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Research Article

Effect Of *Candida Albicans* Cell Concentration on DNA Isolation Results Using Modified *Alkaline Lysis* Method

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ABSTRACT

Candida albicans is one of the leading causes of morbidity and mortality in various countries, with the prevalence of infection reaching 17,640 cases with an average incidence of 1.5 million people, causing more than one billion people, and the adverse effects of fungal infections can threaten >1.6 million lives. This study aimed to determine the effect of Candida albicans cell concentration on DNA isolation results. The method used was the modified Alkaline lysis using cell cultures with concentrations of 10^8, 10^9, and 10^0 cells/mL. The results showed that the growth curve of the sample showed an increase in cell concentration directly proportional to the absorbance of the UV-Vis spectrophotometer results. Cell suspensions in SDB media were incubated for 2-3 days, then the absorbance was measured, resulting in a value of 5.307 nm after multiplying the dilution factor. The results of Candida albicans DNA isolation were visualized using 2% agarose gel electrophoresis, with no DNA bands found in all samples and negative results. In contrast, smear bands appeared in positive controls. Analysis using a Nanodrop spectrophotometer showed the purity of DNA isolates at concentrations of 10^8 and 10^9 < 1.8, while at 10^{10} it was 1.82. The average DNA concentration obtained was < 100 ng/µL. Based on the results of statistical tests, it can be concluded that the p-value <0.05 indicates the effect of cell concentration on the results of DNA isolation using the modified Alkaline lysis method.

***Keywords:** Cell concentration, Candida albicans, Alkaline lysis, DNA isolation*

INTRODUCTION

Candida albicans is one type of fungus that is still one of the highest causes of mortality and morbidity in various countries, which is evidenced by the prevalence of *Candida albicans* fungal infection cases as many as 17,640 cases with an average incidence of 1.5 million people causing more than one billion people, the adverse effects of fungal infections can also threaten >1.6 million lives (Bongomin et al., 2017).

Generally, *Candida albicans* is part of the normal flora of the microbiota, namely organisms found on the surface of the human body and the majority can be found on mucosal surfaces and the digestive tract which grows optimally at a temperature of 25-30° C. *Candida albicans* cell walls

have dynamic properties that are structured like layers and consist of several different carbohydrates. Other conditions have an impact on candidiasis, such as diabetes, thyroid disease, immune disorders, and cytostatics (Jenkinson & Douglas, 2002).

DNA isolation is also the foundation for developing more effective and personalized genetic-based therapies. However, currently used DNA isolation methods, including *Alkaline lysis,* have some limitations and advantages. *Alkaline lysis* is a simple method, often used for DNA isolation in bacteria, but has not been widely applied for DNA isolation in fungi such as *Candida albicans* (Faradisa et al., 2021). This method involves cell lysis using a strong base solution such as NaOH and DNA precipitation with ethanol, but without further purification (Faradisa et al., 2021).

Previous studies have shown that the *Alkaline lysis* method is often less effective in producing pure, high-quality DNA in *Candida albicans.* Therefore, modifications or variations to this method are needed, for example, by adding variations in *Candida* cell concentration to the culture to increase the efficiency of DNA isolation. Several studies have modified culture media to improve DNA isolation results, but further research is still needed to determine the best method that can be applied in general.

Based on this phenomenon, researchers feel challenged to research the effect of *Candida albicans* cell concentration on the results of DNA isolation using the modified *Alkaline lysis* method. This research is expected to fill the gaps in previous research. As shown by Putri et al. (2024), the *Alkaline lysis* method in *Candida albicans* DNA isolation is often less effective in producing high-purity DNA. One of the main obstacles faced is the presence of contamination and less-than-optimal isolation efficiency. Research conducted by Faradisa et al. (2021) shows that alkaline lysis results in poor method performance, and it is recommended to modify the NaOH concentration. Then, further research has been carried out by Putri & Prayekti (2024) by changing the NaOH concentration without varying the *Candida albicans* culture. The results showed an increase by adding 2.0 N NaOH, but the visualization results were not visible on electrophoresis.

The novelty of this research lies in modifying the *Alkaline lysis* method explicitly developed for *Candida albicans* DNA isolation, which aims to see the concentration, Purity, and visualization of DNA bands on electrophoresis.

