

Formulation and Physical Evaluation of Toothpaste from the Combination of Breadfruit Leaves Extract (*Artocarpus altilis*) and Lime (*Citrus aurantifolia*)

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Received 28 August 2021; Accepted 12 September 2021

Abstract: Breadfruit leaves (*Artocarpus altilis*) contain of antibacterial substances toward *Streptococcus mutans* causing dental caries, with the inhibition in amount of 21,37 mm in the concentration of 20% (very strong). Besides caries, the teeth color is also known as a dental problem that has a relation with someone's aesthetic. Lime (*Citrus aurantifolia*) is one of the natural ingredients that contain of citric acid that can be used as the teeth whitener. This observation was intended to know about the formula and physical evaluation of toothpaste also to find out the effect of variation of breadfruit leaves extract concentration to the physical evaluation of toothpaste. This observation used experimental method with 3 variation of breadfruit leaves extract concentration in amount of 20%, 15%, 10%. The result that obtained (numeric data) was analyzed by SPSS with Kruskal-Wallis test for the data of pH and One Way ANOVA test for the data of foam elevation. The result of foam elevation from the formulas sequentially are 5,7 cm; 6,1 cm; and 6,7 cm with the pH values are 7,74; 7,68; and 7,79. The best evaluation's result of the formulas is the 3rd formula (10% of breadfruit leaves extract) that obtained the toothpaste with stingless odor and taste, homogeneous texture of toothpaste, weak alkaline pH, and the best foam elevation compared with 1st formula (20% of breadfruit leaves extract) and 2nd formula (15% of breadfruit leaves extract). Based on the hedonic test, the 1st formula is the best formula in color category, and 3rd formula is the best formula in odor, texture and foam category. The conclusion is the variation of breadfruit leaves extract concentration will affect the pH of toothpaste and not affect the foam elevation of toothpaste that made.

Keywords: Toothpaste, breadfruit leaves extract, lime, physical evaluation.

I. INTRODUCTION

Caries is a chronic dental disease that has a long process, in the form of chronic and continuous loss of mineral ions from the enamel surface on the crown or root surface of teeth, it is caused by bacteria and the product they produce. Dental caries usually caused by *Streptococcus mutans* and it can be prevented by chemical and mechanical preventive measures. Mechanically, the thing that can be done to reduce dental caries is by brushing the teeth. To brush the teeth, we need toothpaste, so the tooth cleaning is done mechanically and chemically. Toothpaste (*Pasta Dentifriciae*) is a thick mixture that consisting of powder and glycerin which is used for cleaning teeth. Toothpaste is generally used for adhesion to mucous membranes to obtain a local effect. Paste usually made by mixing the large amounts of powdered medicinal ingredients with vaseline or liquid paraffin with a lean base made with glycerol mucillago, or soap. A toothpaste usually contains abrasive agent, surface active agent, humectant, binder and flavoring. The functions of toothpaste are to clean teeth from food's or beverage's residue, maintain the healthy teeth and gums, eliminate the bad breath, prevent tooth decay that caused by mouth bacteria, prevent the tartar and gingivitis, and for the aesthetic purpose of tooth color^[1]. One of the common antibacterial substances added to toothpaste is herbal ingredient, the use of herbal toothpaste can provide a chemical effect to control plaque formation. The previous studies have found that herbal toothpaste can reduce the number of the main bacteria in the oral cavity, namely *Streptococcus mutans*^[1].

One of the herbal plants that can be used as antibacterial is breadfruit leaves. Breadfruit (*Artocarpus altilis*) is an Indonesian natural ingredient which has been known only as a fruit but actually it has medicinal efficacy. Breadfruit leaves has the antibacterial efficacy that can inhibit the growth of *Streptococcus mutans* at the concentration of 10% has the inhibition of 12,44 mm, at the concentration of 15% has the inhibition of 16,23 mm, and at the concentration of 20% has the inhibition of 21,37 mm which categorized as the strong and very strong inhibition category^[2]. Breadfruit leaves contain the antibacterial compounds such as flavonoid, tannin, saponin, and phenol^[2]. Tannin is the active substance that can cause protein denaturation by producing the

protein complex. Flavonoid can disturb bacterial wall synthesis when it interacts with bacterial DNA. Phenol has an antibacterial activity by disturb bacterial cell permeability and the function of cell membrane as a selective layer, while the saponin has a function to ruin the bacterial protein cell wall^[3].

