The Saudi Dental Journal 36 (2024) 1006–1009

Contents lists available at ScienceDirect

The Saudi Dental Journal

journal homepage: www.ksu.edu.sa
www.sciencedirect.com

Original Article

Mixing ratio of nano hydroxyapatite and Epigallocatechin-3-gallate (EGCG) towards viscosity and antibacterial effect as a potential pulp capping Material: An experimental study

Kun Ismiyatin [a,*], Tamara Yuanita [a], Widya Saraswati [a], Mardikaning R. Saptaningrum [b], Dinsa C. Putri [b], Rara A. Miranda [c], Bagus A. Wibowo [c]

[a] Department of Conservative Dentistry, Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia
[b] Resident of Conservative Dentistry Specialist Program, Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia
[c] Undergraduate Student, Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia

ARTICLE INFO

Keywords:
Antibacterial
EGCG
Medicine
Nano-hydroxyapatite
Pulp capping
Viscosity

ABSTRACT

Background: Finding a new natural scaffold is challenging due to crucial impact on long-term treatment outcomes in pulp capping. In this context, nano hydroxyapatite (nano-HA) is a potential candidate having similar properties to bone tissue in the body. The compound is often synthesized with Epigallocatechin-3-gallate (EGCG) which offers anti-inflammatory and antibacterial properties. Therefore, this study aims to contribute novel insights into the development of effective pulp capping materials by determining the viscosity ratio of the combination of nano-HA and EGCG applied to the cavity according to standard pulp capping material, as well as proving the antibacterial effect against *Lactobacillus acidophilus*.

Methods: The combination of nano-HA – EGCG is divided into three treatment groups, (G1) 1:1 ratio, (G2) 1:1.5 ratio, (G3) 1:2 ratio, as well as control group G4 ($Ca(OH)_2$ and aquadest) with a ratio of 1:1. Meanwhile, each group is tested for viscosity using a Brookfield viscometer. The well diffusion method is used to determine the antibacterial activity by measuring the diameter of the inhibition zone for each treatment, with C1 ($Ca(OH)_2$ and aquadest) as control group at a ratio of 1:1, and three treatment groups (nano-HA – EGCG), (C2) 0.5:1 ratio, (C3) 1:1 ratio, and (C4) 2:1 ratio.

Results: The results show that there is a difference in the viscosity of each group with G3 having a viscosity of 12.0183 cP, which is closest to control. Furthermore, significant differences are also reported in antibacterial activity between control and treatment groups.

Conclusion: The ratio of 1:2 (G3) has a viscosity that closely matches the standard of pulp capping materials. The combinations of nano-HA and EGCG are proven to have antibacterial power against *Lactobacillus acidophilus*.

1. Introduction

Pulp capping is a conservative pulp treatment that does not require tissue removal, and is minimally invasive compared to other treatment options. Therefore, the purpose of the treatment is to stop the caries process, as well as stimulate pulp to form tertiary dentin and render protection from inflammation (Alex, 2018). The selection of the right pulp capping material greatly affects the long-term results of vital treatment. In this context, new materials serving as better candidates for pulp capping must be obtained.

An alternative material for pulp capping is nano hydroxyapatite (nano-HA) from eggshells widely consumed. The shells represent a cost-effective and abundant raw material, contributing to cost reduction and environmental benefits through recycling (Horta et al., 2020). Eggshell nano-HA is used in early carious lesions for remineralization, reducing tooth sensitivity, and enhancing mechanical properties, as well as promoting the formation of tertiary dentin (Elline and Ismiyatin, 2021). Nano-HA is an important aspect of pulp capping materials due to similar properties to bone tissue and also serves as a drug and gene carrier through interaction with cells (Chu et al., 2017). This compound is often

* Corresponding author at: Department of Conservative Dentistry, Faculty of Dental Medicine, Universitas Airlangga, JL. Prof. Dr. Moestopo No. 47, Surabaya 60132, Indonesia.
E-mail address: kun-is@fkg.unair.ac.id (K. Ismiyatin).

