Effect of Ginger

By Abu Bakar

Effect of Ginger (Zingiber Officinale) Rhizome in Inhibiting Growth Oral Candida (Scoping Review)

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Abstract

Treatments used for oral candidiasis such as ketoconazole bring many side effects such as allergies, nausea and in some cases causes irritation. Long-term use 3 an also cause Candida albicans resistance problems to drugs. On 12 f the traditional treatments that can inhibit the growth of Candida albicans is red ginger rhizome (Zingiber Officinale var Rubrum).

The objective of this research zas to determine the benefits of ginger rhizome (Zingiber Officinale) as a bioactive compound in inhibiting the growth of Candida albicans and to determine the content of ginger rhizome (Zingiber Officinale) which plays a role in inhibiting the growth of Candida albicans. The method used in this research was literature study. The data was carried out by searching the PubMed, Science Direct and Google Scholar databases.

The results of the scoping review of most articles obtaine 2 supported the proven benefits of ginger rhizome (Zingiber Officinale) as a bioactive compound in inhibiting the gro2th of Candida albicans. The content of ginger rhizome (Zingiber Officinale) which played a role in inhibiting the growth of Candida albicans included essential oils, flavonoids, alkaloids, tannins, glycosides, saponins, steroids and triterpenoids. The conclusion of this 3 coping review is that ginger extract (Zingiber Officinale) can be used as a traditional treatment to inhibit the growth of Candida albicans.

Review (J Int Dent Med Res 2023; 16(3): 1309-1316)

Keywords: Ginger Rhizome (Zingiber Officinale), Candida albicans, Oral Candidiasis. **Received date:** 26 June 2023 **Accept date:** 19 August 2023

Introduction

The oral cavity is the entry and exit point for various microorganisms. In the oral cavity there are many normal flora. Normal flora under normal circumstances do not cause disease. However, if there is an immune disorder, the normal flora can turn into a pathogen. One of the normal flora that can be found in the oral cavity is Candida albicans. Candida albicans is a normal microflora of the oral cavity that often causes opportunistic infections in patients who have decreased body defenses caused by infection. by aging, diabetes and AIDS, iatrogenic factors. Candida albicans often colonizes the oral cavity by 30-60%. ^{2,3}

Infections caused by Candida albicans are oral candidiasis found on the dorsum of the tongue, buccal mucosa, labial mucosa and the

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area around the palate.³ The prevalence of oral candidiasis caused by Candida albicans in healthy humans without systemic disease is 20-75%. Meanwhile, oral candidiasis in humans has systemic disease and causes an increase in mortality rate of 71-79%. Because of the high number, it is necessary to do treatment.⁴

Treatments used for oral candidiasis such as ketoconazole have many side effects such as allergies, nausea and in some cases irritation. Long-term use can also cause Candida albicans resistance problems to drugs. Therefore, it is necessary to treat with natural ingredients that are expected to reduce side effects. According to the World Health Organization (WHO), 80% of the world's population still Relies on traditional medicine, including the use of medicines derived from plants.⁵

Traditional treatments that can inhibit the (17) wth of Candida albicans is red ginger rhizome (Zingiber Officinale var Rubrum). Red ginger (Zingiber Officinale var Rubrum) is a spice plant originating from South Asia, and now has spread throughout the world, including Indonesia. ^{6,7} Red ginger (Zingiber Officinale var Rubrum) is a plant

of the Zingiberaceae tribe which is widely used as a spice, traditional medicine ingredient, sweets and refreshing drinks.⁸

Red ginger rhizome (Zingiber Officinale var Rubrum) has activities such as antibacterial, antioxidant, anti-inflammatory, anticarcinogenic, antimutagenic and antitumor. The rhizome of red ginger (Zingiber Officinale var Rubrum) has 2 condary metabolites that have antifungal properties such as flavonoids, tannins, saponins, alkaloids and several active components such as essential oils, this has been proven in in vitro experiments. Research on the essential oil contained in the rhizome of red ginger (Zingiber Officinale var Rubrum) has been shown to inhibit the growth of Condida albicans with the highest effect obtained at a concentration of 100% with an inhibition zone diameter of 39,6 mm. 10