MATERIAL AND METHODS

This research is included in the experimental research. This research was conducted from December 2024 to February 2025 at the Microbiology Laboratory of Nahdlatul Ulama University Surabaya and the TTDC (*Tropical Disease Diagnostic Center)* Laboratory, ITD *(Institute of Tropical Disease)* Airlangga University. The sample used was a pure culture of *Candida albicans* ATCC 10231 obtained from BBLK Jl. Karangmenjangan No.18 Surabaya. The sample size used was calculated using the Federer formula $(t-1)(r-1) \geq 4.75$ (5), where it is the treatment group consisting of 5 groups resulting of 5 repetitions. So, the total number of treatment groups was 25 samples for five treatment groups, rounded up to 30 samples to meet the data analysis requirements on SPSS. The sampling method in this study is *Simple random sampling.* Where this sampling goes through several processes, namely, *Candida albicans* cultures will be cultured on SDA (*Sabouraud Dextrose Agar*) media stored at 37^{o}C for 2-3 days. Furthermore, the culture that has been obtained is divided into three different concentrations, which can then be used for the DNA isolation stage. In this study, there are three stages, namely:

1) Pre-Analytic

First, submit an ethical license to conduct research. Next, *Candida albicans* cell culture was prepared with 3 different concentrations, namely 10^8, 10^9, and 10^{10} CFU/mL. Dressing the concentration values of 10^8, 10^9, and 10^{10} CFU/ml is by making a fungal growth curve by making the McFarland standard, then homogenizing and diluting in several AF solutions to test the turbidity suspension. After that, check the spectrophotometer and then calculate the OD (*Optical density)* value in each tube and implant it in several cups. The results are calculated on the *colony counter*. Then make a suspension on SDB (*Sabouraud Dextrose Broth*) media incubated for 2x24 hours at 37ºC. After planting, there is turbidity, then vortex to obtain a pellet, followed by a 1:3 dilution (1 ml of pure SDB media and 2 ml of SDB media suspension then pour into a cuvette, and then read the absorbance). After obtaining the desired absorbance results, multiply by the dilution factor, connect with the absorbance value, and enter the graph into Excel. Before proceeding to the DNA isolation stage, the suspension is first calculated using the dilution formula, M1 X V1, and then the desired results will be obtained.

2) Analytical
   a) DNA Isolation Modified *Alkaline Lysis* method

      The working procedure in the modified *Alkaline lysis* method is: each concentration of fungi to be tested is transferred into the tube as much as 1 µL, then centrifuged at 13,000 RPM for 2 minutes until there is a pellet, and the supernatant is discarded. Then the pellet is suspended in a solution of 10 mM EDTA as much as 150µL, add 150 µL NaOH 2.0 N, then vortexed and incubated for 10 minutes at room temperature. Then add 150 µL of potassium acetate, pH 5.2, and vortex. Add 2 drops (80 µL) of chloroform, then vortex and centrifuge for 3 minutes at 10,000 RPM. The supernatant is transferred to a new tube and 150 µL ethanol is added, vortexed, and centrifuged at 13,000 RPM for 10 minutes at 4^0c. The p*ellet* is dried, and a 50 µLTE buffer is added (Faradisa et al., 2021).

   b) Isolation of Control DNA

      The working procedure in the positive control treatment is in accordance with what is stated on the QIAGEN QIAamp DNA mini kit. The use of the QIAGEN QIAamp DNA mini kit is advantageous because it has the advantage of being able to produce DNA up to 50 kb in size. DNA with this length is denatured thoroughly and has the highest amplification efficiency (Kuzuoglu-Ozturk et al., 2025). As for treating negative controls, only use Nuclease Free Water as much as 2 µLper sample.

   c) Quantitative Test

      By looking at the results of the Purity and concentration of DNA isolation carried out with a nanodrop spectrophotometer with a wavelength of A260 and A280 nm, namely by entering 2 µL samples of DNA isolation results on a nanodrop spectrophotometer, which is then read the graph. If the results obtained are between the values of 1.8-2.0 and the concentration is greater than 100 µg/µL, the results of the quantity of DNA are good (Faradisa et al., 2021).

   d) Qualitative Test

      By looking at the results of the visualization of DNA bands carried out with electrophoresis tools. This is made of a 2% agarose gel composition with an electric voltage of 100 volts for 30 minutes. Then the gel is soaked in running buffer and then observed under UV light using a UV-Transilluminator tool (Koentjoro et al., 2021).

3) Post Analytical

Observing the results by comparing the quality and quantity of *Candida albicans* DNA that has been divided into three different concentrations in the *Alkaline lysis* method and the positive and negative control methods. Each treatment sample's purity value and DNA concentration, with the A260/A280 ratio. Then, data processing and analysis were carried out using the SPSS statistical data application until the results and conclusions were obtained.

