Sustained Calcium Ion Release from Gelatin-Monetite Composite Sponges for Hemostatic Applications

Azizah Intan Pangesty[1*], M. Naufal Misbah[1] , M. Akif Tholibul Huda[1], Sunarso[2], Abdul Halim Abdullah[3], and Myrna Nurlatifah Zakaria[4]
[1]Department of Metallurgical and Material Sciences, Faculty of Engineering, Universitas Indonesia, Indonesia
[2] Department of Dental Materials, Faculty of Dentistry, Universitas Indonesia, Indonesia.
[3] School of Mechanical Engineering, College of Engineering, Universiti Teknologi MARA 40450 Shah Alam, Selangor, Malaysia
[4] Department of Restorative Dentistry, College of Dentistry, Ajman University, Ajman, P.O.Box 346
*Corresponding author's email: azizah.ip@ui.ac.id

Abstract. Uncontrolled bleeding (hemorrhage) remains a critical concern in trauma and surgical settings, often leading to multi-organ failure and mortality. Gelatin-based sponges are widely used as hemostatic agents due to their excellent biocompatibility and fluid absorption capabilities. However, their functionality can be further improved. This study explores the enhancement of gelatin sponges by incorporating monetite ($CaHPO_4$), a calcium-based compound known to stimulate coagulation through sustained calcium ion (Ca^{2+}) release. Composite sponges containing 3%, 5%, and 10% monetite were fabricated via freeze-drying. All samples exhibited interconnected porous networks (350–700 μm) and homogeneously dispersed monetite particles (5–20 μm). Increasing monetite concentration reduced porosity, which affected both swelling behavior and degradation kinetics. Swelling ratios for 0%, 3%, 5%, and 10% monetite sponges were 1000%, 1300%, 1000%, and 900%, respectively. The addition of monetite significantly slowed degradation, extending the material's structural integrity up to 48 hours. Calcium release was sustained, increasing from 1.3 ppm at 15 minutes to 2.0 ppm at 60 minutes. In vitro cytocompatibility assessment using the MTT assay showed over 80% cell viability for all groups. These results suggest that gelatin-monetite sponges combine structural durability with pro-coagulant ion release, offering a biocompatible and effective hemostatic material for rapid intervention in severe bleeding scenarios.

Keywords: Hemostasis, Gelatin Sponge, Monetite ($CaHPO_4$), Ca ion release, Biocompatibility.

1 Introduction

Uncontrolled hemorrhage remains a leading cause of preventable death among trauma patients. In the United Kingdom, it accounts for approximately 50% of trauma-related

S. C. