Insisiva Dental Journal: Majalah Kedokteran Gigi Insisiva
Website: http://journal.umy.ac.id/index.php/di/index

Research Article

Application of Rambutan Honey Toothpaste with Color Indicator Effect on Salivary Malondialdehyde Levels

Euis Reni Yuslianti[1]*, Ratih Widyasari[2], Bayu Syamsul Arif[1]
[1]Departement of Oral Biology and Biomedical, Faculty of Dentistry, Universitas Jenderal Achmad Yani Cimahi, Indonesia
[2]Departement of Conservative Dentistry, Faculty of Dentistry, Universitas Jenderal Achmad Yani Cimahi, Indonesia

Received date: April 11st, 2024; revised date: October 17th, 2024; accepted: November 23rd, 2024
DOI: 10.18196/di.v13i2.22087

Abstract

Oxidative stress in the oral cavity, driven by an imbalance between free radicals and antioxidants, can lead to lipid peroxidation, as reflected by elevated malondialdehyde (MDA) levels in saliva. Proper oral hygiene, such as regular tooth brushing, is vital in mitigating oxidative damage. This study aimed to evaluate the effects of rambutan honey toothpaste with a color indicator on reducing oxidative stress in the oral cavity by measuring salivary MDA levels. This research was conducted using a laboratory experimental design, with saliva samples collected from students at the Faculty of Dentistry, Universitas Jenderal Achmad Yani. Participants were assigned to five groups: rambutan honey toothpaste with a color indicator (RHTCI), rambutan honey toothpaste without a color indicator (RHT), color-indicated toothpaste without honey (TCI), base toothpaste (BT), and distilled water (DW). The thiobarbituric acid reactive substances (TBARs) method was applied to assess MDA levels, and statistical analysis was conducted using Kruskal-Wallis and Mann-Whitney tests. The results showed a significant reduction in salivary MDA levels following the use of RHTCI ($p = 0.0001$). A notable difference was also found between RHTCI and TCI ($p = 0.001$), while no significant difference was observed between RHTCI and RHT ($p = 0.190$). These findings suggest that rambutan honey toothpaste with a color indicator effectively reduces salivary MDA levels, highlighting its potential antioxidant benefits.

Keywords: malondialdehyde; rambutan honey; toothpaste

INTRODUCTION

Dental and oral health in Indonesia demands focused attention from both governmental initiatives and dental health practitioners through Basic Health Survey (Riskesdas) findings, and caries prevalence stands at 45.3%. Additionally, the incidence of swollen gums, or abscesses, has surged by 14% across Indonesia.[1] The predominant oral health issue among the populace remains tooth decay, closely linked to fluctuations in saliva pH. This interplay underscores the prevalence of dental caries and periodontal diseases within the Indonesian context.[2]

Inflammatory processes within cells, coupled with the assault of free radicals on the body, instigate lipid peroxidation.[3] Inflammatory processes within cells, coupled with assaults from free radicals, instigate lipid peroxidation, leading to an escalation in malondialdehyde (MDA) levels.[4] When the production of free radicals surpasses antioxidant defense mechanisms, oxidative stress ensues, manifesting as heightened lipid peroxidation.[5] This imbalance disrupts the equilibrium between free radical generation and the antioxidant arsenal, giving rise to reactive oxygen species (ROS) that inflict cellular damage.[6,7] This oxidative cascade

* Corresponding author, e-mail: ery.unjani@yahoo.co.id

perpetuates within cell membranes, catalyzing the breakdown of fatty acid chains and culminating in the generation of various byproducts, including MDA.[8] Elevated MDA concentrations signify ongoing oxidative processes within cell membranes, a state commonly reflected in bodily fluids such as urine, blood, and saliva.[9] Saliva plays a pivotal role in oral tissue protection, offering mechanical cleansing, plaque reduction, dental lubrication, inhibition of microbial colonization, bacterial activity, and enzymatic digestion.[10] Notably, saliva hosts a reservoir of antioxidants, with enzymes and uric acid constituting approximately 70% of its antioxidant content.[11] These antioxidant molecules serve as biochemical sentinels, exerting a defensive shield against oxidative insults. Honey emerges as a potent antioxidant agent, harboring flavonoids that combat free radicals and facilitate cellular regeneration.[12] Research by Yuslianti et al. in 2015 underscored honey's efficacy in mitigating oxidative stress by harnessing its antioxidant properties. In summary, the intricate interplay between oxidative stress, saliva composition, and antioxidant interventions, such as honey, underscores the multifaceted approach required to safeguard dental and oral health within the Indonesian populace.[13]

Rambutan honey (*Nephelium lappaceum*), found abundantly in Indonesia, boasts a glucose content of 30% along with a substantial presence of *rutin* group flavonoid antioxidants and vitamin C.[14] Extensive research has validated its commendable free radical scavenging activity both in vitro and in vivo.[15] Incorporating toothpaste into oral hygiene practices is essential for maintaining dental health, as it aids in teeth cleaning and alleviating bad breath. Typically, toothpaste formulations comprise abrasive cleaning agents, thickening agents, humectants, surfactants, flavors, and therapeutic agents.[16] With technological advancements and innovative breakthroughs, toothpaste manufacturers have ventured into incorporating additional ingredients aimed at enhancing properties. Herbal toothpaste, featuring safe and comfortable ingredients with minimal side effects, has gained prominence. Notably, herbal formulations, such as those containing rambutan honey, have shown potential in reducing salivary MDA levels, owing to the antioxidant properties inherent in rambutan honey.[8] Furthermore, the inclusion of coloring agents in toothpaste formulations has garnered attention.[17] Dragon fruit (*Hylocereus costaricensis*), a commonly cultivated fruit plant in Indonesia, offers anthocyanin-rich extracts from its peel. Anthocyanins, belonging to the flavonoid family, exhibit water-soluble properties and impart a red hue. Their characteristic of undergoing color changes at different pH levels renders them suitable as indicators for acid-base titrations.[18]

Therefore, researchers are intrigued by the prospect of exploring the effects of applying color-indicated rambutan honey toothpaste on salivary MDA levels. Such formulations, derived from natural ingredients known for their beneficial properties, not only contribute to overall bodily health but also offer the potential to reduce salivary MDA levels through the antioxidant effects of rambutan honey.[11]

MATERIALS AND METHODS

This study employed an analytical quasi-experimental design, utilizing a pre- and post-test framework with a control group. A group of 20 subjects meeting specific inclusion and exclusion criteria was selected. Inclusion criteria encompassed individuals aged 18-25, of any gender, willing to provide informed consent, possessing a healthy oral cavity and saliva, free from caries, and enrolled as students at the Faculty of Dentistry, Universitas Jenderal Achmad Yani, within the classes of 2020 to 2023. Exclusion criteria included subjects with systemic conditions that could alter saliva composition, such as Sjögren's syndrome,

diabetes, or autoimmune diseases, subjects utilizing fixed or removable orthodontic devices or prostheses, exhibiting crowded teeth, undergoing antibiotic treatment or mouthwash use during the study, possessing a smoking habit, or having allergies to rambutan honey and dragon fruit. Allergies to dragon fruit are considered an exclusion criterion in this study to prevent potential allergic reactions or adverse effects that could compromise the health and safety of participants. Since dragon fruit may be used as a component or ingredient in the study, individuals with known allergies could experience allergic symptoms, which might confound the study's results by introducing unrelated health issues. Additionally, allergic reactions could interfere with the participant's oral and systemic health, which may skew the study outcomes related to the oral cavity and saliva being analyzed.

Respondents who are allergic to rambutan honey or super red dragon fruit may experience an allergic reaction when using toothpaste that contains these ingredients. This allergic reaction can disturb the comfort and health of respondents and will hinder research because respondents cannot be continued or must be replaced with new respondents. Therefore, respondents who have allergies to rambutan honey and super red dragon fruit are included in the exclusion criteria.

Subjects Preparation

A total of 20 subjects, meeting specific inclusion and exclusion criteria, were recruited from the Faculty of Dentistry, Universitas Jenderal Achmad Yani, focusing on students from the 2020 to 2023 classes. Recruitment began with information sessions where interested students learned about the study's purpose, procedures, and potential benefits and risks. Volunteers then completed an initial questionnaire assessing their eligibility based on oral health, habits, and systemic conditions affecting saliva. Those preliminarily eligible underwent a final oral examination to confirm they met all criteria, including a healthy oral cavity and absence of orthodontic devices. Eligible students provided informed consent and were randomly assigned to one of five treatment groups, each group using a different brushing regimen: color-indicated rambutan honey toothpaste, rambutan honey toothpaste without color indication, color-indicated toothpaste without honey, base toothpaste, or *aquadest* (distilled water), ensuring unbiased group allocation. A questionnaire administered via Google Form aided in subject selection, followed by offline verification at the Integrated Dentistry Laboratory, Faculty of Dentistry, Universitas Jenderal Achmad Yani. Informed consent forms were obtained from willing participants.

Toothpaste Preparation

The production process for rambutan honey toothpaste with color indication involves freeze-drying the skin of super red dragon fruit, which will be used as a natural coloring agent and standardization of rambutan honey. Standardization begins by heating rambutan honey in a sterile glass via a water heater for 24 hours to reduce the water content. Standardized rambutan honey is combined with super red dragon fruit skin, which has gone through the freeze-drying stage and is then processed into herbal toothpaste in the pharmaceutical technology laboratory.

Saliva Preparation

Saliva samples were collected from 20 participants in the morning to minimize circadian variation in antioxidant levels. Before collection, participants were instructed to rinse their mouths with distilled water and wait for 5 minutes to clear any food residue or recent contamination. Unstimulated whole saliva was collected by passive drool, where participants allowed saliva to accumulate on the floor of the mouth and then drooled into a sterile collection tube without

chewing or swallowing. This method avoids introducing additional variability caused by stimulation. The samples were collected in sterile 15 mL conical tubes and immediately placed on ice to preserve MDA stability. Within 30 minutes of collection, the samples were transferred to a laboratory for processing. Samples were centrifuged at 3000 rpm for 10 minutes at 4°C to remove debris and cells. The supernatant was then aliquoted into clean microcentrifuge tubes and stored at -80°C until further analysis.

MDA Level Examination (The TBARs Assay)

The TBARs assay was performed to measure malondialdehyde (MDA) levels as an indicator of lipid peroxidation. First, 0.5 mL of saliva was mixed with 0.5 mL of 30% trichloroacetic acid (TCA) to precipitate proteins, followed by the addition of 0.5 mL of 0.75% thiobarbituric acid (TBA). The mixture was heated in a boiling water bath at 100°C for 10 minutes to form the MDA-TBA complex, then immediately cooled in an ice bath. The samples were centrifuged at 3000 rpm for 10 minutes at 4°C, and the supernatant was collected. The absorbance of the supernatant was measured at 532 nm using a spectrophotometer, with MDA concentrations calculated based on a standard curve generated from known MDA concentrations.

Subjects brushed their teeth with the designated toothpaste twice daily (morning and night), employing the Bass technique. Post-test saliva collection occurred in the morning prior to food or beverage intake (excluding water) and was timed meticulously. Twenty participants were instructed to brush their teeth with a different toothpaste each day, with a 24-hour washout period between treatments to prevent carryover effects. On day one, participants brushed with color-indicated rambutan honey toothpaste; on day two, with rambutan honey toothpaste; on day three, with color-indicated toothpaste without honey; and on day four, with basic toothpaste. Saliva samples were collected after each brushing session, immediately stored at -18°C, and preserved until analysis. This washout interval ensured that the impact of each toothpaste on oxidative stress markers in saliva was measured independently. Before the research was carried out, the samples were taken out of the refrigerator and waited for 1 hour until the samples melted. Then, the research was carried out at the Biochemistry Laboratory of the Medicine and the Unjani Pharmacy Laboratory for 4 days with 25 samples per day.

The research was conducted at the Oral Biology Laboratory, Faculty of Dentistry, Universitas Jenderal Achmad Yani, and the Faculty of Pharmacy, Universitas Jenderal Achmad Yani, with ethical clearance obtained (Ethical Letter Number: 1424/UN6.KEP/EC/2023).

Data analysis entailed descriptive analysis to illustrate pre- and post-treatment scores, followed by normality and homogeneity tests (Shapiro-Wilks and Levene, respectively). The Kruskal-Wallis non-parametric test assessed the impact of color-indicated rambutan honey toothpaste, followed by post hoc Mann-Whitney analysis.

The procedure in this research can be seen in Figure 1.

Figure 1. Research procedure. (a. selection of respondents, b. supervision of toothbrushes, c. research, d. rambutan honey toothpaste super red dragon fruit color indicator)

Statistical Analysis

Data from the TBARs assay were analyzed using appropriate statistical tests (Kruskal-Wallis and Mann-Whitney tests) to determine the significance of differences in MDA levels across treatment groups. Statistical significance was set at $p < 0.05$

RESULT

Figure 1 illustrates the impact of rambutan honey toothpaste on salivary malondialdehyde (MDA) levels, as reflected by the mean values for each treatment group.

