Majalah Kedokteran Gigi Indonesia
Vol 9 No 2 – August 2023
ISSN 2460-0164 (print), ISSN 2442-2576 (online)
Available online at https://jurnal.ugm.ac.id/mkgi
DOI: http://doi.org/10.22146/majkedgiind.82071

RESEARCH ARTICLE

Evaluation of viscosity and pH of *Zingiber officinale* var. *officinale* juice in mouthwash formulation

Rosita Stefani, Gisela Ellenia Vanessa*, Eko Fibryanto**✉**

*Study Program of Dentistry Education, Faculty of Dentistry, Universitas Trisakti, Jakarta, Indonesia
**Department of Conservative Dentistry, Faculty of Dentistry, Universitas Trisakti, Jakarta, Indonesia
**Jl Kyai Tapa No 260 Grogol Petamburan, West Jakarta, Indonesia; ✉ correspondence: eko.fibryanto@trisakti.ac.id

Submitted: 5th February 2023; Revised: 7th June 2023; Accepted: 12nd July 2023

ABSTRACT

Zingiber officinale var. officinale juice has many benefits, including as a mixture of mouthwash. This research aims to analyze the differences in pH and viscosity values of *Zingiber officinale var. officinale*-containing mouthwashes with concentrations of 3.125%, 6.25%, and 12.5% on days 0, 14, 28, 42, and 56. *Zingiber officinale var. officinale*-containing mouthwashes with concentrations of 3.125%, 6.25%, and 12.5% were mixed with propylene glycol, PEG-40 hydrogenated castor oil, oleum menthae, benzoic acid, sodium benzoate, calcium lactate, sorbitol 70% and calcium thiocyanate. The formulation was measured with a pH meter (Jenway, United Kingdom) and a viscometer (Brookfield, Massachusetts) for 56 days. pH data was analyzed using GLM repeated measures ANOVA and one-way ANOVA ($p < 0.05$). Viscosity data was analyzed using GLM repeated measured ANOVA and the Kruskal-Wallis test ($p < 0.05$). The pH value of the 3.125% formulation showed significant difference for 56 days in the range of 5.50-5.61. The viscosity value showed no significant difference for 56 days in the range of 3.03-3.09 cP. The pH and viscosity value of the 6.25% formulation showed no significant difference for 56 days with pHs of 5.78-5.83, while the viscosity is 3.12-3.13 cP. The pH and viscosity value of the 12.5% formulation showed no significant difference for 56 days with pHs of 4.90, while the viscosity was 3.43-3.50 cP. The *Zingiber officinale var. Officinale* mouthwash formulation with a concentration of 3.125% was unstable, but it had the lowest viscosity value and was stable for 56 days. The pH and viscosity value of the 6.25% and 12.5% formulations were stable for 56 days. The highest pH value was in the 6.25% formulation.

Keywords: herbal mouthwash; pH; viscosity; *Zingiber officinale var. officinale*

INTRODUCTION

The prevalence of oral disease is increasing gradually with growing urbanization and changing living conditions in most countries with low to middle income.[1] Dental caries, considered as the most common dental and oral disease, is associated with biofilm or dental plaque,[2] which can be removed with mouthwash.[3] Mouthwash can also improve oral health, reduce plaque or biofilm accumulation, prevent dental caries, and freshen the breath.[3,4]

There are two types of mouthwashes: chemical mouthwashes and herbal mouthwashes.[5] Although chemical mouthwashes have a good effect on the oral cavity, they tend to cause discoloration of the teeth and can produce other side effects on the oral cavity. Herbal mouthwashes can eradicate oral pathogens, relieve pain instantly, and have fewer side effects compared to chemical mouthwashes.[6]

Each ingredient of mouthwash has its own role in establishing mouthwash formulation.[7] Benzoic acid and sodium benzoate act as preservatives and buffer solutions.[8,9] Propylene glycol (humectant) helps prevent evaporation of active ingredients, thus maintaining the stability and duration of mouthwash contact on the teeth.[10] Surfactant (PEG-40 hydrogenated castor oil) lowers the surface tension of the solution, so the substances contained become more soluble and enhance hydrophilic penetration.[11,12] Oleum menthae acts as a solvent and flavoring.[9] Calcium lactate and potassium thiocyanate act as therapeutic agents.[13] The function of sorbitol 70% is as an artificial sweetener.[9]