RESULTS AND DISCUSSION

Result

Based on observations made in the *Germ Tube test*, yeast cells are found with a sprout-like shape, which can be seen in Figure 1.

Figure 1. The positive result of the *Candida albicans* germ tube test with a 400x magnification binocular microscope

This study showed microscopic results of *Candida albicans* cells. They included the development of a sprout-like shape on blastospores with racket-shaped morphology, as shown in Figure 1, which is a positive result of the *Germ Tube Candida albicans.*

Based on the results of determining the concentration of *Candida albicans* cell culture, 10^8, 10^9, and 10^{10} can be seen in Figure 2. This shows that the greater the cell concentration, the resulting curve also rises.

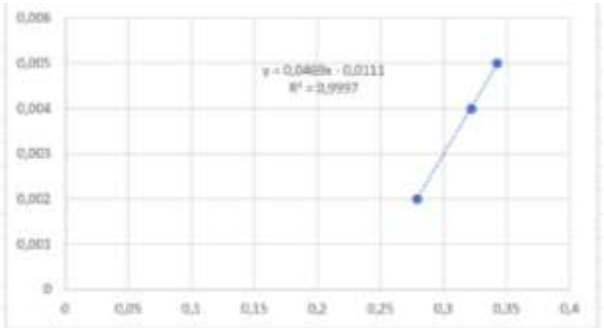

Figure 2. Growth curve of Candida albicans fungus

Figure 2 is a *Candida albicans* fungal growth curve where cell concentration can affect the fungal growth curve formed as measured by a wavelength of 620 nm. These results show that the concentration is directly proportional to the absorbance value; the greater the concentration of *Candida albicans* fungi, the higher the absorbance value produced. With the results of the fungal growth regression equation, y = 0.0469x-0.0111. The results of the linearity value are shown by the correlation coefficient (r) value of 0.997. The value (r) obtained is close to 1, indicating that the regression equation is linear.

1. Quality and Quantity Test with Nanodrop Spectrophotometer

This test was conducted to determine the purity and concentration of DNA at the A260/A280 ratio. Optimal DNA isolation results are indicated by concentrations > 100 ng/ul and purity between 1.8 - 2.0. The results of DNA quality and quantity tests can be seen in Tables 1 and 2.

Table 1. DNA Quality Test Results

Repetition	Purity of DNA 10^8	Purity of DNA 10^9	Purity of DNA 10^{10}	DNA Purity Control (+)	DNA Purity Control (-)
1	1,86	1,92	1,95	2,08	0,98
2	1,62	1,96	1,89	2,10	0,87
3	1,44	1,68	1,86	2,02	1,01
4	1,67	1,88	1,87	2,10	1,25
5	1,76	1,67	1,68	2,18	0,98
6	1,59	1,32	1,70	1,92	1,46
Average ± SD	1,65 ± 0,14	1,73 ± 0,23	1,82 ± 0,10	2,06 ± 0,08	1,09 ± 0,21

Table 2. DNA Quantity Test Results

Repetition	DNA 10^8 Concentration	DNA 10^9 Concentration	DNA 10^{10} Concentration	Control DNA Concentration (+)	Control DNA Concentration (-)
1	18,6	14,8	10,5	17,7	0,1
2	12,6	15,2	10,9	15,6	0,1
3	18,8	16,9	14,8	20,0	0,2
4	11,4	9,7	10,1	29,0	0,2
5	17,8	13,7	12,6	38,7	0,0
6	11,2	12,2	12,4	25,4	0,4
Average ± SD	15,06 ± 3,69	13,75 ± 2,52	11,88 ± 1,75	24,40 ± 8,58	0,16 ± 0,13

2. Visualization of DNA results by Agarose Gel Electrophoresis

The results of DNA isolation were then visualized using agarose gel electrophoresis. DNA visualization was carried out on all samples that had passed five treatments, namely concentration 10^8, $10^{9,}$ and 10^{10}, positive control, and negative control. The following is the documentation of the visualization of the DNA bands obtained.

Figure 3. Visualization results of DNA bands in concentration samples 108 and 109. U1-U6 on the left side is the sample concentration 108 replicates 1-6, M is a 1200 bp marker, and U1-U6 on the right side is the sample concentration 109 replicates 1-6.

