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Formulation and Inhibitory Test of Feminine Cleansing Soap Combination of Young Areca Extract *(Areca cathechu L.)* and Manjakani Extract *(Quercus infectoria*) on the Growth of Candida Albicans

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ABSTRACT

One of the reproductive health problems that women often experience is vaginal discharge. About 85-95% vaginal discharge is caused by the fungus Candida albicans. To maintain the cleanliness of the female organ system, feminine cleansing soap is usually used. The use of traditional ingredients has smaller side effects and the price is also relatively affordable. Traditional ingredients that can be used are young areca nut (*Areca catechu L.*) and Manjakani (*Quercus infectoria*). Young areca nut seeds contain tannins, flavonoids, and saponins, while Manjakani fruit contains tannins and flavonoids which have anti-fungal activity. This study aims to determine the inhibitory power of feminine cleansing soap from areca nut extract (*Areca cathechu L.)* and Manjakani extract (*Quercus infectoria*) on the growth of Candida albicans. This research is a purely experimental laboratory which begins with the extraction process. 5 formulations of feminine cleansing soap were prepared, a combination of young areca nut extract (*Areca cathechu L.*) and Manjakani extract (*Quercus infectoria*) with a concentration percentage ratio of 5:10, 7.5:7.5, 10:5, 15:0 respectively and 0:15. The resulting preparations were tested for inhibition of the growth of *Candida albicans*. The results showed that a feminine cleansing soap combination of young areca nut extract (*Areca cathechu L.*) and Manjakani extract (*Quercus infectoria*) had an inhibitory effect on the growth of Candida albicans, namely F1, F2, F3, F4 and F5 which had average inhibition respectively of 21.33 ± 0.58 mm, 21.67 ± 0.58 mm, 22 ± 0 mm, 19.67 ± 1.53 mm. Thus, the findings show that all feminine cleansing soap formulations of a combination of young areca nut extract (*Areca cathechu L.*) and Manjakani fruit extract (*Quercus infectoria*) have an inhibitory effect on the growth of Candida albicans. Of the five formulations tested, the combination of extracts with a ratio of 0:15 (F5) showed the highest inhibition against Candida albicans with a mean inhibition zone diameter of 22.33 ± 0.58 mm.

Keywords: Feminine cleansing soap; antifungal; Candida albicans.

INTRODUCTION

Reproductive health is a health effort that needs attention. The female reproductive system, such as the vagina, isan important area to care for and needs special attention because of its closed position. There are lots of impacts if a woman does not pay attention to the cleanliness of her genital area, including infections caused by fungi, bacteria,parasites and viruses such as vaginal discharge, bad odors and so on (Rahmi et al., 2017).

One of the reproductive health problems that women often experience is vaginal discharge. *Leucorrhea* is usually clear white in color, when it sticks to underwear it will be bright yellow in color, consistency like mucus, runny or thick depending on hormone cycles, odorlessand does not cause complaints. About 85- 95% vaginal discharge is caused by the *fungus Candida albicans* (Lolok et al., 2020).

To maintain the cleanliness of the female organ system, women's health products (feminine hygiene) are usually used. Feminine cleansing soap is included in feminine cleaning products. Productsspecially formulated for the sensitivegenital environment can help maintain a normal acidic pH and bacterial flora, thereby preventing colonization andovergrowth of pathogenic bacteria (Baki, 2022). The use of antifungals that are not in accordance with the rules is often thecause of fungal resistance. One

of theefforts made is to use traditional materialsbecause they are considered to have less side effects compared to chemicals and theprice is also relatively affordable (Lolok et al., 2020).