Majalah Kedokteran Gigi Indonesia. August 2023; 9(2): 163-170
ISSN 2460-0164 (print)
ISSN 2442-2576 (online)

Most herbal extracts contain antimicrobial properties.[5] *Zingiber officinale var. officinale* is one of them. *Zingiber officinale var. officinale* is less spicy than *Z. officinale* var. *Rubrum* and also has a better antibacterial property than *Z. officinale* var. *Amarum*. Thus, it may offer excellent potential as mouthwash ingredient.[14] Evaluation of mouthwash formulations must be carried out before they undergo clinical trials. The tests include organoleptic tests (odor, color, taste, and consistency), pH (acidity), viscosity, sedimentation, and density.[15] The purpose of this study is to analyze the differences of *Zingiber officinale var. officinale*-containing mouthwashes with concentrations of 3.125%, 6.25%, and 12.5% on days 0, 14, 28, 42, and 56.

MATERIALS AND METHODS

This study used a true experimental research design with a posttest-only control group design. Mouthwash formulations were produced at the Dental Material and Testing Center of Research and Education Laboratory (DMTCORE), Faculty of Dentistry, Universitas Trisakti, Jakarta, Indonesia. pH and viscosity tests were carried out at the Pharmaceutical Physics Laboratory, Faculty of Pharmacy, University of Indonesia, Depok, Indonesia. Equipment used in this study were analytical balances (Fujitsu, Japan), measuring cups (Pyrex, China), beakers (Pyrex, China), magnetic stirrers (Toption, China), Whatman filter paper no. 1 (Midland Scientific, USA), pipettes (Bomex, China), an autoclave (Tomy, Japan), a pH meter (Jenway, United Kingdom), a viscometer (Brookfield, Massachusetts, USA), and grated ginger. The materials used in this study were propylene glycol (Dow Chemical Pacific, Singapore), PEG-40 hydrogenated castor oil (Lambertispa, Italy), oleum menthae (Anhui Province Yifan Spice Co., LTC, China), benzoic acid (Wuhan Youji Industries Co., LTD, China), sodium benzoate (Wuhan Youji Industries Co., LTD, China), calcium lactate (Galactic, Belgium), potassium thiocyanate (Merck Millipore, Germany), sorbitol 70% (Sorini Towa Berlian Corporindo, Indonesia), rhizome of *Zingiber officinale var. officinale* (Balittro, Indonesia), chlorhexidine gluconate 0.2% (Minosep, Indonesia), Enkasari mouthwash herbalcare protection fresh mint flavor (Enkasari, Indonesia), and aquadest.

One kilogram of 10-month-old *Zingiber officinale var. officinale* was cleaned, peeled, and washed with sterile aquadest. It was then mashed and filtered with Whatman filter paper no.1. The *Zingiber officinale var. officinale* juice was diluted to reach concentrations of 3.125%, 6.25%, and 12.5%. The *Zingiber officinale var. officinale* mouthwash was formulated by dissolving calcium lactate (50 mg) and potassium thiocyanate (100 mg) in aquadest (M1). Next, benzoic acid

Table 1. The formulation of juice of *Zingiber officinale var. officinale*

Materials	Function	F1	F2	F3
Zingiber officinale var. *officinale* juice	*Active materials*	3.125%	6.25%	12.5%
Propylene glycol (mL)	Humectant	5	5	5
PEG-40 hydrogenated castor oil (g)	Detergent	1	1	1
Oleum menthae (drops)	Solvent	10	10	10
Benzoic acid (mg)	Preservative	5	5	5
Sodium benzoate (g)	Preservative	2	2	2
Calcium lactate (mg)	Therapeutic agent	50	50	50
Sorbitol 70% (mL)	Flavoring agent	15	15	15
Potassium thiocyanate (mg)	Therapeutic agent	100	100	100

