Malassezia furfur which cause excema, dandruff and tinea versicolor in humans. Fractionation of the extract would obtain a specific compound based on the polarity of the solvent. This research aims to know the active fraction of leaves and stem bark of orange jasmine which had antifungal activity against Malassezia furfur. The simplicia powder of leaves and stem bark orange jasmine was macerated with 96% ethanol solvent and then fractionated as gradually with n-hexane, ethyl acetate, and water solvent. The antifungal activity of ethanol extract and fractions was tested against Malassezia furfur with 80; 90; 100% concentration by disk diffusion method at 37˚C for 48 hours of incubation*. The data of antifungal activity was analyzed by two-way ANOVA. The result of this research showed antifungal activity from active fraction as water fraction of leaves and stem bark of orange jasmine against Malassezia furfur. The diameter of inhibition zones for the active fraction of leaves and stem bark of orange jasmine such as 8.6 – 14 mm and 12.3 – 15.8 mm respectively.*

Keywords**:** *Antifungal, active fraction*, *Malassezia furfur, Murraya paniculata*

ABSTRAK

Daun dan kulit batang kemuning memiliki kandungan senyawa aktif seperti fenol dan flavonoid yang dapat tersari dalam pelarut organik dan berpotensi sebagai antifungi terhadap fungi *Malassezia furfur* penyebab eksim, ketombe dan panu pada manusia. Fraksinasi ekstrak akan diperoleh senyawa spesifik berdasarkan kepolaran pelarut. Penelitian ini bertujuan untuk mengetahui fraksi aktif daun dan kulit batang kemuning yang memiliki aktivitas antifungi terhadap *Malassezia furfur*. Serbuk simplisia daun dan kulit batang kemuning diekstraksi secara maserasi dengan pelarut etanol 96% dan dilanjutkan fraksinasi secara bertingkat dengan pelarut n-heksan, etil asetat dan air. Aktivitas antifungi ekstrak etanol dan fraksi-fraksi diujikan terhadap fungi *Malassezia furfur* dengan konsentrasi 80; 90; 100% menggunakan metode difusi cakram pada inkubasi dengan suhu 37˚C selama 48 jam. Data aktivitas antifungi dianalisis secara statistik menggunakan anava dua jalan. Hasil penelitian ini menunjukkan fraksi aktif yang memiliki aktivitas antifungi terhadap *Malassezia furfur* adalah fraksi air daun dan kulit batang kemuning. Diameter daerah hambat dari fraksi aktif daun dan kulit batang kemuning masing-masing sebesar 8,6-14 mm dan 12,3-15,8 mm.

Kata kunci: Antifungi, fraksi aktif, *Malassezia furfur, Murraya paniculata*.

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INTRODUCTION

Orange jasmine leaves, one of the thirtieth medicinal plants, have focused on research and development of "jamu" sciencetifaction (Menteri Kesehatan RI, 2013). Therefore, it needs to research pharmacological activity such as antifungal activity to enrich scientific evidence. Orange jasmine leaves were used to relieve cough by the community of Jagaraga village in Indonesia (Ni Nengah et al., 2019). This efficacy is related to bioactive compounds. The aqueous extracts of orange jasmine leaves contained alkaloids, flavonoids, phenolics, and tannins with total phenolics and flavonoids content respectively at 263±0.62 (mg GAE/g) and 63±0.19 (mg QE/g) (Sabnam et al., 2020).

Hydroalcoholic extract (70% ethanolic) of orange jasmine leaves has proven antifungal activity against *Candida albicans* with MIC 0.625-10% w/v (Kusuma et al., 2017). Methanolic extracts of orange jasmine leaves have proven antifungal activity against *Pichia kudriavzevii*, *Lasiodiplodia theobromae*, dan *Fusarium oxysporum* (Nesa et al., 2021). Ethanolic, aqueous, and n-hexane extracts at 300-500 µg concentrations have antifungal activity against *Aspergillus niger* (Sundaram et al., 2011).

Orange jasmine stem barks were bioactive compounds such as meksotioin, 5-7-dimetoksi-8-(2,3-dihidroksiisopentil) kumarin (RI, 2016). Ethanolic extract of orange jasmine stem barks has proved antibacterial activity against *Salmonella typhi* at 25-75% concentrations and total flavonoid and phenolic content respectively 982.35 mg/100g QE and 2089.345 mg/100g GAE (Putu et al., 2018).