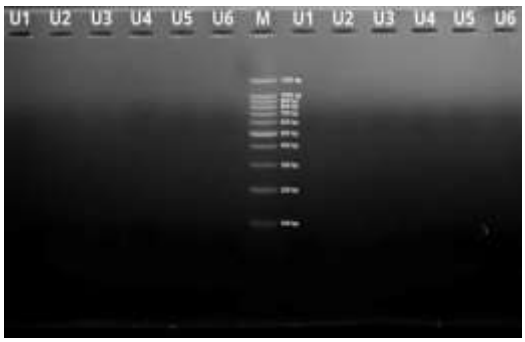

Figure 4. Visualization results of DNA bands in the 1010 concentration sample and control (-). U1-U6 on the left side is the 1010 concentration sample 1-6, M is the 1200 bp marker, and U1-U6 on the right side is the negative control sample 1-6.

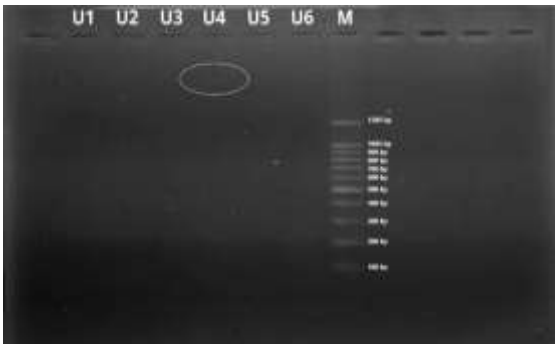

Figure 5. Visualization results of DNA bands in control samples (+) U1-U6 are positive control samples 1-6, and M is a 1200 bp marker. There is a smear DNA band in U4 in the circled image.

Discussions

Figure 1 shows a positive result of the *Candida albicans Germ Tube test*. This is in accordance with previous studies that found sprout-shaped and racket-like cells in the *Candida albicans Germ Tube test* (Putri & Prayekti, 2024).

Figure 2 shows Candida albicans fungus's growth curve where cell concentration can affect the fungal growth curve formed. Absorbance measurements were taken using a wavelength of 620 nm because the wavelength is optimal for reading the OD of *Candida albicans* fungal suspension. (Arzmi et al., 2015).

The growth curve of *Candida albicans* fungus shows that the concentration is directly proportional to the absorbance value; the greater the concentration of the fungus, the higher the absorbance value produced. The fungal growth regression equation y = 0.0469x - 0.0111 was obtained in the absorbance measurement. The results of the linearity value are shown by the correlation coefficient (r) value of 0.997. The value (r) obtained is close to 1, indicating that the regression equation is linear, so it can be said that absorbance and concentration have a robust correlation (Satria, 2021).

The determination of *Candida albicans* fungal cell concentration is based on the results of the OD fungal cell density obtained in this study, which is 5.307 nm. According to research (Karo et al., n.d.), the OD value obtained indicates that the density of fungal cells is very high, so that it can be continued to the next test.

After obtaining the optimal *Candida albicans* cell culture concentration, the DNA isolation process was continued with the modified *Alkaline lysis* method. The use of the *Alkaline lysis*

modification method in this study is because, in this method, the results of DNA isolation are not optimal, even though modifications have been made to the NaOH reagent. NaOH reagent plays an important role in destroying *Candida albicans* cell walls in the cell lysing stage (Putri & Prayekti, 2024).

After DNA isolation, the quality and quantity of DNA were tested using a nanodrop spectrophotometer. Table 1 shows that the average purity of the sample DNA isolate is 1.73. Table 2 shows the average concentration of the sample DNA isolate of 11.9 ng/µL. In the treatment of 1010 concentration, the ideal purity result is 1.82, and in the treatment of 108 concentration, the highest concentration result is 15.06 ng/µL.

In this study, the higher the concentration of *Candida albicans* cells, the lower the results of DNA isolation tend to be. This can occur because the thick Candida albicans cell wall makes the lysis process difficult and causes DNA to be trapped. In addition, excessive cell numbers can cause reagent overload, increased sample viscosity, and accumulation of contaminants that reduce DNA quality, and can even cause DNA fragmentation due to too intensive physical treatment(Putri & Prayekti, 2024;Wasdili et al., 2022).

In this study, DNA isolate results were obtained with low purity and concentration compared to the positive control. According to (Faradisa et al., 2021), the factors that affect the concentration of DNA are the number of cells used in the sample, sampling, and the process of making an imperfect suspension, which will affect the number of cells isolated. The factors that affect DNA quality are an incomplete cell wall lysing process and a less-than-optimal precipitation process. This is due to the complex fungal cell wall, which makes it difficult to perform the lysing process, so the quality of DNA obtained is low.

