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Hydrogel-forming microneedles with epigallocatechin gallate and 4-(hydroxymethyl)-phenylboronic acid for antibacterial wound healing and drug release

Naritsara Suwatsrisakun[1], Duangkanok Tanangteerapong[1,*] and Jindarat Ekprasert[2]

[1] Department of Chemical Engineering, Faculty of Engineering, Khon Kaen University, Khon Kaen 40002, Thailand
[2] Department of Microbiology, Faculty of Science, Khon Kaen University, Khon Kaen, 40002, Thailand
[*]Corresponding author: duangkanok@kku.ac.th

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Abstract

Wounds in diabetic patients represent a major therapeutic challenge, necessitating advanced treatment strategies with sustained drug delivery and infection control. This research introduces a hydrogel-based microneedle dressing incorporating epigallocatechin gallate (EGCG) and 4-(hydroxymethyl)-phenylboronic acid (HPBA), focusing on the crosslinking interactions that govern their structural, mechanical, and functional performance. Among the tested formulations, the hydrogel containing EGCG and HPBA in a 1:1 ratio exhibited the greatest swelling ability, which was likely due to its efficient capacity to retain water. Meanwhile, the HPBA-only hydrogel showed the lowest swelling ability due to its dense polymer network. The 1:1 formulation also exhibited superior mechanical strength and flexibility, enabled by efficient crosslinking that enhanced structural integrity. Drug release studies revealed that the EGCG-HPBA (1:2) hydrogel allowed for rapid initial drug release, while the 1:1 formulation provided a slower, sustained release profile, making it more suitable for controlled drug delivery. Moreover, EGCG demonstrated significant bactericidal activity toward *E. coli* and *S. aureus*, and this activity was retained upon integration with HPBA. The results demonstrate that the EGCG-HPBA (1:1) hydrogel microneedle system is a promising multifunctional dressing for chronic wound management, combining mechanical resilience, controlled drug release, and antibacterial efficacy.

Keywords: EGCG, Microneedle, Crosslinking, Drug release

1. Introduction

Diabetes mellitus refers to a long-term metabolic condition involving the disrupted control of blood sugar levels. This condition is generally divided into two major categories. Type 1 diabetes is caused by a lack of insulin production due to an autoimmune attack on the pancreatic β-cells. On the other hand, Type 2 diabetes results from both the body's decreased sensitivity to insulin and impaired insulin production. Additionally, there are rarer forms of diabetes that may stem from genetic abnormalities or the side effects of specific drugs [1]. Diabetes has become an increasingly common condition among adults worldwide, with its prevalence steadily rising over the past years. Future projections indicate a continued upward trend, signaling a growing concern for public health on a global scale [2]. One of the major complications associated with diabetes is delayed wound healing, primarily due to an impaired immune response and sustained hyperglycemia. Elevated glucose levels inhibit cellular repair mechanisms and create a favorable environment for microbial proliferation, which increases the risk of infection. In severe cases, this may lead to limb amputation [3]. Consequently, proper wound care and strategies to prevent infection are essential for minimizing the complications associated with diabetes.

Epigallocatechin gallate (EGCG) is a major polyphenol compound found in green tea that has garnered significant interest in the scientific community due to its wide range of biological effects. These effects include potent antioxidant capabilities, reduced inflammation, immune system modulation, and the regulation of metabolic processes. Studies have demonstrated that EGCG can alleviate oxidative stress and inflammation, which are central factors in the development of chronic conditions such as diabetes, cardiovascular diseases, and

cancer [4]. Recent studies also suggest that EGCG promotes wound healing by stimulating cell proliferation and exhibiting antibacterial properties, making it a promising candidate for diabetic wound care applications [5]. However, despite its therapeutic benefits, EGCG has been reported to exhibit dose-dependent toxicities (e.g., hepatotoxicity and gastrointestinal irritation at high concentrations), particularly upon oral administration. Topical applications and incorporation into biomaterials at controlled doses significantly mitigate these adverse effects, supporting the safe use of EGCG in wound healing systems [6,7].

4-(Hydroxymethyl) phenylboronic acid (HPBA) is a boronic acid derivative featuring both phenylboronic and hydroxymethyl groups [8]. This unique structure enables HPBA to form dynamic covalent bonds through the reversible formation of boronate esters with diol-containing compounds such as glucose. These bonds can repeatedly dissociate and reform under physiological conditions, imparting responsiveness and adaptability to hydrogel networks [9]. Such reversible bonding allows the hydrogel crosslink density to change in response to environmental stimuli, enabling sustained or stimuli-responsive drug release when glucose levels fluctuate [10]. This mechanism makes HPBA particularly suitable for the development of glucose-sensitive wound dressings capable of on-demand drug delivery. While HPBA is generally considered appropriate for biomedical applications, boronic acid derivatives have shown varying degrees of cytotoxicity depending on their dose and chemical structure, highlighting the need for evaluating the biocompatibility of final formulations [11].

Crosslinking is a critical process in materials engineering that involves the creation of chemical or physical linkages among polymer chains to improve their overall structural strength, mechanical strength, and stability under physiological conditions. In wound dressing applications, crosslinking provides enhanced resistance to microbial invasion and improves the moisture retention properties of the dressing, which are essential factors for effective healing and tissue regeneration [12]. Microneedles (MNs) are an innovative, minimally invasive technology with potential uses in areas such as transdermal drug administration, wound healing, and tissue repair. These structures can be created from a range of materials, including polymers, metals, and hydrogels, and they can be tailored to carry therapeutic agents for gradual and targeted release within the skin layers. This approach improves drug bioavailability, reduces dosing frequency, and facilitates localized therapeutic action features that are particularly beneficial for chronic wound treatment in diabetic patients [13]. The objective of this research is to examine the physicochemical characteristics and the drug release behavior of a glucose-responsive microneedle patch formed by crosslinking EGCG and HPBA. The functional group interactions, water absorption capacity, tensile strength, surface morphology, antimicrobial activity, and drug release kinetics of the prepared hydrogel-based microneedles are characterized. The outcomes of this study provide insights into the development of an advanced wound dressing tailored to the needs of diabetic patients with the potential to enhance healing efficacy and prevent complications.

