

Development Formulation of Aloe Vera and Citrus Limon (L) Burm Extracts (ALOEMON) towards “Minimum Inhibitory Concentration” and “Minimum Kill Concentration” of Streptococcus SP

Nia Afdilla¹, Diah Fatmasari*², Masrifan Djamil³

^{1,2,3} Dental Therapist and Hygienist Department, Poltekkes Kemenkes Semarang
Tirto Agung Rd, Semarang Jawa Tengah 50258, Indonesia

Abstract:- Aloe Vera and Citrus Lemon are herbal plants that have various properties as antibacterial and antimicrobial. The combination of Aloe Vera and Citrus Lemon extracts is formulated in the form of a solution named ALOEMON that can be used as a natural disinfectant. Previous research has shown it can inhibit the growth of gram-negative and gram-positive bacteria. Streptococcus sp is one of the most common bacteria found after tooth extraction. The purpose of the study was to determine the effectiveness of ALOEMON as natural disinfectants by testing the Minimum Inhibitory Concentration (KHM) and the Minimum Killing Concentration (KBM) test, as well as to formulate and determine the physical stability. Using Quasy Experiment pretest-posttest with control group design. Sampling was done by identifying tooth extraction tools exposed to Streptococcus sp media Nutrient Agar (NA). Bacterial testing using spectrophotometry is a fast way to count the number of bacteria in a solution using the liquid dilution method. Subjects were divided into 2 groups, namely the intervention and control groups. This research uses a pharmaceutical chemistry laboratory and a microbiology laboratory. Statistical test using paired sample test, One way ANOVA. Results: effectiveness of inhibition ($p=0.001$), the effectiveness of the killing power of 75% concentration ($p=0.002$), the effectiveness of the killing power of the concentration of 50% ($p=0.007$). Conclusion: The formulation ALOEMON extracts has potential against KHM and KBM of bacteria.

Keyword:- Aloe Vera and citrus Lemon, Minimum Inhibitory Concentration, Minimum Kill Concentration.

I. INTRODUCTION

Aloe Vera is a thick-leaved plant that stores water and contains many active compounds[1]. While Citrus Lemon has bioactive compounds contained in lemons, each of which has antibacterial properties. The natural content contained in lemon can be useful as an antibacterial [2].

The Citric acid (48.6 g/100 g) contained in lemon juice has antibacterial power[3]. The presence of lemonades in citrus species, which have efficacy against clinically isolated bacteria. Lemonades obtained from lemons, showed good antimicrobial activity[2]. The content of essential oils (monoterpenes and sesquiterpenes) such as limonene (97%) has antibacterial activity[3]. Based on the results of phytochemical tests, lemon juice contains alkaloids, phenolic, and flavonoids (70%) [4]. The results of the phytochemical identification test of Aloe Vera extract contained flavonoid antibacterial compounds, Saponins, Tannins, Anthraquinones, and Phenolics[5]. Active compounds such as Lignin and Anthraquinone are substances that function as antibacterial[6].

Streptococcus sp is a gram-positive bacterium that is spherical shape and arranged like a chain during its growth period[7]. *Streptococcus sp* is one of the bacteria that is commonly found after tooth extraction, this bacterium produces various extracellular substances and enzymes.

Dental health workers in carrying out dental care have the risk of being exposed to infection from patient to patient or patient to doctor which is referred to as cross-infection [8]. Transmission of infection can occur by direct contact with microorganisms through sources of infection or indirectly through dental hygiene devices contaminated with saliva and blood[9]. Efforts that can be made to prevent infection are to provide a formulation of Aloe Vera and Citrus Lemon extracts.

Previous studies have reported that Aloe Vera has been shown to be effective against bacteria including: *Staphylococcus aureus*, *Candida albicans*, *Streptococcus mutans*, *Escherichia coli*, *Streptococcus*, *Staphylococcus*, *Lactobacillus*. Sedangkan Citrus Lemonyaitu *Staphylococcus aureus*, *Edwardsiella tarda*, *Streptococcus sanguinis*, *Streptococcus mutans*, *Escherichia coli*, *Aeromonas hydrophila*.

The formulation of a product must pay attention to the stability of a comma, because it takes a long time to use it. The formulation of Aloe Vera and Citrus Lemon extract in the form of a solution can be said to be stable if the time of storage and use, the nature and characteristics of the active substances contained in the preparation remain the same or stable. Therefore, it is necessary to carry out organoleptic tests and physical stability tests.