https://doi.org/10.1016/j.sdentj.2024.04.009
Received 7 January 2024; Received in revised form 22 April 2024; Accepted 25 April 2024
Available online 26 April 2024

synthesized with Epigallocatechin-3-gallate (EGCG), offering antioxidant, anti-inflammatory, and antibacterial properties (Elline et al., 2022). The strong antioxidant properties are obtained from hydroxyl groups (–OH groups), which effectively capture nitric oxide (NO) free radicals in inflammation and tissue damage. This process causes blood vessels to constrict, reducing capillary permeability. Therefore, fewer neutrophil cells migrate to the injury site, speeding up the resolution of the acute inflammatory phase and increasing macrophage activity to create a secondary defense mechanism (Widjiastuti et al., 2019). The antibacterial ability of (–OH) groups also contributes to the destruction of bacterial cell walls (Jahangir et al., 2021). Even though nano-HA's alkaline nature damages bacterial cell membranes and proteins, disrupting the integrity, the organic scaffold is remineralized with EGCG (Aprilisna et al., 2015; Pushpalatha et al., 2023).

The developed nano-HA and EGCG delivery platform is biocompatible and shows promise in enhancing the stability of the adhesive-dentin interface due to unique advantages (Yu et al., 2021). Viscosity is crucial in handling dental materials, showing the ease in flow and dental materials vary in viscosity based on intended use. For cavity liners, low-viscosity materials are preferred in wetting the cavity walls to enhance marginal adaptation and reduce microleakage (Loumprinis et al., 2021).

In the etiology of caries process, the most important factor is the presence of cariogenic bacteria (Ahirwar et al., 2019). Caries occur when large numbers of bacteria produce acid to demineralize the tooth structure. Meanwhile, *Lactobacillus* is the most important microorganism in the development of cavities found to possess acidogenic and aciduric properties. During the fermentation process of glucose, *Lactobacillus acidophilus* is one of the *Lactobacillus* rods that mostly produce lactic acid (Karpiński and Szkaradkiewicz, 2013).

This study was conducted to determine an effective combination suitable in viscosity applied to the cavity according to standard pulp capping material and sufficient antibacterial effect against *Lactobacillus acidophilus*. The aim is to develop an effective and biocompatible pulp capping material to improve dental treatments.

2. Materials and methods

2.1. Viscosity

This research was conducted at the Research Center, Faculty of Dental Medicine, Universitas Airlangga, under the ethical code 534/HRECC.FODM/IX/2021. Nano-HA derived from eggshells in powder form with a particle size of 50–60 nm, was obtained from the Pro-db brand in PT Pertiwi Parahita Teknologi, Bogor, Indonesia. Meanwhile, EGCG in the form of a white powder was obtained from Xi'An Rongsheng Biotechnology Co., Ltd, China. To obtain a solution with a concentration of 0.5 mg/100 ml, 0.5 mg pure EGCG powder was diluted by adding 100 ml aquadest (Kwon et al., 2017). Subsequently, 0.1 g nano-HA powder was prepared per sample (Horta et al., 2020).

In making the combination of nano-HA and EGCG, 0.1 g nano-HA powder was mixed with the solution, at a ratio of (G1) 1:1 (0.1 g nano-HA powder was mixed with 0.1 ml EGCG solution), (G2) ratio 1:1.5 (0.1 g nano-HA powder was mixed with 0.15 ml EGCG solution), and (G3) ratio 1:2 (0.1 g nano-HA powder was mixed with 0.2 ml EGCG solution). In control group (G4), $Ca(OH)_2$ powder (PT Merck Chemicals and Life Sciences, Indonesia) was mixed with aquadest in a ratio of 1:1 (Mohammadi and Dummer, 2011). The solution and nano-HA powder were mixed according to the ratio of each group and stirred for 1–2 min until homogeneous.