2. Materials and methods

2.1 Materials

Pure-EGCG™ (green tea extract, 98% EGCG), 4-(hydroxymethyl) phenylboronic acid (≥98%), collagen, triethanolamine, and a microneedle mold (25 × 15 mm, H = 600 μm, 10 × 10, S = 600 μm, D = 300 μm, conical) were acquired from MySkinRecipes (Bangkok, Thailand). Polyvinyl alcohol and acetic acid were obtained from RCI Labscan (Bangkok, Thailand).

2.2 Bacterial isolates

A 5 mM EGCG solution was prepared by dissolving EGCG in 100 mL of deionized (DI) water at room temperature. HPBA was then added in a specific molar proportion (1:1, 1:2, or 2:1), and this mixture was stirred until fully combined. Then, 1 mL of 1% (w/v) triethanolamine (TEA) was introduced to adjust the pH to between 5.5 and 6.5, followed by further stirring at room temperature until the solution was uniform. In a separate step, 10 g of collagen powder was dispersed in 100 mL of 1% (v/v) acetic acid solution and refrigerated at 4 °C for 12 hours. Meanwhile, 10 g of polyvinyl alcohol (PVA) was dissolved in 100 mL of distilled water at 90 °C, and this mixture was continuously stirred for 30 minutes until complete dissolution was achieved. After bringing the collagen solution and PVA solution to room temperature, equal volumes of these two solutions were mixed and stirred to obtain a single homogeneous collagen+PVA solution. Then, the EGCG+HPBA solution and collagen+PGA solution were combined in a 1:2 volume ratio and cast into a PDMS mold (dimensions 25 × 15 mm, height 600 μm, diameter 300 μm). Crosslinking was performed using a freeze-thaw method involving three cycles of freezing at 4 °C for 2 hours and thawing at 25 °C for 1 hour [14]. The resulting hydrogel microneedles were then collected for further use.

2.3 Fourier transform infrared (FTIR) spectroscopy

The chemical characteristics of the hydrogels were analyzed by an FTIR spectrophotometer (Bruker TENSOR27). The FTIR spectra were collected across the wavenumber range of 4000 to 500 cm^{-1} at a temperature of 25 °C [15].

2.4 Water uptake test

The water uptake of the EGCG-HPBA microneedles was analyzed as follows: first, a dry sample with dimensions of 2 cm × 2 cm was kept under vacuum at room temperature for 6 hours, and the dry weight (Wi) was then recorded. Next, the dry sample was immersed in distilled water at room temperature for a specified length of time to measure the swollen weight (Wf). Water uptake was then quantified using Equation (1) [16].

$$\text{Swelling ratio (\%)} = \frac{(W_f - W_i)}{W_i} \times 100 \quad (1)$$

Where Wi is the initial dry weight of the sample and Wf is the weight of the sample after immersion in water.

2.5 Scanning electron microscopy (SEM)

The surface structures of the hydrogel microneedles were observed using a LEO 1450 VP scanning electron microscope. The hydrogels mainly consisted of water. Therefore, prior to imaging, each hydrogel was freeze-dried to maintain its original architecture. After freeze-drying, a fine gold coating was applied to each sample to improve its electrical conductivity. SEM analysis was performed using an accelerating voltage of 10 kV with settings optimized for detailed examination [17].

2.6 Micro universal testing machine (UTM)

The evaluation was carried out with a universal testing machine (UTM, model EZ-LX) featuring a 5000 N load cell. Hydrogel specimens with dimensions of 6 × 2 cm were employed for tensile testing at a constant elongation speed of 50 mm/min. The resulting data produced a stress-strain curve for each sample, and the stress (kPa) was determined according to Equation (2) [16].

$$\sigma = \frac{F}{A} \quad (2)$$

Where σ is the stress (kPa), F is the force (N), and A is the area (m^2).

2.7 Antibacterial testing

The antibacterial properties of the hydrogel samples were tested using the disc diffusion technique on Mueller-Hinton agar (Himedia, India) following the Clinical and Laboratory Standards Institute (CLSI) guidelines. Separate cultures of the Gram-positive (*S. aureus*) and the Gram-negative (*E. coli*) bacteria were grown in nutrient broth (Himedia, India) and incubated at 37 °C under agitation at 150 rpm for 24 hours. The bacterial suspensions were then diluted to reach an optical density of 0.1 at OD_{600nm} before being evenly spread onto Mueller-Hinton agar plates. Each hydrogel microneedle specimen (6 mm in diameter) was carefully positioned on the agar plate under sterile conditions using disinfected forceps. Ciprofloxacin discs (Himedia, India) were used as the positive control, and sterile distilled water discs were used as the negative control. The reference antibiotic (ciprofloxacin) also served as a quality control to ensure that the bacterial inoculum density was within the acceptable CLSI range [18]. Following placement, the agar plates were incubated at 37 °C for 24 hours [19]. Antibacterial efficacy was evaluated by observing and measuring the diameters of the inhibition zones that developed around the samples.