Bioactive compounds played a role as antifungals can dissolve on polar, medium polar, and nonpolar solvents such as water, ethanol, ethyl acetate, and n-hexane. Those bioactive compounds need to be verified as antifungal activity against Malassezia furfur fungi. These fungi as lipophilic yeast, and microfloral in human skin, could cause of skin infections (Saleh et al., 2020). Flavonoids are found on leaves and stem barks of orange jasmine and dissolved in water, ethanol, ethyl acetate, and n-hexane solvents. Fractionation for extract was done with different polarity of solvents that could obtain simpler than its crude extract.

Exploration of natural compounds is carried out today because we want to find active compounds as drug candidates. The stages started with collecting plant raw materials, extraction, isolation and purification, activity testing, chemical structure characterization, and optimization of active compounds (Chaachouay & Zidane, 2024). At the isolation and purification stage, active compounds are separated into more specific ones through fractionation and purification methods. Fractionation can use the separating funnel method which uses solvents of different polarities (Abubakar & Haque, 2020). These solvents will extract active compounds and have the potential for pharmacological activity. *Allium chinense* G.Don bulb extracts and fractions showed antifungal activity against *Candida albicans*, but the ethyl acetate fraction had a larger diameter of inhibitory zone than the other fractions (Supomo et al., 2021). So, it needs to be investigated further to obtain the active fraction from the natural extract of the orange jasmine plant as an antifungal.

The research of orange jasmine leaves and stem barks previously showed antifungal potential so it can develop continuously against other fungi such as *M. furfur*. This research aims to know the active fraction of orange jasmine (*Murraya paniculata*) leaves and stem barks that have antifungal activity against *M. furfur*.

METHOD

Materials and Tools

The tools are used oven, rotary evaporator (Heidolph), glassware, autoclave (All American), and laminar airflow (Airtech). The materials are used orange jasmine leaves and stem barks fresh, 95% ethanol, n-hexane, ethyl acetate and aquadest, Saboraud Dextrose Agar (SDA), and Saboraud Dextrose Broth (SDB) media, Malassezia furfur fungi, dimethylsulfoxide, ketoconazole (20µg/disk).

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Methods

Collection of Raw Materials and Sample Preparation

Orange jasmine leaves and stem barks were obtained from Kaligarang village Jepara Central Java. This orange jasmine has determined to confirm the truth of the plant. Orange jasmine leaves were used in old leaves while stem barks were used main stem or branch with a diameter of more than 10 cm and then they were exfoliated with size, length, and width particularly (Menteri kesehatan RI, 2011). After harvested material plants, plants were sorted, washed, drained, and dried at 50°C and 40°C in the oven for leaves and stem barks. The simplicia of leaves and stem barks were obtained and then they ground until they become powders.

Extraction and Fractionation

Simplicia powders were soaked in 96% ethanol solvent with a ratio of 1:10 for 3 days of maceration and 2 days of remaceration (Departemen Kesehatan Republik Indonesia, 1986). Macerate was obtained by filtering the result of maceration and remaceration. Macerates evaporate their solvent by rotary evaporator at 50°C until become thick extracts. Two hundred grams and 70 grams of ethanol extract of orange jasmine leaves and stem barks respectively were used for fractionation.

Fractionation was done to extract ethanol from orange jasmine leaves and stem barks by the separation funnel method (Abubakar & Haque, 2020). The crude extract was moistened with water (1:10) then entered into a separating funnel and added the nonpolar solvent (n-hexane) (1:1). The separating funnel was shaken until the content could settle. The aqueous layer was removed and the n-hexane dissolved collected in another flask. This aqueous layer entered again into a separating funnel and added n-hexane again with equal volume, shaken and separating again until after added n-hexane, shaken and n-hexane solvent still clear. The same procedure was performed for the ethyl acetate solvent. The water, ethyl acetate, and n-hexane fraction were evaporated until thick.

Antifungal Activity Test

Antifungal activity test followed by disk diffusion method (EUCAST, 2023). The *Malassezia furfur* fungi were rejuvenated first by replanting them in SDA media and incubating them at 37°C for 48 hours. The results of this fungal rejuvenation were used to make fungal suspensions in SDB media with the same incubation conditions as before. This fungal suspension was then diluted with 0.9% NaCl solution until the turbidity was similar to the McFarland 0.5 standard which is equivalent to 0.5 x 108 CFU/mL. This equivalent fungal suspension was mixed into SDA media using the pour plate method and used as a medium for testing antifungal activity. Ethanol extract,

ethyl acetate, and n-hexane fraction were made solution by dimethylsulfoxide solvent while water fraction by sterile aquadest. All samples were made at 80%, 90%, and 100% concentration. The negative and positive control used samples solvent (DMSO and aquadest) and ketoconazole respectively. This test was repeated 3 times replications.