Based on this, a study was conducted to determine the effectiveness of the combination of Aloe Vera and lemon extracts (ALOEMON) as antibacterial and antimicrobial which has a great effect on the inhibition and killing power of *Streptococcus sp* bacteria in tooth extraction tools after tooth extraction.

II. METHODOLOGY

The design of this research is Quasy Experiment with Randomized Pretest-Posttest design with control group design. This experimental research will be carried out in a microbiology laboratory and a pharmaceutical laboratory. The minimum sample size is calculated based on the Federer formula. The samples were divided into three groups, namely the 75% concentration group, 50% concentration group for the intervention group and 0.5% chlorine solution control.

The sample in this study was the number of colonies of *Streptococcus sp* bacteria obtained from the identification of tools after tooth extraction. *Streptococcus Sp* colonies growing on Nutrient Agar (NA) were treated and incubated at 37°C for 24 hours.

The dilution method was used to measure the Minimum Inhibitory Concentration (KHM) and Minimum Kill Concentration (KBM). The advantage of this dilution method is that one concentration of the antimicrobial agent under test can be used to test several test microbes. The method used is the serial dilution method with spectrophotometric testing methods.

The stages of making the dosage formulation are as follows;

1. Sorting, Aloe Vera and lemon with a good category, sorting the separation process is carried out from foreign objects.
2. Drying with a temperature of 40-50°C ie the drying process is carried out until the aloe and lemon are easily crushed. The dry material in the form of simplicial or powder is then stored in a dry container.

3. Maceration, namely simplicial or powder macerated with 96% solvent. The solution was stored in an airtight maceration tube and protected from sunlight for 4-5 days and stirred daily with a glass stirrer for 30 minutes.
4. Rotary evaporator is a rotary evaporator process at temperatures with hot temperatures of 40-60°C and cold temperatures of 12.4°C to remove the solvent. Then dried with a bath for 2 days to obtain the extract.

Table 1:- Formulation of Aloe Vera and Citrus lemon

Ingredients	Formula		function
	I	II	
Aloe Vera and lemon extract	2,5 gr : 2,5 gr	5 gr : 2,5 gr	Active Substance
Lemon juice	100 ml	100 ml	Active Substance
Carbopol	0,5 gr	0,5 gr	Gelling agent
Triethanolamine (TEA)	1 gr	1 gr	Neutralizing agent
Propylene glycol	15 gr	15gr	Cosolvent
Propylparaben	0,2 gr	0,2 gr	Preservative
Methylparaben	0,02 gr	0,2 gr	Preservative
Aquadest	100 ml	100ml	Solvent

The herbal formulations were made by mixing Aloe Vera and Citrus Lemon extracts together with several chemicals, including: Carbopol as an emulsion stabilizer, Triethanolamine (TEA) as an emulsifier, Propylparaben as an antimicrobial preservative, Propyleneglycol as an antimicrobial preservative, Methylparaben as an antimicrobial preservative. The result of mixing Aloe Vera extract and Citrus Lemon and aquadest into a sterile bottle.

Evaluation of the dosage formulation using the cycling test method. Samples were stored at 4°C for 24 hours and then transferred to a hot oven at 40°C for 24 hours (one cycle). The test was carried out for 6 cycles and then organoleptic observations (changes in color, scent, texture) and physical stability (changes in the pH of the solution) were carried out.

III. RESULT AND DISCUSSION

A. Organoleptic Test

The results of the observation of the cycling method for the organoleptic test which was carried out visually showed that the texture, color and aroma of the base and the two formulas after cycling test for 6 cycles did not experience any change or separation.

Formulation	Before Cycling Test		
	Color	Scent	Texture
75%	Dark brown	Lemon	liquid
50%	Dark brown	Lemon	liquid
Formulation	After Cycling Test		
	Color	Scent	Texture
75%	Dark brown	Lemon	liquid
50%	Dark brown	Lemon	liquid

Table 2:- Aloe Vera and Citrus Lemon Extract Organoleptic Test by Method Cycling test

B. Physical Stability Test

The results of changes in temperature after a cycling test for six cycles have a significant effect on changes in the pH of the preparation. The pH value of the solution from the base and the two concentrations after the cycling test decreased and met the SNI standard No. 06-2588 pH of the preparation solution, namely in the interval of pH 4.5 – 6.5