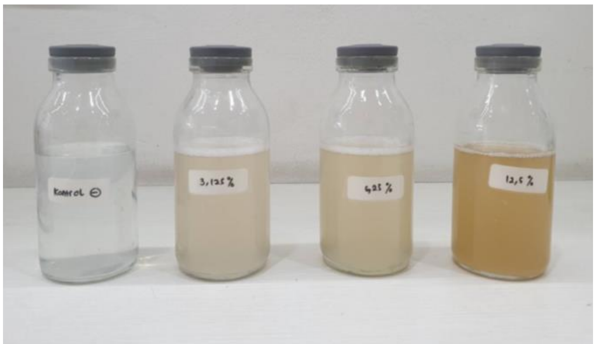


Figure 1. *Zingiber officinale var. officinale* juice mouthwash formulation

(5 mg) and ginger juice with a predetermined concentration were dissolved with ten drops of oleum menthae (M2). In the third step, M2 was emulsified with PEG-40 hydrogenated castor oil (1 gram) and propylene glycol (5 mL) was added gradually and stirred using a magnetic stirrer until the solution was homogeneous (M3). M1 was added little by little to the M3 solution and stirred until it was homogeneous. Fifteen mL of sorbitol 70% was added gradually and stirred until homogeneous. Finally, sodium benzoate (2 grams) was dissolved in aquadest and added to the mouthwash solution to obtain the appropriate pH of the mouthwash. The formulation was presented in Table 1. The formulations of the mouthwashes were stored in glass bottles at room temperature (Figure 1).

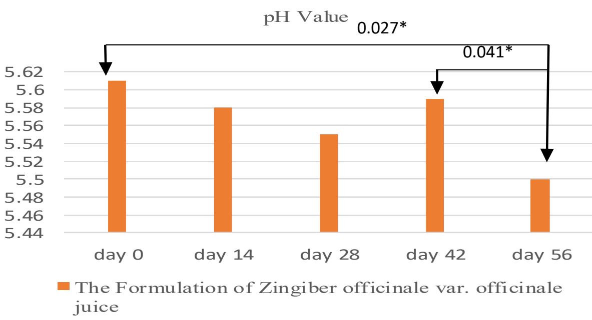
The pH values were measured by a pH meter (Jenway, United Kingdom), and the values were the average of three consecutive measurements. pH measurements were taken on days 0, 14, 28, 42 and 56. The viscosity value was measured by a viscometer (Brookfield, Massachusetts). Similar to the pH values, the results of the viscosity measurement were the average of three consecutive measurements. Viscosity measurements were taken on days 0, 14, 28, 42 and 56. Data normality was tested using the Shapiro-Wilk test. pH value data was analyzed using GLM repeated measures ANOVA and one-way ANOVA ($p < 0.05$). Viscosity value data was analyzed using GLM repeated measures ANOVA and the Kruskal-Wallis test ($p < 0.05$). Data was analyzed using SPSS version 25.0 (IBM SPSS Statistics, United States of America).

RESULTS

The pH value of the mouthwash formulations ranged from 5.46 to 5.83 (Table 2). The data was normally distributed ($p > 0.05$), and the results of GLM repeated measures ANOVA test of 0%, 6.25% and 12.5% mouthwash formulations were not significantly different in 56 days ($p > 0.05$). In contrast, the 3.125% mouthwash formulation showed a significant difference ($p < 0.05$). The results of the post-hoc paired wise comparison test of the 3.125% mouthwash formulation group is displayed in Figure 2.

The positive controls (chlorhexidine and Enkasari) were tested using a paired sample t-test because the test was only carried out on days 0 and 56. The paired sample t-test showed that there was no significant difference in the pH value of chlorhexidine and Enkasari on the day of the test ($p > 0.05$). One-way ANOVA test showed there were significant differences in pH values between the mouthwash groups with one-time measurement on days 0, 14, 28, 42, and 56 ($p < 0.05$). The results can be seen in Table 2.

The viscosity value of the mouthwash formulations ranged from 3.03 to 3.50 cP (Table 3). The data was normally distributed ($p > 0.05$) and the results of GLM repeated measures ANOVA test of 0%, 3.125%, 6.25%, and 12.5% mouthwash formulations were not significantly



*: significantly different ($p < 0.05$)

Figure 2. The pH value of juice of *Z. officinale* var. *officinale* mouthwash formulation 3.125% (*post-hoc paired wise comparison* ($p < 0.05$)).

