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Antifungal Activity of Red Ginger (*Zingiber officinale var. Rubrum*) and Garlic (*Allium sativum)* against HIV Patients-Isolated *Candida albicans*

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Abstract: The most of *Candida* strain in oral candidiasis is nystatin resistance strain. Hence, it become important to investigate the natural products like red ginger (*Zingiber officinale var. Rubrum*) and garlic (*Allium sativum*) as antifungal against HIV patient-isolated *Candida albicans*. This experimental study used two antifungal assays (Disc diffusion and antibiofilm assay). Both red ginger and garlic extract were extracted by maceration method. *Candida albicans* isolate was isolated from a volunteer HIV Patient with oral candidiasis. The outcomes included the diameter of the inhibition zone and optical density (OD) that were expressed as mean and standard deviation and analysed by Kruskal-Walis. This study showed that the highest concentration of both red ginger (0.67 ± 0.55 mm) and garlic extract (0.67 ± 0.46 mm) had the widest diameter of inhibition zone. Meanwhile, the highest inhibition of biofilm formation was found in the lowest concentrations (25%) of red ginger (2.22 ± 1.24) and garlic extract (3.65 ± 0.24). Any concentration of red ginger or garlic extract did not significantly affect the antifungal activity (P-Value: 0.392). Overall, it can be concluded that both red ginger and garlic extract at any concentration showed a weak antifungal activity against HIV patient-isolated *Candida albicans* strain.

Keywords: Antifungal; *Candida albicans*; Garlic; HIV; Red ginger

Introduction

Candidiasis does not only become a serious health burden in some countries but also a national health burden. Kemal et al. (2017) also reported that the rate of invasive candidiasis in Ciptomangunkusumo General Hospital was 12.3%. Another study by Yusri et al. (2012) in Adam Malik General Hospital reported a similar result. Yusri et al. (2012) reported that there were 109 patients out of 309 total patients (35.28%) suffer from Vulvovaginal candidiasis as the most common opportunistic infection (Kalista et al., 2017; Ratha, 2019). Some risk factors reported to affect the incidence of candidiasis to become opportunistic, including local or systemic factors. Local factors include dentures, smoking, inhaled steroids, hyperkeratosis, microflora imbalance, and both quantity and quality of saliva. Meanwhile, the systemic factors include immunosuppressive diseases, chemotherapy, and immunodeficiency diseases (Sadeghi et al., 2020).

Some drugs have been used to treat candidiasis; the most common is nystatin. Nystatin is an active polyene macrolide with pharmaceuticals such as oral suspension, topical cream, and oral pastille. However, this drug has some inconvenient adverse drug effects, including nausea, vomiting, diarrhoea, and mildly irritation for topical pharmaceutical. Ironically, Paula et al. (2015) also found five Candida albicans isolates with nystatin resistance activity in HIV-infected patients in Londrina-PR, Brazil. Due to this reason, it has become important to look for newer antifungal compounds with fewer adverse drug effects and higher efficacy. Some

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studies have looked for natural products potentially acting as a newer natural antifungal drug. Some of these natural products were garlic and red ginger (de Paula et al., 2015).

The community has widely used garlic (*Allium sativum*) as an herb. Previous studies have reported that garlic extract has pharmacological properties, including anti-inflammatory, anti-diabetic, antibacterial, antifungal, antioxidant, and antiprotozoal. These pharmacology properties are due to the sulfur-contain phytochemicals, including allicin, diallyl disulfide, and diallyl trisulfide. Allicin is an organosulfur compound with characterised and pungent odour with antimicrobial activity. Furthermore, Ayesha et al. (2022) reported that garlic had an anti-biofilm formation for *Candida albicans* with MIC of 12.5 g/ ml (Fahim et al., 2022; Rahmatika & Oktaria, 2021; Zainal et al., 2021).

Another local natural product widely studied is red ginger or *Zingiber officinale var. Rubrum*). It has higher essential oil (3.9%) and oleoresin (7-10%) levels than other ginger type. Both essential oil and oleoresin have antibacterial activity, inhibiting cell wall formation (Zainal et al., 2021)**.** Khalaf et al. (2020) reported that ginger alcoholic extract had potential antifungal activity against *Candida albicans*. The concentration of 50 mg/ ml, 100 mg/ ml, and 150 mg/ ml of ginger alcoholic extract form 18 mm, 21 mm, and 25 mm rates of inhibition zone, respectively (Khalaf et al., 2020). Another study by Suraini et al. (2021) reported that ginger and Curcuma infusion also inhibited the growth of Candida albicans at a concentration of 100% (Suraini & Putri, 2018). Interestingly, some studies also reported that white ginger has antifungal activity against *Candida albicans* and antibacterial activity against *Pseudomonas aeruginosa* (Kasetty et al., 2021).