Viscosity testing was conducted using a Brookfield viscometer (Brookfield AMETEK DV1-LV, USA) prepared by connecting to electricity and setting the water bath temperature to 25 °C. A cone-shaped spindle was used due to the small size of the samples and the plate was installed to adjust the distance. Turning on the viscometer, the rotating speed was set on the monitor, and the motor button was pressed to start rotating the tool. Meanwhile, the viscosity results were shown on a digital indicator and recorded in centipoise (cP).

After obtaining the data, the processing was carried out through Shapiro-Wilk test to determine the normality of the distribution, followed by a homogeneity analysis using Levene's test. To determine the difference in all treatment groups, One-way ANOVA test was performed. In contrast, Tukey HSD analysis test was conducted to determine the treatment group with significant differences.

2.2. Antibacterial Activity Against Lactobacillus acidophilus

This research was conducted at the Research Center, Faculty of Dental Medicine, Universitas Airlangga, under the ethical code 538/HRECC.FODM/IX/2021. A Post Test-Only Control Group Design was used with 4 treatment groups, consisting of 6 replications and the sample used was *Lactobacillus acidophilus* ATCC 4356 PK/5 (Thermo Scientific, USA). Combinations of nano-HA and EGCG were made by mixing the solutions prepared by dissolving 0.5 mg powder with 100 ml aquadest (Kwon et al., 2017).

Combinations of nano-HA and EGCG in the treatment group were prepared in a (C2) 1:2 ratio (0.05 g nano-HA to 0.1 ml EGCG), a (C3) 1:1 ratio (0.10 g nano-HA to 0.1 ml EGCG) and a (C4) 2:1 ratio (0.20 g nano-HA with 0.1 ml EGCG). Meanwhile, a combination of (C1) 0.10 g nano-HA with 0.1 ml aquadest was used as control. A stock of *Lactobacillus acidophilus* was prepared on Brain Heart Infusion Broth (BHIB) media (Oxoid, Thermofisher Scientific, UK) which was incubated for 24 h at 37 °C, and bacterial concentration with standardized Mc Farland turbidity was 0.5 (1.5×10^8).

The prepared bacteria were rubbed evenly on Mueller Hinton Agar (MHA) media, (Oxoid, Thermofisher Scientific, UK) in a petri dish using a spreader, and 4 wells were made in MHA media with a diameter of 5 mm. The first well was filled with nano-HA samples (C1), while the second, third, and fourth wells were filled with combined samples of nano-HA and EGCG at a ratio of C2 (0.05 g: 0.1 ml), C3 (0.1 g: 0.1 ml), and C4 (0.2 g: 0.1 ml) incubated for 24 h at 37 °C.

The antibacterial activity was assessed by observing the formation of inhibition zones, measured in millimeters using a caliper. The average was calculated by summing the largest and smallest diameters and dividing by 2. Furthermore, data normality was assessed with the Shapiro-Wilk test, followed by homogeneity analysis using Levene's test. The differences among treatment groups were analyzed using One-way ANOVA, with significant differences determined by Tukey HSD analysis.

3. Results

3.1. Viscosity

According to the viscosity measurements, there were differences in viscosity in each treatment group, as shown in Table 1. G1, G2, G3, and G4 had a value of 16,042 cP, 13,828 Cp, 12,018 Cp, and 12,793 Cp, respectively. Based on the results presented, the ratio with the closest viscosity to control group G4 was G3.

Table 1
The Mean value and standard deviation of viscosity.

Group	n	Mean (cP)	Standard Deviation (SD)
1	6	16.042	0.258
2	6	13.828	0.175
3	6	12.018	10.537
4	6	12.793	0.409

Information:
Group 1 (G1) = combination of nano-HA and EGCG ratio 1:1.
Group 2 (G2) = combination of nano-HA and EGCG ratio 1:1.5.
Group 3 (G3) = combination of nano-HA and EGCG ratio 1:2.
Group 4 (G4) = combination of $Ca(OH)_2$ and Aquadest ratio 1:1 (control group).
cP = Centipoise.

