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The Effect of Arabica Coffee Extract (*Coffea Arabica* L.) on the Progression of Lactobacillus Cervicovaginal Microbiome Biomarkers

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ABSTRACT

Cervical infection or cervicitis is an inflammation of the cervical epithelium that can progress to chronicity and potentially lead to cervical cancer. Lactobacillus crispatus, which is normal vaginal flora, can migrate to the cervix and cause inflammation. Mandailing arabica coffee (Coffea arabica L.) is rich in phenolic compounds and antioxidant activity, with antibacterial potential. This research aims to assess the effect of Mandailing arabica coffee (Coffea arabica L.) extract on the growth of Lactobacillus crispatus as an effort to reduce the progression of cervicovaginal microbiome biomarkers. This laboratory experimental study used a completely randomized design (CRD) with 25%, 50%, and 100% concentrations of Mandailing arabica coffee extract. The antibacterial activity test was carried out by liquid dilution, solid dilution, and disc diffusion methods. Data were analyzed using a one-way ANOVA test followed by the Least Significant Difference post hoc test. Mandailing arabica coffee extract contains alkaloids, flavonoids, saponins, tannins, and triterpenoids. Liquid and solid dilution tests showed inhibition of Lactobacillus crispatus growth at all extract concentrations. The disc diffusion test produced the greatest average inhibition at 100% concentration (6.62 cm), followed by 50% (5.19 cm), and 25% (4.81 cm). ANOVA analysis showed a significant effect of extract administration on the growth of Lactobacillus crispatus ($p < 0.001$). Mandailing arabica coffee (Coffea arabica L.) extract has antibacterial activity against Lactobacillus crispatus, with growth inhibition increasing alongside increasing extract concentration. This indicates the potential of Mandailing arabica coffee in preventing cervical inflammation and the progression of precancerous lesions.

Keywords: Mandailing arabica coffee (Coffea arabica L.), Lactobacillus crispatus, antibacterial, cervical inflammation, cervical cancer

INTRODUCTION

Cervicitis, or cervical infection, is a clinical condition characterized by inflammation of the columnar epithelium of the endocervix (Shroff, 2023). It can be acute or chronic, and symptoms range from asymptomatic cases to patients with significant mucopurulent discharge and systemic symptoms. Complications associated with this condition include pelvic inflammatory disease, salpingitis, and endometritis, all of which can have serious health consequences. If left untreated, chronic cervical infection can lead to epithelial changes that can potentially progress to cervical cancer, a leading cause of morbidity and mortality in women worldwide (Marrazzo et al., 2020; Taylor et al., 2019).

Cervicitis can be caused by a variety of pathogens, including sexually transmitted infections such as gonorrhea and syphilis, as well as bacterial infections originating from the normal vaginal flora. Under certain conditions, the normally harmless vaginal microbiota can migrate and invade the cervix, causing inflammation that progresses to chronicity.

Cervicitis can be caused by a variety of pathogens, including sexually transmitted infections such as gonorrhea and syphilis, as well as bacterial infections originating from the normal vaginal flora. Under certain conditions, the normally harmless vaginal microbiota can migrate and invade the cervix, causing inflammation that progresses to chronicity. This untreated inflammatory process can trigger changes in the cervical epithelium, increasing the

risk of malignant transformation and potentially developing into cervical cancer (Pollett et al., 2018; Young & Argáez, 2017). In addition, other factors such as *human papillomavirus* (HPV) infection also contribute significantly to the development of cervical cancer. The cervical microenvironment is very complex, consisting of various immune cells and specific microbiota that play a role in modulating the local immune response.

Although numerous studies have focused on detecting the cervical microbiome and its role in local immune modulation and as a predictive biomarker for HPV infection and the development of cervical neoplasia, few have explored the potential use of natural ingredients as therapeutic agents. One such potential natural ingredient is Mandailing Arabica coffee (*Coffea arabica* L.), which grows in North Sumatra, Indonesia. This coffee is known to be rich in phenolic compounds and has strong antioxidant activity, potentially providing various health benefits, including antibacterial activity.