Based on the information above, it becomes important to investigate the antifungal activity from red ginger (*Zingiber officinale var. Rubrum*) and garlic (*Allium sativum*) against *Candida albicans* that was isolated from an immunosuppressive patient especially HIV patients, by antibiofilm and disc diffusion methods. When the nystatin-resistance *Candida albicans* was high in community.

Method

This experimental study used two methods: disc diffusion and antibiofilm. This study was performed in Microbiology and Integrated Laboratory, Universitas Sumatera Utara, Medan, from June 2023 to July 2023. Research procedure is also described in Figure 1.

This study used some materials, including red ginger, garlic, 96% ethanol, HIV Patient-isolated Candida albicans strain, sterile distilled water, normal saline, phenol cotton blue staining, KOH solution, 10% DMSO solution, SDA (Sabouroud Dextrose Agar), and SDB (Sabouroud Dextrose Broth).

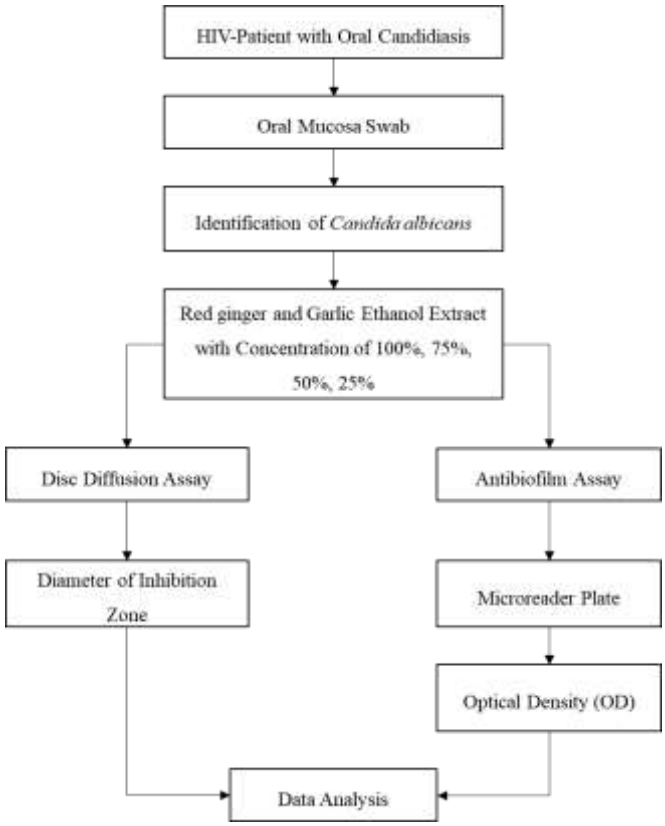

Figure 1. Research flow

Both red ginger and garlic were cleaned and washed under running water. Then, red ginger and garlic were peeled and cut into small pieces. After that, these red ginger and garlic were dried without sunlight exposure, and these dried red ginger and garlic meshed into simplicial powder. Both simplicial powders were extracted by maceration method. Five hundred grams of red ginger and garlic were soaked into 1,500 millilitres of 96% ethanol solution for 3 days and stirred regularly twelve times, fifteen minutes each time. Then, it was filtered, and a rotary evaporator evaporated the filtrate until it formed a concentrated extract (Chiuman, 2019).

This study used two different extracts that were red ginger and garlic. Both concentrated extracts were diluted into four variation concentrations, which were 100%, 75%, 50%, and 35%. Amounts of 1.00 gram, 0.75 gram, 0.50 gram, and 0.25 gram of concentrated extract were diluted into 100 millilitres of 10% DMSO to form concentrations of 100%, 75%, 50%, and 35%, respectively (Gulo et al., 2021; Suhartomi et al., 2020).

Preparation of media was performed based on SDA and SDB manufacturer's instructions. SDA and SDB media were made by dissolving 65 grams of SDA powder and 30 grams of SDB powder into a litre of distilled water, then heating and stirring with a magnetic

stirrer until completely dissolved. After that, these media were sterilised by autoclave at a temperature of 121oC and a pressure of 1.5 atm for 15 minutes (Chiuman et al., 2023; Kaul et al., 2020).