Table 3:- Aloe Vera and Citrus Lemon Extract pH Test Using Cycling Test Method

Formulation	pH		p-value
	Before Cycling Test	After Cycling Test	
	Mean ±SD	Mean ±SD	
75%	6.103±1.006	4.966±1.064	0.005
50%	6.330±1.355	4.973±0.889	0.003

*Paired Samples Test



Fig 1:- Formulation Aloe Vera and Citrus Lemon Extracts

C. Minimum Inhibitory Concentration (KHM) and Minimum Kill Concentration (KBM)

Table 4 shows that the data effectiveness test is paired. This indicates that the p-values of the intervention group with a concentration of 75% and a concentration of 50% are 0.002 and 0.007 (p <0.05), meaning that Aloe Vera and Citrus Lemon extracts have an effective killing power against *Streptococcus sp*. The p-value of the control group was 0.002 (p <0.05), which means it has an effective killing power against *Streptococcus sp*.

Table 4:-Paired-Data Effectivity Test

Variable	Paired-Data Test		p-value
	Mean±SD		
Minimum Kill Concentration (KBM)			
Concentration 75%	pre	1.91±0.550	0.002
	post	1.87±0.537	
Concentration 50%	pre	2.00±0.516	0.007
	post	1.94±0.498	
Chlorine solution 0,5%	pre	1.88±0.565	0.002
	post	1.80±0.557	

*Paired samples test

Table 5 shows the effectiveness of the unpaired data test. The pre-post (Δ) value showed that the p-value between the intervention and control groups was 0.027 (p < 0.05), meaning that the Aloe Vera and Citrus extracts were more effective in killing *Streptococcus sp* than the control group. This is evidenced by the average value of change (Δ) in the intervention group that was better than the killing power in the control group, namely the intervention group, namely 0.045, 0.038 and 0.027. The effectiveness test of the minimum inhibitory concentration showed that the value of 0.001 (p < 0.05) means that the Aloe Vera and Citrus extracts of the model were more effective against *Streptococcus sp* than the control group. This is evidenced by the average value of the intervention group is better than the inhibition in the control group, namely the intervention group, namely 6.50, 4.25 and 2.13.

The results of the post hoc test or unpaired data showed that the 75% concentration group had greater effectiveness against the killing and inhibiting power of *Streptococcus sp* bacteria compared to the 50% concentration group and the control group.

Table 5:-Non-Paired Data Effectivity Test

Variable	Non-paired data effectivity test (Δ)*		
	Mean ±SD Pre-Post Test	p-value	
Concentration 75%	Minimum Killed Concentration (KBM)		
	0.045±0.132	0.027	
Concentration 50%	0.038±0.006		
Chlorine Solution 0,5%	0.027±0.015		
Post Hoc Non-paired data effectivity test (Δ)**			
p-value	75% -0,5%	75% -50%	50% - 0,5%
	0.022	0.479	0,07
Minimum Inhibitory Concentration (KHM)			
Concentration 75%	6.50±0.926	0.001	
Concentration 50%	4.25±1.38		
Chlorine Solution 0,5%	2.13±1.45		
Post Hoc Non-paired data effectivity test (Δ)**			
p-value	75% -0,5%	75% -50%	50% - 0,5%
	0.001	0.006	0.009

*One Way Anova **Post Hoc Tukey

IV. DISCUSSION

Based on the results of the study, it was concluded that Aloe Vera and Citrus Lemon extracts are products that can be used as a preventive in preventing cross-infection which has great benefits for killing and inhibiting bacteria. Extracts of Aloe Vera and Citrus Lemon proved effective in killing and inhibiting the growth of *Streptococcus sp*. evidenced by the results of the microbiology laboratory and statistical analysis of the value (p-value (p <0.05), table 4).

The results of the organoleptic test of the preparation did not change or separate in color, scent, texture, because the disinfectant preparations from the Aloe Vera and Citrus Lemon formulations had good stability in the storage process, as well as for the herbal disinfectant base before and after storage there was no change or separation. One study stated that the organoleptic test was carried out using the five senses or visually which included the components of color, texture, scent, using the cycling test method[10].

The results of temperature changes in physical tests that occur after cycling testing for 6 cycles have a significant effect on changes in the pH of the preparation. The pH value of the base, 75% concentration, 50% concentration after the cycle test decreased. This is evidenced by the results of the paired data test, the p-values are 0.006 and 0.005 ($p < 0.05$), meaning that there is a difference in effectiveness on the pH of the preparation before and before the cycling test for 6 cycles.