Another problem that can occur in the teeth is the color of the teeth. Tooth discoloration has a relation with someone's aesthetic especially in the anterior teeth which are clearly visible when someone interact with other, or when talking or smiling and it can occur a psychological impact in that person. One of the natural ingredients that can be used as the teeth whitener is lime. Lime has some benefits as the antibacterial, antifungal, anticancer, antioxidant, and as the teeth whitener^[4]. Lime, at the concentration of 2,5% can bleach the teeth because it contains citric acid on its flesh of fruit that has a similar pH with the natural whitener pH such as the sour strawberry^[5].

II. MATERIALS AND METHODS

2.1 Plant Material Collection and Authentication

Simplicia preparation was carried out by searching and collecting the breadfruit leaves and lime fruit in Klepu Village, Donorojo District, Pacitan Regency, East Java, Indonesia. The determination of breadfruit and lime plants was carried out in B2P2TOOT, Tawangmangu, Karanganyar Regency, Central Java, Indonesia.

2.2 Chemicals

The ingredients used in this research are breadfruit leaves extract, lime, calcium carbonate, Na-CMC, Sodium lauryl sulfate, glycerin, methyl paraben, propyl paraben, sorbitol, and aquadest.

2.3 Preparation and Extraction of Plant Material

Taking 7 kilograms of breadfruit leaves which has a dark green and not wrinkled, then wet sorting is done by separating the dirt materials from breadfruit leaves. Then washing it using clean flowing water by cleaning one by one then chopping it to reduce its size like a haksel. Chopping breadfruit leaves is done to simplify the drying and pollination process. Drying breadfruit leaves done by using an oven at the temperature of 60°C. If it already dried, do the dry sorting to separate the dirt left behind in the simplicia, then the simplicia mashed to be the dried powder. The next step is measuring the dried powder using analytical scale in amount of 800 grams and putting it in a maceration container, macerating it using 8 liter of 70% ethanol for 5 days in a container which protected from light, and then filtering it using flannel. The filtered macerate that has been collected will be thickened using a rotary evaporator and a water bath to obtain a thick extract, and then evaluate it for the organoleptic, specific gravity, drying shrinkage, moisture content, and also phytochemical screening.

2.4 Phytochemical Screening of Breadfruit Leaves Extract

2.4.1 Flavonoid Test

Putting 1 ml of breadfruit leaves extract into a test tube, then 2 drops of 10% NaOH were added and shaken strongly. Positive samples contain flavonoid when the solution's color change into a very flashy color to be yellow, red, or brown^[6].

2.4.2 Tannin Test

Reacting 1 ml of breadfruit leaves extract with 10% FeCl, the discoloration to be blue, dark blue or greenish black color show that there are polyphenol and tannin substances^[7].

2.4.3 Saponin Test

Putting the extract into a test tube, adding 10 ml of hot water then cooled and shaken strongly for 10 seconds. A stable foam is formed for 10 minutes as high as 1-10 cm on the addition of 2N HCL, the foam does not disappear^[7].

2.4.4 Phenol Test

Breadfruit leaves extract in amount of 0,2 grams were added with 1% FeCl solution. The positive result is indicated by the formation of green, red, purple, dark blue, blue or greenish dark color^[7].

2.5 Making Toothpaste Procedure

Toothpaste is made by weighing the ingredients that used. Putting CMC Na into the mortar then adding aquadest, stirring it using the stamper until mucilago is formed, adding calcium carbonate and stirring homogeneously. Pouring the breadfruit leaves extract that has been dissolved into the hot aquadest previously and then stirring it homogeneously. Pouring the methyl paraben and propyl paraben that has been dissolved into the glycerin, pouring them into the toothpaste preparation and stirring them homogeneously. Dissolving sodium

lauryl sulfate and sorbitol into aquadest then mixing it into the toothpaste preparation, stirring it until homogeneous. The formula of toothpaste can be seen in the Table 1.