2.8 In vitro drug release

The in vitro release profile of EGCG from the microneedles was examined using a simulated physiological environment. A PBS solution (pH 7.4) containing 200 mg/dL of glucose was used to replicate diabetic conditions. The microneedles were immersed in this solution and kept at 25 °C for a total duration of 30 hours. At predetermined intervals, aliquots were collected for analysis. The amount of EGCG released was determined by measuring the absorbance at approximately 275 nm with a UV-visible spectrophotometer (Agilent 8453) [20]. The data obtained were then used to construct a time-dependent release profile of EGCG from the microneedles.

3. Results and discussion

3.1 FT-IR analysis

The FTIR spectrum of EGCG (Figure 1) exhibits a broad absorption band between 3500 and 3200 cm^{-1}, which is attributed to the hydroxyl (–OH) groups of phenolic compounds. Moreover, a distinct peak around 1600 cm^{-1} reflects the C=C stretching vibrations in the aromatic ring, while signals observed from 1300 to 1200 cm^{-1} correspond to the C–O stretching of the phenolic moiety. These spectral features align well with those reported in earlier FTIR analyses of EGCG [16]. The FTIR spectrum of HPBA also exhibits a broad –OH band in the same range (3500–3300 cm^{-1}) due to the hydroxyl groups from both the phenol and boronic acid moieties of this compound. Moreover, a distinctive B–O absorption peak characteristic of boronic acid compounds appears between 1300–1200 cm^{-1} [21], and a C=C absorption peak is observed around 1600 cm^{-1}. The FTIR spectrum of the EGCG–HPBA crosslinked product shows distinct functional group changes, indicating the formation of covalent bonds between the hydroxyl groups of EGCG and the $B(OH)_2$ groups of HPBA. These dynamic covalent bonds, which are primarily generated via boronate ester formation [19,22], are reversible under physiological conditions, providing the hydrogel network with both stability and adaptability. Additionally, alterations in the B–O stretching region (1400–1300 cm^{-1}) confirm the covalent interaction between boronic acid and hydroxyl groups of EGCG, supporting the formation of a crosslinked network. Mechanistically, the boronate ester bonds stabilize the hydrogel structure, enhance resistance to degradation, and improve mechanical strength and elasticity while allowing controlled swelling and drug release in response to environmental stimuli [22,23]. This FTIR analysis serves as a reliable tool for confirming the crosslinking between EGCG and HPBA by observing changes in the –OH and B–O regions. Overall, this covalent crosslinking enhances the physicochemical stability of the resulting hydrogel, modulates its mechanical properties, and contributes to improved performance for stimuli-responsive drug delivery and wound healing applications.

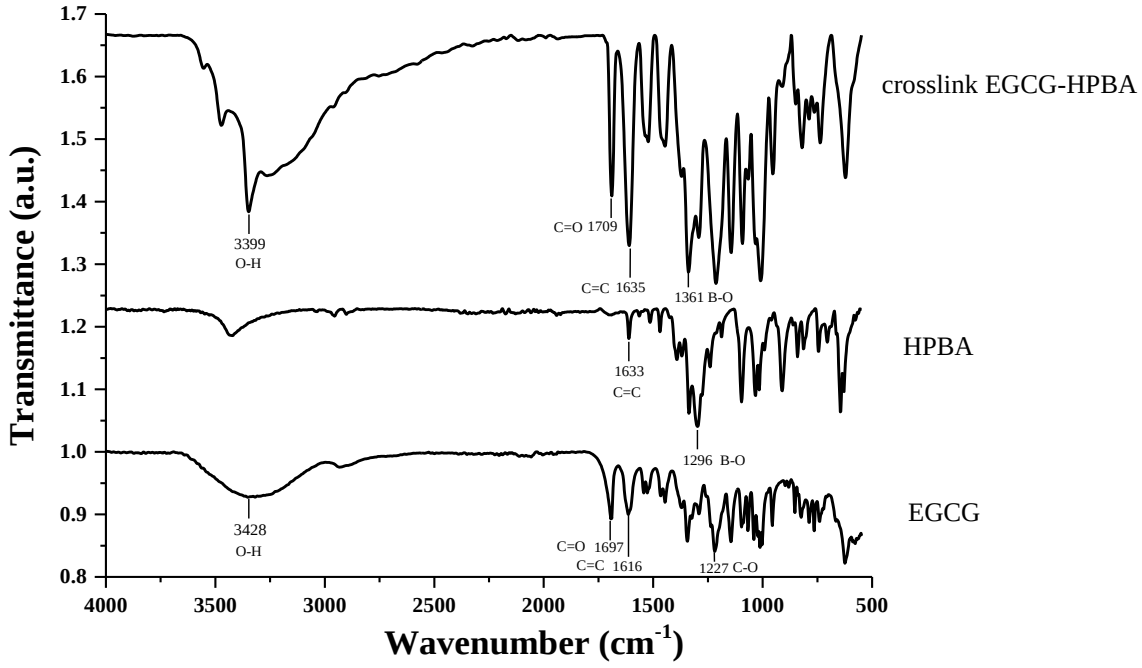

Figure 1 FT-IR results of the EGCG, HPBA, and EGCG-HPBA crosslink.

3.2 Water uptake testing

The water uptake capacities of EGCG, HPBA, and EGCG-HPBA hydrogels prepared with various ratios were evaluated. As shown in Figure 2, the EGCG-HPBA (1:1) hydrogel has the highest water uptake capacity. This is due to the 1:1 ratio providing an optimal balance between hydrogen bonding from the hydroxyl groups of EGCG and covalent crosslinking with HPBA, allowing efficient water retention within a stable polymer network [24]. Meanwhile, the hydrogels prepared with 2:1 and 1:2 ratios exhibit lower water uptake capacities. The EGCG-HPBA (2:1) hydrogel exhibits abundant hydrogen bonding but insufficient crosslinking, resulting in a less stable

network, while the EGCG-HPBA (1:2) hydrogel has a densely crosslinked, rigid structure leading to limited water diffusion. The pure HPBA hydrogel shows the lowest water uptake due to its highly crosslinked, dense network that restricts water absorption [25]. These results, which are aligned with previous studies, demonstrate that the strong hydrogen bonding of EGCG enhances water retention. However, excessive HPBA content decreases the water uptake capacity by excessively increasing the crosslinking density of the hydrogel network, which limits water absorption [26]. Overall, the 1:1 ratio of EGCG to HPBA provides the best balance between water absorption and network stability.