Ginger es 13 ntial oil (Zingiber Officinale) contains active compounds such as gingerol, shagaol, zingeron, zingiberen and phenos One of the derivatives of phenolic compounds that can inhibit the growth of Candida albicans is eugenol. The mechanism of eugenol is as follows, eugenol is bound to ergosterol on the cell membrane of Candida albicans which can interfere with the transport of macromolecules and ions in Candida albicans cells, causing irreversible destruction, inhibiting the enzyme squaleneepoxydase and decreasing the synthesis of ergosterol, inhibiting the lipid biosynthesis of Candida albicans. especially ergosterol present in cell membranes, inhibits DNA synthesis, affects the function of microtubules or nucleic acid synthesis and polymerization and can inhibit Hyphae Cell Wall Synthesis And Mitosis. 11

The results of research conducted in vitro on ginger rhizome extract (Zingiber Officinal) proved to show a significant inhibition of the growth of Candida albicans. Therefore, the authors are interested in reviewing articles relating the effect of gar rhizome (Zingiber Officiale) in inhibiting the growth of Candida albicans in the oral cavity.

Materials and methods

The article criteria used in this scoping review are articles that cover the topic of the effect of anger rhizome (Zingiber Officiale) in inhibiting the growth of Candida albicans in the oral cavity.

The search strategy is a combination of keywords that are used to repeat (and or modify)

keywords that already exist in the previous scoping revie. consider whether keywords are specific (precise) or broad (comprehensive). The author uses keywords for a journal or article search strategy through a database.

Results

The results of the selection of sources of evidence obtained were 20 articles. The article search and selection process consists of several stages, namely for the first stage to search for articles in databases such as PubMed, Science Direct and Google Scholar using initial keywords. "Zingiber Officinale, Ginger, Candida albicans, Fungi, Antimicrobial, Antifungal". The article search process using these initial keywords for PubMed contained 346,290 articles, Science Direct 14,427 articles and for Google Scolar 26,108 articles. The total articles in the search process using initial keywords were 386,825 articles. The next step is to search for articles in the database with the final keyword "Zingiber Officinale OR". Ginger AND Candida albicans OR Fungi AND Antimicrobial OR Antifungal " on PubMed there are 89 articles, Science Direct there are 161 articles, and finally for Google Scholar there are 1,840 articles, so the total of searches is 2,090 articles. Furthermore, the article was continued with the issuance of double articles using Mendeley, namely 179 articles then the total articlesafterthe issuance of double articles were 1,911 articles.

The next stage for article selection is based on articles that are not available in abstracts, which are not on topic, not published in 2011-2021, cannot be accessed, articles in the form of theses and theses, research articles in the form of (literature review, systematic review and meta-analysis),1,858 articles were issued. The remaining 53 articles in full text form after selecting articles based on the criteria above, then 33 articles were issued again because they did not fit the topic and did not discuss further. As a result, 20 articles were selected according to the topic and qualified for review.

Characteristics Sources of Evidence

The characteristics of 20 articles to be reviewed have been identified based on the year of publication, articles in 2011 there were 5% articles, in 2012 there were 5% articles, in 2013 there were 5% articles, in 2014 there were 10%

articles, in 2015 there were 10%, in 2016 there were 15%, in 2017 there were 5%, in 2018 there were 20% articles. In 2019 there are 5%, in 2020 there are 5% articles, and in 2021 there are 15% articles. Based on location there are 45% articles come from Indonesia, 20% articles come from India, 15% articles come from Iraq, 5% articles come from Iran, 5% articles come from Turkey, 5% articles come from Malaysia, 5% articles come from Nigeria.

Based on the method used in the research, each article that will be reviewed is the same, namely using the in vitro experimental method with a percentage of 100%. In addition, the research sample was 11 articles using 55% Candida albicans, 1 article with Candida albicans, Pseudomonas aeruginosa and Staphylococcus aureus 5% research samples, article using Staphylococcus aureus, Escheria coli and Candida albicans 5% research samples, 1 article with research samples Candida albicans and Trichophyton rubrum 5%, 1 article with research samples Pseudomonas aeruginosa and Candida albicans 5%, 1 article with study samples Staphylococcus aureus and Candida albicans 5%, 1 article with research samples Candida albicans, Penicillum spp and Aspergillus spp 5%, 1 article with research samples Candida albicans, Geotrichum candidum, Trichophyton rubrum, Aspergillus flavus, Fusarium oxysporum and Scopulariopsis brevicaulis 8%, 1 article with research samples Bacillus subtilis. aureus, Staphylococcus Escherichia Pseudomonas aeruginosa, Candida albicans and Aspergillus niger 5% 1 article with a research mple of Candida albicans, E nterococcus faecalis, Enterobacter aerogenes, Enterococcus durans, Enterococcus faecium, Escherichia coli, Klebsiella pneumoniae, Listeria moonocytogenes, Listeria innocua, Pseudomonas aeruginosa, Pseudomonas fluorescence, Salmonella infantis, Salmonella kentucky, Salmonella thypimurium and Staphylococcus aureus 5%. Furthermore, based on the type of article to be reviewed, there are 20 articles with the type of journal article publication with a percentage of 100%. The characteristics of the sources of evidence in the articles that fall into the inclusion criteria are presented in table 1.