The normality tests conducted using the Shapiro-Wilk test showed that the data were normally distributed. The homogeneity test carried out using the Levene test reported that the data variance was homogeneous. According to One-way ANOVA test, there were significant differences in the treatment groups and Tukey HSD test showed that the groups had significant differences between treatment groups (Table 2).

3.2. antibacterial activity against Lactobacillus acidophilus

A preliminary study was carried out by measuring the pH of the combination ingredients according to the treatment. The pH measurements of C2, C3, and C4 groups were 7.49, 7.85, and 8.02, respectively. The results of the antibacterial activity through the diameter of the inhibition zone using the diffusion method are presented in Fig. 1 and Table 3.

According to Table 3, the groups with the highest and lowest means were C4 and C1, which had a ratio of 2:1 (0.2 g nano-HA + 0.1 ml EGCG) and nano-HA without EGCG, respectively. One-way ANOVA test showed a significant value of 0.001 ($p < 0.05$), reporting a difference in treatment effects. Therefore, the treatment groups showed activity in inhibiting the growth of *Lactobacillus acidophilus*. The results of Tukey HSD test in Table 4 reported that not all combinations had a p-value < 0.05. Significant differences in antibacterial power were observed between various combinations of C1 C3, and C4; C2, C4, C3, and C1; as well as C4, C1, and C2.

4. Discussion

The viscosity of nano-HA with EGCG decreases due to the increase in EGCG ratio, with G3 (1:2 ratio) showing the closest viscosity to control group. This decrease occurs because higher EGCG ratios alter the mixture's structure, leading to dilution. Lower viscosity facilitates higher ionic dissociation, while high molecular weight solvents maintain the paste in the desired area for longer periods (Mohammadi and Dummer, 2011). Various factors influence viscosity, including solution concentration, dissolved molecule weight and size, intermolecular strength, temperature, and pressure (Lumbantoruan and Erislah, 2016; Juhantoro and Ariana, 2012). Meanwhile, higher solution concentration results in greater viscosity due to increased friction between dissolved particles (Lumbantoruan and Erislah, 2016).

Intermolecular forces in liquids maintain close molecular proximity while allowing for relative movement. In this context, neutral molecules show dispersion and dipole–dipole forces, as well as hydrogen bonds. The dispersion forces operate universally and strengthen with molecular weight to enhance polarizability since dipole–dipole forces intensify the polarity. Hydrogen bonds, stronger than other forces, are prevalent, and ion–dipole forces become significant in polar solvent solutions with ionic compounds. In addition, higher viscosity correlates with stronger intermolecular forces (Brown et al., 2015). Previous studies confirmed high viscosity in nano-HA and EGCG combination due to the large relative masses, enhancing dipole formation and hydrogen bonding. The compounds' polarity amplifies van der Waals forces to elevate viscosity.

Table 2
Results of the Post Hoc Tukey HSD Test Analysis.

Group	1	2	3	4
1		0.000*	0.000*	0.000*
2	0.000*		0.000*	0.001*
3	0.000*	0.000*		0.009*
4	0.000*	0.001*	0.009*	

Information:
*) Significant or significant difference $p < 0.05$.
Group 1 (G1) = combination of nano-HA and EGCG ratio 1:1.
Group 2 (G2) = combination of nano-HA and EGCG ratio 1:1.5.
Group 3 (G3) = combination of nano-HA and EGCG ratio 1:2.
Group 4 (G4) = combination of $Ca(OH)_2$ and Aquadest ratio 1:1 (control group).