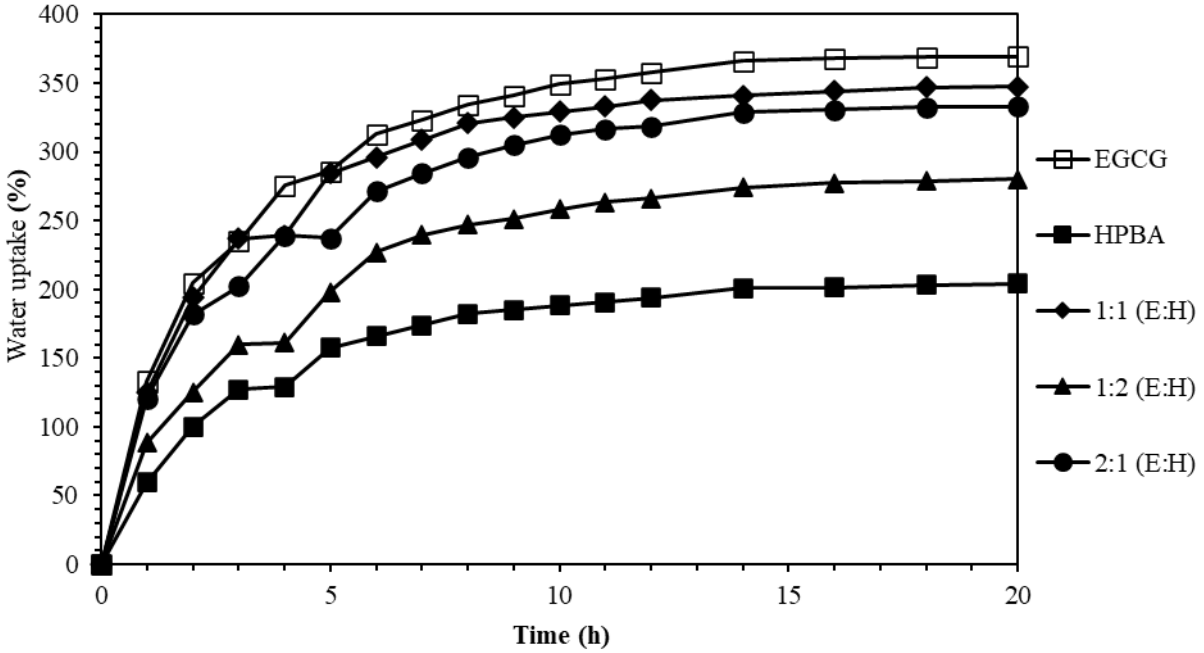

Figure 2 Water uptake capacities of EGCG, HPBA, EGCG-HPBA (1:1), EGCG-HPBA (1:2), and EGCG-HPBA (2:1).

3.3 Mechanical property of hydrogel

The stress-strain curves of the prepared EGCG, HPBA, and EGCG-HPBA hydrogel microneedle samples are displayed in Figure 3. This mechanical testing reveals that the addition of HPBA significantly improves the hydrogel strength through covalent crosslinking between the boronic acid groups of HPBA and the diol groups of EGCG, forming a dynamic network that can efficiently dissipate stress [19]. The pure EGCG hydrogel exhibits a high tensile strain of 582%, demonstrating excellent flexibility. However, this hydrogel has a relatively low tensile stress of 16 kPa, indicating a soft polymer structure suitable for applications requiring high elasticity. The EGCG-HPBA (1:1) hydrogel exhibits superior mechanical properties, achieving a maximum tensile stress of 35.4 kPa along with a tensile strain of 448%. This reflects an optimal balance between strength and flexibility. The enhanced mechanical performance of this hydrogel is attributed to the formation of a well-distributed crosslinked network in which dynamic boronate ester bonds enable efficient stress transfer and self-healing, reducing the risk of fracture during use [19,27]. In contrast, the EGCG-HPBA (1:2) hydrogel, despite having more HPBA, shows a decreased tensile stress of 14.3 kPa. This decline is attributed to excessive crosslinking density leading to excessive rigidity and brittleness, resulting in a loss of flexibility, poor tensile performance, and easier fracture [28]. Meanwhile, the EGCG-HPBA (2:1) hydrogel, which has higher EGCG content and lower HPBA content, exhibited the lowest tensile stress of 12.5 kPa and a tensile strain of 396%. This is ascribed to insufficient crosslinking and weaker structural reinforcement. The pure HPBA hydrogel has a higher tensile stress (23.2 kPa) but lower tensile strain (322%) than the pure EGCG hydrogel (16 kPa stress and 582% strain), illustrating their contrasting mechanical properties. EGCG provides a softer, more flexible network with lower strength, while HPBA contributes higher strength but less elasticity. Therefore, combining EGCG and HPBA at an appropriate ratio of 1:1 is crucial for obtaining hydrogels with balanced mechanical properties suitable for biomedical microneedle applications, consistent with previously reported dynamic hydrogel networks.

