

Original Article

Activity of Carboxymethyl Chitosan-Based Torch Ginger Flower Extract Nanoparticles on Biofilm Degradation in Oral Cavity

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KEY WORDS

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ABSTRACT

Background: An imbalance in the oral cavity's microbial biofilm can lead to dental caries and periodontitis. Torch ginger (*Etilingera elatior*) possesses antibiofilm properties that may be enhanced through nanoparticle formulation using carboxymethyl chitosan.

Purpose: This study aimed to evaluate the biofilm degradation activity of torch ginger flower extract nanoparticles formulated with carboxymethyl chitosan against oral pathogenic bacteria.

Materials and Method: The experiment was conducted from December 2024 – March 2025 at the Faculty of Medicine, Jenderal Soedirman University. An *in vitro* laboratory study was conducted with five treatment groups: torch ginger extract nanoparticles at concentrations of 15, 25, and 35mg/mL; a positive control (0.2% chlorhexidine gluconate); and a nanoparticle formulation without extract (formulation control). Biofilm degradation was assessed using the microtiter plate assay method with 1% crystal violet staining. Data analysis was performed using one-way ANOVA followed by LSD post hoc test.

Results: All nanoparticle concentrations exhibited significant biofilm degradation activity ($p < 0.05$) against *Streptococcus sanguinis*, *Streptococcus mitis*, *Fusobacterium nucleatum*, *Prevotella intermedia*, and *Porphyromonas gingivalis*. The 15mg/mL concentration showed equivalent effectiveness to 0.2% chlorhexidine gluconate against *Streptococcus sanguinis*; 25mg/mL against *Fusobacterium nucleatum* and *Porphyromonas gingivalis*; and 35mg/mL against *Streptococcus mitis* and *Prevotella intermedia*.

Conclusion: Torch ginger flower extract nanoparticles based on carboxymethyl chitosan are effective in degrading oral bacterial biofilms and demonstrate potential as a natural alternative for plaque control.

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Introduction

Oral health is a crucial aspect that significantly influences an individual's quality of life. The most common oral health issues are dental caries and periodontitis [1-3]. Dental caries is the destruction of tooth hard tissues caused by acids produced by plaque bacteria [4], while periodontitis is the inflammation of the supporting tis-

ues of the teeth, involving an immune response to microbial biofilms [5].

Biofilms are bacterial colonies protected by an extracellular polymeric substance (EPS) matrix. Various bacterial species such as *Streptococcus sanguinis* (*S. sanguinis*), *Streptococcus mitis* (*S. mitis*), *Fusobacterium nucleatum* (*F. nucleatum*), *Porphyromonas gingivalis*

(*P. gingivalis*), and *Prevotella intermedia* (*P. intermedia*) play essential roles in plaque formation and the pathogenesis of periodontal diseases, particularly under conditions of oral flora imbalance [6–9].

Biofilm control can be achieved through both mechanical and chemical methods. Chlorhexidine gluconate (CHX) is considered the gold standard of chemical mouthwash due to its effectiveness; however, it may cause adverse effects such as tooth discoloration [10–11]. This has encouraged the development of safer natural alternatives. One promising candidate is torch ginger (*Etilingera elatior*), which is rich in antibacterial compounds including flavonoids, tannins, alkaloids, saponins, steroids, terpenoids, and phenols [12–13].

Previous studies by Putri *et al.* [12] and Ichsyani *et al.* [14] have shown that torch ginger extract has biofilm degradation activity. However; its limited stability necessitates modification into a nanoparticle form to enhance its efficacy. Carboxymethyl chitosan (CMChi), a water-soluble and safe derivative of chitosan, can be used as a nanoparticle matrix that enhances the antibacterial activity of plant extracts [15–19]. Earlier studies by Hardening *et al.* [20], Khairunnisa *et al.* [21], and Suhesti *et al.* [22] have demonstrated that combining plant extracts with CMChi or chitosan nanoparticles significantly enhances antibacterial and antibiofilm activity.

This study aims to evaluate the biofilm degradation activity of CMChi-based torch ginger flower extract nanoparticles against *S. sanguinis*, *S. mitis*, *F. nucleatum*, *P. intermedia*, and *P. gingivalis*, with the expectation of achieving higher efficacy than pure extract.