Data Analysis

Antifungal activity was shown by the formation of an inhibition zone around the paper disk. The diameter of inhibition zones was measured and calculated their mean ±SD. The data was statistically analyzed to determine the difference of antifungal activity from the water fraction of leaves and stem barks orange jasmine by a two-way ANOVA with a significance of $p<0.05$ to determine the differences in antifungal activity of the water fractions of leaves and bark of orange jasmine.

RESULT AND DISCUSSION

Extract and Fraction of Orange Jasmine Leaves and Stem Barks

The yields of extract and fractions of orange jasmine leaves and stem barks are shown in Table I. The weight of the fractions obtained has different weights, this is because the ability of each solvent to attract compounds is very different. As is the case with the like-dissolve-like system where polar compounds tend to dissolve in polar solvents because they have a high dielectric constant while non-polar compounds will dissolve in non-polar solvents because they have a low dielectric constant (Zhuang et al., 2021). The water fraction of leaves and bark of orange jasmine had the highest yield compared to the n-hexane fraction and the ethyl acetate fraction. The highest yield of several fractions of beet leaf extract is the water fraction, this is due to the presence of compounds with complex structures with high molecular weights that are easily soluble in water such as several types of sugars, glycosides, carbohydrates, and saponins and the large number of polar compounds contained (Anjaswati et al., 2021).

Table 1. The results of extraction extract and fractions from orange jasmine leaves and stem bark

Parts of the orange jasmine plant	Weight (g)				
	Simplicia powder	Ethanol extract	Fraction		
			n-Heksan	Ethyl acetate	Water
Leaves	1250	253.6	16.3	15.1	38
Stem barks	2250	146.2	7.6	6.5	11.9

The color profile of each extract and fraction of orange jasmine leaves and bark are presented in Table 2. The different colors of the extracts and fractions are due to the pigment content that is absorbed in these solvents. Green color appears in the ethanol extract, n-hexane fraction, and ethyl acetate of orange jasmine leaves, it is possible that chlorophyll pigment was absorbed into these solvents. Chlorophyll has been proven to be leachable in ethanol and n-hexane solvents (Lefebvre et al., 2020). The water fraction of orange jasmine leaves has a brown color, which indicates that chlorophyll pigment is not present in the water fraction. This shows that nonpolar and semipolar compounds have been extracted in the solvents n-hexane and ethyl acetate. The color of the kemuning bark is brown, the brown color is due to the presence of tannin compounds (Erfiza et al., 2021). The dark brown and slightly orange-brown color in the water

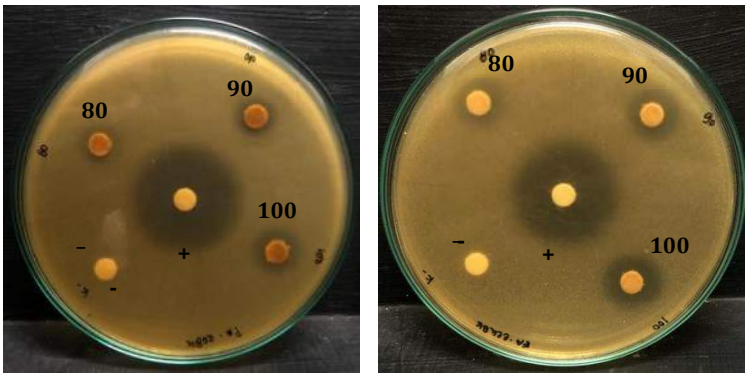
fraction of the leaves and bark of orange jasmine possibly indicates the presence of tannin compounds.

Table 2. The color of extract and fraction from leaves and stem bark of orange jasmine

Parts of the orange jasmine plant	Color			
	Ethanol extract	Fraction		
		n-Heksan	Ethyl acetate	Water
Leaves	Deep dark green	Dark green	Dark green	Dark brown
Stem barks	Dark brown	Greenish brown	Brown	Slightly orange brown

Antifungal Activity Test

The antifungal activity test results of the ethanol extract, n-hexane fraction, and ethyl acetate fraction of orange jasmine leaves and bark at concentrations of 80%, 90%, and 100% did not have antifungal activity against *M. furfur*. Only the water fraction of leaves and bark of orange jasmine has antifungal activity against *M. furfur* (Figure 1), so this fraction is the active fraction.