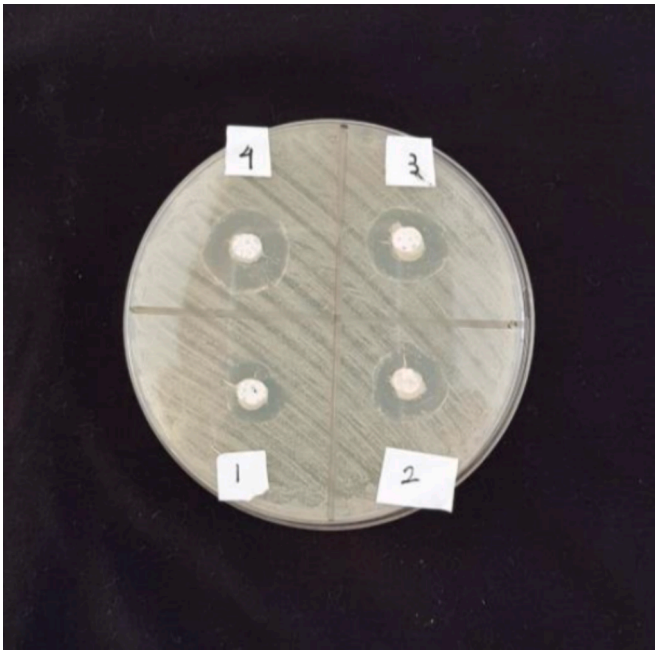

Fig. 1. (1) C1 (control) = 1:1 ratio (0.10 g nano-HA: 0.1 ml aquadest); (2) C2 = 1:2 ratio (0.05 g nano-HA: 0.1 ml EGCG); (3) C3 = 1:1 ratio (0.10 g nano-HA to 0.1 ml EGCG), and (4) C4 = 2:1 ratio (0.20 g nano-HA with 0.1 ml EGCG).

Table 3
The mean (mm) and standard deviation of the treatment group's inhibitionagainst *Lactobacillus acidophilus*.

Group	n	Mean	Standard Deviation (SD)
1	6	6.63	1.159
2	6	8.25	1.458
3	6	9.58	1.708
4	6	11.04	1.771

Information:
Group 1 (C1) = 0.10 g nano-HA + 0.1 ml Aquadest (control).
Group 2 (C2) = combination of nano-HA and EGCG ratio 1:2.
Group 3 (C3) = combination of nano-HA and EGCG ratio 1:1
Group 4 (C4) = combination of nano-HA and EGCG ratio 2:1.

Table 4
Results of Tukey HSD Test Analysis.

Group	1	2	3	4
1		0.292	0.017*	**0.000***
2	0.292		0.458	**0.025***
3	**0.017***	0.458		0.381
4	**0.000***	**0.025***	0.381	

Information:
*) Significant or significant difference $p < 0.05$.
Group 1 (C1) = 0.10 g nano-HA + 0.1 ml Aquadest (control).
Group 2 (C2) = combination of nano-HA and EGCG ratio 1:2.
Group 3 (C3) = combination of nano-HA and EGCG ratio 1:1
Group 4 (C4) = combination of nano-HA and EGCG ratio 2:1.

Nano-HA and EGCG combination shows potent antibacterial properties and promotes dentinal bridge formation. EGCG, rich in polyphenols, serves as a natural antibacterial agent to inhibit bacterial adhesion and biofilm formation against antibiotic-resistant strains (Du et al., 2012). Nano-HA, known for osteoinductive and osteoconductive properties, facilitates dentinal bridge formation effectively (Chu et al., 2017). In this context, G3 with a ratio of 1:2 (0.1 g nano-HA powder was mixed with 0.2 ml EGCG solution) can be a suitable candidate as pulp

capping material in terms of viscosity, due to the level corresponding with the standard. Pulp capping materials with viscosity possess better antibacterial properties, causing slower ion dissociation. This enables the antibacterial properties from the combination of nano-HA and EGCG to work optimally and last for a longer time.

Antibacterial properties are crucial in pulp capping materials to preserve vitality for maintaining tooth homeostasis and durability (Aprilisna et al., 2015). Table 2 shows the antibacterial efficacy across all treatment groups, attributed to nano-HA release of hydroxide ions (OH–) with strong oxidizing properties, effectively targeting bacteria. Additionally, the alkaline nature of hydroxyapatite proves detrimental to bacterial cell membranes and proteins, disrupting the integrity (Aprilisna et al., 2015). These high pH levels can be particularly detrimental to *Lactobacillus acidophilus*, which thrives in a narrower pH range of 5.5 to 6.0.