2.6 Physical Evaluation of Toothpaste from The Combination of Breadfruit Leaves Extract and Lime

2.6.1 Organoleptic Test

Organoleptic test is done by observing the texture, color, odor and taste of the toothpaste that made ^[8].

2.6.2 Homogeneity Test

Homogeneity test is done by seeing the spread of toothpaste. When the sample that smeared does not show any powders or spots, the sample of toothpaste is homogeneous. Taking 0,1 gram of toothpaste as the sample and then smearing it on the object glass, observing its homogeneity.

2.6.3 pH Test

pH test is done to find out whether the pH of the toothpaste that made is appropriate with the mouth pH (4,5-10). This pH test is done by dipping the digital pH meter stick into the toothpaste which previously calibrated with the buffer solution, then the result can be observed after a few minutes at the monitor screen. The constant value at the monitor screen shown the pH of the sample ^[9].

2.6.4 Foam Elevation Test

Foam elevation test is done by putting 1 gram of toothpaste into the measuring glass of 50 mL, then adding 10 mL of aquadest shaken strongly and measuring the formed foam ^[10].

2.6.5 Hedonic Test

Hedonic test is done to rate a sample by involving several panelists or volunteer which then asked to give their opinions or responses toward the quality of the sample. Hedonic test was done by 20 panelists which were male nor female toward the toothpaste that made and asked to rate the organoleptic of toothpaste such as color, odor, taste, texture and foam. In processing data, the result of hedonic test can be analyzed using a scoring method ^[11].

2.7 Data Analysis

The data analysis method that used in this observation are parametric test (One Way ANOVA) and nonparametric test (Kruskall Wallis). The result interpretation from One Way ANOVA test is when it obtained the *P* value from the significance column is $<0,05$ so it means that there is a significant difference between the tested samples. But when it obtained the *P* value from the significance column is $>0,05$ so it means that there is no significant difference between the tested samples ^[12]. The result interpretation from Kruskal Wallis test showed by *Asymp.Sig* value. When it obtained the *P* value from the significance column is $<0,05$ so it means that there is a significant difference between the dependent towards independent variable ^[13].

III. RESULTS AND DISCUSSION

Based on the result of breadfruit and lime plants determination, it is stated that the plants which observed is the correct species of *Artocarpus altilis* for the breadfruit plant and *Citrus aurantifolia* for the Lime plant. From the 7 kilograms of breadfruit leaves that has been dried using an oven at the temperature of 60°C, obtained simplicia in amount of 2,106 kilograms with 70% of the LOD (Loss on Drying) value. The LOD determination of breadfruit leaves is done to give the maximum range of the substances that lost during the drying process. From the result that obtained showed that the amount of evaporated or lost substances due to heating in amount of 70%, so the remaining content in the simplicia is 30%. The remaining content is probably the water and the substance that does not disappear during the heating because the temperature that is used in the oven is 60°C while the boiling point of water is 100°C, so not all water evaporates during the drying process but some are still trapped in the simplicia cells of breadfruit leaves ^[14]. Breadfruit leaves simplicia was taken in amount of 800 grams for extraction using maceration method with the solvent of 70% ethanol and obtained the weight of the thick extract in amount of 57,874 grams with 7,23% of yield value, which means that in 800 grams of breadfruit leaves simplicia that has been extracted with 8 liters solvent of 70% ethanol solution contains 7,23% thick extract of breadfruit leaves. Then the thick extract was evaluated organoleptically. The thick extract that obtained has the form of an extract, thick, blackish brown color, distinctive odor and bitter taste. The density of breadfruit leaves extract obtained was 1,01 with a water content of 4,86% and drying loss of 7,24%. The result of phytochemical screening showed that the breadfruit leaves extract contains flavonoid, phenol, saponin, and tannin as antibacterial against *Streptococcus mutans* ^[2]. The phytochemical screening result of breadfruit leaves extract can be seen at Table 2.