Article Characteristics	Number of Articles (n=20)	Percentage (%)
Publication Year		
2011	1	5
2012	1	5
2013	1	5
2014	1 2 2 3 1	10
2015	2	10
2016	3	15
2017	1	5
2018		20
2019	1	5
2020	1	5
2021	3	15
Study Location :		
Indonesia	9	45
India	4	20
Iraq	4 3 1	15
Iran		5
Turkey	1	5
Malaysia	1	5
Nigeria	1	5
Research methods :		
Experimental in vitro	20	100

Table 1. Characteristics of Evidence Sources.

Resea	arch Sample:		
1)	Candida albicans	11	55
2)	Candida albicans, Pseudomonas aeruginosa and Staphylococcus	1	5
	aureus		
3)	Staphylococcus aureus, Escheria coli and Candida albicans	1	5
4)	Candida albicans and Trichophyton rubrum	1	5
5)	Pseudomonas aeruginosa and Candida albicans	1	5
6)	Staphylococcus aureus and Candida albicans	1	5
7)	Candida albicans, Penicillium spp dan Aspergillus spp	1	5
8)	Candida albicans, biofilm, Trichophyton red, Aspergillus flavus,	1	5
	Fusarium oxysporum dan Scopulariopsis brevicaulis		
9)	Bacillus subtilis, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Candida albicans dan Aspergillus niger	1	5
10)	Candida albicans, biofilm Candida albicans, Enterococcus faecalis, Enterobacter aeroqenes, Enterococcus durans, Enterococcus	1	5
11)	Candida albicans, biofilm, Candida albicans, Enterococcus faecalis, Enterobacter aeroqenes, Enterococcus durans, Enterococcus faecalis Escherichia coli, Klebsiella pneumoniae, Listeria moonocytogenes, Listeria innocua, Pseudomonas aeruginosa, Pseudomonas fluorescence, Salmonella infantis, Salmonella kentucky, Salmonella thypimurium and Staphylococcus aureus	1	5

Table 2. Characteristics of Evidence Sources.

Results from Each Source of Evidence Based on the results of the selection of articles, the total inclusion was 20 articles. The results of each source of evidence in the form ofauthor data, method, type of ginger, concentration of ginger extract, inhibition, microorganisms studied and the content of active components of ginger extract. The results from each source of evidence are presented in tabel 2.

No	Author I	Method	Types of Ginger	Concentration Extract	Inhibition Zone (mm)	Active Component Content
1	Setiadi et al.12	Disc diffusion	Red ginger	20-100%	8.3 -39.6	Phenol
2	Supreetha et al. ¹³	Disc diffusion	Ginger Extract	1g, 2g and 4g	16-24	Gingerol, Shagaol
3	Santoso et al.º	Maceration	White ginger	30%	12	4 contents
4	Mutmainah et al ¹⁴	Maceration	Red ginger	10, 15, 20%	NA	Shagaol, Zingerone
5	Aghazadeh et al ¹⁵	Microdilution	Ginger extract	0.625 mg/ml	NA	NA
6	al.10	Steam distillation	Red ginger	0.125%-1%	0.9-0.28 nm,	Terpenoids
7	Hiregoudar et al.16	Agar well	Ginger Extract	,	8.22	Gingerol
8	Suraini et al. ¹⁷	Disc diffusion	Ginger Extract		7.3	Phenols
9	Sari et al.18	Agar well diffusion	ginger	100g	10.7	Gingerol, Zingerone
10	Prastiyanto et al.19		4 types of ginger,		12-14	Flavanoids
11	Hadyprana et al.20	Pure quantitative	White ginger	20-100%	6-15	4 contents
12	Sukandar et al.21	Agar well diffusion	I Ginger extract	2048 g/ µl	NA	4 contents
13	Khalaf et al 22	Agar well diffusion	I Ginger extract	50, 100, 150%	18-25	4 contents
14	Agi et al. 23	Association of Official Analytical Chemists (AOAC)		25-100%	NA	NA
15	Ghasemzade h et al.24	3 methods	Ginger Extract	100%	12-25	NA
16	Sharma et al.25	Disc diffusion	Ginger essential oil	1-10 l/ml	12.5 mm	Essential oil
17	Sener et al.25	Hydrodistillati on method	Ginger essential oil	(3.125–100 g/ml)	NA	Essential oil
18	Al-Hussainy ²⁷	Agar well	Ginger Extract	50-200 mg/ml	2.14-3.24	5 contents
19	Tamore et al.28	Agar well	I Ginger Extract	(50, 80 and 100) mg/ml	16-18	NA
20	Ali et al 29	Disc Diffusion	Ginger Extract	2.5, 5, 10, 20%	2-20	4 contents