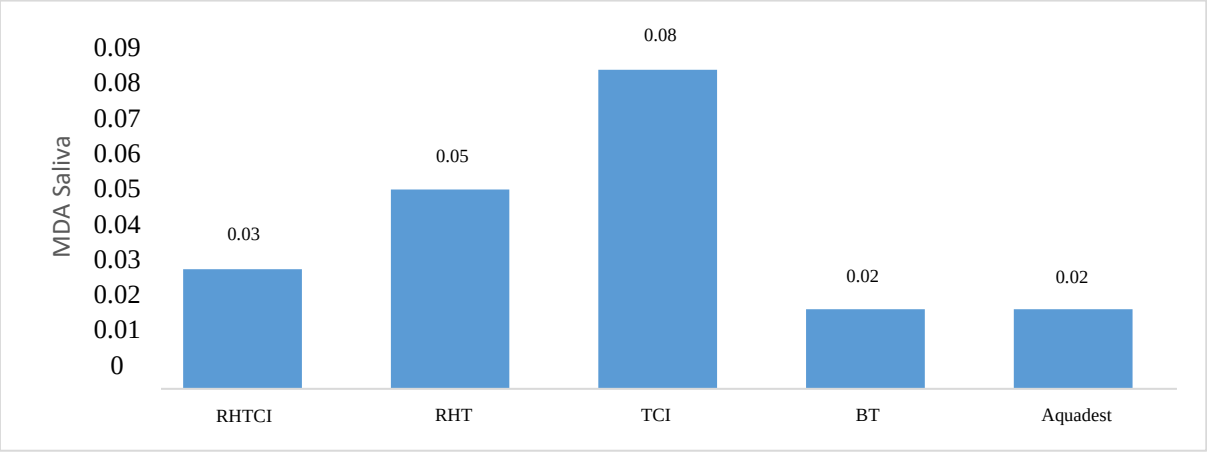

Figure 2. This diagram illustrates the effect of applying color-indicated rambutan honey toothpaste on salivary malondialdehyde (MDA) levels across different treatment groups: rambutan honey toothpaste with a color indicator (RHTCI), rambutan honey toothpaste (RHT), toothpaste with a color indicator (TCI), base toothpaste (BT), and distilled water.

Figure 2 illustrates that within the RHTCI group, the mean salivary malondialdehyde level was notably low at 0.03 mg/dl. Statistical analysis employed the Kruskal-Wallis test due to the non-normal distribution and lack of homogeneity in the data. The results yielded a p-value of less than 0.05, indicating a significant effect of RHTCI on reducing salivary malondialdehyde levels, as summarized in Table 1.

Table 1. Effect of RHTCI application on salivary malondialdehyde levels.

Test Group	n	Average ±SD	P value
RHTCI	40	0.03±0.017	0.0001
RHT	40	0.05±0.040	
TCI	40	0.08±0.061	
BT	40	0.02±0.156	
Aquadest	40	0.02±0.002	

Table 2. Test results differ in the influence of RHTCI, RHT, TCI, and BT.

Group	Aquadest	RHTCI	RHT	TCI	BT
Aquadest					
RHTCI	0.036*				
RHT	0.115	0.190			
TCI	0.0001*	0.001*	0.031*		
BT	0.0001*	0.0001*	0.004*	0.0001*	

Note: Mann-Whitney test. $p < 0.05$ (significant)
RHTCI: Rambutan Honey Toothpaste with Color Indicator, RHT: Rambutan Honey Toothpaste, TCI: Toothpaste with Color Indicator, BT: Base Toothpaste

Table 1 presents the outcomes of statistical tests conducted within the research group. The p-value for the variable of saliva MDA examination exceeded 0.05 ($p > 0.05$), indicating nonsignificance. Thus, it can be elucidated that there exists no significant disparity in mean salivary MDA levels between the RHTCI group compared to RHT ($p = 0.190$) and between RHT and distilled water ($p = 0.115$).