DNA bands resulting from electrophoresis visualization are ideal if they appear thick, clear, and free of smears (Green & Sambrook, 2012). In this study, the visualization results of DNA isolate samples were not visible on electrophoresis. Visualization using agarose gel becomes invisible or DNA cannot migrate, because several factors cause it (Surzycki & Surzycki, 2000). The possible factors that influence the non-formation of DNA bands in this study are the low concentration of DNA samples, DNA samples having small fragmentation, and insufficient sample volume, so that DNA bands do not appear.

The concentration of DNA isolates plays a role in determining the visualization results of DNA bands (Yuenleni, 2019). DNA concentrations that are too high can make it challenging to visualize DNA bands, while concentrations that are too low can produce faint or very thin DNA bands (Putri & Prayekti, 2024).

Candida albicans DNA samples in this study may have small DNA fragmentation as indicated by the results of the quantity and purity of *Candida albicans* DNA which is relatively low According to (Sambrook & Russell, 2006) DNA samples that have small fragmentation are recommended to be visualized using high agarose gel electrophoresis such as 2% because it is more effective in separating DNA fragments with smaller sizes (about 100-500 bp) because the gel pores are tighter. So, if the isolated DNA is fragmented into small pieces, 2% agarose gel will provide better resolution in separating and visualizing the fragments.

Whereas in this study, no DNA bands were formed after visualization. This can occur because the sample volume used in this study is relatively low, namely 4 µLsample and 2 µL of loading dye, so that it can cause the band to not be seen. The electrophoresis process uses a fairly low volume of DNA isolate samples, comprising 6 micro (4 µLsample and 2 µLloading dye). As

for the volume of DNA samples that are too small on agarose gel electrophoresis, the amount of DNA loaded can be too low, so the DNA bands are not clearly visible or are not detected at all.

This can result in suboptimal separation and difficulty in analyzing the results. To ensure good results, it is important to use an appropriate sample volume so that the DNA concentration is sufficient to produce clear bands and can be analyzed appropriately (Sambrook & Russell, 2006). In addition, thick and complex cell walls can also cause the lysis process to be incomplete, resulting in DNA failing to exit the cell (Putri & Prayekti, 2024; Wasdili et al., 2022). For DNA bands to be visible on electrophoresis, the minimum concentration of DNA required is generally around 10-20 ng/µL, or a total of ≥100 ng of DNA loaded into one well of the gel (Green & Sambrook, 2012).

In this study, the results of DNA isolation showed that higher cell concentrations (10^9 and 10^{10} cells/mL) affected the quantity and quality of DNA. However, no DNA bands were found on agarose gel electrophoresis, and the purity of DNA isolates at cell concentrations of 10^8 and 10^9 was <1.8, indicating suboptimal results. The average DNA concentration obtained was also <100 ng/µL.

On the other hand, (Faradisa et al., 2021) *Alkaline lysis* method, showed the results of DNA quantity at a concentration of 108 cells/mL, namely (3.40 µg/mL) and obtained a concentration of 10^9 cells/mL, namely (8.20 µg/mL) which is categorized as a low DNA quantity result. While the results of DNA quality at cell concentrations of 10^8 and 10^9 with the *Alkaline Lysis* method measured by the A260/A280 ratio showed that the results could not be identified because both results were zero.

The research results (Faradisa et al., 2021) show that cell concentration affects the results of DNA isolation. This is in line with this study, which shows that *Alkaline lysis* still has a significant effect even though the results are less than optimal.

CONCLUSION AND SUGGESTION

Based on the results of this study, it can be concluded that the optimal *Candida albicans* cell concentration is found in the 10^8 cell concentration treatment, with the highest average DNA concentration of 15.06 ± 3.69, which provides significance to the results of DNA isolation. At cell culture concentrations of 10^8, $10^{9,}$ and 10^{10}, no DNA bands were found on a 2% agarose gel run for 30 minutes at 100 volts. There is a significant difference in the use of *Candida abicans* cell concentration on the quality and quantity of DNA obtained using the modified *Alkaline lysis* method, with significant results obtained using the *one-way ANNOVA* Parametric test with a p-value of 0.00 and the *Kruskal-Wallis non-parametric* test with *a p-value* of 0.00. Future research is expected to perform additional procedures at the DNA band visualization stage using PCR to prove the quality and quantity of the DNA isolation obtained.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest related to the publication of this article. No financial, personal, or professional relationships could be considered to have influenced the work reported in this paper.

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