Tabel 3. Results from Each Source of Evidence.

Synthesis of Results

Overall, the results of research conducted by researchers found that ginger rhizome extract (Zingiber Officinale) had antifungal effects, especially against Candida albicans. However, there are some differences in various aspects, such as the type of ginger extract (Zingiber Officinale), the method or method of processing ginger extract (Zingiber Officinale) and the content of active compounds in ging (Zingiber Officinale) which play an active role in inhibiting

the growth of Candida albicans. Several studies orted that ginger extract (Zingiber Officinale) could inhibit the growth of Candida albicans and there were also several studies reporting that ginger extract (Zingiber Officinale) could not inhibit the growth of Candida albicans

The discussion regarding the formulation of the problem is taken from articles collected from various types of ginger extract (Zingiber Officinale) which play a role in inhibiting the growth of Candida albicans. Of the 20 articles, 6articles conducted research using the agar well diffusion). Based on the results of article 7, article 9, article 13, article 18 and article 19, it was wed that ginger extract (Zingiber Officinale) could inhibit the growth of Candida albicans with the highest inhibition zone. Furthermore, in article 12, research conducted by Sukandar et al.20 stated that the ethanolic extracts of Zingiber Rhizom var Rubrum could inhibit the growth of Candida . albicans but has low activity. From the results of the phytochemical screening test in the 6 articles, it was said that ginger extract (Zingiber Officinale) contains active compounds gingerol, zingerone. flavanoids, alkaloids. terpenoids and phenols. The study conducted by Tamore et al. (2018). showed that there were no compounds that played an active role in inhibiting the growth of Candida albicans.²⁸

Based on 5 articate using the disc diffusion method, namely article 2, article 16, article 1, article 8 and article 20. Based on article 16, article 1 and article 8 stated that ginger extract (Zingiber Officinale) can inhibit the growth of Candida albicans. In article 1, a study conducted by Set 14 di et al. (2014), proved that the essential oil extract of red ginger (Zingiber Officination of 100% could inhibit the growth of Candida albicans with the highest into ition zone of 39,6 Based on the test results that the red ginger (Zingiber Officinale var Rubrum) essential oil extract has a compound that plays an active role, namely essential oil. 12

Based on article 2 research conducted by Supretha et al (2011), stated that ginger extract at a concentration of 4g at cold temperatures showed a maximum inhibition zone with a diameter of 23 mm at 24 hours but at 48 hours the diameter of the inhibition zone decreased to a diameter of 17 mm. Furthermore, article 20 conducted by Ali et al (2012), stated that ginger extract (Zingiber Officinale) can inhibit the growth

of Candida albicans. Ginger extract (Zingiber Officinale) was tested at concentrations of 2.5%, 5%, 10% and 20%13 nd produced inhibition zones with diameters of 15 mm, 18 mm, 20 mm and 22 mm, respective 5 Based on the test results, it was concluded that the higher the concentration of ginger extract (Zingiber Officinale), the higher the inhibition zone produced.¹³