Conversely, the results of the saliva MDA examination yielded p-values below 0.05 ($p < 0.05$), signifying significance. Hence, it can be deduced that a notable mean difference exists between various comparisons, including the RHTCI groups compared to TCI, RHTCI compared to BT, RHTCI compared with distilled water, RHT compared with TCI, RHT compared with BT, TCI compared with BT, RHTCI compared with distilled water, and BT compared with distilled water.

DISCUSSION

Rambutan honey is renowned for its rich composition, comprising a 30% glucose content, notable levels of rutin group flavonoid antioxidants, and vitamin C. Its efficacy in scavenging free radicals has been corroborated through both *in vitro* and *in vivo* studies.[15] Antioxidants, typically administered orally through food or supplements, can also be topically applied in formulations such as mouthwashes, gels, and pastes. The bioactive compounds present in rambutan honey possess the ability to inhibit free radical activity and shield cells from oxidative damage.[11]

Free radicals, characterized by one or more unpaired electrons, result from oxidation reactions and ROS. These entities instigate lipid peroxidation, generating reactive lipid aldehydes, notably MDA, which exert toxic effects and cause cellular damage.[19] MDA levels serve as pivotal biomarkers for assessing lipid peroxidation,

with elevated concentrations indicating heightened oxidative stress. Factors contributing to increased MDA levels include exposure to air pollution, smoking, poor dietary habits, and chronic stress. Notably, MDA levels can be gauged in various bodily tissues or fluids, including saliva.[11,20]

Rambutan honey, utilized in herbal toothpaste formulations, exhibits a capacity to reduce salivary MDA levels and thereby mitigate free radical activity. Factors influencing the antioxidant potential of rambutan honey encompass its high sugar and low water content, pH level, methylglyoxal (MGO), as well as the presence of flavonoids, phenolics, polyphenols, glycosides, and hydrogen peroxide. The primary function of antioxidants lies in inhibiting lipid oxidation.[11]

Previous research highlighted the neutral pH value of rambutan honey toothpaste, like the pH of the oral cavity, thus enhancing its antioxidant properties. Clinical trials have elucidated the safety and efficacy of bee-based products, including toothpaste, mouthwash, and chewing gum, in ameliorating various oral ailments.[21] Moreover, color-indicated rambutan honey toothpaste, incorporating super red dragon fruit skin as a coloring agent, capitalizes on the anthocyanin-rich composition of the fruit peel. Anthocyanins, renowned for their pH-sensitive color-changing properties, serve as effective indicators for monitoring oral hygiene practices, as evidenced by Purbaningtyas 2020 study showcasing the efficacy of super red dragon fruit peel mucoadhesive gel in dental plaque staining.[22]

The antioxidant capacity within individual oral environments varies, with oxidative stress ensuing when the balance between oxidative and antioxidant mechanisms is disrupted. Reacting with antioxidants, free radicals undergo electron transfer, thereby attenuating bodily damage. The anthocyanin-rich skin of super red dragon fruit, boasting antimicrobial properties and vivid pigmentation, emerges as a promising coloring agent for dental applications.[23,24]

Research endeavors focusing on toothpaste formulations incorporating rambutan honey and freeze-dried super red dragon fruit as color indicators underscore their potential in reducing free radicals, as evidenced by assessments of MDA levels in saliva.[21]

Based on the outcomes of the Kruskal-Wallis non-parametric statistical analysis, it is evident that the utilization of RHTCI, RHT, TCI, and BT exerts a statistically significant influence on reducing salivary malondialdehyde (MDA) levels. This underscores the efficacy of color-indicated rambutan honey toothpaste in MDA reduction, aligning with findings from prior research, such as Yuslianti et al.'s 2015 study, which highlighted the antioxidant properties of honey and its potential to mitigate MDA levels.[13]

Among the treatment groups, the TCI group exhibited the highest mean MDA level at 0.08 mg/dl, while the lowest mean was observed in the color-indicated rambutan honey toothpaste group at 0.03 mg/dl. MDA absorbance measurements were conducted using the TBARS spectrophotometry method, wherein MDA molecules react with thiobarbituric acid (TBA) to produce a pink color. The intensity of this color correlates with MDA levels, with darker hues indicating higher concentrations. Notably, the composition of TCI, derived from dried super red dragon fruit skin, imparts a red pigment, leading to pink staining during the TBARS method, consistent with MDA measurement.