The use of spectrophotometry in this study is a fast way to calculate the number of bacteria in solution, this is in line with the preparation of Aloe Vera and Citrus Lemon extract formulations in the solution texture for the intervention and control groups[11]. Measurements using spectrophotometry were carried out before and after 24 hours incubation at 37°C which was seen through the results of measuring absorbance values before and after incubation. If the absorbance value at the beginning of incubation is higher than the absorbance value at the end after incubation, there is a killing power against *Streptococcus sp*. This is evidenced by the p-value ($p < 0.05$), meaning that the intervention group and the control group have the potential to kill *Streptococcus sp*. Incubation is carried out with the aim of the development and growth of bacteria[12].

Analysis of the results of the research on the successful formulation of Aloe Vera and Citrus Lemon extracts seen from the turbidity value of the minimum inhibitory concentration from the test results using the turbid metric method of the growth of *Streptococcus sp*[13].

Testing using the turbid metric method according to the McFarland 1 turbidity standard, all tube media treatments were incubated for 1x24 hours at 37°C then the results of all solutions in the intervention group tube with a concentration of 75% and 50% concentration showed clarity and then viewed the turbidity value using spectrophotometry. This indicates that the presence of inhibition against *Streptococcus sp* is evidenced by the p-value ($p < 0.05$).

The mechanism of tannin compounds in Aloe Vera and lemon is by way of bacterial walls that have been lysed due to saponins and flavonoids, causing tannin compounds to easily enter bacterial cells and coagulate protoplasm, as a result the cells cannot carry out live activities and their growth is stunted or even dead. Tannins also inhibit antibacterial growth and are able to inactivate microbial cell adhesions as well as inactivate enzymes, and interfere with protein transport in the inner layer of cells[14], [15].

The mechanism of action of Aloe Vera and lemon flavonoids is to provide antibacterial effects, inhibit nucleic acid synthesis, inhibit cytoplasmic membrane function and inhibit energy metabolism[16]. Cell membranes can be damaged by flavonoid compounds by inhibiting the synthesis of macromolecules. Flavonoids can also depolarize cell membranes and inhibit the synthesis of RNA, DNA and protein. In addition, the function of the cytoplasmic membrane and energy metabolism in bacteria can be inhibited by flavonoid compounds[17]. Flavonoids will also cause lysis and inhibit the process of cell wall formation. The above mechanism causes Aloe Vera to kill or inhibit the formation of bacteria[18].

The mechanism of action of citric acid contained in lemon juice can denature bacterial cells by damaging the cell wall and entering the nucleus of bacterial cells, disrupting the process of cellular respiration, inhibiting the activity of bacterial enzymes and suppressing the translation of the regulation of certain gene products. The presence of citric acid compounds cause proteins to experience denaturation which causes changes in their molecular structure so that proteins in bacterial cells cannot perform their functions so that bacterial cells will experience[19].

Saponins are alkaloid substances that can damage the acid (DNA and RNA) of bacteria. The mechanism of action of saponins is an antibacterial group that interferes with the permeability of bacterial cell membranes, which results in damage to cell membranes and causes the release of various important components in bacterial cells, namely proteins, nucleic acids, nucleotides[20].

The mechanism of anthraquinone in Aloe Vera works by phenolic compounds found in the sap. Aloe Vera contains several anthraquinone glycosides (aloin, aloe-emodin, barbaloin). Aloe-emodin is bactericidal against gram-positive bacteria by inhibiting electron transfer in the mitochondrial respiratory chain. Anthraquinones found in Aloe Vera work like tetracyclines, which inhibit protein synthesis in bacteria so that they cannot grow in media that is given a concentration of Aloe Vera leaf extract[21].