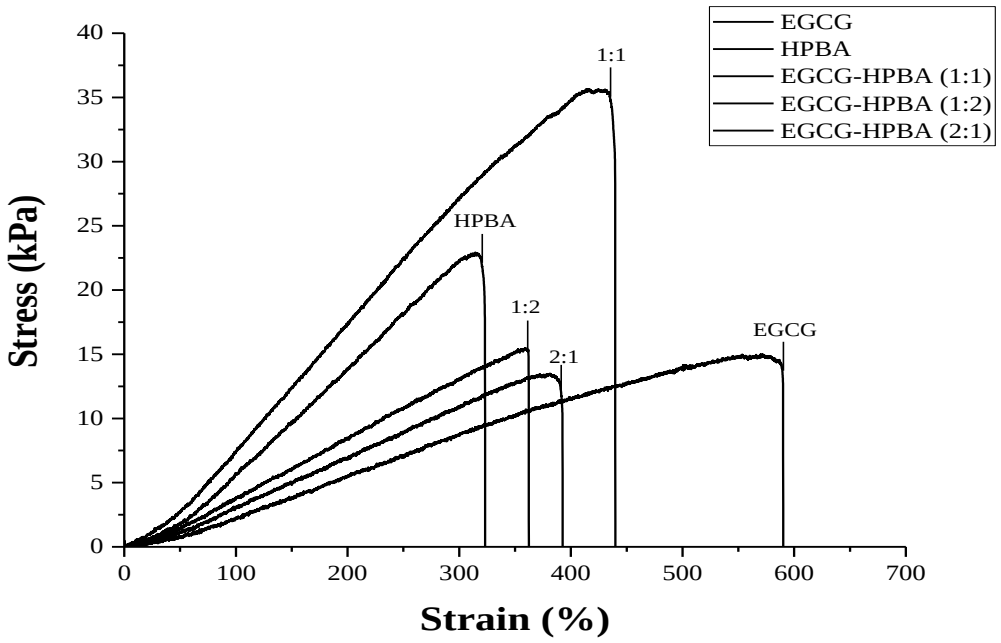

Figure 3 3 Stress-strain curves of EGCG, HPBA, EGCG-HPBA (1:1), EGCG-HPBA (1:2), and EGCG-HPBA (2:1).

3.4 Surface morphology analysis

Digital photographs and SEM images of the prepared hydrogel needles are shown in Figure 4 and Figure 5, respectively. Clearly, the ratio of EGCG and HPBA significantly influences the morphological characteristics and functional performance of these hydrogel-based microneedles. The pure EGCG microneedles exhibit a highly porous structure (pore size: 33.27 ± 4.6 μm), which facilitates enhanced water absorption and drug release but compromises mechanical stability due to increased brittleness. In contrast, the pure HPBA microneedles have a smooth, low-porosity surface that provides improved mechanical strength while limiting fluid uptake and controlled release efficiency. Adjusting the EGCG-to-HPBA ratio of the crosslinked hydrogels offers a strategic approach to achieving desirable properties. The microstructure of the EGCG-HPBA (2:1) microneedles shows a network with large, interconnected pores (10.2 ± 2 μm), supporting water uptake and drug diffusion with moderate structural integrity. Meanwhile, the EGCG-HPBA (1:1) sample exhibits a balanced microstructure (19.6 ± 5.2 μm), combining adequate porosity with mechanical robustness and sustained release performance. In contrast, the EGCG-HPBA (1:2) microneedles show a denser matrix (16.4 ± 6.9 μm), reducing both the absorption and release capabilities of this hydrogel. These findings highlight the importance of selecting appropriate material compositions to customize microneedle characteristics for biomedical uses, especially in wound repair and targeted drug administration, where maintaining mechanical strength and precise drug release are essential. The water absorption, mechanical strength, and morphology analyses of these EGCG-HPBA hydrogel microneedles reveal a strong correlation among these properties, with the precursor ratio playing a critical role. Specifically, the EGCG-HPBA (1:1) hydrogel provides the most balanced performance. In terms of swelling, this ratio achieves the maximum water uptake due to the synergy between hydrogen bonding, which facilitates water absorption, and covalent crosslinking, which maintains structural integrity. Unlike other ratios that result in reduced swelling or structural collapse, the 1:1 ratio maintains both high swelling capacity and good stability. Typically, high water absorption requires a loose network that compromises mechanical strength [29]. However, in the EGCG-HPBA (1:1) hydrogel, boronate ester crosslinking between EGCG and HPBA creates a flexible yet robust polymer matrix. This enables the microneedles to resist fracture while conforming to irregular surfaces. Morphological analysis shows that this ratio also produces uniformly distributed, moderate-sized pores, enhancing both the swelling and controlled drug release properties without enabling structural degradation. In contrast, a 2:1 ratio leads to excessive porosity and brittleness, while a 1:2 ratio results in low porosity and stiffness. Overall, the EGCG-HPBA (1:1) hydrogel offers the optimal combination of good water absorption, mechanical resilience, flexibility, and favorable porosity for sustained drug delivery. These characteristics render this hydrogel highly suitable for biomedical uses, including wound sealing and targeted drug delivery.

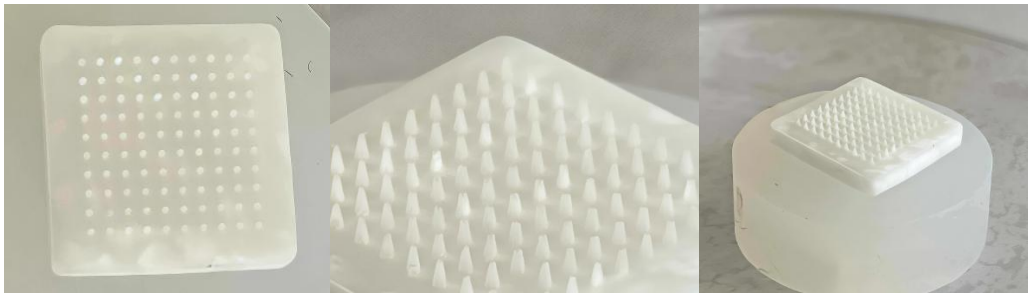

Figure 4 Digital photographs of EGCG-HPBA microneedles.