Traditional ingredients that can be used are young areca nut (*Areca catechu L.*) and Manjakani (*Quercus infectoria*). Young areca nut seeds contain flavonoid compounds including quercetin, tanninssuch as catechin and epicatechin compounds, other compounds are fatty acids, such as galled acid, lauric acid, decanoic acid, myristic acid and tetrad conoid acid which can inhibit the growth of Candida albicans (Asrianto et al., 2022). Areca nut seeds also contain phenol and alkaloid compounds which can inhibit the growth ofCandida albicans (Al-Bayati, 2016; Putriningrum et al., 2016). Manjakani fruit contains gal Manjakani, hydrolyzed tannins namely pyrogallol, flavonoids, phenols, gallic acid, and elagatic acid which can inhibit the growth of Candida albicans (Baharuddin et al., 2015; Yanti et al., 2016; Magbool et al., 2018). However, although some of these studies show the antimicrobial potential of areca nut and Manjakani seeds, their application in feminine cleansing soap formulations has not been studied in depth.

There has been no research that examines the effectiveness of the combination of areca nut extract and Manjakani in one formulation to inhibit the growth of Candida albicans. In addition, most existing studies focus on in vitro tests, while clinical testing of the effectiveness and safety of feminine hygiene products based on these two extracts has not been carried out comprehensively. Therefore, the purpose of this study was to determine the inhibition of feminine cleansing soap based on areca nut extract (*Areca cathechu L.*) and Manjakani extract (*Quercus infectoria*) against the growth of Candida albicans. This study is expected to contribute in providing a scientific basis for the development of more effective and safe feminine hygiene products using natural ingredients. In addition, the results of the study can introduce the use of a combination of areca nut and Manjakani extracts in the formulation of feminine cleansing soap, which can be a new innovation in the personal care product industry. As well as providing valuable information for further research on the use of natural ingredients in health and personal care products.

METHODS

This research is a purely experimental laboratory research conducted at the Pharmaceutical Technology and Pharmaceutical Technology Laboratory, Faculty of Pharmacy, Universitas Mahasaraswati Denpasar and MicrobiologyLaboratory, Biology Study Program,Faculty of Mathematics and Natural Sciences, Udayana University in January- June 2023. Samples of young areca nut (*Areca cathechu L.*) was obtained from Bitera Village, Gianyar District, Gianyar Regency, Bali and Manjakani fruit (*Quercus infectoria*) was obtained from City of Surabaya, East Java.

Tools and materials

The tools used are blender, glass jar, Erlenmeyer, measuring cup, beaker glass,water bath, homogenizer, rotary evaporator, universal pH, thermometer,stir bar, Buchner funnel, dropping pipette,volume pipette, oven, autoclave, micropipette, spirit lamp, tweezers, wire loops, incubators, calipers, Petri dishes. The ingredients used are young areca nutseeds (*Areca cathechu L.*) and Manjakani fruit (*Quercus infectoria*), 96% ethanol, methyl paraben, sodium lauryl sulfate (SLS), CMC-Na, Na4EDTA, aquadest, SDA medium (Sabouraud Dektrose Agar),female liquid soap preparations on themarket, 0.9% NaCl.

Procedures Preparation of Young Areca Nut Seeds and Manjakani Fruit Simplicia

Young areca nut seeds are taken from fruit that is still green in color and the Manjakani fruit used is dried Manjakani fruit young areca nut seeds are split intofour parts, then washed and dried in thehot sun for 2 days. Then cut into smallpieces and then do dry sorting. After thedry sorting process, the simplicia wascrushed to obtain a coarse powder. Thenthe powder was sieved using a 60mesh sieve to obtain fine simplicia.

Extraction of Young Areca Nut Seeds and Manjakani Fruit

The process of extracting young areca nut and manjakani fruit seeds uses the maceration method with 96% ethanol solvent. Put 1,353 g of young areca nut seed powder and 1,684 g of Manjakani fruit simplicia powder into each macerator, add 13.53 L and 16.84 L of 96% ethanol solvent respectively. Soaking was carried out for the first 6 hours with occasional stirred, then allowed to stand for 18 hours. The macerate was separated by filtration using a Buchner funnel, then the dregs were re-macerated for 2 days with the same type of solvent (half the amount of solvent in the first extraction). The macerate obtained is filtered. The results of maceration and remaceration were collected and then evaporated using a rotary evaporator at 60°C to obtain a thick extract.

