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Synthesis of Silver Nanoparticles Using Turmeric Infused and Antifungal Activity Against *Malassezia furfur* ATCC 14521

Sintesis Nanopartikel Perak Menggunakan Infusa Kunyit dan Aktivitas Antifungi *Malassezia furfur* ATCC 14521

Eliya Mursyida*[1], Olvaria Misfa[2], Santi Widiasari[3], Bellanera Alifia Safitri[4], Sabrina Hayati[5]
[1,2]*Department of Microbiology, Abdurrab University, Pekanbaru*
[3]*Department of Pharmacology, Abdurrab University, Pekanbaru*
[4]*Faculty of Medicine, Abdurrab University, Pekanbaru*
[5]*Department of Biochemistry, Abdurrab University, Pekanbaru*
Email koresponden: eliya_mursyida@univrab.ac.id

ABSTRACT

Malassezia furfur is a lipophilic fungus and part of the normal flora of the skin. Under certain conditions, Malassezia furfur can cause Pityriasis versicolor (Tinea versicolor). Pityriasis versicolor can generally be treated with azole antifungals. However, recently it has been widely known that *Malassezia furfur* has experienced resistance. Therefore, a nanoparticle approach was sought. This research aims to synthesize and characterize turmeric infused silver nanoparticles, as well as test the antifungal activity of silver nanoparticles against *Malassezia furfur*. This research method begins with preparation of turmeric infusion, synthesis of silver nanoparticles using turmeric infusion and characterization using a UV-Vis spectrophotometer, and testing the antifungal activity of silver nanoparticles with ratios of 1:2, 1:4, and 1:6 at a stirring time of 3 hours, 6 hours, and 24 hours using the well method. The results showed that the color of the solution changed from yellow to yellowish brown. Characterization of silver nanoparticles using a UV-Vis spectrophotometer obtained the highest absorbance value at a ratio of 1:6 with a stirring time of 24 hours with a wavelength of 393nm. The antifungal activity test showed that the highest inhibition zone was at a ratio of 1:6 with a stirring time of 6 hours with an average diameter of the inhibition zone of 8.17mm and the lowest was at a ratio of 1:6 with a stirring time of 24 hours with an average diameter of the inhibition zone of 2.78mm. Turmeric infusion can be used as a bioreduction in the synthesis of silver nanoparticles.

Keywords: Antifungal Activity, *Malassezia furfur*, Silver Nanoparticles, Turmeric Infusion

ABSTRAK

Malassezia furfur merupakan jamur lipofilik dan merupakan bagian dari flora normal kulit. Pada kondisi tertentu, *Malassezia furfur* dapat menyebabkan *Pityriasis versicolor* (*Tinea versicolor*). *Pityriasis versicolor* umumnya dapat diobati dengan antijamur azol. Namun, belakangan diketahui secara luas bahwa *Malassezia furfur* telah mengalami resistensi. Oleh karena itu, pendekatan nanopartikel dicari. Penelitian ini bertujuan untuk mensintesis dan mengkarakterisasi nanopartikel perak infus kunyit, serta menguji aktivitas antijamur nanopartikel perak terhadap *Malassezia furfur*. Metode penelitian ini diawali dengan pembuatan infusa kunyit, sintesis nanopartikel perak menggunakan infusa kunyit dan karakterisasi menggunakan spektrofotometer UV-Vis, serta pengujian aktivitas antijamur nanopartikel perak dengan

perbandingan 1:2, 1:4, dan 1:6 pada suhu kamar. waktu pengadukan 3 jam, 6 jam, dan 24 jam dengan menggunakan metode sumur. Hasil penelitian menunjukkan bahwa warna larutan berubah dari kuning menjadi coklat kekuningan. Karakterisasi nanopartikel perak menggunakan spektrofotometer UV-Vis diperoleh nilai serapan tertinggi pada perbandingan 1:6 dengan waktu pengadukan 24 jam dengan panjang gelombang 393nm. Uji aktivitas antijamur menunjukkan zona hambat tertinggi pada perbandingan 1:6 dengan waktu pengadukan 6 jam dengan rata-rata diameter zona hambat 8,17 mm dan terendah pada perbandingan 1:6 dengan pengadukan. waktu 24 jam dengan rata-rata diameter zona hambat 2,78mm. Infus kunyit dapat digunakan sebagai bioreduksi dalam sintesis nanopartikel perak.