This research demonstrates the significant impact of RHTCI, RHT, TCI, and BT on reducing salivary MDA levels. Specifically, a notable difference was observed in the comparison between RHTCI and TCI, signifying the superior efficacy of color-indicated rambutan honey toothpaste. Conversely, comparisons between RHTCI and RHT, as well as with

distilled water, did not yield significant differences. Consequently, it can be inferred that the application of color-indicated rambutan honey toothpaste effectively reduces MDA levels, with superior potential compared to RHT, TCI, and BT formulations.[25]

CONCLUSION

Based on the research findings and subsequent data analysis, it is evident that the application of rambutan honey toothpaste color indicator (RHTCI) exerts a discernible influence on salivary malondialdehyde (MDA) levels. Furthermore, compared to rambutan honey toothpaste (RHT), toothpaste with a color indicator (TCI), and base toothpaste (BT), rambutan honey toothpaste color indicator (RHTCI) demonstrates a notably greater impact on reducing salivary malondialdehyde levels.

ACKNOWLEDGEMENTS

Our gratitude goes to the Faculty of Dentistry, Universitas Jenderal Achmad Yani Cimahi.

REFERENCE

1. Riset Kesehatan Dasar 2018. Badan Penelitian dan Pengembangan Kesehatan Kementerian Kesehatan RI. Jakarta: Kementerian Kesehatan RI. 2018.
2. Syauqy, A., & Iskandar, M. Perbandingan pH saliva setelah konsumsi buah nanas dan buah belimbing. Jambi Medical Journal: Jurnal Kedokteran dan Kesehatan. 2022.10(1), 26-36. https://doi.org/10.22437/jmj.v10i1.13201
3. Suryadinata RV. Pengaruh radikal bebas terhadap proses inflamasi pada penyakit paru obstruktif kronis (ppok). Amerta Nutr. 2018;2(4):317. https://doi.org/10.20473/amnt.v2i4.2018.317-324
4. Rahayu, P. N. Hubungan Kadar Gula Darah Puasa dan Profil Lipid Pada Penderita Diabetes Melitus Tipe 2 dengan Kejadian Stroke Iskemik di RSUD R.A Basoeni Mojokerto. Jurnal Biosains Pascasarjana, 2020. 22(2) 50–62. https://doi.org/10.20473/jbp.v22i2.2020.50-62
5. Kamilatussaniah, Yuniasti A, Iswari R. Pengaruh suplementasi madu kelengkeng terhadap kadar tsa dan mda tikus putih yang diinduksi timbal (pb). J MIPA Unnes. 2015;38(2)(2):108–14.
6. Nurdyansyah F, Pangan T, Teknik F. Stres oksidatif dan status antioksidan pada latihan fisik. jendela olahraga. 2017;2 (1):105–9. https://doi.org/10.26877/jo.v2i1.1288
7. Murphy MP, Bayir H, Belousov V, Chang CJ, Davies KJA, Davies MJ, Dick TP, Finkel T, Forman HJ, Janssen-Heininger Y, Gems D, Kagan VE, Kalyanaraman B, Larsson NG, Milne GL, Nyström T, Poulsen HE, Radi R, Van Remmen H, Schumacker PT, Thornalley PJ, Toyokuni S, Winterbourn CC, Yin H, Halliwell B. Guidelines for measuring reactive oxygen species and oxidative damage in cells and in vivo. Nat Metab. 2022 Jun;4(6):651-662. https://doi.org/10.1038/s42255-022-00591-z
8. Yuslianti ER. Radikal bebas dan antioksidan. 1st ed. Yogyakarta; 2017. 30–73 p.
9. Yulianti MEP. Ekstrak labu siam (sechium edule) dapat menurunkan kadar serum malondialdehid pada tikus putih (rattus norvegicus) yang diberikan pakan kolesterol. J Telenursing. 2022;4(1):128–34. https://doi.org/10.31539/joting.v4i1.3587
10. Haripa PE, Lestari C, Mahata I. Perbedaan antara obat kumur a - mangostin 0,5 % dan Klorhesidin 0,2% terhadap ph saliva pada penderita gingivitis. J B-Dent,. 2016;3(2):75–82. https://doi.org/10.33854/JBDjbd.61
11. Yuslianti ER, Sutjiatmo AB, Meliawaty F, Zhafarina M. Efek aplikasi gel madu rambutan pada mukosa labial inferior terhadap kadar malondialdehid (mda)