Phytochemical Screening of Young Areca Extract and Manjakani Extract

Alkaloid test

The extract is dripped on 3 drip plates. One part is used as a control and two parts are dripped with Mayer's reagent and Dragendorf's reagent. The result is positive containing alkaloids if Mayer's reagent is added it will form a white precipitate (yellowish white) and if added Dragendrof reagent it produces an orange red precipitate (Slamet et al., 2020).

Steroid/triterpenoid test

Two drops of extract on the drip plate. One side is used as a control and the other side is added with the Lieberman-Burchard reagent, so that a red or violet color is formed, this result indicates a positive test for terpenoids, the formation of green or blue color indicates a positive test result for steroids (Slamet et al., 2020).

Flavonoid Test

Extract as much as 0.1 g added ethanol until submerged and then heated. The filtrate was added with H2SO4, the formation of a red color due to the addition of H2SO4 indicated the presence of flavonoid compounds added with

concentrated H2SO4, forming a red color indicating the presence of flavonoids (Slamet et al., 2020).

Saponin Test

The extract is dripped into two test tubes. One side was used as a control and the other side was boiled with 20 ml of water in a water bath. The filtrate was shaken and left for 15 minutes. Formation of foam indicates a positive test result for saponins (Slamet et al., 2020).

Tannin Test

As much as 1 ml of extract was put into a test tube, then 2-3 drops of 1% FeCl3 were added. Positive samples contain tannins when they change color into blackish green (Huliselan, 2015).

a. Formula Design

Table 1
Feminine Cleansing Soap Formulas

Material	Concentration (%) F1	F2	F3	F4	F5	Negative Control	Function
Areca nut extract	5	7,5	10	15	-	-	Active substance
Manjakani extract	10	7,5	5	-	15	-	Active substance
Sodium laurylsulfate	1	1	1	1	1	1	Surfactant
Na4EDTA	0.1	0.1	0.1	0.1	0.1	0.1	Cheating
Methyl paraben	0.3	0.3	0.3	0.3	0.3	0.3	Preservative
CMC-Na	0.5	0.5	0.5	0.5	0.5	0.5	Emulsifier
Aquadest	d 100ml	d 100ml	d 100ml	l 100ml	l 100ml	ad 100 ml	Carrier

b. Making Formula

CMC-Na was dispersed with distilled water, then stirred using a homogenizer until homogeneous (mixture 1). Put the remaining aquadest, sodium laurylsulfate, Na4EDTA, methyl paraben into a100 ml beaker glass, then heat it over a water bath at 65oC while stirring until the mixture is homogeneous (mixture 2). The extract was dissolved with the remaining distilled water in the mortar until homogeneous (mixture 3), then mixed 1was added to mixture 3 while stirring untilhomogeneous, then mixed 2 was added,stirred until homogeneous.

Antifungal Activity Testing

a. Tool Sterilization

Sterilization of glassware, growing media and bacterial growth using an autoclave at 121°C for 15 minutes. The loops and tweezers are sterilized by directheating using a Bunsen flame until they are red.

b. Making SDA Media

Weighed 65 g of SDA media, put it in into Erlenmeyer, then dissolved with distilled water up to 1,000 ml. Then shaken and heated in boiling water while shaking occasionally for 1 minute or untilthe powder dissolves completely. Enter the media that has been homogenized into 2 petri dishes as much as 15 ml each.Sterilized in an autoclave at 121oC for 15 minutes, and then allowed the media to solidify.

c. Making Solution Mc. Farmlands 0.5%

A total of 0.05 ml of 1% Barium Chloride (BaCl2) in aquadest was added to 9.95 ml of 1% H2SO4, then shaken until a turbid solution was formed which would be used as a standard comparison for theturbidity of the tested mushroom suspension.

d. Antifungal Activity Testing

Antifungal activity test was carried outby well diffusion method. First a petri dish was prepared, then 200 µL of Candida albicans suspension was deposited, then15 mL of SDA media was added and then shaken simultaneously to get even fungal growth. A total of 20 µL of the test samplewas put into the wells previously made with a cock borer in each petri dish. Thenthe petri dish was incubated at 370C for 24 hours. Inhibitory power can be seen by the formation of the diameter of the inhibition zone around the well. The inhibition zone formed was measured using a caliper.