Candida albicans isolate was obtained from a volunteer HIV patient with oral candidiasis. After that, a cotton swab was swabbed into a white-coated membrane in the oral cavity, and this cotton swab was sterilely delivered to Microbiology and Integrated Laboratory, Universitas Sumatera Utara, Medan to undergo enrichment, multilevel dilution, and purification by quadrant streak plate method. Thus, it resulted in the HIV patient-isolated Candida albicans isolates in SBA Media (Harijani et al., 2013; Irza et al., 2021).

The obtained Candida albicans isolates in SBA media were initially identified by KOH and phenol cotton blue staining under a microscope. After the isolation was confirmed, the isolate was suspended in SDB media and chilled at room temperature for 18-24 hours. After that, this suspension was vortex until it was cloudy and determined the absorbance at 625 nm wavelength. This study required a suspension with 0.5 McFarland standard, equal to absorbance of 0.08-0.13 and indicated an enumeration of Candida albicans colony was 1.0 x 106 CFU/ ml (Mutia et al., 2021).

Disc diffusion assay was performed by streaking the HIV patients-isolated Candida albicans suspension into the surface of SDA media with a sterile cotton swab. All disc papers were diffused into various concentrations, positive control (nystatin) and negative control (distilled water). These disc papers were placed on the surface of SDA. Finally, all Petri dishes were incubated at 30oC for 24 hours, and the inhibition zone was measured by a calliper (Chiuman et al., 2023; Mutia et al., 2021).

Biofilm formation assay used Microtiter Plate Biofilm Assay methods in microplate flexible U-bottom PVC 96-well. Ten microlitres of all concentrations of red ginger and garlic extract, negative and positive control, were filled into each column, followed by adding 10 µL of Candida albicans fungal suspension, and it was incubated for 24 hours at 37oC. After 24 hours, the microplate was washed thrice with sterile Phosphate Buffer Saline (PBS). Then, it was added by 200 µL of methanol for 15 minutes, discarded, and dried. After that, it was added by 200 µL of 2% crystal violet, waited for five minutes, washed the microplate with PBS, and added 200 µL of 33% glacial acetic acid. Finally, the biofilm formation was measured by spectrophotometry at a wavelength of 570nm, and it was expressed as an absorbance or optical density (OD) (Nasution et al., 2023).

All data were expressed as Mean and standard deviation for descriptive statistics. After that, the diameter of the inhibition zone and optical density (OD) were analysed by Kruskal-Walis.

Result and Discussion

The antifungal activity of the red ginger extract against the *Candida albicans* based on the Disc diffusion method is described in Table 1.

Table 1. Antifungal Activity of Red Ginger Extract against the *Candida Albicans*

Conc.	Diameter of Inhibition Zone, mm			Mean	SD	P-Value
	1st	2nd	3rd			
100%	0.4	0.3	1.3	0.67	0.55	0.392
75%	0.2	0.3	1.3	0.60	0.61	
50%	0.2	0.3	1.2	0.57	0.55	
25%	0.1	0.3	1.0	0.47	0.47	

Table 1 showed that the widest inhibition zone was found in 100% of red ginger extract, that was 0.67 ± 0.55 mm, followed by 75% of red ginger extract (0.60 ± 0.61 mm), 50% of red ginger extract (0.57 ± 0.55 mm), and the narrowest was 25% of red ginger extract (0.47 ± 0.47 mm). Furthermore, the antifungal activity of another sample, that was garlic extract based on the disc diffusion method, is described in Table 2.

Table 2. Antifungal Activity of Garlic Extract against the *Candida albicans*

Conc.	Diameter of Inhibition Zone, mm			Mean	SD	P-Value
	1st	2nd	3rd			
100%	0.4	0.4	1.2	0.67	0.46	0.392
75%	0.2	0.4	1.2	0.60	0.53	
50%	0.2	0.3	1.2	0.57	0.55	
25%	0.1	0.3	1.0	0.47	0.47	

Table 2 showed that the widest inhibition zone was found in 100% of garlic extract, that was 0.67 ± 0.46 mm, followed by 75% of garlic extract (0.60 ± 0.53 mm), 50% of garlic extract (0.57 ± 0.55 mm), and the narrowest was 25% of garlic extract (0.47 ± 0.47 mm). On the other hand, this study also has two control groups, which were positive and negative groups and the antifungal activity from these control groups is described in Table 3.