Previous studies have shown that Mandailing Arabica coffee extract has significant antibacterial effects against various bacteria, including gram-positive bacteria. Furthermore, this coffee is also known to have strong anti-inflammatory effects and can act as a chemopreventive agent and chemotherapy against various types of cancer. The main proposed mechanism is through the activation of the Nrf2 system by phenolic phytochemicals in coffee, which stimulates the expression of cellular defense genes (Sepdian Luri et al., 2021). Activation of this system may help prevent infection by *Lactobacillus crispatus* in the cervical epithelium, which may contribute to the prevention of the development of inflammation-induced precancerous lesions (Kusumaningrum et al., 2017; Chu, 2012).

Research conducted by Luisa in 2020 revealed that in vitro roasted Arabica coffee extract can inhibit the growth of Lactobacillus sp., thanks to the content of chlorogenic acid, galactomannan, arabinogalactan type 2, caffeine, and trigonelline in the coffee. Another study by Stephen S. in 2023 showed that consumption of Mandailing Arabica coffee was associated with a reduced risk of endometrial cancer, especially in women with a body mass index ≥25 kg/m2, as well as a reduced risk of esophageal squamous cell carcinoma in a prospective cohort study in Europe (Sthepan et al., 2022; Zhu et al., 2021).

This study aims to evaluate the potential of Mandailing Arabica coffee as an antimicrobial agent against *Lactobacillus crispatus* using in vitro methods, including the liquid dilution method to measure the Minimum Inhibitory Concentration (MIC) and the diffusion method to determine the sensitivity of the test microbes to antimicrobial agents (Mattson et al., 2016). The results of this study are expected to provide new insights into the use of natural ingredients as alternative therapeutic agents to prevent the development of cervical cancer, with a particular focus on the role of cervical microbiota in local immune modulation and prevention of chronic infections that can lead to malignancy.

METHOD

This study used a laboratory experimental design with a Completely Randomized Design (CRD) approach that utilized Arabica coffee extract (*Coffea arabica L.*) at several concentrations, namely 25%, 50%, and 100%. This in vitro study aimed to evaluate the interaction and effectiveness of phenolic compounds in Arabica coffee against *Lactobacillus crispatus*, which has the potential to facilitate HPV invasion into the epithelial tissue and cervical mucosa, thereby triggering the formation of precancerous lesions and cervical cancer.

This research was conducted at the Integrated Laboratory of the Faculty of Medicine, Muhammadiyah University of North Sumatra.

The subject used in this study was Arabica coffee. The Arabica coffee used in the study was Arabica coffee (*Coffea arabica)* grown in a garden in the Mandailing area, from which the extract was taken for use in this study. The use of Arabica coffee extract (*Coffea arabica* L.) was divided into several concentrations, namely 25%, 50%, and 100%.

In the process of making Arabica coffee extract using the maceration method. By using two thousand five hundred grams of washed Arabica coffee beans, then cut into small pieces, dried and blended until crushed. And in this method also uses 96% ethanol solvent, where the coffee beans that have become powder will be put into a glass container and added with 96% ethanol. After that, the dilution and diffusion method will be carried out for the isolation process *of Lactobacillus Crispatus*. By using several tubes that have been sterilized and labeled P1, P2, P3, Kp, Kn each tube is filled with 1 ml of aquadest medium except for tube P3 and control. Tube P3 is filled with filtrate with a concentration of 100% as much as 2 ml, taken from tube P3 as much as 1 ml is put into tube P2 (50% concentration). Tube P2 is taken 1 ml, put into tube P1 (25% concentration). Tube Kp is filled with 1 ml of test medium and 1 ml of extract. The KN tube was filled with 1 test medium and 1 ml of distilled water. All tubes were added with 1 ml of bacterial suspension, except the control tube, then incubated at 37°C for 24 hours. Samples from tubes 1–3 were taken using a cotton swab and smeared on de Man Rogosa Sharpe Agar media labeled according to the concentration of Mandailing Arabica coffee bean extract. MIC was determined by observing the turbidity and clarity of each incubated test medium and comparing it with the control media solution. The lowest concentration indicating bacterial growth inhibition was indicated by the clarity of the test medium. MBC was determined by observing the presence or absence of bacterial growth in the agar medium after incubation. The lowest concentration indicating bacterial death (no growth) was the MBC value. The diffusion method was carried out using paper discs. Paper discs were inserted into the agar medium that had been inoculated with bacteria and filled with the test compound. Clear areas on the surface of the agar medium indicated that the antimicrobial agent inhibited the growth of microorganisms.