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Kata kunci: Aktivitas Antifungi, *Malassezia furfur*, Nanopartikel Perak, Infusa Kunyit

INTRODUCTION

Malassezia furfur is a lipophilic fungus that is oval, cylindrical or round, singly or in pairs and sprouts, sometimes forming short chains, and can be found as part of the normal flora on human skin. Under certain conditions, this fungus causes Pityriasis versicolor and attacks all ages which is characterized by discrete macules, serpentine, and hyper or hypopigmentation of the skin. Several factors that can cause Pityriasis versicolor include a person's immune system, genetic factors, increased temperature and humidity (Riedel *et al*., 2019).

Pityriasis versicolor cases in Indonesia have not been reported accurately because most patients do not seek treatment at health care facilities (Wahid, 2021). However, research by Kristanty in Duy *et al*, (2020) proves that cases of Pityriasis versicolor isolated from Cipto Mangunkusumo Hospital, Jakarta prove that of the 98 patients infected it was caused by *Malassezia furfur* (42.9%), *M. sympodialis* (27.5%), *M. globosa* (13.3%), *M. slooffiae* (7.7%), *M. obtuse* (7.7%), and *M. limita* (2.2%). *Malassezia furfur* is well distributed in rural and urban, and mostly isolated on the back (39.56%), face (23.99%), and chest (16.51%).

Pityriasis versicolor caused by *Malassezia furfur* can usually be treated using azole antifungal. However, recent research has found that *Malassezia furfur* has developed resistance to the azole group, making treatment ineffective. Research by Yogiswara *et al*, (2018) shows that the antifungal miconazole has 62.5% resistance to *Malassezia furfur*. According to research by *Pote et al*, (2020) it also shows that *Candida* sp has experienced resistance to the antifungal itraconazole (78%), fluconazole (63%), clotrimazole (52%), and ketoconazole (43%). Apart from that, research by Shi *et al*, (2014) states that the azole group used topically has side effects, including causing erythema and dry skin or a burning sensation. Systemically, the side effects of the azole group are diarrhea, nausea, bloating and can be hepatotoxic (Gaol *et al*., 2022). Therefore, we are looking for alternative medicines based on natural ingredients using a nanoparticle approach (Laokor & Juntachai, 2021).

Nanoparticles are materials that include particles with a size of less than 100nm. Some of the most widely used metal nanoparticles are gold (Au), platinum (Pt), silver (Ag), and palladium (Pd) (Laurent *et al*., 2010 in Khan *et al*., 2019). Nanoparticles produced biosynthetically are known to have advantages, some of which are higher antimicrobial activity and more controlled size and shape (Zhao *et al*., 2022).

Turmeric is a plant that can be used as a bioreductant in the silver nanoparticle process. Turmeric is known to contain active compounds such as curcuminoids which include curcumin, desmetoxycurcumin (10%), and bisdesmetoxycurcumin (1-5%), essential oils which include sesquiterpenoid ketones, turmeron, tumeon (60%), zingiberen (25%), felandrene, sabinen, borneol, and cineole (Kusbiantoro & Purwaningrum, 2018). This research aims to synthesize and characterize turmeric infused silver nanoparticles, as well as test the antifungal activity of turmeric infused silver nanoparticles in inhibiting *Malassezia furfur* ATCC 14521.

METHODS

Tools and materials

The tools used in this research include UV-Vis spectrophotometer. The materials used in this research included turmeric rhizomes obtained from the plantation of the Faculty of Agriculture, Riau Islamic University, isolate *Malassezia furfur* ATCC 14521 obtained from the Microbiology-Parasitology Laboratory of Abdurrab University, silver nitrate ($AgNO_3$), distilled water, Whatmann paper No. 1, ketoconazole, Potato Dextrose Agar (PDA), Barium Chloride ($BaCl_2$) 1%, Sulfuric Acid (H_2SO_4) 1%, and Sodium Chloride (NaCl) 0.9%.