Based on 3 articles using the maceration method, namely article 3, article 4 and article 10. In article 3 research conducted by Santoso et al (2014), stated that the ethanol extract of small white ginger (Zingiber Officinale var Amarum) can inhibit the growth of Candida albicans with a concentration of 30% had a 12 mm inhibition zone. While in article 10 conducted by Prastiyanto et al (2021), it was stated that the higher the concentration of ginger extract (Zingiber Officinale), the higher the inhibition zone produced. Phytochemical screening test results prove that ginger extract (Zingiber Officinale) contains active compounds, namely flavonoids. 18

Based on article 4 research conducted by Mutmainah et al (£15), stated that the higher the concentration of red ginger (Zingiber Officinale var Rubrum) extract, the higher the inhibition zone produced. However, in this study there was a difference which did not indicate the value of the resulting inhibition zone. Based on the results of the hytochemical screening test, it was stated that red ginger extract (Zingiber Offic lale var Rubrum) contains active compounds that can inhibit the growth of Candida albicans, namely shagaol and zingerone. 13

Based on 20 article 10 6 articles used different methods, namely article 5, article 6, article 11, article 14, article 15 and article 17. In article 5 research conducted by Aghazadeh et al (2016), this study used the microdilution method which states that the ethanol extract of ginger (Zingiber Officinale) can inhibit Candida albicans starting at a concentration of 5mg/ml with inhibition zones of 3 mm and 1 mm. Meanwhile, at a concentration of 40 mg/ml did not show an inhibition zone. Based on the results of phytochemical screening, it did not show compounds that played an active role in inhibiting the growth of Candida albicans.¹⁴

Based on article 6 research conducted by Rinanda et al (2018), this stugy using the steam distillation method states that red ginger (Zingiber Officinale var Rubrum) essential oil starting at a

concentration of 1% produc an inhibition zone with a diameter of 0.28 nm. At a concentration of 0.5% produces inhibition zone with a diameter of 0.58 nm. At a concentration of 0.25% produces inhibition zone with a diameter of 0.62 nm. At a concentration of 0.125% produces an inhibition zone with a diameter of 0.9 nm. Based on the results of the study, it was proven that red ginger (Zingiber Officinale var Rubrum) essential oil contains active compounds, namely terpenoids. 15

Based on article 11 research conducted by Hadyprana et al (2025), using a pure quantitative method stated that the higher the concentration of white ginger extract, the higher the inhibition zone produced in inhibiting the growth of Candida albicans. Based on the results of phytochemical screening of extracts of white ginger (Zingiber Officinale var Amarum) showed positive results on all the compounds tested. namely flavonoids, alkaloids, tannins, saponins, steroids and terpenoids. 19 Furthermore, article 14 conducted by Agi et al (2019) using the Association of Official Analytical Chemists (AOAC) method stated that sterilized and unsterilized ginger (Zingiber Officinale) extracts inhibited the growth of Candida albicans. Based on the test results, it was found that the sterilized concentration I 100g/100ml had a high inhibition zone compared to the unsterilized extract. While the concentration II 100g/50ml which was sterilized had a lower inhibition zone than the unsterilized extract.22

Based on 15 research articles conducted by Ghasemzadeh et al (2018), using 3 methods, namely the Open Sun Drying (OSD) method, this method states that ginger extract (Zingiber Officinale) can inhibit the growth of Candida albicans at a concentration of 100% producing an inhibition zone with diameter 12mm. Furthermore, the Solar Tunner Drying (STD) metho stated that ginger extract (Zingiber Officinale) inhibited growth of Candida albicans at a concer13tion of 100% producing an inhibition zone with an inhibition zone of 16 mm. Furthermore, the Hot Air Drying (HAD) method gated that ginger extract (Zingiber Officinale) inhibited the growth of Candida at a concentration of 100% producing an inhibition zone with a diameter of 25 mm.23

Based on 17 research articles conducted by Sener et al (2017), using the hydrodistillation method stated that ginger (Zingiber Officinale) essential oil extract can inhibit the growth of Candida albicans. However, this study did not show the resulting inhibition zone value. Based on the results of the phytochemical screening test, this study also did not show the content of ginger extract compounds (Zingiber Officinale) which played an active role in inhibiting the growth of Candida albicans. ²⁵

Discussion

Based on the results of the search for sources of evidence and passing through the article selection process, this is a scoping review on based on the formulation of the problem, namely the benefits of ginger rhizome (Zingiber Officinale) as a bioactive compound in inhibiting growth Candida albicans and the content of ging rhizomZingiber Officinale) which plays a role in inhibiting the growth of Candida albicans in the results of a scoping review.