RESULTS AND DISCUSSION

The results of phytochemical content tests on Mandailing Arabica coffee beans (*Coffea arabica* L.) are shown in the table below.

Table 1. Results of Phytochemical Content of Arabica Coffee Beans (*Coffea arabica L.*) Mandailing

Contents	Reaction
Alkaloid	+
Flavonoid	+
Saponin	+
Tannin	+
Triterpenoid	+

Source: Research data, 2024

Table 1 above shows that the results of phytochemical tests on Mandailing Arabica coffee beans (*Coffea arabica* L.) are alkaloids, flavonoids, saponins, tannins and triterpenoids.

Table 2. Observation Results of Liquid Dilution Test on Mandailing Coffee Bean Extract (*Coffea arabica L.*) Against *Lactobacillus crispatus*

Group	MIC Test Results
KN	Cloudy
KP	Clear (++++)
P1	Clear (+)
P2	Clear (++)
P3	Clear (+++)

Source: Research data, 2024

Table 2 above shows that the results of the liquid dilution test observations on Mandailing coffee bean extract (*Coffea arabica* L.) against *Lactobacillus crispatus* where in the negative control, cloudy observation results were obtained in the test tube, while in the positive group, and in the groups given 25%, 50% and 100% Mandailing coffee bean extract, clear results were obtained.

Table 3. Results of the Solid Dilution Test Observations on Mandailing Coffee Bean Extract (*Coffea arabica L.)* Against *Lactobacillus crispatus*

Group	KBM Test Results
KN	+
KP	-
P1	-
P2	-
P3	-

Source: Research data, 2024

Table 3 above shows that the results of the solid dilution test observations on Mandailing coffee bean extract (*Coffea arabica* L.) against *Lactobacillus crispatus* where in the negative control, the positive observation results showed the presence of *Lactobacillus crispatus* , while in the positive group, and in the group given Mandailing coffee bean extract (*Coffea arabica* L.) 25%, 50% and 100%, there was no *Lactobacillus crispatus* .

Table 4. Observation Results of the Diffusion Method on Mandailing Coffee Bean Extract (*Coffea arabica L.)* Against *Lactobacillus crispatus*

Group	H1	H2	H3	H4	Mean
KN	7.5	7.5	7	7	7.25
KP	0.25	0.25	0.25	0.25	0.25
P1	5	5	4.75	4.5	4.81
P2	6	5	5	4.75	5.19
P3	7	6.5	6.5	6.5	6.62

Source: Research data, 2024

Table 4 above shows that the results of observations of the diffusion method on disc paper given Mandailing coffee bean extract (*Coffea arabica* L.) against *Lactobacillus crispatus* where the average result in the positive control was 7.25 cm, the negative control was 0.25 cm, Mandailing coffee bean extract (*Coffea arabica* L.) 25% with an average of 4.81 cm,

Mandailing coffee bean extract (*Coffea arabica* L.) 50% with an average of 5.19 cm, and Mandailing coffee bean extract (*Coffea arabica* L.) 100% with an average of 6.62 cm.

Table 5. Normality Test

Group	P Value
KN	0.224
KP	0.291
P1	0.272
P2	0.103
P3	0.301

Source: Data analysis using Shapiro-Wilk test, 2024

Table 5 above shows the results of the normality test on the negative control with a value of p = 0.224, positive control p = 0.291, Mandailing coffee bean extract (*Coffea arabica* L.) 25% p = 0.272, Mandailing coffee bean extract (*Coffea arabica* L.) 50% p = 0.103, Mandailing coffee bean extract (*Coffea arabica* L.) 100% p = 0.301. Based on the results of the normality test value where the P Value in each group is p> 0.05 which means the data is normally distributed, so it can be continued to be carried out the ANOVA test.