Majalah Kedokteran Gigi Indonesia. August 2023; 9(2): 163-170
ISSN 2460-0164 (print)
ISSN 2442-2576 (online)

Table 2. The pH value of juice of *Z. officinale* var. *officinale* mouthwash formulation for 56 days

Groups (n = 3)	Mean ± Standard deviation					p
	day 0	day 14	day 28	day 42	day 56	
Chlorhexidine (positive control)	4.89	-	-	-	4.88	0.478
Enkasari (positive control)	4.77	-	-	-	4.76	0.225
Z. officinale var. *officinale* mouthwash 0% (negative control)	5.48 ± 0.005	5.47	5.46 ± 0.005	5.47 ± 0.008	5.47	0.366
Z. officinale var. *officinale* mouthwash 3.125%	5.61 ± 0.005	5.58 ± 0.008	5.55 ± 0.011	5.59 ± 0.005	5.50	0.004*
Z. officinale var. *officinale* mouthwash 6.25%	5.78 ± 0.008	5.81 ± 0.008	5.78 ± 0.011	5.83 ± 0.005	5.80	0.081
Z. officinale var. *officinale* mouthwash 12.5%	4.97 ± 0.011	4.95 ± 0.005	4.93 ± 0.005	4.93 ± 0.005	4.90 ± 0.005	0.064
p	0.001†	0.001†	0.001†	0.001†	0.001†	

*GLM Repeated Measures ANOVA test ($p < 0.05$)
†One-way ANOVA test ($p < 0.05$)

Table 3. The viscosity value of juice of *Z. officinale* var. *officinale* mouthwash formulation for 56 days

Groups (n = 3)	Mean ± Standard deviation					p
	day 0	day 14	day 28	day 42	day 56	
Chlorhexidine (positive control)	4.42	-	-	-	4.34 ± 0.010	0.005ˣ
Enkasari (positive control)	5.17	-	-	-	5.03 ± 0.231	0.423
Z. officinale var. officinale mouthwash 0% (negative control)	1.91	1.93 ± 0.012	1.95 ± 0.021	1.96 ± 0.015	1.96 ± 0.008	0.180
Z. officinale var. officinale mouthwash 3.125%	3.03	3.09 ± 0.055	3.06 ± 0.025	3.06 ± 0.025	3.08 ± 0.021	0.588
Z. officinale var. officinale mouthwash 6.25%	3.12	3.12 ± 0.008	3.12 ± 0.008	3.12 ± 0.008	3.13 ± 0.008	0.491
Z. officinale var. officinale mouthwash 12.5%	3.50 ± 0.033	3.44 ± 0.074	3.43 ± 0.071	3.50 ± 0.011	3.43 ± 0.044	0.482
p	0.005*	0.024*	0.017*	0.019*	0.006*	

* Kruskal Wallis test ($p < 0.05$)
ˣ Paired sample t-test ($p < 0.05$)

different ($p > 0.05$). The paired sample t-test was carried out to analyze the viscosity values of the positive controls (chlorhexidine and Enkasari) because the tests were only taken on days 0 and 56. The test showed that there was a significant difference in the chlorhexidine viscosity values on days 0 and 56 ($p < 0.05$). Meanwhile, the results of the Enkasari test showed that there was no significant difference on days 0 and 56 ($p > 0.05$). Table 3 shows the results of the analysis.

Based on the results of the normality test, the data was not normally distributed ($p < 0.05$); therefore, one-way ANOVA test could not be performed. As an alternative, the data could be analyzed using the Kruskal-Wallis test which is a non-parametric test. The Kruskal-Wallis test showed that there was a significant difference in pH values of the mouthwash groups on days 0, 14, 28, 42, and 56 ($p < 0.05$). The results of the analysis are presented on Table 3.

DISCUSSION

In this research, the mouthwash formulation contained *Zingiber officinale var. officinale* juice with concentrations of 3.125%, 6.25%, and 12.5%. The mouthwash formulations used in this study contain various ingredients that can maintain oral health. Propylene glycol functions as a humectant, antimicrobial, disinfectant, cosolvent, and stabilizer.[16,17] *Oleum menthae* is used as a flavoring agent, solvent, anti-inflammatory, anti-spasmolytic, and antibacterial agent which acts as a bactericidal against pathogens such as *Escherichia coli* and *Staphylococcus aureus*.[18] Sorbitol functions as a sugar substitute sweetener which has calorific value, low glycemic index, and free of carcinogenic effects. In addition, sorbitol prevents the formation of plaque and tooth decay owing to resistance to the metabolism of oral bacteria.[19] The preservatives are sodium benzoate and benzoic acid,[8,9] which have an activity as antifungal and antibacterial agents. Benzoic acid and sodium benzoate act as buffer in mouthwash.[20] Polyoxyl 40 (PEG-40) hydrogenated castor oil is used as surfactant to lower the surface tension in the solution, solubilize fat-soluble components, and increase hydrophilic penetration.[12] The therapeutic agents are calcium lactate and potassium thiocyanate. The functions of calcium lactate are to strengthen tooth structure, and as antibacterial agents, antitartar agents, and bone substitute materials.[13] Potassium thiocyanate acts as an antifungal and anti-caries agent in teeth.[21]