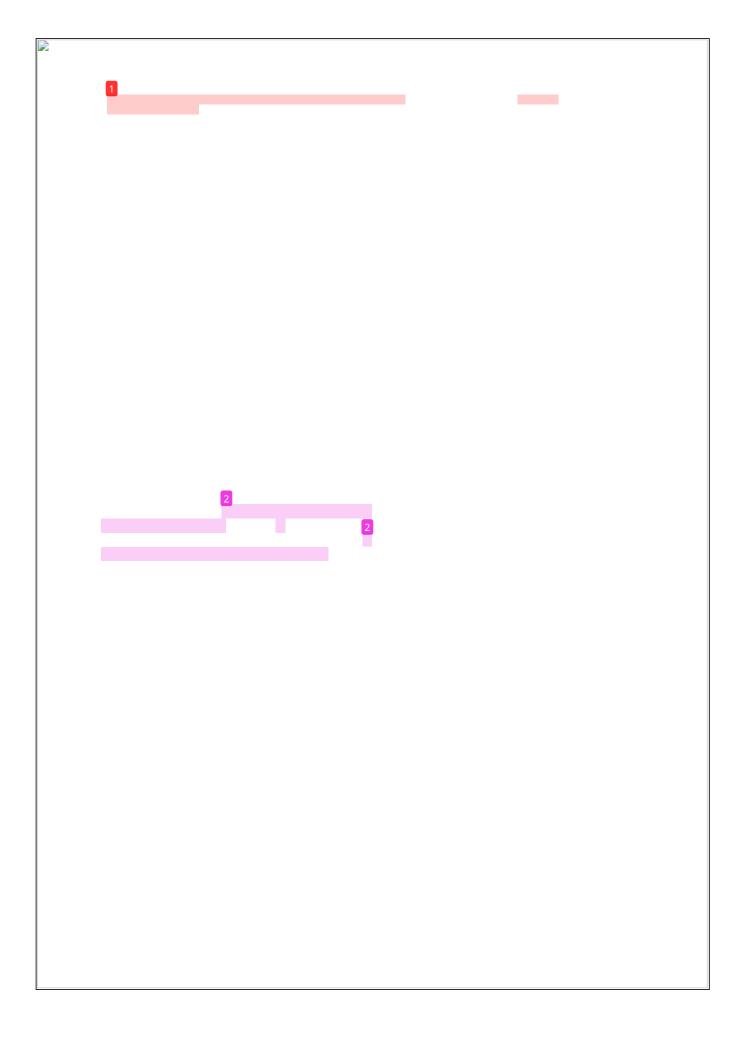
According to Sari et al. (2013) fresh extracts of ginger rhizomes were able to inhibit the growth of the test microbes by varying the diameter of the microbial-free area formed. This is because the fresh extract of ginger rhizome contains anti-microbial compounds. Fresh extract of ginger-ginger rhizome contains several volatile oil components consisting of -pinene, champhene, caryophyllene, -pinene, cineol, dl-camphor, isokaryophyllene, caryophylleneoxide and germacron which can inhibit microgal growth. 18