Green Synthesis of Silver Nanoparticles

Preparation of Plant Infusion

The turmeric (*Curcuma longa*) rhizomes that have been obtained are washed thoroughly using running water, then cut into small pieces and air-dried. Next, 400g of turmeric rhizomes were added to 800mL of distilled water and heated for 5 minutes. After that, the turmeric decoction was filtered using Whatmann No.1 paper and cooled (modified Siampa *et al*., 2020). Turmeric infusion is used as a reducing agent for silver nanoparticles.

Biosynthesis of Silver Nanoparticles

10mL of 1mM silver nitrate was mixed with 20mL, 40mL, and 60mL of turmeric infusion, then stirred using a magnetic stirrer at a speed of 150rpm at room temperature for 3 hours, 6 hours, and 24 hours. Next, the formation of silver nanoparticles was characterized using a UV-Vis Spectrophotometer (Marissa *et al*., 2016).

Characterization of Silver Nanoparticles

The characterization of silver nanoparticles can be observed by color changes and confirmation using a UV-Vis spectrophotometer. Where, the change in color of the solution from yellow to yellowish brown is an indicator of the formation of silver nanoparticles. Analysis of the results of the synthesis of silver nanoparticles using a UV-Vis spectrophotometer was carried out at a wavelength of 300-700nm at a stirring time of 3 hours, 6 hours and 24 hours (Siampa *et al.*, 2020).

Antifungal Activity of Silver Nanoparticles

Preparation of McFarland 0.5 Standard Solution

Making McFarland 0.5 solution is done by taking 9.95mL of 1% H_2SO_4 solution, then putting it in a test tube, and adding 0.05ml of 1% $BaCl_2$ solution. Next, the solution is homogenized until a cloudy solution is formed (Tomi *et al*., 2022).

Preparation of Positive Control Solution

A positive control was made by grinding the antifungal ketoconazole 200mg until finely ground. Next, 0.05g of ketoconazole was weighed and dissolved in 10mL of distilled water, then homogenized (Rahmawati & Rasiyanto, 2019).

Preparation of Fungal Suspension

The *Malassezia furfur* suspension is made by taking 2-3 loop of 48 hour old fungal colonies, then placing them in 10mL of 0.9% NaCl solution and homogenizing. The suspension made was compared with McFarland standard solution (Tomi *et al*., 2022).

Antifungal Test of Silver Nanoparticles Using the Well Diffusion Method

Malassezia furfur suspension which has been adjusted to the Mc Farland standard 0.5 is swabbed on PDA medium using a sterile cotton swab and left for 5 minutes. After that, 5 holes

were made using a 6mm diameter cork borer. Next, turmeric infused silver nanoparticles were inserted into each well hole at a concentration of 1:2, 1:4, 1:6 at the 3, 6, and 24 hours of stirring, positive control (ketoconazole), and negative control (distilled water) 20µL each, then incubated for 24 hours at 25^{o}C. After the incubation time, the inhibition zone formed around the well was measured using a caliper and calculated using the formula of well diameter minus the diameter of the inhibition zone.

Data analysis

The data obtained was analyzed descriptively, and presented in the form of tables and figures.

RESULTS AND DISCUSSION

The results of the synthesis of silver nanoparticles using turmeric infusion with varying stirring times showed a change in the color of the solution from yellow to yellowish brown (Figure 1). In the results of characterization of silver nanoparticles using a UV-Vis spectrophotometer at a wavelength of 300-700nm, the maximum absorbance value was obtained, namely 2.92 for a 1:6 ratio, 3 hours of stirring time at a wavelength of 393nm, 3.2 for a 1:6 ratio, 6 hours of stirring time. hours at a wavelength of 373nm, and 3.25 for a 1:6 ratio of 24 hours of stirring time at a wavelength of 393nm (Figure 2).

Based on the results of the synthesis of silver nanoparticles using turmeric infusion, it showed a change in the color of the solution from yellow to yellowish brown from 3 hours to 24 hours of observation. This indicates that more silver nanoparticles are formed as the reduction time increases. This research is in accordance with Alsammarraie *et al*, (2018) who found that curcumin extract isolated from turmeric with the addition of $AgNO_3$ was able to reduce Ag^+ ions after incubation at room temperature for 24 hours which was characterized by the formation of a color change from yellow to light brown, brown, and finally reddish brown. The results of the synthesis of silver nanoparticles occur because the compounds found in natural materials are able to convert Ag^+ ions into Ag^0 (Haryani *et al.*, 2016).