Zingiber officinale var. officinale is a natural ingredient which has antimicrobial and antifungal effects to prevent caries and oral candidiasis; therefore, ginger may help maintain oral health.[22] Phytochemical test of *Zingiber officinale var. officinale* shows that it contains alkaloids, flavonoids, quinones, saponins, monoterpenoids, and sesquiterpenoids.[23] Previous studies have demonstrated that mouthwashes containing natural ingredients are safe and have fewer side effects.[24]

Stability tests were performed to evaluate changes in the mouthwash preparation to determine the mouthwash suitability. The pH test showed the value was in the range of 4.90-5.83. The pH of quality standard of herbal mouthwash ranges from 5 to 7.[25] In this study, the mouthwash formulations with 0%, 3.125% and 6.25% concentrations of ginger met the quality standards of herbal mouthwash with a pH in the range of 5.46-5.83. The 12.5% mouthwash formulation had a pH from 4.90 to 4.97, which was the lowest, and it may indicate that it did not meet the quality standards of herbal mouthwashes because it was too acidic. When mouthwash solution proven too acidic, it makes the bacteria grow faster and may irritate to the oral cavity.[3,26] Surprisingly, when the 12.5% mouthwash formulation was compared to commercial mouthwash, which is a positive control in this study, it showed that the pH of the mouthwash was higher than the commercial mouthwash. The pH values of *Zingiber officinale var. officinale*-containing mouthwashes with concentrations of 0%, as a negative control, 6.25%, and 12.5% were stable for 56 days. However, the pH value of the mouthwash formulation with a concentration of ginger of 3.125% was unstable for 56 days. In

Majalah Kedokteran Gigi Indonesia. August 2023; 9(2): 163-170
ISSN 2460-0164 (print)
ISSN 2442-2576 (online)

addition, the mouthwash formulations across the three different percentages showed different pHs, both in negative and positive control at one-time measurement. It is highly likely that differences in the mouthwash ingredients could affect the pH value of the mouthwash.

The viscosity test showed that the value was in the range of 3.03-3.50 cP. The best mouthwash viscosity is the one that is closest to the viscosity of water, which is 0.89 cP.[27] It is mainly by considerations of convenience when patients rinse their mouth. The viscosity values of mouthwash formulations containing *Zingiber officinale var. officinale* juice were found higher than the viscosity value of standard mouthwash. This could be caused by the relatively high content of *Zingiber officinale var. officinale* and sorbitol in the mouthwash. In comparison with commercial mouthwashes, which were the positive controls in this study, it was found that the viscosity values of the mouthwash formulations with concentrations of ginger of 3.125%, 6.25%, and 12.5% were closer to the viscosity of water than that of the commercial ones. The mouthwash formulation in this test showed a stable viscosity for 56 days. In addition, there were differences in the viscosity values between the positive controls (Enkasari and chlorhexidine), negative controls, and the three mouthwash formulations (3.125%, 6.25%, and 12.5%) at one-time measurement tested on days 0, 14, 28, 42, and 56. Taken together, differences in mouthwash ingredients could affect the viscosity value of the mouthwash. This study found that the higher the concentration of *Zingiber officinale var. officinale*, the higher the viscosity of the mouthwash. One unanticipated result in this study was that the mouthwash formulations had cloudy colors, whereas mouthwash formulations should have clear color to appeal the public. Mouthwash formulations have to pass various tests such as organoleptic, density, sedimentation and toxicity tests. These tests, however, had not been carried out in this study. Further research, which incorporates these tests to determine the feasibility of the mouthwash, is therefore recommended.