Table 6. *ANOVA Test*

	H1	H2	H3	H4	Mean	P Value
KN	7.5	7.5	7	7	7.25	
KP	0.25	0.25	0.25	0.25	0.25	
P1	5	5	4.75	4.5	4.81	0,000
P2	6	5	5	4.75	5.19	
P3	7	6.5	6.5	6.5	6.62	

Source: Data analysis using one-way ANOVA, 2024

Table 5 above shows that the results of the ANOVA test in the research group obtained a P value <0.001 where there was an effect of administering Mandailing coffee bean extract (*Coffea arabica* L.) on *Lactobacillus crispatus.*

Table 7. *Post Hoc Test*

	KN	KP	P1	P2	P3
KN		0,000	0,000	0,000	0,000
KP	0,000		0,000	0,000	0.144
P1	0,000	0,000		1,000	0,000
P2	0,000	0,000	1,000		0,000
P3	0,000	0.144	0,000	0,000	

Source: Data analysis using LSD test, 2024

Table 7 above shows, the post hoc test above which appears to have a significant difference in the KN group with KP (p = 0.000) where the average inhibitory power in KP is greater than KN, as well as in KN with P1, P2, and P3 (P = 0.000) which means there is a significant difference in the average inhibitory power where the inhibitory power of KN is smaller. Comparison of P1 with KN, KP, and P3 (P = 0.000) which means there is a difference in bacterial inhibitory power between P1 with KN, KP and P3. While in the P1 and P2 groups (P

= 1.000) where there is no significant difference. P2 with P3 (p = 0.000) which means there is a significant difference.

Bacteria are prokaryotic microorganisms that are naturally found in various parts of the human body and outside the human body. Some bacteria can be opportunistic, meaning they are normally beneficial, but under certain conditions they can become pathogens that cause infections in humans. Some examples of bacteria commonly found in the human body include *Escherichia coli, Staphylococcus mutans, Staphylococcus epidermidis, Staphylococcus aureus, Lactobacillus* sp., and others. Treatment of bacterial infections is generally treated with antibiotics. However, the increasing development of antibiotic resistance has triggered the search for new sources of drugs from natural sources, one of which is from plants. As noted by Paul et al. (2019) and Rachmatiah et al. (2020), one plant that can be empirically used as an antibacterial drug is coffee.

The results of this study, where the results of qualitative phytochemical screening showed that the extract of Mandailing Arabica coffee beans (*Coffea arabica* L.) contains alkaloids, flavonoids, saponins, tannins and triterpenoids. In accordance with previous research by Febriani et al. (2023) where Mandailing Arabica coffee (*Coffea arabica* L.) contains polyphenolic compounds alkaloids, flavonoids, saponins, phenolics/tannins and triterpenoids. Research by Munira et al. (2020) where Arabica coffee beans contain alkaloids, flavonoids, saponins, tannins, triterpenoids. Research by Ajhar and Meilani (2020) results of phytochemical tests of Arabica coffee (*Coffea arabica* L.) contain alkaloids, flavonoids, saponins, tannins, and steroids. The main compounds responsible for the antimicrobial action of coffee extract are polyphenolic compounds including chlorogenic acid, caffeic acid, and caffeine as well as minor compounds such as trigonelline, α-dicarbonyl compounds, and protocatechuic acid. These polyphenolic compounds are divided into two groups, namely flavonoids (flavones, flavanols, flavanones, isoflavones, anthocyanidins, and chalcones) and tannins (phenolic acid polymers, catechins, or isocatechins). In this study, both groups were present. Polyphenolic compounds deactivate bacterial cellular enzymes that depend on the rate of penetration of a substance into the cell or are caused by changes in membrane permeability. The antibacterial mechanism of flavonoid compounds is by damaging the permeability of the bacterial cell wall. As described by Farhadi et al. (2020) and Khameneh et al. (2019), alkaloids function as antibacterials by disrupting the peptidoglycan components of bacterial cells, so that the cell wall layer is not formed completely and causes cell death.