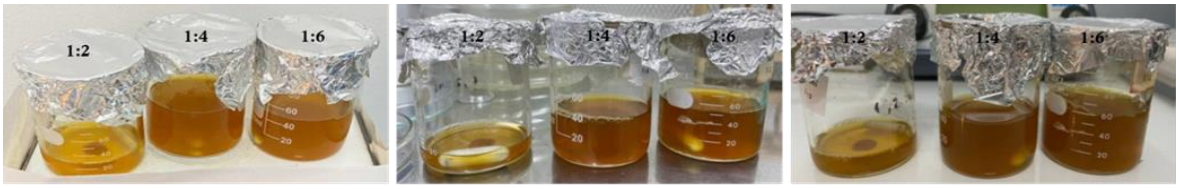

Figure 1. Synthesis of silver nanoparticles using turmeric infusion. (A). Stirring time 3 hours, (B). Stirring time 6 hours, and (C). Stirring time 24 hours.

The results of the antifungal activity test of silver nanoparticles showed that silver nanoparticles were able to inhibit the growth of *Malassezia furfur* which was characterized by the formation of a clear zone around the well (Figure 3). The highest inhibitory zone diameter was found in a ratio of 1:6 with a stirring time of 6 hours with an average diameter of 8.71mm, while the lowest inhibitory power was found in a ratio of 1:6 with a stirring time of 24 hours with an average diameter of 2.78mm (Table 1). In the positive control (ketoconazole) the largest average diameter of the inhibition zone was 5.28 mm, whereas in the negative control no inhibition zone was formed around the wells.

In Figure 2, the results of the nanoparticle characterization test using a UV-Visible spectrophotometer show that the wavelength of silver nanoparticles ranges from 300-442nm with an absorption value of 1.4-3.25. This shows that turmeric infusion acts as a bioreductor in the formation of silver nanoparticles. Previous research, Haryani *et al*, (2016) said that the longer the solution synthesis time, the greater the resulting absorption value until no more Ag^+ is reduced to

Ag^0. Sari *et al*, (2017) said that time influences the process of forming silver nanoparticles, because the absorption spectrum of silver nanoparticles tends to increase as the synthesis time increases. According to Nidianti *et al*, (2021) the wavelength of turmeric extract nanoparticles ranges from 270-420nm with an absorption value of 3.8-4.2. Several factors cause differences in absorbance results in nanoparticle synthesis, including the extraction process used, the concentration used (Clara *et al*., 2022).