Processing

Processing of inhibition data in this study used IBM SPSS statistics 22 and with a confidence level of 95%. Before statistical testing was carried out, theresearch data were tested for normality first with the Shapiro-Wilk Test, and the variance of the data was tested withLevine's Test analysis. If it fulfills the requirements of a normal distribution andthe same variance, then the data from the results of the inhibition test can be analyzed statistically with the One-Way ANOVA test. Conversely, if the data is not normally distributed and does not have the same variance, then the data is testedwith a non-parametric test, namely the Kruskal Wallis test, followed by MannWhitney analysis to determine the significant differences in the inhibition ofeach test group.

RESULT AND DISCUSSION

Extraction Results

The process of extracting young areca nut and Manjakani fruit seeds uses the maceration method with 96% ethanolsolvent. The use of the maceration method because this method has an easyway of working and the equipment used is simple (Tena & Asuero, 2022). The choice of using 96% ethanol solvent is because it is selective, non-toxic, has good absorption and high dissolving ability so that it can extract compounds which are non-polar, semi- polar and polar (Wendersteyt et al.,

2021). In addition, 96% ethanol is able to attract flavonoid compounds contained in young areca nutextract and Manjakani extract, where flavonoid compounds are polar compounds, so in general, flavonoids are quite soluble in polar solvents such as ethanol, methanol, butanol (Riwanti et al., 2020).

Compared to other methods such as Soxhlet or supercritical CO2, the maceration method is more economical, simple, and does not require expensive or complex equipment. However, the extraction time may be longer compared to other methods. The main weakness of the maceration method is the relatively low extraction efficiency because the process is slow, requiring proper temperature and time settings for maximum results (Rasul, 2018). Nevertheless, this method is safe, affordable, and effective for extracting bioactive compounds from plants such as flavonoids in young areca nut and Manjakani extracts, which have potential applications in biopharmaceutical and pharmacological research.

From the extraction results, 140.076 grams and 200.146 grams of young areca nut viscous extracts were obtained, respectively. Young areca nut viscous extract obtained is blackish brown in color, has a distinctive odor with a yield percent of 10.35%, meanwhile theManjakani viscous extract is yellowishbrown in color, has a distinctive odor witha yield percent of 11.88%.

Table 2

Organoleptic Observations of Young Areca Extract and Manjakani

Extract	Observation Result		
	Consistency	Colour	Smell
Young areca nut extract(*Areca cathechu L.*)	Thic	Brownish black	Special extract
Manjakani extract (*Quercus infectoria*)	Thic	Yellowish-brown	Special extract

Results of Phytochemical Screening of Young Areca Extract and Manjakani Extract

Phytochemical screening is an initial stage in a phytochemical research which aims to provide an overview of the class of compounds contained in the plant under study (Simaremare, 2014).

Table 3

Results of Young Areca Extract Phytochemical Screening

Compound Target	Method	Results
Alkaloids	Color Reaction	Negative
Steroids/Triterpenoids	Color Reaction	Triterpenoid positive
Flavonoids	Color Reaction	Positive
Saponins	Color Reaction	Positive
tannins	Color Reaction	Positive

Table 4

Results of Manjakani Extract Phytochemical Screening

Target Compound	Method	Results
Alkaloids	Color Reaction	Negative
Steroids/Triterpenoids	Color Reaction	Negative
Flavonoids	Color Reaction	Positive
Saponins	Color Reaction	Negative
tannins	Color Reaction	Positive

Based on tables 3 and 4 of the phytochemical screening results, it is known that young areca nut extract contains flavonoids, tannins and saponins, while Manjakani extract contains flavonoids and tannins which are thought to have inhibitory antifungal activity.