Materials and Method

This study was approved by the Health Research Ethics Committee, Faculty of Health Sciences, Jenderal Soedirman University (Ref. No: 119/KEPK/PE/XII/2024). It was an *in vitro* experimental laboratory study with a posttest-only control group design. The research was conducted at the Plant Systematics Laboratory, Pharmaceutical Biology Laboratory, Pharmaceutical Preparation Technology Laboratory, and Research Laboratory of Jenderal Soedirman University, as well as the Integrated Laboratory of Yogyakarta State University, from December 2024 to March 2025. Fresh flower samples of torch ginger were collected and subjected to

taxonomic identification at the Herbarium of the Plant Systematics Laboratory, Universitas Jenderal Soedirman. The identification process was conducted by a certified botanist, Professor Pudji Widodo, Ph.D., M. Sc, and the plant was authenticated under reference letter #B/81/UN23.6.10/TA.00.01/2025. This *in vitro* study consisted of five groups: torch ginger extract nanoparticles at concentrations of 15, 25, and 35 mg/mL; a positive control using 0.2% CHX; and a nanoparticle formulation without extract as the negative control. The bacterial strains tested included *S. sanguinis* ATCC 10556, *S. mitis* ATCC 49456, *F. nucleatum* ATCC 25586, *P. intermedia* ATCC 25611, and *P. gingivalis* ATCC 32277. The torch ginger flower extract was obtained via maceration using 70% ethanol. A total of 10 kg of fresh torch ginger flowers produced 1.4 kg of dried simplicia. Maceration was performed by immersing 1.4 kg of simplicia powder in 5 L of 70% ethanol for 24 h. The extract was filtered, and the residue was re-macerated twice under the same conditions. The combined filtrates were concentrated using a rotary evaporator and further evaporated in a water bath to obtain a thick blackish-brown extract of *Etilingera elatior* flowers. The maceration process yielded 236 grams of thick extract, with a yield of 16.8%. Phytochemical screening confirmed the presence of active compounds including flavonoids, tannins, alkaloids, saponins, terpenoids, phenols, and steroids (Table 1). Torch ginger extract nanoparticles based on CMChi were synthesized using the ionic gelation method. Nanoparticles were synthesized through ionic gelation with CMChi and CaCl₂. In the first step, CMChi was dissolved in 100mL of distilled water and stirred using a magnetic stirrer at 700rpm for 1h until homogeneous. In the second step, a CaCl₂ solution was prepared by dissolving 100mg of CaCl₂ in 40mL of distilled water and then added to the

Table 1: Phytochemical Screening Results

No	Active Compound	Test Result	Description
1	Flavonoid	(+)	Color change to dark brown
2	Tannin	(+)	Color change to black
3	Alkaloid	(+)	Formation of brown precipitate
4	Saponin	(+)	Foam formation
5	Terpenoid	(+)	Color change to red
6	Phenol	(+)	Color change to dark red
7	Steroid	(+)	Color change to green

Note: (+)= presence of compound

CMChi solution, followed by stirring at 700 rpm for 1 h. In the third step, *Etilingera elatior* flower extract (1500 mg, 2500 mg, and 3500 mg) was dissolved in 10 mL of 70% ethanol and mixed according to the predetermined formula. The volume ratio of the CMChi solution to the CaCl₂ solution was 5:2. The mixture was stirred using a magnetic stirrer at 1000 rpm for 2 h [22]. Particle characterization was conducted using a particle size analyzer (PSA) to determine particle size, polydispersity index (PDI), and zeta potential. PSA results (Table 2) showed particle sizes within the 10–1000 nm range, qualifying as nanoparticles. All formulations had PDI values below 0.7, indicating monodispersed particle distribution. However, the zeta potential values were below the ideal threshold for optimal stability.

Bacterial cultures grown on Mueller Hinton agar (MHA) medium were inoculated into brain heart infusion broth (BHIB) medium using 4–5 loops. *S. sanguinis*, *S. mitis*, *F. nucleatum*, and *P. intermedia* were incubated in a CO₂ incubator at 37 °C for 24 h, while *P. gingivalis* was incubated in an anaerobic jar with an anaerobic pack at 37°C. Bacterial suspensions were standardized by diluting them in 0.9% NaCl to match the 0.5 McFarland standard. A total of 100µL of bacterial suspension and 100µL of BHIB medium were added into each well of a microplate. The microplate was then incubated in a CO₂ incubator at 37°C for 48h, after which 200µL of the medium in each well was discarded. The degradation assay was performed on preformed bacterial biofilms by adding 100µL of CMChi-based *Etilingera elatior* flower extract nanoparticles at various concentrations and 100µL of BHIB medium. For the positive control group, 100µL of 0.2% CHX and 100µL of BHIB medium were added. For the formulation control group, 100µL of CMChi nanoparticles without extract and 100µL of BHIB medium were added. For the