CONCLUSION

Based on the results of this research, it can be concluded that the pH of the *Zingiber officinale var. officinale*-containing mouthwash with a concentration of 3.125% was unstable for 56 days with pHs in the range of 5.50-5.61. The viscosity value, however, was stable for 56 days. It had lower viscosity value compared to those with concentrations of 6.25% and 12.5%, which was between 3.03 and 3.09 cP. Mouthwash formulation containing 6.25% concentration of *Zingiber officinale var. officinale* juice had a stable pH and viscosity value for 56 days. It showed a higher pH value compared to pHs of mouthwashes with ginger concentrations of 3.125% and 12.5%, which was in the range of 5.78-5.83, while the viscosity value ranged from 3.12 to 3.13 cP. Mouthwash formulation containing *Zingiber officinale var. officinale* juice with a concentration of 12.5% had a stable pH value for 56 days and had lower pH value compared to the pHs of those with the concentrations of 3.125% and 6.25%, which was between 4.90 and 4.97. The viscosity value was stable and higher compared to those of the mouthwashes with ginger concentrations of 3.125% and 6.25%, which was in the range of 3.43-3.50 cP.

ACKNOWLEDGMENT

The authors' gratitude goes to drg. Wiena Widyastuti, Sp., KG(K), drg. Anastasia Elsa Prahasti, Sp., KG(K), and drg. Dewi Ranggaini, M.K.G. for their suggestions and valuable insights for the improvement of this research.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

1. World Health Organization. Oral Health [Internet]. 2022. Available from: https://www.who.int/news-room/fact-sheets/detail/oral-health.

2. Chen X, Daliri EBM, Kim N, Kim JR, Yoo D, Oh DH. Microbial etiology and prevention of dental caries: Exploiting natural products to inhibit cariogenic biofilms. Pathogens. 2020; 9(7): 1–15. doi: 10.3390/pathogens9070569
3. Iskandar B, Lukman A, Syaputra S, Al-Abrori UNH, Surboyo MDC, Lee CK. Formulation, characteristics and anti-bacterial effects of Euphorbia hirta L. mouthwash. J Taibah Univ Med Sci. 2022; 17(2): 271–282. doi: 10.1016/j.jtumed.2021.08.009
4. der Weijden FAV, der Sluijs EV, Ciancio SG, Slot DE. Can chemical mouthwash agents achieve plaque/gingivitis control? Dent Clin North Am. 2015; 59(4): 799–829. doi: 10.1016/j.cden.2015.06.002
5. Renuka S, Muralidharan NP. Comparison in benefits of herbal mouthwashes with chlorhexidine mouthwash: a review. Asian J Pharm Clin Res. 2017; 10(2): 3–7. doi: 10.22159/ajpcr.2017.v10i2.13304
6. Nigam D, Verma P, Chhajed M. Formulation and evaluation of herbal mouthwash against oral infections disease. Int J Pharm Life Sci. 2020; 11(7): 6746–6750.
7. Sykes L, Comley M, Kelly L. Availability, Indications for use and main ingredients of mouthwashes in six major supermarkets in Gauteng. South African Dent J. 2016; 71(7): 308–313.
8. Sharma R, Hebbal M, Ankola AV, Murugaboopathy V, Shetty SJ. Effect of two herbal mouthwashes on gingival health of school children. J Tradit Complement Med. 2014; 4(4): 272–278. doi: 10.4103/2225-4110.131373
9. Kono SR, Yamlean PVY, Sudewi S. Formulasi sediaan obat kumur herba patikan kebo (Euphorbia hirta) dan uji antibakteri Prophyromonas gingivalis. Pharmacon. 2018; 7(1): 37–46. doi: 10.35799/pha.7.2018.18803
10. Anastasia A, Yuliet Y, Tandah MR. Formulasi sediaan mouthwash pencegah plak gigi ekstrak biji kakao (Theobroma cacao L) dan uji efektivitas pada bakteri Streptococcus mutans. J Farmasi Galenika (Galenika J Pharm). 2017; 3(1): 84–92. doi: 10.22487/j24428744.2017.v3.i1.8144
11. Rachmawati H, Novel MA, Ayu S, Berlian G, Tandrasasmita OM, Tjandrawinata RR, Anggadiredja K. The in vitro–in vivo safety confirmation of PEG-40 hydrogenated castor oil as a surfactant for oral nanoemulsion formulation. Sci Pharm. 2017; 85(2): 4–13. doi: 10.3390/scipharm85020018
12. Radzki D, Wilhelm-Węglarz M, Pruska K, Kusiak A, Ordyniec-Kwaśnica I. A fresh look at mouthwashes—what is inside and what is it for? Int J Environ Res Public Health. 2022; 19(7): 3926. doi: 10.3390/ijerph19073926
13. Simbolon RA, Amna U, Halimatussakdiah H. Uji kadar disolusi tablet kalsium laktat menggunakan titrasi kompleksometri. Quimica. 2020; 2(2): 11-13. doi: 10.33059/jq.v2i2.2618
14. Wibowo DP, Mariani R, Hasanah SU, Aulifa DL. Chemical constituents, antibacterial activity and mode of action of elephant ginger (Zingiber officinale var. Officinale) and emprit ginger rhizome (Zingiber officinale var. Amarum) essential oils. Pharmacognosy Journal. 2020; 12(2): 404–409. doi: 10.5530/pj.2020.12.62
15. Anshula D, Rameshwari R, Poonacha KS, Seema B, Monika K NP. Evaluation of the stability, pH, density and sedimentation of green tea and green tea plus ginger mouthwash: a phytochemical study. J Oral Heal Dent Sci. 2018; 2(1): 1-4.
16. Agency EM. Propylene glycol used as an excipient propylene glycol used as an excipient Table of contents. Comm Hum Med Prod. 2017; 44: 97.
17. Kao TT, Wang MC, Chen YH, Chung YT, Hwang PA. Propylene glycol improves stability of the anti-inflammatory compounds in Scutellaria baicalensis extract. Processes. 2021; 9(5): 1-13. doi: 10.3390/pr9050894
18. Selina C, Darwis I, Graharti RR. Peppermint (Mentha piperita) sebagai pengobatan alternatif pada irritable bowel syndrome (IBS). Major Med J Lampung Univ. 2019; 8(1): 211–219.
19. Dash RP, Srinivas NR, Babu RJ. Use of sorbitol as pharmaceutical excipient in the present