Table 3. Antifungal Activity of Control Groups against the *Candida albicans*

Groups	Diameter of Inhibition Zone, mm
Nystatin (Positive Control)	23.8
Distilled Water (Negative Control)	0

Table 3 showed that both positive and negative control groups underwent no repetitions. Only the nystatin was the positive control group that formed of inhibition zone with a diameter of 23.8 mm. Meanwhile, the negative group did not form any inhibition zone. According to these formed inhibition zones, the degree of antifungal activity was described in Table 4.

Table 4. Degree of Antifungal Activity Based on Diameter of Inhibition Zone in All Groups

Groups	Concentration	Degree of Antifungal Activity
Red Ginger Extract	100%	Weak
	75%	Weak
	50%	Weak
	25%	Weak
Garlic Extract	100%	Weak
	75%	Weak
	50%	Weak
	25%	Weak
Nystatin (Positive Control)		Very Potent
Distilled Water (Negative Control)		None

Table 4 showed that red ginger and garlic extract had only weak antifungal activity against HIV patient-isolated Candida albicans. Meanwhile, the positive group revealed a very potent antifungal activity as a positive control group. Furthermore, this study also evaluated the inhibition of *Candida albicans* biofilm formation activity in red ginger extract, described in Table 5.

Table 5. Inhibition of *Candida albicans* Biofilm Formation in Red Ginger Extract

Conc.	Optical Density (OD) 630nm			Mean	SD	P-Value
	1st	2nd	3rd			
100%	1.263	1.113	1.676	1.35	0.29	0.392
75%	0.706	0.659	0.988	0.78	0.18	
50%	0.632	0.554	0.902	0.70	0.18	
25%	2.924	0.791	2.949	2.22	1.24	

Table 6. Inhibition of *Candida albicans* Biofilm Formation in Garlic Extract

Conc.	Optical Density (OD) 630nm			Mean	SD	P-Value
	1st	2nd	3rd			
100%	3.605	3.143	3.844	3.53	0.36	0.392
75%	3.087	3.098	3.352	3.18	0.15	
50%	3.298	3.710	3.726	3.58	0.24	
25%	3.423	3.907	3.609	3.65	0.24	

Table 5 showed that red ginger extract at the lowest concentration (25%) showed the highest OD630nm, which was 2.22 ± 1.24, followed by the highest concentration (100%) of red ginger extract (1.35 ± 0.29), 75% of red ginger extract (0.78 ± 0.18), and the lowest OD630nm was revealed by 50% of red ginger extract (0.70 ± 0.18). Meanwhile, the inhibition of Candida albicans biofilm formation from garlic extract was described in Table 6.

Table 6 showed that the highest OD630nm was found in 25% of garlic extract, which was 3.65 ± 0.24, followed by a higher concentration (50%) of garlic extract (3.58 ± 0.24), 100% of garlic extract (3.53 ± 0.36), and the lowest OD630nm was revealed by 75% of garlic extract (3.18 ± 0.15). Furthermore, the inhibition of Candida albicans biofilm activity from control groups as the comparison was described in Table 7.

Table 7. Inhibition of Candida albicans Biofilm Formation in Control Groups

Groups	Optical Density (OD) 630nm			Mean	SD
	1st	2nd	3rd		
Nystatin (Positive Control)	0.065	0.069	0.081	0.07	0.01
Distilled Water (Negative Control)	0.081	0.090	0.068	0.08	0.01

Table 7 above showed that the OD630nm from the nystatin group as positive control and distilled water group as negative control were 0.07 ± 0.01 and 0.08 ± 0.01, respectively. According to the OD630nm value above, the degree of inhibition for *Candida albicans* biofilm formation in all groups was described in Table 8.

Table 8. Degree of Inhibition for *Candida albicans* Biofilm Formation in All Groups

Groups	Concentration	Degree of Inhibition
Red Ginger Extract	100%	Weak
	75%	Weak
	50%	Weak
	25%	Weak
Garlic Extract	100%	Weak
	75%	Weak
	50%	Weak
	25%	Weak
Nystatin (Positive Control)		Potent
Distilled Water (Negative Control)		Weak

Table 8 above showed that red ginger and garlic extract at either concentration have weak inhibition activity for *Candida albicans* biofilm formation. Meanwhile, the nystatin as positive control group showed opposite inhibition activity, potent inhibition activity for *Candida albicans* biofilm formation.