growth control group, 100µL of distilled water and 100µL of BHIB medium were added. The microplates were then incubated in a CO₂ incubator at 37°C for 45 min in each treatment group. Biofilm degradation activity was evaluated using a microtiter plate assay, with 1% crystal violet staining and absorbance measurement at 450nm. Biofilm degradation percentage data were analyzed using SPSS v29. Following tests for normality and homogeneity, one-way ANOVA and LSD post hoc tests were applied.

Results

Biofilm degradation was evaluated using the microtiter plate assay with 1% crystal violet staining, and absorbance readings at 450nm. The absorbance for *S. sanguinis* is presented in Figure 1. All nanoparticle concentrations (15, 25, 35mg/mL) showed significantly higher degradation activity compared to the nanoparticle control ($p < 0.05$). No significant difference was found compared to 0.2% CHX, suggesting equivalent effectiveness. The absorbance for *S. mitis* is presented in Figure 2. A significant increase in biofilm degradation was observed at all concentrations compared to the negative control ($p < 0.05$). The 35mg/mL concentration was equivalent in effectiveness to 0.2% CHX, while the 15 and 25mg/mL concentrations were slightly less effective. The absorbance for *F. nucleatum* is presented in

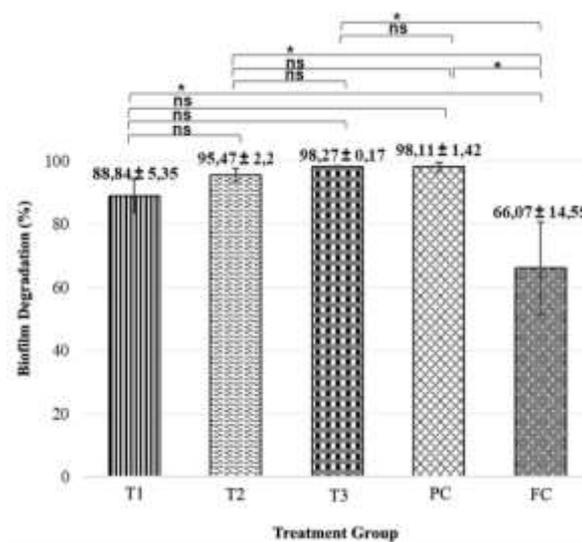


Figure 1: Percentage of *S. sanguinis* biofilm degradation by torch ginger flower extract nanoparticles based on carboxymethyl chitosan compared to 0.2% CHX as positive control (PC) and nanoparticles without extract as formulation control (FC) (Note: * = significantly different, ns = not significantly different, T1 = 15 mg/mL concentration, T2 = 25 mg/mL concentration, T3 = 35 mg/mL concentration, PC = positive control, FC = formulation control)

Table 2: Nanoparticle Characterization via PSA

No	Parameter	Standard	Result			
			T1	T2	T3	FC
1	Particle size	10-1000 nm [22]	187 nm	484 nm	777 nm	248 nm
2	Polydispersity index	< 0.7 [23]	0.2	0.3	0.1	0.6
3	Zeta potential	>±30mV [21]	-4, 5mV	-19, 5mV	-0, 2mV	5, 1mV

Note:

Treatment 1 (T1) = Concentration 15 mg/mL

Treatment 2 (T2) = Concentration 25 mg/mL

Treatment 3 (T3) = Concentration 35 mg/mL

Formulation control (FC) = Nanoparticle without extract

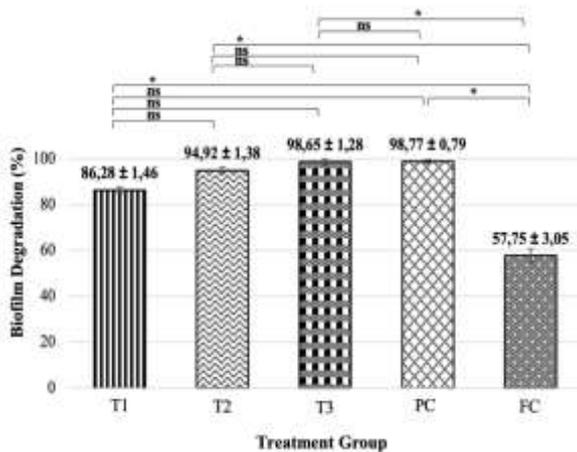


Figure 2: Percentage of *S. mitis* biofilm degradation by torch ginger flower extract nanoparticles based on carboxymethyl chitosan compared to 0.2% CHX (PC) and nanoparticles without extract (FC) (Note: * = significantly different, ns = not significantly different, T1 = 15 mg/mL concentration, T2 = 25 mg/mL concentration, T3 = 35 mg/mL concentration, PC = positive control, FC = formulation control)