3.1 Physical Evaluation of Toothpaste

The toothpaste is made into 4 formulas with the combination of breadfruit leaves extract (*Artocarpus altilis*) and Lime (*Citrus aurantifolia*) that are F1 (20%:2,5%), F2 (15%:2,5%), F3 (10%:2,5%) and F4 as the negative control and obtained the result of physical evaluation as follows:

3.1.1 Organoleptic Test

The result of organoleptic test of toothpaste preparation to describe the color, odor, taste, and texture are shown in Table 3. In the organoleptic test, it can be seen that the toothpaste base was originally has a bone white color before the addition of breadfruit leaves extract and lime, after adding the breadfruit leaf extract and lime the color of resulting toothpaste changed to brownish green with the different intensity color (dark color and bright color) for each formula. The odor and taste that produced also different according to the addition of breadfruit leaves extract concentration in the toothpaste preparation. The higher concentration of the extract that added in the toothpaste preparation will produce darker color, the more pungent odor and the bitter taste of the toothpaste that made.

3.1.2 Homogeneity Test

The result of homogeneity test of the three of toothpaste formulas with a combination of breadfruit leaves extract and lime can be seen in Table 4. In the homogeneity test in formula 1, 2, 3 it appears that there are spots from the added extract, this is because the thick extract that dissolved into the solvent (aquadest) cannot be dissolved completely because the thick extract used has a slightly dry texture, while to elaborate it using a polar solvent (aquadest) is very difficult to do. Even in this composition of this toothpaste, the thick extract cannot be dissolved using ethanol/alcohol which is a polar solvent because the preparation that made is an oral preparation, it should not contain ethanol/alcohol. In addition, the polarity of ethanol/alcohol is lower than aquadest, although it can dissolve the thick extract, it's dissolving ability is also cannot be perfect^[15]. The way that can be done to overcome this problem is by using a liquid extract or a thick extract that has a higher water content (not too thick) so that the decomposition of the extract in the solvent is easier to do, and the result of toothpaste can be more homogeneous without any spots because of the added of extract.

3.1.3 Foam Elevation Test

The foam elevation test is used to determine the amount of foam that produced by the toothpaste preparation that made. The result of the foam elevation test in the three toothpaste formulas can be seen in Table 5. The size of the foam elevation can be associated with the aesthetic value that consumers prefer, with the presence of foam that appears, brushing teeth will feel more comfortable. The addition of extract variation concentration will affect the amount of foam that produced. In formula 4 (negative control), the product of foam is more than the formula with the addition of breadfruit leaves extract. The concentration of extract that used can also affect the foam elevation of the preparation^[16]. Formula 3 which contains the lowest concentration of extract (10%) produces a higher foam elevation than formula 2 that contains 15% of extract and formula 1 that contains 20% extract. Formula 1 produced the lowest foam elevation compared to formula 2 and 3. So, it can be concluded that the variation concentration of breadfruit leaves extract that added into the toothpaste will affect its foam elevation. The higher of breadfruit leaves extract added, the less foam will be produced.

3.1.4 pH Test

The result of pH test of the toothpaste formulas can be seen in Table 6. The toothpaste should have an appropriate pH with the pH of mouth which ranges from 4,5-10^[17]. Toothpaste that has a lower pH (acidic) will damage the teeth enamel and corrosive, while the higher pH (alkaline) of toothpaste will causes the deposition of material which form plaque around the roots of the teeth, as well as on the surface of the teeth facing the salivary glands^[18]. The additional of breadfruit leaves extract and lime will affect the pH of toothpaste. Formula 4 as the negative control has a pH that tend to be alkaline, when added breadfruit leaves extract and lime (formula 1, 2, 3) the pH of toothpaste drops to near neutral but still weakly alkaline. This is because the formula 1, 2, 3 contain lime which is acidic (pH 2,30) which causes the pH of toothpaste to be decrease from the original base. Formula 1, 2, 3 has a pH range of 7 to 8 (alkaline), but as shown in the table formula 3 which has the lowest concentration of breadfruit leaves extract (10%) produces a more alkaline pH than formula 2 and formula 1. Based on the research that conducted by M. Tahir et al., (2017)^[19], the pH of breadfruit leaves extract is 6,42 (weak acid), so that the concentration variation of breadfruit leaves extract will also affect the pH of toothpaste preparation. By added the breadfruit leaves extract, the pH of toothpaste will become lower (acidic).