The resulting study showed that red ginger and garlic extract have weak antifungal activity against HIV patients-isolated Candida albicans. It can be seen from the diameter of the inhibition zone, which was lower than the positive group (Nystatin) and higher than the negative control (distilled water). Furthermore, this

study also showed that red ginger and garlic inhibited Candida albicans biofilm formation. However, the change in extract concentration did not significantly affect the antifungal or inhibition of biofilm formation, as seen from P-Value > 0.05 (P-Value: 0.392).

This study used nystatin as a positive control because this drug has been widely used to treat oral candidiasis. Dwi et al. (2019) reported that oral nystatin still has good sensitivity for antifungal in oral candidiasis cases among the HIV/AIDS patient in RSU dr. Soetomo. The effective dose of nystatin was reported at a range of 400,000-600,000 U/ ml four times a day for 7-14 days (Murtiastutik et al., 2019).

Some previous studies also reported a similar result to a recent study. Rahmawati et al. reported that 25% of n-butanol garlic extract could inhibit *Candida albicans*' growth, equal to positive control (Samsudin et al., 2017). Dubia et al. also reported that garlic ethanol extract can inhibit the growth of *Candida albicans* based on the disc diffusion method. The average inhibition zone for 100%, 80%, 60%, and 40% of garlic ethanol extract were 21.40, 18.60 mm, 14.80 mm, and 11.60 mm, respectively. Moreover, the lowest concentration of garlic extract (20%) did not show any inhibition zone (Andayani & Kurniawan, 2014). Another study by Purify et al. and Indrawaswary et al. reported a weaker antifungal activity. Purify et al. reported the average inhibition zone for 25%, 50%, 75%, and 100% of garlic extract were 0.16 mm, 0.57 mm, 2.33 mm, and 3.04 mm, respectively. Indaswary et al. reported that the average inhibition zone for 75% and 100% garlic was 6.56 mm and 11.15 mm, respectively. The two lowest concentrations, 25% and 50% of garlic extract, showed no antifungal activity against the *Candida albicans* (Indraswari et al., 2022; Sabila et al., 2019).

The antifungal activity of garlic comes from a bioactive compound in the garlic extract. Monica et al. reported that some factor affects the quantity and quality of bioactive compound in garlic extract, including temperature, extraction method, solvent properties, size, and origin of garlic. When the extraction process uses water solvent, it promotes the antimicrobial activity of garlic. On the other hand, an alcohol-based solvent, including methanol and ethanol, promotes garlic's antioxidant activity, which is associated with highly extracted phenolic compounds by alcohol-based solvent. This antifungal activity in garlic extract was due to the presence of allicin in garlic extract. Zainal et al. reported that allicin in garlic extract can inhibit the formation of *Candida albicans* and *Staphylococcus aureus* biofilm. It can be seen from the MIC and MFC that were 8 mg/ ml and 16 mg/ ml, respectively. Meanwhile, both MIC and MBC of *Staphylococcus aureus* were 8 mg/ ml (Zainal et al., 2021).

This study also evaluated antifungal activity from a different sample, red ginger. Some previous studies have reported antifungal activity from red ginger against *Candida albicans*. Aghazadeh et al. reported that ginger extract has significant antifungal activity in two fungal species, including *Candida albicans* and *Candida krusei*. It can be seen from P-Value < 0.05 that the ginger MIC was higher than the fluconazole and nystatin (Aghazadeh et al., 2016). Some factors can affect the quality of red ginger and the quantity and quality of phytochemical and essential oil content in red ginger. These factors include cultivation method, quality of the cultivation, quality of manure, and harvest method (Aidin et al., 2016; Ibrahim et al., 2015; Saputri et al., 2018).

Conclusion

Overall, it can be concluded that both red ginger and garlic extract have antifungal activity against HIV patient-isolated *Candida albicans*. Changes in concentration from 25% to 100% from both extracts did not significantly affect antifungal activity or biofilm formation (P-Value > 0.05). The inhibition antifungal assay also showed the weak inhibition of biofilm formation in *Candida albicans*.

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Author Contributions
Conceptualization: EW, ANN, and SWN; Methodology: EW and ANN; Investigation: EW; Discussion of results: EW; Writing – Original Draft: EW; Writing – Review and Editing: SWN and ANN; Supervision: SWN and ANN; Approval of the final text: EW, ANN, and SWN.