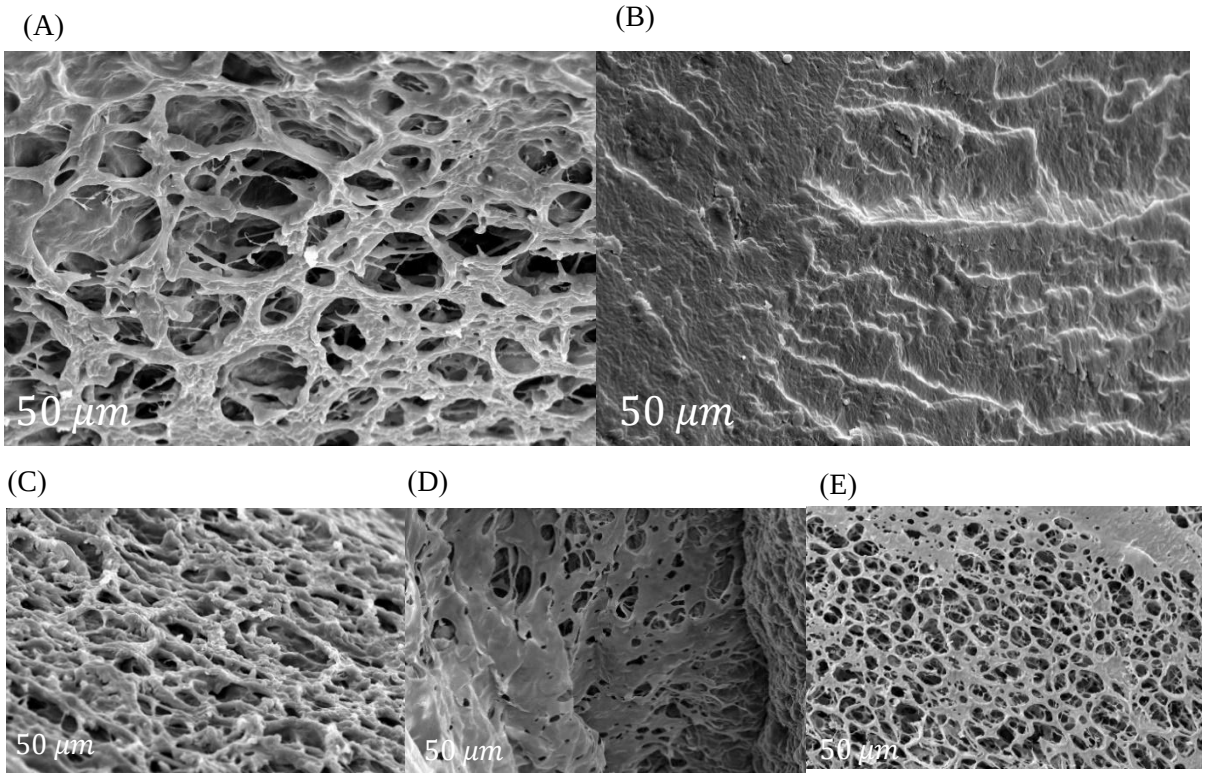

Figure 5 SEM images showing the surface morphology of (A) EGCG, (B) HPBA, (C) EGCG-HPBA (1:1), (D)EGCG-HPBA (1:2), and (E) EGCG-HPBA (2:1).

3.5 Antibacterial activity testing

The antibacterial properties of EGCG and HPBA against *E. coli* and *S. aureus* were investigated, as presented in Figure 6. EGCG alone shows stronger inhibition against *E. coli* (~17.5 mm) than *S. aureus* (~14.8 mm), while HPBA alone exhibits low antibacterial activity. The EGCG-HPBA (2:1) sample provides the largest inhibition zones (21.8 mm for *E. coli* and 19.3 mm for *S. aureus*), with a modest increase in the inhibition zones compared to the individual compounds indicating an additive effect. This conclusion is supported by fractional inhibitory concentration index (FICI) calculations. The calculated FICI value of EGCG-HPBA (2:1) is 0.8, which is within the 0.5–1.0 range consistent with an additive interaction [30]. Greater antibacterial activity is observed against Gram-negative *E. coli*, which is possibly due to the thin layer of peptidoglycan exhibited by Gram-negative bacterial cell walls making these bacteria more vulnerable to drug penetration into the cells. In contrast, the cell walls of Gram-positive bacteria mainly consist of peptidoglycan, which provides more resistance to external chemical intrusion. Moreover, antibacterial efficacy is positively correlated with the EGCG concentration due to the multiple antibacterial mechanisms of this compound, which include binding to cell surface proteins and generating reactive oxygen species. These findings emphasize that the performance obtained by combining EGCG and HPBA shows good promise for the development of effective antimicrobial biomedical materials (such as wound dressings and microneedles) to reliably prevent infection in clinical settings [20].