Flavonoid compounds work as antifungals by inhibiting mitochondrial electron transport which results in a reduction in the mitochondrial membrane potential. Inhibition (inhibition) can occur through the inhibition of protons in the respiratory chain which causes a decrease in ATP production and subsequent fungal cell death. Tannin as an antifungal has a mechanism by inhibiting the synthesis of chitin which is used for the formation of cell walls in fungi and damages cell membranes so that fungal growth becomes inhibited (Agustina et al., 2021; Komala & Siwi, 2020). Saponin compounds as antifungals work by reducing the surface tension of the sterol membrane of the cell wall of the Candida albicans fungus, so that its permeability increases. The increased permeability causes the more concentrated intracellular fluid to be pulled out of the cell so that nutrients, metabolic substances, enzymes, proteins in the cell come out and the fungus experiences death.

Test Results of Inhibitory Power of Feminine Cleansing Soap Combination of Young Areca Extract and Manjakani Extract

Antifungal activity test was carried out To determine the ability of a feminine cleansing soap combination of areca nut extract and Manjakani extract to inhibit the growth of the Candida albicans fungus as indicated by the clear zones formed around the wells.

Based on table 5 of the measurement results, the average inhibitory power obtained is F1 has an average drag of 21.33 mm, F2 is 21.67mm, F3 is 22 mm, F4 is 19.67 mm, F5 is 22.33 mm with an average -the average inhibition result of the positive control was 18.33 mm, while the negative control had no inhibition. From the test results, it canbe classified the strength of the antifungal inhibition tested on the Candida albicans fungus, namely the feminine hygiene soap preparations F1, F2, F3, F5 are included in the very strong inhibition zonecategory with a range of > 20 mm, (Julyasih & Purnawati, 2019; Silitonga 2019).This difference in inhibitory strength between each formulation, is due to the variation in concentration of extracts contained in each formula. Resulting in differences in inhibitory effectiveness with Manjakani extract playing a major role in providing significant antifungal effects.

Table 5
Inhibitory Power Test Results

Formulas	Resistance (mm)			Mean ±S
	Replication 1	Replication 2	Replication 3	
F1	21	22	21	21.33±0.58
F2	22	22	21	21.67±0.58
F3	22	22	22	22±0.00
F4	18	21	20	19.67±1.53
F5	23	22	22	22.33±0.58
Positive Control	21	15	19	18.33±3.05
Negative Control	0	0	0	0

To perceive the difference betweenthe resulting inhibition tests, a statistical test was carried out, where a normality test was first carried out. Table 6 shows the results of F1, F2, and F5 have a p value of 0.001, indicating abnormal data distribution. While F4 and positive control have a p value of 0.637, indicating normal data distribution. Then F3 and negative control did not have a p value listed. Because most of the p values obtained from the normality test are p <0.05, which means that the data is not normally distributed, so the statistical test uses the Kruskal Wallis Test.

Table 6
Normality Test Results

Test of Normality			
Test Parameters	Shapiro-Wilk		
	Statistics	Df	Sig.
F1	0.385	3	0.001
F2	0.385	3	0.001
F3	-	3	-
F4	0.253	3	0.637
F5	0.385	3	0.001
Positive control	0.253	3	0.637
Negative control	-	3	-

Table 6 shows the results of F1, F2, and F5 have a p value of 0.001, indicating abnormal data distribution. While F4 and positive control have a p value of 0.637, indicating normal data distribution. Then F3 and negative control did not have a p value listed. Because most of the p values obtained from the normality test are p <0.05, which means that the data is not normally distributed, so the statistical test uses the Kruskal Wallis Test.