Lemon peel extract contains alkaloids with a working mechanism that acts to interfere with the constituent components of peptidoglycan in bacterial cells so that the cell wall layer is not formed completely, causing cell[22]. Terpenoids can inactivate microbial cell adhesins as well as inactivate enzymes, and interfere with protein transport in the inner layer of cells. The phenolics contained in Aloe Vera are phenol derivative compounds with an antimicrobial mechanism on phenolic compounds against bacteria, namely phenolic compounds and their derivatives that can change the protein properties of bacterial cells. Changes in the protein structure of the bacterial cell wall will increase cell permeability so that cell growth will be inhibited and then the cell will be damaged. Terpenoid has ability to inactivated adhesion [15]

V. CONCLUSION

Infectious diseases can be transferred through dental health services that are routinely exposed to microorganisms in the patient's blood and saliva, so efforts are needed to overcome them with the formulation of Aloe Vera and Citrus Lemon extracts. Within the limitations and based on the results of the study, it can be concluded that the formulation of Aloe Vera and Citrus Lemon extracts in the solution texture was more effective in killing and inhibiting Streptococcus sp as a result of bacterial identification of tooth extraction tools compared to 0.5% chlorine solution. The formulation of Aloe Vera and Citrus Lemon extracts can be used as natural disinfectants in dental health services.

REFERENCES

- [1]. G. Patri and A. Sahu, "Role of herbal agents-tea tree oil and Aloe Vera as cavity disinfectant adjuncts in minimally invasive dentistry-an in vivo comparative study," *Journal of clinical and diagnostic research*, vol. 11, no. 5, p. DC05, 2017.
- [2]. M. H. Jeffrey, J., Sudigdoadi, S., Kurnia, D., & Satari, "A Monoterpenoid Isolated from Citrus Aurantifolia Peel and Its Potential as An Antibacterial for The Inhibition and Eradication of Streptococcus Mutans Biofilm.," *Systematic Reviews in Pharmacy*, vol. 11, no. 6, pp. 1205–1210, 2021.
- [3]. Y. Liu *et al.*, "Inhibitory effects of Citrus Lemon oil and limonene on Streptococcus sobrinus – Induced dental caries in rats," *Archives of Oral Biology*, vol. 118, no. 5, 2020, doi:10.1016/j.archoralbio.2020.104851.
- [4]. E. I. Oikeh, E. S. Omoregie, F. E. Oviasogie, and K. Oriakhi, "Phytochemical, antimicrobial, and antioxidant activities of different citrus juice concentrates," *Food science & nutrition*, vol. 4, no. 1, pp. 103-109., 2016.
- [5]. M. E. Berniyanti T, "Microbiological studies on the production of antimicrobial agent by Saponin Aloe Vera Linn against Streptococcus sanguinis," *Res J Microbiol*, vol. 10, p. 385-92, 2015.
- [6]. F. Korkmaz, M. Ozel, T. Tuzuner, B. Korkmaz, and N. Yayli, "Antimicrobial activity and volatile constituent analysis of three commercial herbal toothpastes containing Aloe Vera L. and Fragaria vesca L. extracts," *Nigerian Journal of Clinical Practice*, vol. 22, no. 5, pp. 718–726, 2019, doi: 10.4103/njcp.njcp_557_18.
- [7]. E. I. Sari, Vivin Nola, "The effect of civil chilli extract (capsicum frutescens, L) on streptococcus sp bacteria on the post tooth removal solution," *Journal of Dentistry*, vol. 5, no. 1, pp. 55–64, 2018.
- [8]. L. Bizzoca, M. E., Campisi, G., & Lo Muzio, "Covid-19 pandemic: What changes for dentists and oral medicine experts? A narrative review and novel approaches to infection containment ZOCA, Maria Eleonora; CAMPISI, Giuseppina; LO M,," *International journal of environmental research and public health*, vol. 17, no. 11, p. 3793., 2021.
- [9]. M. J. Vázquez-Rodríguez, I., Estany-Gestal, A., Seoane-Romero, J., Mora, "Quality of cross-infection control in dental laboratories. A critical systematic review," *International Journal for Quality in Health Care*, vol. 30, no. 7, pp. 496–507, 2018.
- [10]. A. B. Wulansari, Aprilla, Mahdi Jufri, "Studies on the formulation, physical stability, and in vitro antibacterial activity of tea tree oil (Melaleuca alternifolia) nanoemulsion gel," *International Journal of Applied Pharmaceutics*, vol. 9, pp. 135-139., 2017.
- [11]. J. K. Kumari, Arti, "Phyto-Chemical Screening of Root Extracts of Glycyrrhiza Glabra by Spectroscopic Methods (UV-VIS Spectrophotometer, FTIR & HPLC). Kumari, A., and J. Kumar. 'Phyto-Chemical Screening of Root Extracts of Glycyrrhiza Glabra by Spectroscopic Methods (UV-VIS Sp,'" *International Journal of Pharmaceutical Sciences and Drug Research*, vol. 11, no. 6, pp. 376–81, 2019.
- [12]. Y. D. Akinduti, P. A., Motayo, B., Idowu, O. M., Isibor, P. O., Olasehinde, G. I., Obafemi, "Suitability of spectrophotometric assay for determination of honey microbial inhibition," *In Journal of Physics: Conference Series*, vol. 1299, no. 1, p. 012131, 2019.
- [13]. I. Putri, D. K. T., Amirda, F., Muzadi, H., Carabelly, A. N., & Erlita, "The antibacterial activity of actinomycetes against the growth of Streptococcus mutans and Lactobacillus acidophilus. In BIO Web of Conferences," *In BIO Web of Conferences*, vol. 20, p. 03006, 2020.
- [14]. S. Haque, A. Al-Amin, B. Islam, N. Nazneen, S. Karim, and M. Rahman, "Antibacterial effect of Dimethyl sulfoxide extract of Aloe Vera (Aloe barbadensis) leaf gel against Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli and Klebsiella pneumoniae," *Mediscope The Journal of GMC*, vol. 7, no. 2, pp. 67–74, 2020, //doi.org/10.3329/mediscope.v7i2.49444.
- [15]. O. Roanisca, R. Rani, and R. G. Mahardika, "Phytochemical Screening and Antibacterial Potency of Jeruk Kunci Fruit Waste (Citrus x microcarpa Bunge) Extract Against Propionibacterium acnes," *Jurnal Pijar Mipa*, vol. 16, no. 3, pp. 387–392, 2021.
- [16]. T. Widyastari, E. Harlia, and E. T. Marlina, "Effectiveness Of Aloe Vera Outer Leaf As a Natural Disinfectant On Inhibition Potential And Reduction Of Inhibition Total Number Bacteria In Milk Room," *J. Austenit*, vol. 4, no. 4, pp. 1–9, 2020.
- [17]. K. A. Abbaszadegan A, Sahebi S, Gholami A, Delroba A and I. A, "Time-dependent antibacterial effects of Aloe Vera and Zataria multiflora plant essential oils compared to calcium hydroxide in teeth infected with Enterococcus faecalis," *Jurnal Investig Clin Dent*, vol. 7, no. 1, p. 93-101, 2016.
- [18]. Y. H. Nonong, M. H. Satari, R. Indriyanti, and S. Patawulandari, "Antibacterial Test between Aloe Vera and Chlorhexidine Based on the Number of Colony of Streptococcus mutans Atcc 25 175 In Vitro," *International Journal of Science and Research (IJSR)*, vol. 5, no. 1, pp. 1379–1385, 2016, doi: 10.21275/v5i1.nov153049.