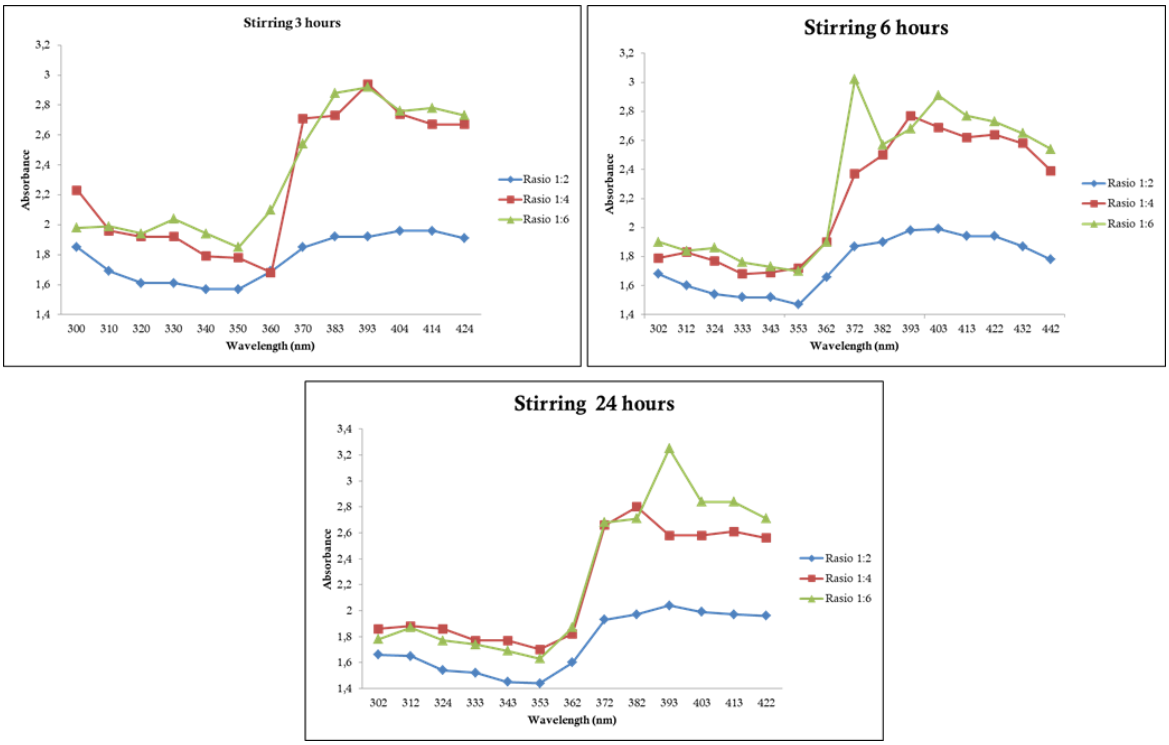

Figure 2. Silver nanoparticle UV-Vis spectrophotometer results.

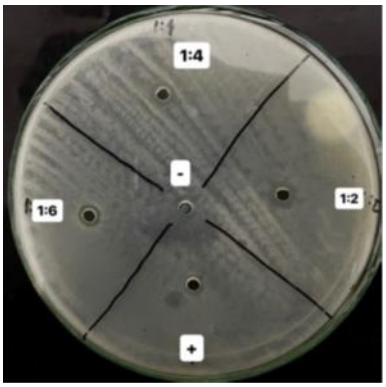

Figure 3. Inhibition zone of silver nanoparticles in inhibiting *Malassezia furfur* on PDA media. Note: (+) = positive control and (-) negative control.

Table 1 shows that silver nanoparticles at various ratios and stirring times were able to inhibit the growth of *Malassezia furfur* on PDA medium. Research by Kosimaningrum *et al*, (2020) stated that silver ions in the medium can inhibit the growth of fungi and fungal spores. The antifungal mechanism of silver nanoparticles begins with the attachment of silver ions to the fungal membrane which causes damage and disrupts the electron transport process. Furthermore, silver

ions enter fungal cells, causing damage to proteins, membranes, deoxyribonucleic acid (DNA), and disrupting nutrient absorption (Cruz-Luna *et al*., 2021).

Table 1. Inhibition zone of silver nanoparticles in inhibiting *Malassezia furfur* at various ratios and stirring times

Treatment	Mean ± SD		
	3 hours	6 hours	24 hours
C-AgNP 1:2	6.51 ± 1.3	5.00 ± 1.35	3.8 ± 0.63
C-AgNP 1:4	5.78 ± 1.49	6.31 ± 0.75	4.26 ± 1.04
C-AgNP 1:6	4.11 ± 1.07	8.71 ± 0.65	2.78 ± 0.64
Control positive	1.48 ± 0.5	4.43 ± 0.9	5.28 ± 0.91
Control negative	0	0	0

Research by Paul *et al*, (2018) found that the synthesis of silver nanoparticles using turmeric infusion was able to inhibit the growth of *Candida* sp. with the diameter of the inhibition zone, namely for *C. glabrata* 12mm, for *C. albicans* 10mm, for *C. krusei* 9mm, for *C. tropica* 8.6mm, for *C. parapsilosis* 8.1mm, and for *C. kefir* 7.8mm. When compared with this study, the inhibitory power results obtained were slightly lower. This is probably because the heating time for the infusion is only short, namely 5 minutes, so that the active turmeric compound obtained is not perfect and the ratio between $AgNO_3$ and the infusion used means that the pharmacological effect may not be good (Sembiring & Suhirman, 2014).

CONCLUSION

Based on the results of the research conducted, it can be concluded that turmeric infusion can be used as a bioreductor. Silver nanoparticles were best demonstrated at a ratio of 1:6 with 24 hours stirring. Silver nanoparticles were able to inhibit the growth of *Malassezia furfur* at all ratios.

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