EGCG enhances bacterial growth inhibition by damaging bacterial lipid bilayer walls (Loumprinis et al., 2021). Meanwhile, C2 combination had no significant antibacterial activity compared to other treatment groups because the amount of nano-HA was small. This study found that C4 showed stronger antibacterial activity compared to C2 and C3. The increased nano-HA content correlates with enhanced bacterial inhibition due to the high pH antibacterial mechanism. Nano-HA synthesized from chicken eggshells, comprising 94 % calcium carbonate (CaCO3), serves as a calcium source for precursor synthesis, contributing to the elevated pH levels (Rivera-Muñoz, 2011). Meanwhile, optimal antibacterial activity occurs when there is a collaboration between nano-HA and EGCG. The combination is effective against the inhibition of *Lactobacillus acidophilus*, due to synergistic effect. This is in accordance with previous studies, where a beneficial combination has a synergistic effect on the active ingredients in the development of medicinal plants (Syahrir et al., 2016).

Concerning the limitation, the effects of the experimental parameters were not thoroughly investigated on mixing, including variations in concentrations of Nano-HA and EGCG, as well as reaction pH and time. Additionally, the stability of the mixtures was not comprehensively assessed in water, buffer, and culture media. These areas should be given priority in future studies.

5. Conclusion

In conclusion, the combination with a ratio of 1:2 was reported to have a viscosity closely matching the standard of pulp capping materials. Meanwhile, the combinations of nano-HA and EGCG had antibacterial activity against *Lactobacillus acidophilus*.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Ahirwar, S.S., Gupta, M.K., Snehi, S.K., 2019. Dental caries and lactobacillus: role and ecology in the oral cavity. Int. J. Pharm. Sci. Res. 11, 4818–4829. https://doi.org/10.13040/IJPSR.0975-8232.10(11).4818-29.

Alex, G., 2018. Direct and indirect pulp capping: a brief history, material innovations, and clinical case report. Compendium 39, 182–189.

Aprilisna, M., Ramadhany, C.A., Sunendar, B., Widodo, H.B., 2015. Karakteristik dan Aktivitas Antibakteri Scaffold Membran Cangkang Telur yang Diaktivasi Karbonat Apatit. Majalah Kedokteran Gigi. Indonesia 1, 59–67. https://doi.org/10.22146/majkedgiind.8993.

Brown, T.L., LeMay, H.E., Bursten, B.E., Murphy, C.J., Woodward PM. 2015. Chemistry: The Central Science. 13th ed. Vol. 57, Chemical and Engineering News. p. 444-454.

Chu, C., Deng, J., Man, Y., Qu, Y., 2017. Evaluation of nanohydroxyapaptite (nano-HA) coated epigallocatechin-3-gallate (EGCG) cross-linked collagen membranes. Mater. Sci. Eng. C 78, 258–264. https://doi.org/10.1016/j.msec.2017.04.069.

Du, X., Huang, X., Huang, C., Wang, Y., Zhang, Y., 2012. Epigallocatechin-3-gallate (EGCG) enhances the therapeutic activity of a dental adhesive. J. Dent. 40, 485–492. https://doi.org/10.1016/j.jdent.2012.02.013.

Elline, E., Ismiyatin, K., 2021. Nanohydroxiapatite using chicken eggshell waste and its characterization. Malay. J. Med. Health Sci. 17, 83–86. https://repository.unair.ac.id/123878/1/7.pdf.

Elline, E., Ismiyatin, K., Budhy, T.I., Bhardwaj, A., 2022. The potential of eggshell hydroxyapatite, collagen, and EGCG (HAp-Col-EGCG) scaffold as a pulp regeneration material. Saudi Dental J. 34, 715–722. https://doi.org/10.1016/j.sdentj.2022.10.004.