- [19]. S. Mulyanti, D. S. Laela, E. Julaeha, A. A. Suwargiani, and D. Aripin, "Formulation of mouth rinse from the essential oils of lime (*Citrus aurantifolia*) and its inhibitory efficacy on the growth of *Streptococcus mutans* – in vitro," *Padjadjaran Journal of Dentistry*, vol. 32, no. 1, p. 39, 2020, doi: 10.24198/pjd.vol32no1.25486.
- [20]. P. Tatekalva and S. R. K. Haripriya Subbaiyan, "Comparative evaluation of antimicrobial potential of herbal extracts on *Streptococcus mutans* and *Enterococcus faecalis*: An in vitro study," *Brazilian Dental Science*, vol. 24, no. 1, 2021.
- [21]. V. A. I. Permatasar, M. H. Nurjanah, and W. T. W. Analisis, "Effectiveness of Ethanolic Extract of Aloe Vera Leaves against *Staphylococcus aureus*," *Journal of Medical Laboratory Science Technology*, vol. 3, no. 2, pp. 36–40, 2020, doi: 10.21070/medicra.v3i2.760.
- [22]. M. Goudarzi, M. Mehdipour, B. Hajikhani, S. Sadeghinejad, and B. Sadeghi-Nejad, "Antibacterial Properties of Citrus limon and Pineapple Extracts on Oral Pathogenic Bacteria (*Streptococcus mutans* and *Streptococcus sanguis*)," *International Journal of Enteric Pathogens*, vol. 7, no. 3, pp. 99–103, 2019, doi: 10.15171/ijep.2019.21.