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Conflicts of Interest
The authors declare no conflict of interest.

References

Adhikari, K. L. N., Bastola, A., Devkota, L., Bhandari, P., Dhungel, B., Bipin Adhikari, U. T. S., Banjara, M. R., Rijal, K. R., & Ghimire, P. (2020). Biofilm-producing candida species causing oropharyngeal candidiasis in hiv patients attending sukraraj tropical and infectious diseases hospital in kathmandu, nepal. *HIV/AIDS - Research and Palliative Care*, *12*, 211–220. https://doi.org/10.2147/HIV.S255698

Aghazadeh, M., Bialvaei, A. Z., Aghazadeh, M., Kabiri, F., Saliani, N., Yousefi, M., Eslami, H., & Kafil, H.

S. (2016). Survey of the antibiofilm and antimicrobial effects of Zingiber officinale (In vitro study). *Jundishapur Journal of Microbiology*, *9*(2), 1–6. https://doi.org/10.5812/jjm.30167

Aidin, A., Sahiri, N., & Madauna, I. (2016). The Effect of Rhizome Types and The Composition of Planting Media on The Growth of Red Ginger (Zingiber Officinale Rosc.). *E-J. Agrotekbis*, *4*(4), 394–402. Retrieved from http://jurnal.faperta.untad.ac.id/index.php/agrotekbis/article/view/37

Andayani, D., & Kurniawan, R. A. (2014). Uji Daya Hambat Ekstrak Etanol Bawang Putih Tunggal (Allium Sativum L.) terhadap Jamur (Candida Albicans) Dahlia. *Jurnal Ilmu Kesehatan Dan Farmasi*, *2*(1), 15–19. Retrieved from https://ejournal.unwmataram.ac.id/jikf/article/view/124

Chiuman, L. (2019). Protective Effect of Curcuma zedoria Against Copper in Rats' White Blood Cell. *American Scientific Research Journal for Engineering, Technology, and Sciences (ASRJETS)*, *59*(1), 142–148. Retrieved from https://core.ac.uk/download/pdf/235050884.pdf

Chiuman, L., Sherlyn, Aritonang, N. S., Rudy, & Suhartomi. (2023). In Vitro Study of Antibacterial Activity of Snake Fruit Extract against Extended Spectrum Beta Lactamase (ESBL) Escherichia coli. *Jurnal Aisyah : Jurnal Ilmu Kesehatan*, *8*(2), 715–720. https://doi.org/10.30604/jika.v8i2.1962

de Paula, S. B., Morey, A. T., Santos, J. P., dos Santos, P. M. C., Gameiro, D. G., Kerbauy, G., Sena, E. M., Ueda, L. T., Carneiro, M., Pinge-Filho, P., Yamauchi, L. M., & Yamada-Ogatta, S. F. (2015). Oral Candida colonization in HIV-infected patients in Londrina-PR, Brazil: Antifungal susceptibility and virulence factors. *Journal of Infection in Developing Countries*, *9*(12), 1350–1359. https://doi.org/10.3855/jidc.6970

Fahim, A., Himratul-Aznita, W. H., Abdul-Rahman, P. S., & Alam, M. K. (2022). Efficacy of bakuchiol-garlic combination against virulent genes of Candida albicans. *PeerJ*, *10*(e12251), 1–13. https://doi.org/10.7717/peerj.12251

Gulo, K. N., Suhartomi, Saragih, A. D., Raif, M. A., & Ikhtiari, R. (2021). Antioxidant Activity of Flavonoid Compounds in Ethanol and Ethyl Acetate Extract from Citrus Sinensis. *AIMS 2021 - International Conference on Artificial Intelligence and Mechatronics Systems*, 1–6. https://doi.org/10.1109/AIMS52415.2021.9466078

Harijani, N., Rahadi, U. S. E., & Nazar, D. S. (2013). The Isolation of Escherichia coli from the Meat Some Traditional Markets in the South Surabaya. *Veterinaria Medika*, *6*(1), 39–44. Retrieved from https://journal.unair.ac.id/filerPDF/abstrak_614128_tpjua.pdf

Huang, F., Song, Y., Chen, W., Liu, Q., Wang, Q., Liu, W., Wang, X., & Wang, W. (2019). Effects of Candida albicans infection on defense effector secretion by human oral mucosal epithelial cells. *Archives of Oral Biology*, *103*(February), 55–61. https://doi.org/10.1016/j.archoralbio.2019.05.013

Ibrahim, A. M., Sriherfyna, F. H., & Yunianta. (2015). Pengaruh Suhu dan Lama Waktu Ekstraksi Terhadap Sifat Kimia dan FIsik pada Pembuatan Minuman Sari JAhe Merah (Zingiber officinale var. Rubrum) dengan Kombinasi Penambahan Madu sebagai Pemanis. *Jurnal Pangan Dan Agroindustri*, *3*(2), 530–541. Retrieved from https://jpa.ub.ac.id/index.php/jpa/article/view/171

Indraswari, N. M. W. S., Setyowati, D. I., & Hamzah, Z. (2022). Efektivitas Ekstrak Bawang Putih dan Bawang Hitam dalam Menghambat Pertumbuhan Candida albicans. *Pustaka Kesehatan, 10*(2), 114-119. Retrieved from https://garuda.kemdikbud.go.id/documents/detail/2895456

Irza, D. A., Lister, I. N. E., Sihotang, S., & Fachrial, E. (2021). Isolation, Characterization, Molecular Identification of Probiotic Bacteria from Meconium. *IOP Conference Series: Earth and Environmental Science*, 1–10. https://doi.org/10.1088/1755-1315/755/1/012041

Kalista, K., Lie, K., Wahyuningsih, R., & Rumende, C. (2017). Karakteristik Klinis dan Prevalensi Pasien Kandidiasis Invasif di Rumah Sakit Cipto Mangunkusumo. *Jurnal Penyakit Dalam Indonesia*, *4*, 56. https://doi.org/10.7454/jpdi.v4i2.104

Kasetty, S., Mould, D. L., Hogan, D. A., & Nadell, C. D. (2021). Both Pseudomonas aeruginosa and Candida albicans Accumulate Greater Biomass in Dual-Species Biofilms under Flow. *American Society for Microbiology*, *6*(3), 2021. https://doi.org/10.1128/msphere.00416-21

Kaul, D. R., Flanders, S. A., Beck, J. M., Saint, S., Kartikawati, E., Deswati, D. A., Pramudita, B., Limper, M., Eeftinck Schattenkerk, D., de Kruif, M. D., van Wissen, M., Brandjes, D. P. M., Duits, A. J., van Gorp, E. C. M., Hendra, R., Masdeatresa, L., Almurdani, M., Abdulah, R., Haryani, Y., & Rahmawati, M. (2020). Antifungal Activity of Red Dragon Peel (Hylocereus polyrhizus). *Jurnal Sabdariffarma*, *21*(1), 124–128.

Khalaf, A. A., Al-Aedany, A. J. M., & Hussein, S. F. (2020). Activity evaluation of ginger (Zingiber

officinale) alcoholic extract against Candida albicans. *AIP Conference Proceedings*, *2290*. https://doi.org/10.1063/5.0029718

Murtiastutik, D., Maharani, C. S., Rahmadewi, & Listiawan, M. Y. (2019). Nystatin profile on Candida species in HIV/AIDS patients with oral candidiasis: A phenomenology study. *Journal of Pure and Applied Microbiology*, *13*(4), 2013–2019. https://doi.org/10.22207/JPAM.13.4.12

Mutia, M. S., Annisa, E., & Suhartomi. (2021). Anti-Bacterial Activity of Ethanol Extract of Indian Borage (Coleus Amboinicus) Leaves against Bacillus Cereus. *Healthy Tadulako Journal (Jurnal Kesehatan Tadulako)*, *7*(1), 30–34. https://doi.org/10.22487/htj.v7i1.151

Mutiawati, V. K. (2016). Pemeriksaan Mikrobiologi pada Candida albicans. *Jurnal Kedokteran Syiah Kuala*, *16*(1), 2016. https://doi.org/10.1016/s0035-9203(03)90055-1

Nasution, A. N., Sari Mutia, M., & Susilo, R. I. (2023). Antibacterial Activity of Mahkota Dewa (Phaleria macrocarpa) Leaves Extract against Propionibacterium acne. *Jurnal Teknologi Laboratorium*, *11*(1), 4–13. https://doi.org/10.29238/teknolabjournal.v12i1.393