Figure 3. All tested concentrations significantly enhanced biofilm degradation compared to the negative control ($p < 0.05$). The 35mg/mL concentration was not significantly different from 0.2% CHX, indicating optimal effectiveness. The absorbance for *P. gingivalis* is presented in Figure 4. All nanoparticle concentrations exhibited significant degradation effects ($p < 0.05$) compared to the nanoparticle control. The 35mg/mL formul-

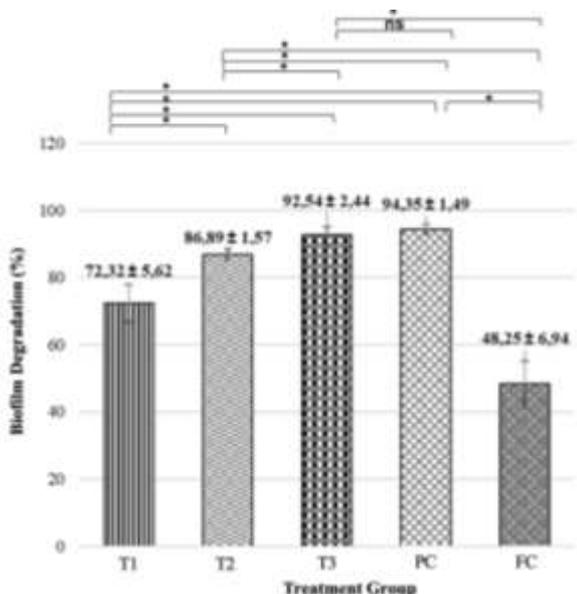


Figure 3: Percentage of *F. nucleatum* biofilm degradation by torch ginger flower extract nanoparticles based on carboxymethyl chitosan compared to 0.2% CHX (PC) and nanoparticles without extract (FC) (Note: * = significantly different, ns = not significantly different, T1 = 15 mg/mL concentration, T2 = 25 mg/mL concentration, T3 = 35 mg/mL concentration, PC = positive control, FC = formulation control)

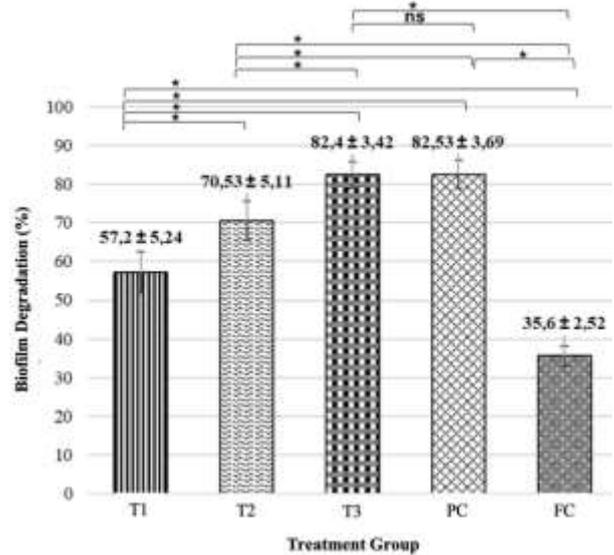


Figure 4: Percentage of *P. gingivalis* biofilm degradation by torch ginger flower extract nanoparticles based on carboxymethyl chitosan compared to 0.2% CHX (PC) and nanoparticles without extract (FC) (Note: * = significantly different, ns = not significantly different, T1 = 15 mg/mL concentration, T2 = 25 mg/mL concentration, T3 = 35 mg/mL concentration, PC = positive control, FC = formulation control)

ation demonstrated comparable results to 0.2% CHX. The absorbance for *P. intermedia* is presented in Figure 5. CMChi-based torch ginger extract nanoparticles at all concentrations demonstrated significantly higher degradation than the negative control ($p < 0.05$). At 35mg/mL, their effectiveness matched that of 0.2% CHX.