3.1.5 Hedonic Test

The hedonic test is carried out to assess a sample by involving several panelists who are then asked to provide their opinions or responses to the quality of a sample. The data that has been obtained from the hedonic questionnaire that has been filled in by SPSS 22 with the result that can be seen at Table 7.

The hedonic test categories carried out include color, odor, texture, and foam sensation with 5 rating scales, namely 1 scale (very dislike), scale 2 (dislike), scale 3 (ordinary), scale 4 (like), scale 5 (very like). In each category, the significant difference between the three formulas can be seen in the resulting subset column. If the data produce 2 different subset columns, then there is a significant difference to the three formulas in the tested categories. The result of the subset values can be seen in Table 6 where the results show that formula 1 has the highest subset value, it means that formula 1 is the most preferred formula by panelist in color category, and formula 3 has the highest subset value in the odor, texture, and foam categories that means formula 3 is the preferred formula by panelists in the odor, texture, and foam categories.

In this observation, data processing was carried out using IBM Statistic SPSS 22, where the data were analyzed for normality and homogeneity to determine the further test that will be used. The processed data is the numerical data, that contains of pH's data and foam elevation's data from the toothpaste formulas. The result of the normality and homogeneity test of the pH's data in this observation is normal but it is not distributed homogeneously, the next data analysis method used Kruskal Wallis. While the result of foam elevation's data is normal and homogeneous, the next data analysis method used One Way ANOVA. The result of data processing showed that there was a significant difference in the variation concentration of the breadfruit leaves extract towards the physical evaluation of toothpaste that made.

3.2 Data Analysis

Data analysis method that was used to analyze the pH data is nonparametric test with Kruskal Wallis method and the foam elevation data was analyzed by parametric test with One Way ANOVA method. Kruskal Wallis method obtained the significance value 0,00 that means the significance value is under 0,05, so it can conclude that there is a significant difference between the concentration variation of breadfruit leaves extract towards the pH of toothpaste. While the One-Way ANOVA method obtained the significance value 0,432 which >0,05 so it means that there is no significant difference between the breadfruit leaves extract concentration variation towards the toothpaste foam elevation.

Table 1: The Formula of Toothpaste

Ingredients	Concentration (%)				Function
	F1	F2	F3	F4 (K-)	
Breadfruit Leaves Extract	20	15	10	-	Active substance
Lime	2,5	2,5	2,5	-	Active substance
Na-CMC	2	2	2	2	Making texture
Calcium Carbonate	43	43	43	43	Abrasive
Glycerin	9,5	9,5	9,5	9,5	Humectant
Natrium Lauryl Sulfate	2	2	2	2	Detergent
Sorbitol	0,3	0,3	0,3	0,3	Sweetener
Methyl Paraben	0,075	0,075	0,075	0,075	Preservative
Propyl Paraben	0,025	0,025	0,025	0,025	Preservative
Aquadest	ad 100	ad 100	ad 100	ad 100	Solvent

Table 2: Phytochemical Screening of Breadfruit Leaves Extract

Test	Color Result	Indicator (+)	Result
Flavonoid	Brown	Yellow, red or brown	+
Tannin	Greenish black	Dark blue, greenish black	+
Saponin	Stable foam ± 10 minutes Foam elevation = 3 cm	Stable foam ± 10 minutes Foam elevation = 1-10 cm	+
Phenol	Greenish black	Green, red, blue, dark blue, greenish black	+

Table 3: The Result of Organoleptic Test

Formula	Organoleptic Test			Texture
	Color	Odor	Taste	
1	Brownish green (dark color)	The smell of extract	The taste of extract, a bit sour	Semi solid, soft like a toothpaste
2	Brownish green	The smell of extract	The taste of	Semi solid, soft like a toothpaste

3	Brownish green (bright color)	The smell of extract	extract, a bit sour The taste of extract, a bit sour	Semi solid, soft like a toothpaste
4 (K-)	White bone	No odor	No taste	Semi solid, soft like a toothpaste