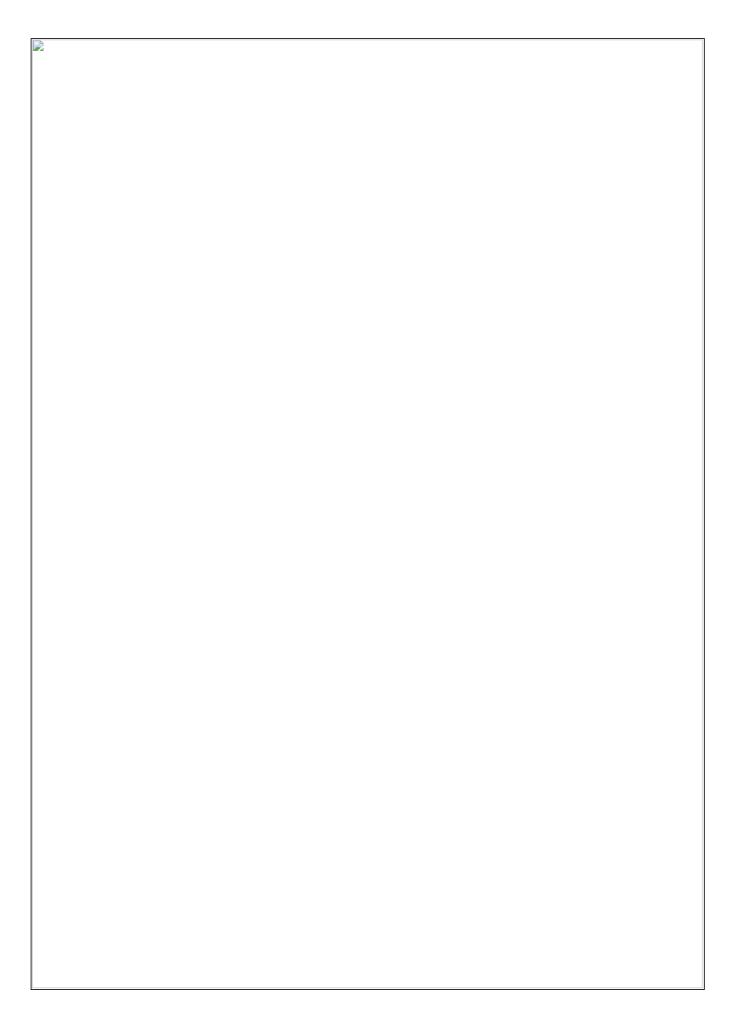
The ethanol extract of small white ginger (Zingiber Officinale var Amarum) has 9an antifungal effect against Candida albicans. The antifungal effect of the ethanol extract of small white inger (Zingiber Officinale var Amarum) was due to the presence of essential oils consisting of active compounds, namely gingerol, shogaol, zingerone, zingiberen and phenol. The of the derivatives of phenolic compounds that can inhibit the growth of Candida albicans is eugenol. The mechanism of eugenol is as follows. eugenol is bound to ergosterol on the cell membrane of Candida albicans which can interfere with the transport of macromolecules and ions in Candida albicans cells, causing irreversible destruction, inhibiting the enzyme squaleneepoxydase and decreasing the synthesis of ergosterol, inhibiting the lipid biosynthesis of Candida albicans. especially ergosterol which is found in cell membranes,

inhibits DNA synthesis, affects the function of microtubules or nucleic acid synthesis and polymerization and can inhibit hyphae cell wall synthesis and mitosis.^{6,11}

Based on a remark review, Mutmainah et al (2015), stated that the ethanolic extract of red ginger (Zingiber officinale var Rubrum) with varying concentrations of 10%, 15% and 20% had antifungal activity against Candida albicans. From the chemical analysis of red ginger (Zingiber Officinale var Rubrum) it can be seen that the content of compounds includes fsvonoids, polyvenols, essential oils, gingerols, limonene, 1,8 cineol, 10-dehydroginger dione, 6gingerdion, alpha linolenic acid, arginine, aspartic, betasitosterol, caprilic acid, capsaicin, chorogenic acid, farnesal, farnes dan farnesol. The active substances shogaol, zingerol, limonene and caprilic acid act as antifungals. The results of the screening process for the test extract in this study were red ginger extract (Zingiber Officinale var Rubrum) containing alkaloids, flavonoids, triterpenoids, essential oils, tannins and shagaol. Shogaol compounds were the most active components against filament formation and growth of Candida albicans, followed by citral and gingerol compounds. 13

Phytochemical screening results from white ginger extract (Zingiber Officinale var Amarum) showed positive results on all tested compounds, namely flavonoids, alkaloids, tannins, glycosides, saponins, steroids and triterpenoids. In flavonoid compounds, a yellow to red color is formed. In the alkaloid compound, a brown to black precipitate is formed. In tannin compounds, a blue-black color is also formed. In glycoside compounds, a blue or greenish color is formed. In the saponin compound, a stable foam is formed. In steroid and tritepenoid compounds, a blue-green ring is formed and a brown or violet ring is formed. These results are consistent with previous studies which state 17 at the secondary metabolite compounds in the n -hexane and ethyl acetate fractions of red ginger extract (Zingiber Officinale var Rubrum) are alkaloids, flavonoids, phenolics, and triterpenoids. On (Zingiber Officinale) essential oil contains sesquiterpenes and monoterpenes which contain phenolic compounds and alcohol which have antifungal properties. This compound has the working principle of binding sterols to form fungal cell membranes, causing interference with cell membrane synthesis so that fungal cells die. 19





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