The antibacterial mechanism of triterpenoids is to react with porins (Trans Membrane Proteins) on the outer membrane of bacterial cell walls, forming strong polymer bonds that cause damage to the porins. As documented by Rini et al. (2017) and Sani et al. (2019), tannin compounds inhibit bacterial growth by inactivating microbial adhesins (molecules that attach to the host) found on the cell surface and enzymes and disrupting protein transport in the inner layer of cells, tannins also have targets on cell wall polypeptides that cause cell wall damage. The mechanism of action of saponins as antibacterials is by denaturing proteins. Because saponins are surface active substances, they can be used as antibacterials where the surface tension of bacterial cell walls will be reduced and the permeability of bacterial membranes is damaged. According to Marsya et al. (2021) and Amalia (2020), coffee also contains many compounds that have antibacterial activity, namely chlorogenic acid, caffeine, and trigonelline. Chlorogenic acid works by increasing the permeability of the plasma membrane, thereby

reducing the function of bacterial cell defenses and causing leakage of nucleotides and cytoplasmic contents. Trigonelline also has antibacterial activity that is more or less the same as chlorogenic acid, namely by disrupting the stability of the bacterial cytoplasmic membrane. Membrane instability disrupts bacterial nutrient exchange, inhibiting bacterial metabolism and growth. As reported by Kuncoro et al. (2018), caffeine, a crystalline xanthine alkaloid, has an antibacterial mechanism that inhibits cell wall synthesis, leading to cell lysis, and subsequent cell death.

The results of this study indicate that Mandailing Arabica coffee (*Coffea arabica* L.) has an effect in inhibiting the antibacterial *Lactobacillus crispatus* at a concentration of 25%-100% Mandailing Arabica coffee bean extract. The results indicate that coffee has a bacteriostatic effect. Where it is seen in the liquid dilution test and solid dilution, there is inhibition with a clear appearance in the liquid dilution observation, while the solid dilution does not show any bacterial growth in the media. Meanwhile, in the observation of the diffusion method on disc paper given Mandailing coffee bean extract against *Lactobacillus crispatus* where the average result in the positive control was 7.25 cm, negative control 0.25 cm, Mandailing coffee bean extract 25% with an average of 4.81 cm, Mandailing coffee bean extract 50% with an average of 5.19 cm, and Mandailing coffee bean extract 100% with an average of 6.62 cm so it can be concluded that the higher the dose, the higher the inhibitory power. Paula et al.'s (2020) research examined the effect of roasted Mandailing Arabica coffee extract with caffeine (*Coffea arabica*) and decaffeinated coffee (*Coffea cenephora*) on the growth of probiotic bacteria in vitro, where roasted Arabica coffee extract (*Coffea arabica*) limited the growth of *Lactobacillus* sp. Where the study stated that the caffeine contained in Arabica coffee extract (*Coffea arabica*) inhibited probiotic bacteria, while decaffeinated coffee (*Coffea cenephora*) encouraged their growth. The results of the study also showed that coffee consumption can selectively increase the growth of probiotic strains, thus provide a prebiotic effect, and show that roasting and decaffeination of coffee affect this property and that different strains utilize different coffee components to grow.

This study is in accordance with previous studies that examined the potential antimicrobial properties of coffee beans and coffee by-products against *vibrio cholerae*, where the content found as antibacterial is chlorogenic acid, caffeic acid, and caffeine. According to Rawangkan et al. (2022), the study examined the minimum inhibitory concentration and minimum bactericidal concentration against 20 isolates of V. *cholerae*. Where the results showed that all strains tested were sensitive to coffee extract, with minimum inhibitory concentration and minimum bactericidal concentration values ranging from 3.125–25.0 mg/mL and 12.5–50.0 mg/mL, respectively. Almeida's 2018 study, as cited by Wijaya et al. (2017), proved with the results of their research that the caffeine content in Mandailing Arabica coffee bean extract can affect the growth of *Streptococcus mutans* bacteria at a concentration of 2.0 mg/mL and the higher concentration of caffeine provides stronger and longer inhibition. Robusta coffee bean extract is known to have an inhibitory effect on the growth of *Lactobacillus acidophilus bacteria* at concentrations of 100% and 75%, while Arabica coffee bean extract at concentrations of 50% and 25% does not have an inhibitory effect on the growth of *Lactobacillus acidophilus bacteria.*