Table4: The Result of Homogeneity Test

Formula	Homogeneity
1	Inhomogeneous
2	Inhomogeneous
3	Inhomogeneous
4 (K-)	Homogeneous

Table5: The Result of Foam Elevation Test

Formula	Foam elevation (cm)
1	5,7 ± 0,26
2	6,1 ± 0,11
3	6,7 ± 0,21
4 (K-)	7,2 ± 0,20

Table6: The Result of pH Test

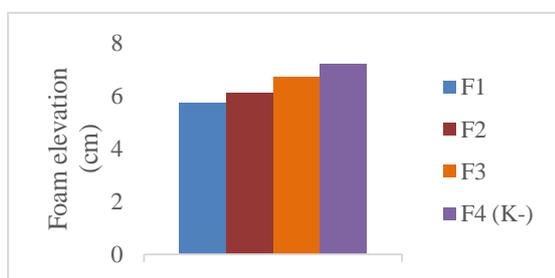
Formula	pH
1	7,74 ± 0,06
2	7,68 ± 0,21
3	7,79 ± 0,04
4 (K-)	9,10 ± 0,21

Table7: The Hedonic Test Result from the Three of Toothpaste Formula

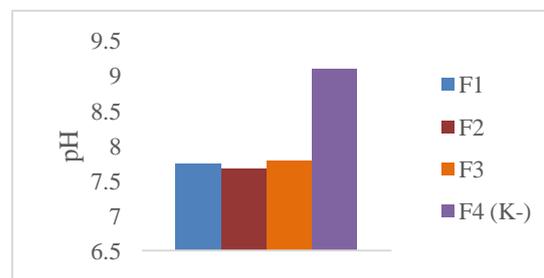
Test Category	Subset Value			Best Formula
	F1	F2	F3	
Color	3,70	3,55	3,60	F1
Odor	2,65	3,00	3,05	F3
Texture	3,20	3,60	3,90	F3
Foam	3,30	3,30	3,70	F3

Fig 1: Diagram of the Foam Elevation and pH Test Result

A. The Diagram of Foam Elevation Test Result



B. The Diagram of pH



IV. CONCLUSION

Based on the research that has been done, it can be concluded that the formulation and physical evaluation of toothpaste from the combination of breadfruit leaves extract and lime produced different homogeneous texture, color, odor, taste, pH, and foam elevation between the three formulas. The evaluation result of the best formula is in the formula 3 (10%:2,5%), formula 3 produces toothpaste with taste and odor that is not too strong, has inhomogeneous toothpaste texture, weak alkaline pH, and the best foam elevation compared with formula 1 and formula 2. Formula 1 is the best formula in the color category and formula 3 is the best formula in odor, texture and foam category based on the hedonic test. There is a significant difference between the concentration variation of breadfruit leaves extract toward the pH of toothpaste and there is no significant difference between the concentration variation of breadfruit leaves extract toward the foam elevation.

ACKNOWLEDGEMENTS

We would like to thank the Laboratory Assistant and The Head of Pharmacy Study Program of Indonusa Polytechnic of Surakarta for providing all the facilities required to carry out this work.

Abbreviations

Na-CMC: Sodium Carboxymethyl Cellulose. NaOH: Sodium dioxide. NaCl: Sodium Chloride.