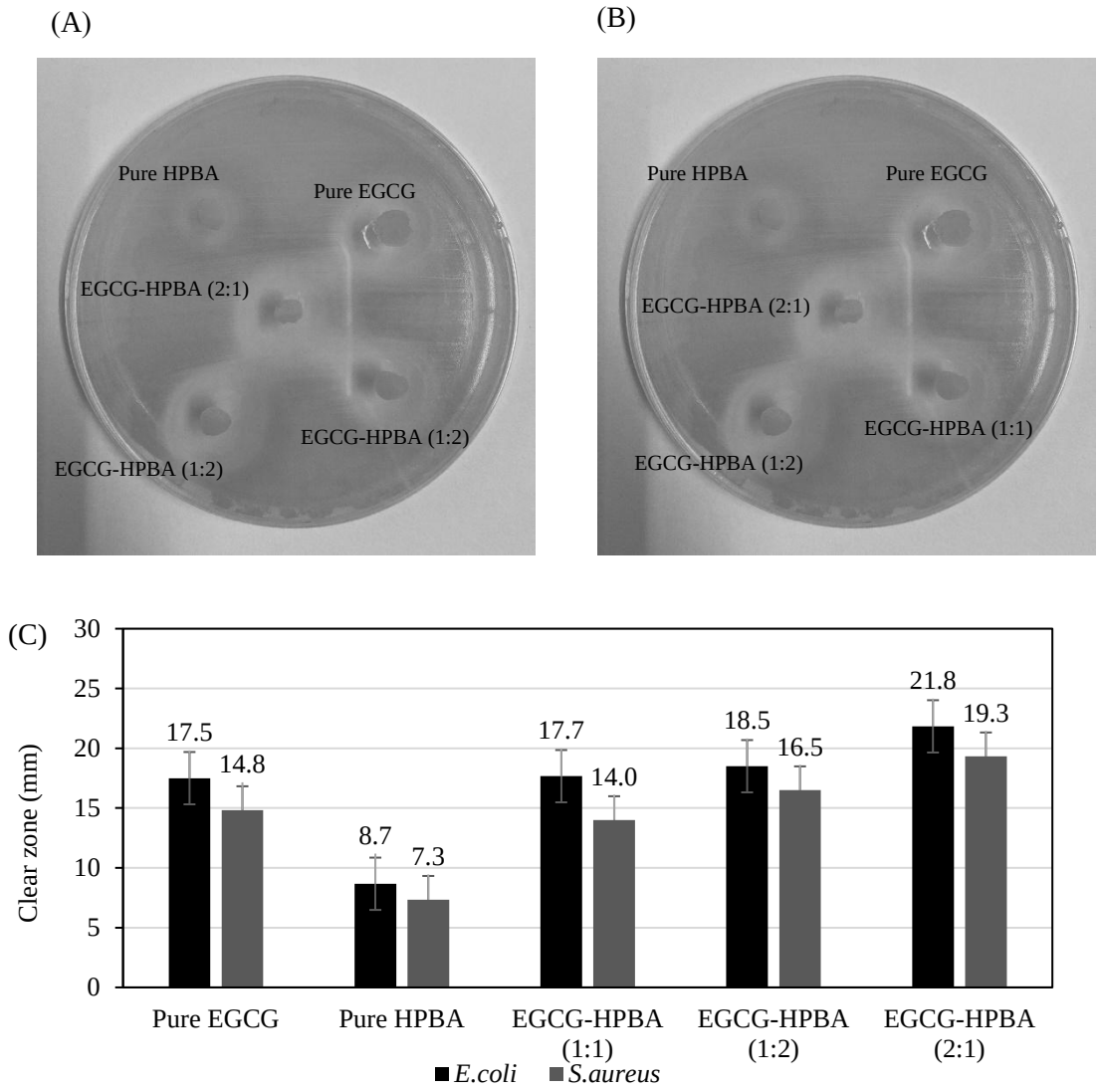

Figure 6 6 Antibacterial activity test results of EGCG, EGCG-HPBA (1:1), EGCG-HPBA (1:2), and EGCG-HPBA (2:1) against (A) *E. coli* and (B) *S. aureus*; (C) comparison of antibacterial inhibition zones for *E. coli* and *S. aureus.*

3.6 Drug release evaluation

In this study, hydrogel microneedles were prepared using epigallocatechin gallate (EGCG) and 4-(hydroxymethyl)-phenylboronic acid (HPBA) for use as a controlled drug release system. The crosslinking interactions between EGCG and HPBA significantly influenced the chemical structure, swelling behavior, mechanical properties, and surface morphology of the hydrogel microneedles. Among the tested formulations, the EGCG-HPBA (1:1) ratio exhibited the highest water uptake capacity due to an optimal balance between hydrogen bonding and crosslinking, enabling effective water retention. This formulation also showed superior mechanical strength and flexibility, indicating a stable structure suitable for microneedle applications. Drug release tests revealed that the 1:1 formulation provided a sustained and controlled release profile, unlike the 1:2 formulation, which showed rapid initial drug release. Additionally, EGCG exhibited strong antibacterial effects against both *E. coli* and *S. aureus*, and this activity was retained after crosslinking with HPBA. SEM analysis showed that the 1:1 formulation had a uniform porous structure conducive to water absorption and sustained drug release. These results confirm that the EGCG-HPBA (1:1) hydrogel microneedle system possesses the most favorable properties in terms of structure, mechanical strength, and drug delivery, indicating its excellent promise for upcoming medical applications in healing wounds and regulating drug delivery.