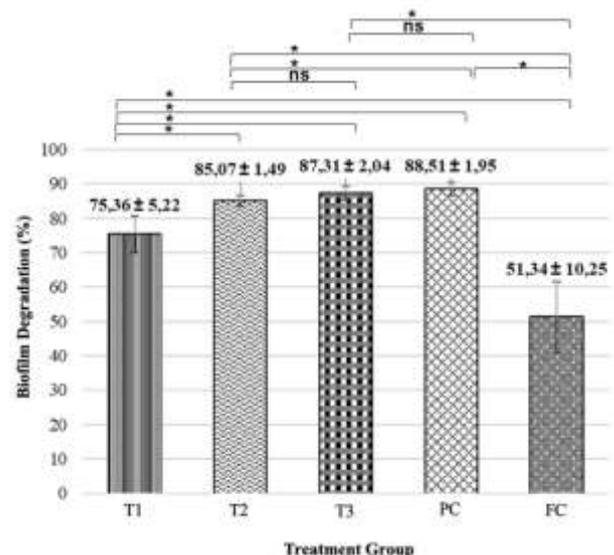


Figure 5: Percentage of *P. intermedia* biofilm degradation by torch ginger flower extract nanoparticles based on carboxymethyl chitosan compared to 0.2% CHX (PC) and nanoparticles without extract (FC) (Note: * = significantly different, ns = not significantly different, T1 = 15 mg/mL concentration, T2 = 25 mg/mL concentration, T3 = 35 mg/mL concentration, PC = positive control, FC = formulation control)

Discussion

Periodontitis is a chronic inflammatory disease of the periodontal supporting tissues driven by dysbiosis microbial communities. These pathogenic microorganisms induce the destruction of the periodontal ligament and alveolar bone, resulting in periodontal pocket formation, clinical attachment loss, gingival recession, alveolar bone resorption, tooth mobility, and ultimately tooth loss in advanced stages. The etiology of periodontitis is closely associated with subgingival biofilms dominated by anaerobic gram-negative bacterial species [23-24].

The primary therapy for periodontitis involves eliminating etiologic factors through plaque control using scaling and root planing (SRP). Mouthrinses are commonly used as adjuvant therapy to help control bacterial accumulation following SRP [23]. Conventional mouthrinses such as CHX gluconate often contain alcohol and, with long-term use, may cause adverse effects including tooth staining, mucosal irritation, disruption of the normal oral flora, and xerostomia [10-11]. These limitations have encouraged the development of natural-based mouthrinse alternatives that are safer and associated with fewer side effects [26].

Torch ginger species is *Etilingera elatior* (Jack) R.M. Sm. within the genus *Etilingera*, family Zingiberaceae, and is categorized as a perennial herbaceous plant [13]. Torch ginger, locally known as *kecombrang* in Indonesia, has long been consumed as both food and spice. Traditionally, its flowers are used as flavoring agents in various culinary preparations [25]. Extraction of torch ginger flowers with 70% ethanol yielded 16.8%, which is considered satisfactory as it exceeds the minimum standard of 9.8% set by the Indonesian Ministry of Health [17]. Phytochemical screening revealed that the extract contains flavonoids, tannins, alkaloids, saponins, terpenoids, phenols, and steroids—compounds widely recognized for their antibacterial and antibiofilm activities [14, 16, 27-28].

Previous studies by Putri *et al.* [12] and Djati *et al.* [29] have demonstrated that torch ginger (*Etilingera elatior*) extract possesses biofilm degradation activity against *F. nucleatum* and *P. gingivalis*, two major periodontopathogens in oral biofilm development. Due to its viscous texture, large particle size, and limited compound stability, the extract was formulated into nanoparticles using CMChi through the ionic gelation meth-

od with CaCl_2 as a cross-linker. This approach was intended to enhance stability and penetration of the active constituents [14]. A similar strategy was applied in the present study using extract of spirulina and longan seed, which showed stronger antibacterial activity when encapsulated in chitosan nanoparticles compared to the free extract [20-21].

Characterization showed that the nanoparticles ranged from 187 to 777 nm, which falls within the nanoparticle classification of 10–1000 nm. All formulations had PDI values below 0.7, indicating uniform and stable particle distribution [28–29]. The zeta potential values were below ± 30 mV, suggesting moderate stability. Although not meeting the ideal threshold, the homogeneous particle size distribution contributed to maintaining stability [2,22].