day formulations–issues and challenges for drug absorption and bioavailability. Drug Dev Ind Pharm. 2019; 45(9): 1421–1429. doi: 10.1080/03639045.2019.1640722
20. Krátký M, Vinšová J, Buchta V. In vitro antibacterial and antifungal activity of salicylanilide benzoates. ScientificWorldJournal. 2012; 2012: 290628. doi: 10.1100/2012/290628
21. Mariyam D, Farida N, Wijaya HW, Dasna IW. Studi karakterisasi dan aktivitas antibakteri senyawa kompleks dari zink (II) klorida, kalium tiosianat dan 2-Aminopiridina. J Riset Kimia. 2022; 13(1): 100–110. doi: 10.25077/jrk.v13i1.465
22. Aghazadeh M, Bialvaei AZ, Aghazadeh M, Kabiri F, Saliani N, Yousefi M, Eslami H, Kafil HS. Survey of the antibiofilm and antimicrobial effects of Zingiber officinale (in vitro study). Jundishapur J Microbiol. 2016; 9(2): e30167. doi: 10.5812/jjm.30167
23. Yulianti AB, Tejasari M, Dewi MK, Furqaani AR. Penelusuran campuran senyawa aktif ekstrak air bawang putih, jahe gajah, dan lemon lokal: Potensi pengatur profil lipid pada tikus tua yang terpapar pakan tinggi Lemak [Laporan penelitian]. Bandung: Fakultas Kedokteran Universitas Islam Bandung; 2021. 28.
24. Olejnik E, Szymanska J. Active ingredients of mouthwashes. Acta Pol Pharm - Drug Res. 2021; 77(6): 825–32. doi: 10.32383/appdr/128897
25. Yelfi Y, Susilo H, Kurnia NM. Mouthwash of Amaranthus hybridus L. Leaf extract with ethyl acetate as a Streptococcus mutans antibacterial. Jurnal Ilmiah Farmasi Farmasyifa. 2022; 5(1): 79–90. doi:10.29313/jiff.v5i1.8379
26. Ardini D, Ratnasari E, Mulatasih. Streptococcus mutans antibacterial study: Mouthwash preparations formulation using cinnamon and betel leaf essential oils (Cinnamomum burmannii) (Piper betle L). Int J Innov Creat Chang. 2020; 13(2): 85–95.
27. Baitariza A, Ghazali A, Rosmiati. Formulasi larutan obat kumur pencegah plak gigi ekstrak kulit nanas (Ananas comosus L. Merr). J Sabdariffarma. 2022; 6(1): 33–42. doi: 10.53675/jsfar.v2i1.29