Noguchi, H., Iwase, T., Omagari, D., Asano, M., Nakamura, R., Ueki, K., Shinozuka, K., Kaneko, T., Tonogi, M., & Ohki, H. (2017). Rapid detection of Candida albicans in oral exfoliative cytology samples by loop-mediated isothermal amplification. *Journal of Oral Science*, *59*(4), 541–547. https://doi.org/10.2334/josnusd.16-0717

Rahmatika, D., & Oktaria, S. (2021). Perbedaan Uji Daya Antibakteri Jahe Merah (Zingiber Officinale Var. Rubrum) Dan Bawang Putih (Allium Sativum) Terhadap Pertumbuhan Bakteri Staphylococcus Aureus. *Jurnal Kedokteran Ibnu Nafis*, *10*(1), 1–8. https://doi.org/10.30743/jkin.v10i1.94

Ratha, P. P. (2019). The Characteristics of Opportunistic Infections Among AIDS Patiaents in BRSU Tabanan in 2019. *WMJ (Warmadewa Medical Journal)*, *4*(2), 50–56. Retrieved from https://www.ejournal.warmadewa.ac.id/index.php/warmadewa_medical_journal/article/view/1201

Sabila, P., Ngadiani, & Budiarti, F. F. (2019). Uji Banding Ekstrak Bawang Hitam dan Ekstrak Bawang Putih (Allium sativum) Sebagai Antifungi Terhadap Pertumbuhan Candida albicans. *Journal of Pharmacy and Science*, *4*(2), 101–104. https://doi.org/10.53342/pharmasci.v4i2.147

Sadeghi, G., Mousavi, S. F., Ebrahimi-Rad, M., Mirabzadeh-Ardekani, E., Eslamifar, A., Shams-Ghahfarokhi, M., Jahanshiri, Z., & Razzaghi-Abyaneh, M. (2020). In vivo and in vitro pathogenesis and virulence factors of candida albicans strains isolated from cutaneous candidiasis. *Iranian Biomedical Journal*, *24*(5), 319–327. https://doi.org/10.29252/ibj.24.5.319

Samsudin, R. R., Kunsah, B., & Widyastuti, R. (2017). The effect of pacitan's sweet orange's (Citrus sinensis (L.) osbeck) peel powder on the lipid profile of male dyslipidemia rats (Rattus novergicus). *Bali Medical Journal*, *6*(3), 51. https://doi.org/10.15562/bmj.v6i3.720

Saputri, L., Hastuti, E. D., & Budihastuti, R. (2018). Respon Pemberian Pupuk Urea dan Pupuk Kandang terhadap Pertumbuhan dan Kandungan Minyak Atsiri Tanaman Jahe Merah [Zingiber officinale (L,) Rosc var. rubrum]. *Jurnal Biologi*, *7*(1), 1–7. Retrieved from https://ejournal3.undip.ac.id/index.php/biologi/article/view/19615

Suhartomi, Gulo, K. N., Saragih, A. D., Martinus, A. R., & Ikhtiari, R. (2020). Antioxidant Properties of Sweet Orange Peels in Several Fractions of Methanolic Extract. *Proceedings of the International Conference on Health Informatics and Medical Application Technology - Volume 1: ICHIMAT*, 371–378. https://doi.org/10.5220/0009515503710378

Suraini, & Putri, N. (2018). Efektifitas Anti Jamur Campuran Rebusan Jahe (Zingiber officinale) dan Kunyit (Curcuma domestica) terhadap Pertumbuhan Candida albicans. *Prosiding Seminar Kesehatan Perintis*, *1*(2), 73–77. Retrieved from https://jurnal.upertis.ac.id/index.php/PSKP/article/download/126/119

Tsui, C., Kong, E. F., & Jabra-Rizk, M. A. (2016). Pathogenesis of Candida albicans Biofilm. *Journals Investing in Science*, *74*(4), 1–13. https://doi.org/10.1093/femspd/ftw018

Zainal, M., Mohamad Zain, N., Mohd Amin, I., & Ahmad, V. N. (2021). The antimicrobial and antibiofilm properties of allicin against Candida albicans and Staphylococcus aureus – A therapeutic potential for denture stomatitis. *Saudi Dental Journal*, *33*(2), 105–111. https://doi.org/10.1016/j.sdentj.2020.01.008

Zdanavičienė, E., Sakalauskienė, J., Gleiznys, A., Gleiznys, D., & Žilinskas, J. (2017). Host responses to Candida albicans. A review. *Stomatologija*, *19*(4), 109–123. Retrieved from https://www.sbdmj.com/174/174-02.pdf