Previous research has shown that ethanol extracts of Arabica and Robusta coffee beans can inhibit the growth of *Lactobacillus acidophilus bacteria* at a minimum inhibitory concentration (MIC) of 25% and a minimum bactericidal concentration (MBC) of 50%, but there are

differences in the inhibitory zone at concentrations of 75-100%. This is due to differences in the active components contained in the extract. As noted by Sholichah et al. (2017), caffeine and trigonelline are major components of alkaloids in coffee beans that have antibacterial properties. Research on other bacteria by Parnomo (2021) shows that Arabica coffee bean extract can be used to inhibit the growth of *Enterococcus faecalis bacteria* at concentrations of 50% (10.3 mm) and 100% (14.6 mm). The higher the extract concentration, the larger the inhibition zone produced, as is also the case with research by Widyasari et al. (2021) at the same extract concentration, it can inhibit the growth of *Staphylococcus epidermidis bacteria* with an inhibition zone diameter of 6.8 mm at a 50% concentration and 9 mm at a 100% concentration. According to Dafale et al. (2019), differences in the inhibition zone at each concentration in each treatment can be caused by several factors consisting of the culture medium, bacterial sensitivity, incubation conditions seen from temperature, pH, time, media composition, bacterial concentration, and the rate of substance diffusion into the agar.

Paputungan et al. (2019) stated that the growth of *Staphylococcus aureus* and *Escherichia coli bacteria* can be inhibited by ethanol extract of Arabica coffee beans fractionated using solvents with varying degrees of polarity, namely methanol, ethyl acetate, and n-hexane. The results obtained showed that the diameter of the inhibition zone of *Staphylococcus aureus* and *Escherichia coli bacteria* formed at a fraction concentration of 30% was larger than that of the fraction concentrations of 10% and 20%. This proves that the higher the concentration of the test solution, the larger the diameter of the inhibition zone formed. The results obtained from the methanol, ethyl acetate and n-hexane fractions at a concentration of 30%, the diameter of the inhibition zone formed was larger against *Staphylococcus aureus bacteria*, this is because gram-positive bacteria have a cell wall structure with thicker peptidoglycan content but little lipid, and do not have a lipopolysaccharide layer so that hydrophilic and hydrophobic antibacterial compounds can easily pass through the cell wall. Damage to bacterial cells that occurs on the wall, membrane and internal parts of the cell will cause the bacteria to be unable to withstand high osmotic pressure from within the cell, resulting in cell lysis. As explained by Breijyeh et al. (2020), in accordance with this study where *Lactobacillus crispatus* is a gram-positive bacterium and the higher the concentration of Arabica coffee bean extract Mandailing, the higher the inhibition power will also be seen in the concentration of Arabica coffee Mandailing at a concentration of 100% the largest inhibition power is with an average of 6.62 cm.

Based on the results of the analyzed literature study, Arabica coffee bean extract Mandailing has antibacterial activity. This antibacterial property can be used as a source of natural antibiotics. The link between the above articles is that Arabica extract can inhibit the growth of various bacteria even though the extraction is carried out with different methods and concentrations, and the secondary metabolite content varies. Of these several parameters, Arabica coffee bean extract has the best antibacterial activity against the growth of *Lactobacillus crispatus bacteria.*

CONCLUSION

Phytochemical tests on *Mandailing Arabica coffee beans (Coffea arabica L.)* revealed the presence of alkaloids, flavonoids, saponins, tannins, and triterpenoids. In antibacterial tests against *Lactobacillus crispatus*, liquid dilution showed clear inhibition at 25%, 50%, and 100%

extract concentrations, while solid dilution resulted in complete absence of *Lactobacillus crispatus* at all tested concentrations. The disc diffusion method demonstrated the strongest inhibition at 100% concentration, with an average inhibition zone of 6.62 cm. Statistical analysis using ANOVA confirmed a significant inhibitory effect of the coffee extract on *Lactobacillus crispatus* growth ($p < 0.001$). Future research could explore the specific mechanisms underlying the antibacterial activity of these phytochemicals and assess their potential effects in vivo on cervicovaginal microbiota balance and cervical health.

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