REFERENCES

- [1]. Depkes RI. (1995). *Indonesian Pharmacope 4th edition*. Jakarta: Departemen Kesehatan Republik Indonesia.
- [2]. Yuliastri, Wa Ode, dkk. (2019). Breadfruit Leaves (*Artocarpus altilis*) Herbal Toothpaste Formulation and Its Antibacterial Activity Test Towards *Streptococcus mutans*. *Indonesia Mandala Pharmacon Journal*, Vol. 05, No. 01. <https://doi.org/10.35311/jmpi.v5i01.35>.
- [3]. Bempa, S. L. P., Fatimawali., & Perengkuan, W. G. (2016). Breadfruit Leaves Extract (*Artocarpus altilis*) Inhibition Test On Bacteria *Streptococcus mutans* Growth. *Pharmacon*, Vol.5, No. 4. 2302-2493. <https://doi.org/10.35799/pha.5.2016.13967>.
- [4]. Makasenda, E. F. ., Wicaksono, D. A., & Khoman, J. A. (2018). The Discoloration of Composite Resin On Immersion In Vinegar (Asetic acid) and Lime (*Citrus aurantifolia*). *E-GIGI*. <https://doi.org/10.35790/eg.6.2.2018.20149>
- [5]. Prastiwi, S. S., & Ferdiansyah, F. (2017). Article Review: The Substances and Pharmacological Activity of (*Citrus aurantifolia s.*). *Farmaka*.
- [6]. Lisi, A. K. F., Runtuene, M. R. J., Wewengkang, D. S. (2017). Phytochemical Test and Antioxidant Activity From Soyogi Flower Methanol Extract (*Saurauia bracteosa* DC.). *Pharmacon* Vol.6 No.1. 2302-2493.
- [7]. Hanani, Endang. (2015). *Phytochemical Analysis*. Jakarta: EGC.
- [8]. Tauchitul Alfiyah Agustin, T. D. K. (2017). Physical Quality of Pineapple Peel Extract Toothpaste (*Ananas Comosus* L.) With The Variation concentration of CMC-Na as A Binder. *Journal of Chemical Information and Modeling*, accessed on December 1st, <http://repository.pimedu.ac.id/id/eprint/8>.
- [9]. Auna Mahdalin, Elis Widarsih, dan K. H. (2017). Physical and Chemical Test In The Formulation of Gambir Toothpaste With The Natural Sweetener of Stevia Leaves. *The 6th University Research Colloquium 2017*. Vol. 4, No. 2252-7311.
- [10]. Maesaroh, Imas., Nurhayati, Euis. (2018). The Effectiveness Test of Using Kepok Banana Peel Extract Toothpaste (*Musa paradisiaca* L.) as Teeth Whitener. *Pharmacy Science Journal*. Vol.9 No.1.
- [11]. Kusmayadi. (2004). *Descriptive Tourism Statistic*. Jakarta: PT. Gramedia Pustaka Umum.
- [12]. Usman, Husaini dan Purnomo, S. A. R. (2004). *Social Research Methodology*. Jakarta: Bumi Aksara.
- [13]. Santoso, Singgih. (2006). *Using SPSS For Nonparametric Statistic*. Jakarta: Elc Media Komputindo.
- [14]. Depkes RI. (2000). *General Standard Parameter of Medicinal Plant Extract*. Jakarta: Departemen Kesehatan Republik Indonesia.
- [15]. Sa'adah, H., Henny Nurhasnawati. (2015). The Comparison of Ethanol and Water as The Solvents in The Manufacture OF Tiwai Onion (*Eleutherine americana* Merr.) Using The Maseration Method. Samarinda Pharmacy Academy. *Manuntung Scientific Journal*, Vol. 1, No.2, Page: 149-153.
- [16]. Marlina, Dewi., Nilma Rosalini. (2017). Formulation Gel Toothpaste from Breadfruit Leaves Extract (*Artocarpus altilis*) With Na-CMC as The Gelling Agent and Its Physical Stability Test. Palembang's Helath Journal, Vol.12, No.1, Page: 36-50.
- [17]. National Standardization Institution. SNI 12-354-1995. Toothpaste. Jakarta: 1-16.
- [18]. Oktafria, Satya dkk. 2016. The Description of The Acidity Degree of Saliva and The Amount of Caries In Students at The Intinung Dormitory, North. Yogyakarta: Yogyakarta Health Polytechnic-Press.
- [19]. M.Tahir, M., Zainal, & Darma. (2017). Antioxidant Activity and Organoleptic Characteristic of Breadfruit Leaves Beverage (*Artocarpus Altilis*) With The Addition of Jasmine (*Jasminum sambac* Ait.). *Journal of Agritech Science*.

Iin Suhesti, et. al. "Formulation and Physical Evaluation of Toothpaste from the Combination of Breadfruit Leaves Extract (*Artocarpus altilis*) and Lime (*Citrus aurantifolia*)." *IOSR Journal of Pharmacy (IOSRPHR)*, 11(09), 2021, pp. 29-35.