Horta, M.K.D.S., Moura, F.J., Aguilar, M.S., Westin, C.B., Campos, J.B.D., Peripolli, S.B., Ramos, V.S., Navarro, M.I., Archanjo, B.S., 2020. Nanostructured hydroxyapatite from Heń s eggshells using sucrose as a template. Mater. Res. 23 https://doi.org/10.1590/1980-5373-MR-2020-0266.

Jahangir, M.U., Islam, F., Wong, S.Y., Jahan, R.A., Matin, M.A., Li, X., Arafat, M.T., 2021. Comparative analysis and antibacterial properties of thermally sintered apatites with varied processing conditions. J. Am. Ceram. Soc. 104, 1023–1039. https://doi.org/10.1111/jace.17525.

Juhantoro, N., Ariana, I. M. & Sanuri, S. 2012. Penentuan Properties Bahan Bakar Batubara Cair untuk Bahan Bakar Marine Diesel Engine. Jurnal teknik ITS, 1, G271-G275. 10.12962/j23373539.v1i1.2005.

Karpiński, T.M., Szkaradkiewicz, A.K., 2013. Microbiology of dental caries. J. Biol. Earth Sci. 3, M21–M24.

Kwon, Y.S., Kim, H.J., Hwang, Y.C., Rosa, V., Yu, M.K., Min, K.S., 2017. Effects of epigallocatechin gallate, an antibacterial cross-linking agent, on proliferation and differentiation of human dental pulp cells cultured in collagen scaffolds. J. Endod. 43, 289–296. https://doi.org/10.1016/j.joen.2016.10.017.

Loumprinis, N., Maier, E., Belli, R., Petschelt, A., Eliades, G., Lohbauer, U., 2021. Viscosity and stickiness of dental resin composites at elevated temperatures. Dent. Mater. 37, 413–422. https://doi.org/10.1016/j.dental.2020.11.024.

Lumbantoruan, P., Erislah, E., 2016. Pengaruh suhu terhadap viskositas minyak pelumas (oli). Sainmatika: Jurnal Ilmiah Matematika Dan Ilmu Pengetahuan Alam 13. https://doi.org/10.31851/sainmatika.v13i2.993.

Mohammadi, Z., Dummer, P.M.H., 2011. Properties and applications of calcium hydroxide in endodontics and dental traumatology. Int. Endod. J. 44, 697–730. https://doi.org/10.1111/j.1365-2591.2011.01886.x.

Pushpalatha, C., Gayathri, V.S., Sowmya, S.V., Augustine, D., Alamoudi, A., Zidane, B., Albar, N.H.M., Bhandi, S., 2023. Nanohydroxyapatite in dentistry: A comprehensive review. Saudi Dental J. https://doi.org/10.1016/j.sdentj.2023.05.018.

Rivera-Muñoz, E.M., 2011. Hydroxyapatite-based materials: synthesis and characterization. Biomed. Eng.-Front. Chall. 75–98 https://doi.org/10.5772/19123.

Syahrir, N.H.A., Afendi, F., Susetyo, B., 2016. Efek Sinergis Bahan Aktif Tanaman Obat Berbasiskan Jejaring Dengan Protein Target. Jurnal Jamu Indonesia 1, 35–46. https://doi.org/10.29244/jji.v1i1.6.

Widjiastuti, I., Ismiyatin, K., Purwanto, D.A., Sukmawati, T., 2019. Effect of hydrogel Epigallocatechin-3-gallate (EGCG) to the number of fibroblast cell proliferation in the perforation of Wistar rat tooth pulp. Conservative Dentistry J. 10.20473/cdj.v9i2.2019.93-96.

Yu, J., Zhang, Z., Guo, R., Peng, W., Yang, H., Huang, C., 2021. Epigallocatechin-3-gallate/nanohydroxyapatite platform delivery approach to adhesive-dentin interface stability. Mater. Sci. Eng. C 122, 111918. https://doi.org/10.1016/j.msec.2021.111918.