A **B**

Gambar 1. The inhibition of zones of water fraction of orange jasmine leaves (A) and stem bark (B) against *Malassezia furfur* in SDA medium

The absence of antifungal activity from the three test samples could possibly be caused by the unique properties of the *M. furfur* fungi. This fungi requires a source of long-chain fatty acids for its growth. Most saturated fatty acids and unsaturated fatty acids that have C12 – C24 chains provide external sources of lipids that are important for the growth of *Malassezia furfur*. This fungi can grow well in media with ghee (Dhanablan et al., 2022) which contains fatty acids such as oleic, arachidis, stearic, and palmitic acids (Pena-Serna et al., 2019) (Putri, 2018). According to research (Shah et al., 2014), orange jasmine herbs contain several fatty acids such as palmitic acid, stearic acid, and methyl stearate, and orange jasmine leaves contain methyl palmitate (Dosoky et al., 2016). This fatty acid can be extracted in the solvent's ethanol, n-hexane, and ethyl acetate. Ethanol solvent has a high ability to filter polar and non-polar compounds. The n-hexane solvent is a non-polar solvent that is capable of filtering non-polar compounds such as fats, fatty acid derivatives, and essential oils (Asmah et al., 2020). Ethyl acetate solvent is also quite capable of extracting fatty acids from Galician Algae (Otero et al., 2018) and essential oils from orange peel (Asmah et al., 2020). The presence of these fatty acids makes *M. furfur* more resistant because it is able to grow well. These results are supported by research results from (Syafriana et al., 2020)

(Syafriana et al., 2020), grape seed extract containing 10-20% oil consisting of fatty acids, was unable to inhibit the growth of *M. furfur*.

The presence of antifungal activity in the water fraction of leaves and bark of orange jasmine (Table 3) is indicated by the formation of an inhibition zone around the disk paper (Figure 1), possibly due to the presence of polar compounds which are mostly absorbed by the water solvent. This is supported by (Wagay et al., 2017) who stated that the water extract of orange jasmine stem bark contains polar compounds such as flavonoids, saponins, and glycosides. Flavonoid compounds, saponins, and glycosides may play an important role in inhibiting *M. furfur*. According to previous research, the water fraction of the ethanol extract of orange jasmine leaves contains active compounds, namely phenolics and flavonoids (Azizah & Ekawati, 2017). It is these phenolic and flavonoid compounds that are thought to act as antifungal agents. Flavonoids work as antifungals by disrupting plasma membranes, inducing mitochondrial dysfunction, inhibiting cell wall synthesis; cell division, protein synthesis, and efflux pumps (Saleh et al., 2020).

Malassezia sp. cell wall which is very thick and has a multilayer structure consisting of 70% sugars, 10% protein, and 15 – 20% lipids (Billamboz & Jawhara, 2023). These sugars tend to be polar so that the water fraction that is polar will more easily penetrate the sugar layer of the M. furfur cell wall compared to the non-polar lipid layer. This is because the lipid content is less than the sugar content of fungal cell walls.

Table 3. The diameter of inhibition zones from water fraction of ethanol extract of orange jasmine leaves and stem bark against *M. furfur*, Ø paperdisk 6mm

Parts of the orange jasmine plant	**The diameter of inhibition zones (mm)**				
	Concentration of water fraction (%)			**Positive control**	**Negative control**
	80	**90**	**100**		
Daun[a]	8.62±0.37	9.43±0.41	14.06±0.43	28.39±0.42	0
Kulit batang[a]	12.23±0.27	13.2±0.44	15.82±0.21	28.21±0.41	0

[a]nilai signifikansi <0.05

The statistical test results showed that there were differences in the antifungal activity of all concentrations of the water fractions of orange jasmine leaves and bark, meaning that the antifungal activity of the two test samples had different potential. At a concentration of 100%, it showed antifungal activity with the diameter of inhibition zone values greater than concentrations of 80 and 90% for both leaves and bark of orange jasmine. The levels of flavonoid compounds in orange jasmine bark are thought to have a higher antifungal effect than in orange jasmine leaves. The flavonoid content in the ethanol extract of kemuning stem bark was 892.35 mg/100 g QE (Putu et al., 2018) while the water extract of orange jasmine leaves was 63 ± 0.19 (mg QE /g) (Sabnam et al., 2020). Apart from that, tannin compounds are also contained in the water fraction of the leaves and bark of orange jasmine, but based on the visible color, they may have different tannin levels. Tannins, which are polyphenolic compounds, also have antifungal activity by inhibiting the enzyme that synthesizes ergosterol (Carvalho et al., 2018).

CONCLUSION

The active fraction that shows antifungal activity is the water fraction from the leaves and bark of orange jasmine. The water fraction of orange jasmine stem bark has higher antifungal activity against M. furfur than the water fraction of kemuning leaves. The water fraction from the leaves and bark of kemuning requires determining the levels of flavonoid and tannin compounds.

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