Table 7
Inhibition Power Difference Test Results

Test Statistics	
	Test Results
Kruskal-Wallis H	17,174
Df	6
Asymp. Sig.	0.009

Table 7 shows the results of the Kruskal-Wallis test to test the difference in the inhibitory power of feminine cleansing soap which is a combination of areca nut extract (*Areca cathechu L.*) and Manjakani extract (*Quercus infectoria*). The test results showed an H value of 17.174 with a degree of freedom (Df) of 6 and a significant value (Asymp. Sig.) of 0.009. The results of this analysis indicate that there is a significant difference in the inhibitory power of feminine cleansing soap which is a combination of areca nut extract (*Areca cathechu L.*) and Manjakani extract (*Quercus infectoria*). To find out which formula is different, it is continued with the Mann Whitney post hoc test.

Table 8 shows the results of the Mann-Whitney post hoc test to see significant differences between the tested groups. The results showed that there were significant differences between the negative control and positive control, F1, F2, F3, F4, and F5, between positive control and F3 and F5, and between F4 and F3 and F5 against Candida growth.

This difference occurs because thereis a combination of different extract concentrations in each formula, where differences in concentration affect the effectiveness of a drug (Lolok et al., 2020). The percentageof Manjakani extract concentration ineach formula affects the resulting inhibition test, where the higher the concentration of Manjakani extract, the higher the active substance content in itso that the antifungal activity will be even greater (Yanti et al., 2016). In addition, the inhibition of the F4 feminine cleansing soap which only contains young areca nut extract with a percentage of 15% can be caused by the ripeness of the areca fruit used in the extraction process (Setyani et al., 2016). Young areca nut seeds contain polyphenol groupcompounds with a range of 17.2-29.8%. Meanwhile, ripe areca nut seeds containpolyphenol group compounds with a range of 11.1-17.8%. Polyphenol group compounds in areca nut seeds are in theform of flavonoids and tannins. The higher the content of these compounds, the greater the antifungal activity produced (Yen et al., 2020).

Table 8

Mann Whitney Post Hoc Test Results

Group	F1	F2	F3	F4	F5	Positive Control	Negative Control
F1		0.0456*	0.114*	0.105*	0.099*	0.105*	0.034**
F2	0.456*		0.317*	0.072*	0.197*	0.072*	0.034**
F3	0.114*	0.317*		0.037**	0.317*	0.037**	0.025**
F4	0.105*	0.072*	0.037**		0.046**	0.658*	0.037**
F5	0.099*	0.197*	0.317*	0.046**		0.046**	0.034**
Positive Control	0.105*	0.072*	0.037**	0.658*	0.046**		0.037**
Negative Control	0.034**	0.034**	0.025**	0.037**	0.034**	0.037**	

Information:
* = Not significantly different (p > 0.05)
** = Significantly different (p < 0.05)

CONCLUSION

This study aims to evaluate the inhibitory power of feminine cleansing soap based on young areca nut extract (*Areca catechu L.)* and Manjakani extract (*Quercus infectoria*) against the growth of Candida albicans. The main results showed that the combination of young areca nut and Manjakani extracts in various formulations had a significant effect in inhibiting the growth of Candida albicans, with most formulations showing strong to very strong inhibition zones. Research shows that the use of natural ingredients such as areca nut (*Areca catechu L.*) and Manjakani (*Quercus infectoria*) in feminine products can be an alternative to maintain vaginal health and prevent yeast infections. This natural-based formulation can also be developed into market-ready products, potentially attracting consumers who want natural and environmentally friendly products. This innovation can improve product competitiveness in the market, especially as the demand for natural and organic products is increasing. However, further research is needed to determine the optimal concentration of extract that gives the best results. Research also needs to be conducted to explore potential synergistic effects with other natural ingredients to increase product effectiveness. In addition, exploration of various formulation techniques can help develop better and safer-to-use products.

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