Therefore, glucose can effectively displace EGCG from the boronate ester bonds, leading to rapid and enhanced drug release. This represents a stimuli-responsive drug release mechanism [28,29,32]. The EGCG-HPBA (1:1) hydrogel provides a balanced amount of EGCG and HPBA, resulting in an optimal number of boronate ester bonds that are not too weak or too strong. This balance enables a high sensitivity to glucose and highly efficient drug release. In contrast, although the EGCG-HPBA (2:1) formulation contains more EGCG, the

lower HPBA content of this hydrogel results in fewer boronic acid groups available for interaction with glucose. This limits the extent to which glucose can displace EGCG, leading to a moderate and less continuous release profile. Meanwhile, the EGCG-HPBA (1:2) formulation, which has an excess of HPBA, forms a dense and rigid polymer network that restricts glucose diffusion into the structure. Consequently, bond exchange and EGCG release are limited, resulting in the lowest release efficiency. Therefore, the EGCG-HPBA (1:1) formulation is the most optimal ratio for glucose-responsive and controlled drug delivery. This hydrogel offers a balanced structure where the number of boronate ester bonds is neither too high nor too low, allowing the system to effectively respond to glucose and release EGCG in a controlled and efficient manner.

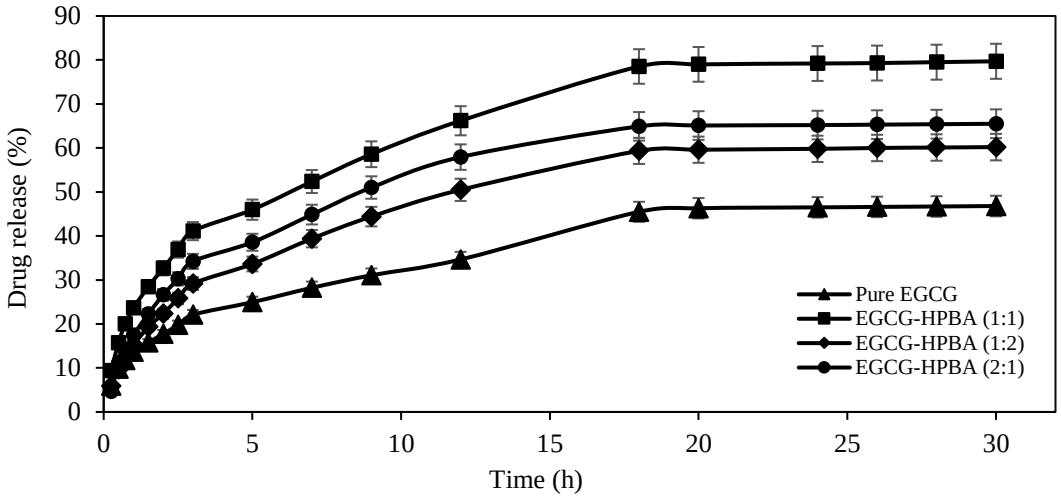

Figure 7 Drug release (%) profiles of EGCG, EGCG-HPBA (1:1), EGCG-HPBA (1:2), and EGCG-HPBA (2:1) in pure PBS solution.

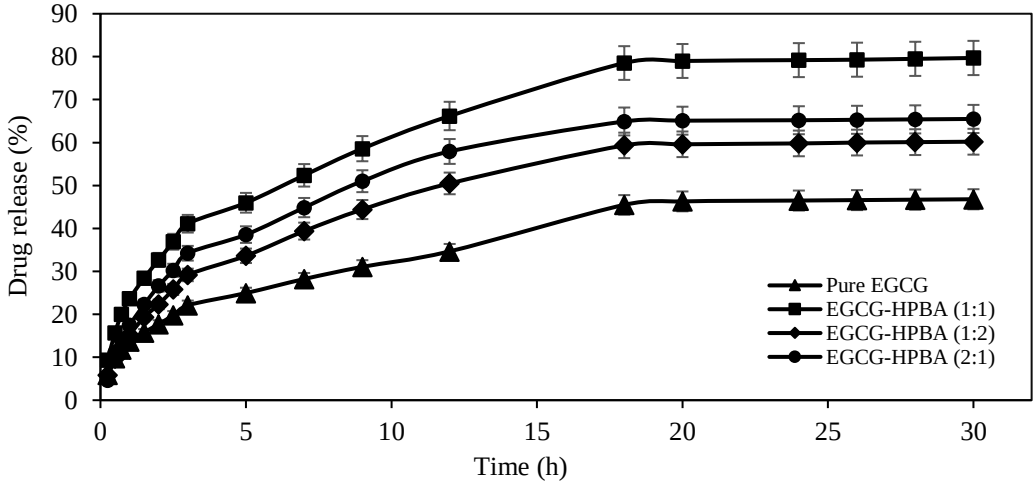

Figure 8 Drug release (%) profiles of EGCG, EGCG-HPBA (1:1), EGCG-HPBA (1:2), and EGCG-HPBA (2:1) in PBS solution with glucose (200 mg/dL).

4. Conclusions

In this study, hydrogel microneedles were prepared using epigallocatechin gallate (EGCG) and 4-(hydroxymethyl)-phenylboronic acid (HPBA) for use as a controlled drug release system. The crosslinking interactions between EGCG and HPBA significantly influenced the chemical structure, swelling behavior, mechanical properties, and surface morphology of the hydrogel microneedles. Among the tested formulations, the EGCG-HPBA (1:1) ratio exhibited the highest water uptake capacity due to an optimal balance between hydrogen bonding and crosslinking, enabling effective water retention. This formulation also showed superior mechanical strength and flexibility, indicating a stable structure suitable for microneedle applications. Drug release tests revealed that the 1:1 formulation provided a sustained and controlled release profile, unlike the 1:2 formulation, which showed rapid initial drug release. Additionally, EGCG exhibited strong antibacterial effects against both

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6. Author Contributions

Suwatsrisakun, N.: Conceptualization, Investigation, Formal analysis, Writing – original draft; Tanangteerapong, D.: Conceptualization, Methodology, Writing – review & editing;Ekprasert, J.: Methodology, Writing – review & editing.

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