saliva. Cakradonya Dent J. 2020;12(2):111–8. https://doi.org/10.24815/cdj.v12i2.18442
12. Rotty M, Runtuwenen MRJ, Kamu VS. Aktivitas penghambatan oksidasi asam linoleat ekstrak metanol daun soyogik (saurauia bracteosa dc) dengan metode ferric thiocyanate. J MIPA. 2017;6(2):42. https://doi.org/10.35799/jm.6.2.2017.17756
13. Yuslianti ER, M. Bachtiar B, F. Suniarti D, B. Sutjiat A. Antioxidant activity of rambutan honey: the free radical-scavenging activity in vitro and lipid peroxidation inhibition of oral mucosa wound tissue in vivo. Res J Med Plant. 2015 Jun;9(6):284–92. https://doi.org/10.3923/rjmp.2015.284.292
14. Yuslianti ER, Sutjiatmo AB, Septiani D. Pemberian madu rambutan (nephelium lappaceum) menurunkan luas luka dan kadar malondialdehid tikus diabetes melitus. Insisiva Dent J Maj Kedokt Gigi Insisiva. 2021;10(1):12–9. https://doi.org/10.18196/di.v10i1.8245
15. Yuslianti ER, Florence M, Afifah SB, Kertamaya S. Pengaruh pemberian madu rambutan secara topikal terhadap proses penyembuhan luka setelah pencabutan gigi kelinci (oryctolagus cuniculus) dilihat dari panjang mesial-distal luka dan kadar alkaline phosphatase. Alami J. 2019;3(2):6–12. https://doi.org/10.24252/alami.v3i2.9359
16. Zahrannisa DL, Dewi IK. Evaluasi mutu fisik sediaan pasta gigi kombinasi ekstrak kayu siwak (salvadora persica) dan daun mint (coleus amboinicus l .). PHARMADEMICA J Kefarmasian dan Gizi. 2022;2(1):31–41. https://doi.org/10.54445/pharmademica.v2i1.25
17. Prasetya F. Formulasi pasta gigi berbahan aktif ekstrak daun sirih hitam sebagai antimikroba penyebab radang gusi (gingivitis) dan gigi berlubang (caries). J Trop Pharm Chem. 2012;2(1):19–25. https://doi.org/10.25026/jtpc.v2i1.44
18. Meganingtyas W, Alauhdin M. Ekstraksi antosianin dari kulit buah naga (hylocereus costaricensis) dan pemanfaatannya sebagai indikator alami titrasi asam-basa. agriTECH. 2021;41(3):278. https://doi.org/10.22146/agritech.52197
19. Mulianto N. Malondialdehid sebagai Penanda Stres Oksidatif pada Berbagai Penyakit Kulit. Cermin Dunia Kedokt. 2020;47(1):39–44.
20. Situmorang N, Zulham Z. Malondialdehyde (mda) (zat oksidan yang mempercepat proses penuaan). J Keperawatan Dan Fisioter. 2020;2(2):117–23. https://doi.org/10.35451/jkf.v2i2.338
21. Choudhary P, Tushir S, Bala M, Sharma S, Sangha MK, Rani H, et al. Exploring the potential of bee-derived antioxidants for maintaining oral hygiene and dental health. Antioxidants. 2023;12(7). https://doi.org/10.3390/antiox12071452
22. Purbaningtyas E, Yuliani F, Ananda AP, Sari R. Disclosing agent from red dragon fruit peel as dental plaque indicator. ODONTO Dent J. 2020;7(1):31. https://doi.org/10.30659/odj.7.1.31-39
23. Nishikito DF, Borges ACA, Laurindo LF, Otoboni AMMB, Direito R, Goulart R de A, et al. Anti-inflammatory, antioxidant, and other health effects of dragon fruit and potential delivery systems for its bioactive compounds. Pharmaceutics. 2023;15(1). https://doi.org/10.3390/pharmaceutics15010159
24. Ida I, Bisnis F, Maranatha UK. Penyuluhan pemeliharaan kesehatan gigi dan mulut pada guru dan siswa sdk bppk Bandung. 2023;09(January):129–36.
25. Yuslianti ER, Hartanto Endro, Anindya Sekar. The potential of rambutan honey toothpaste in reducing the dental plaque index: a Quasi Experimental study.

Padjadjaran Journal of Dentistry. 2023;35(3):199-205. https://doi.org/10.24198/pjd.vol35no3.50310