Biofilm degradation testing demonstrated that CMChi-based torch ginger nanoparticles exhibited significant activity ($p < 0.05$) compared to the negative control (CMChi nanoparticles without extract). Against Gram-positive bacteria such as *S. sanguinis* and *S. mitis*, the effect was particularly pronounced. At 35 mg/mL, the nanoparticles degraded *S. sanguinis* biofilms by $98.27 \pm 0.17\%$, comparable to 0.2% CHX with $98.11 \pm 1.42\%$. For *S. mitis*, degradation at the same concentration reached $98.65 \pm 1.28\%$, similar to CHX at $98.77 \pm 0.79\%$.

The effect on Gram-negative bacteria— including *F. nucleatum*, *P. intermedia*, and *P. gingivalis*—was also strong, though slightly lower. At 35 mg/mL, degradation was $92.54 \pm 2.44\%$ for *F. nucleatum*, $87.31 \pm 2.04\%$ for *P. intermedia*, and $82.4 \pm 3.42\%$ for *P. gingivalis*, with no significant difference compared to 0.2% CHX. The higher effectiveness against Gram-positive bacteria may be explained by structural differences. Gram-positive bacteria, with their thick but permeable peptidoglycan layer, are more susceptible to interaction with polar and cationic agents such as CMChi nanoparticles. In contrast, gram-negative bacteria possess an additional outer membrane enriched with lipopolysaccharides, which acts as a selective barrier, reducing nanoparticle penetration and efficacy [30–31]. This distinction is important in oral biofilm management, as early plaque colonizers are mainly gram-positive *Streptococcus* species that facilitate the attachment of late gram-negative anaerobes such as *P. gingivalis*, *F. nucleatum*, and *P.*

intermedia. By disrupting gram-positive biofilms, torch ginger nanoparticles may interfere with the initial stages of plaque development and indirectly limit the colonization of more pathogenic gram-negative organisms [35].

The effectiveness of biofilm degradation can be attributed to the active compounds within the extract. Flavonoids inhibit bacterial enzymes and virulence factors, as well as interfere with EPS production and adhesion [28, 36]. Tannins penetrate cell membranes, suppress enzyme activity, and modulate biofilm-related genes such as *icaA* and *icaD* [28, 30]. Alkaloids disrupt bacterial membranes, inhibit peptidoglycan synthesis, degrade EPS, interfere with quorum sensing, and suppress biofilm-related genes [12]. Saponins denature bacterial proteins, destabilize membranes, lower surface tension, and degrade the EPS, thereby weakening biofilms [28, 37]. Terpenoids and steroids alter membrane integrity through interactions with proteins and phospholipids, whereas phenols denature bacterial proteins [30, 37].

These results are consistent with previous studies by Putri *et al.* [12] and Ichsyani *et al.* [14] showing that torch ginger extract contains flavonoids, saponins, tannins, alkaloids, terpenoids, steroids, and phenols, which can degrade the biofilms of *P. gingivalis* and *Aggregatibacter actinomycetemcomitans* [12,14]. Similarly, Wijaya *et al.* [37] has reported that extracts of roselle flower and tamarind fruit, which contain alkaloids, tannins, saponins, terpenoids, phenols, steroids, and flavonoids, possess antibacterial activity against *P. intermedia*.

Based on these findings, torch ginger flower extract nanoparticles formulated with CMChi show strong potential to improving their stability and antibacterial performance and supporting their development as adjunctive agents for biofilm control in oral infections, with comparable effectiveness to CHX but potentially fewer side effects. A limitation of this study was the absence of a pure extract control without nanoparticle formulation, which would clarify the added benefit of nanoparticle delivery. Future research should address this limitation and further investigate *in vivo* and clinical applications to support their use in dentistry.

Conclusion

CMChi -based nanoparticles containing torch ginger flower extract exhibit biofilm degradation activity agai-

nst *S. sanguinis*, *S. mitis*, *F. nucleatum*, *P. intermedia*, and *P. gingivalis*. This activity is attributed to the presence of active compounds such as flavonoids, tannins, saponins, alkaloids, terpenoids, steroids, and phenols. A concentration of 15 mg/mL showed comparable degradation activity to 0.2% CHX against *S. sanguinis*, 25 mg/mL against *F. nucleatum*, and *P. gingivalis*, and 35 mg/mL against *S. mitis* and *P. intermedia*.

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Conflict of Interest

The authors declare no conflict of interest in this study.

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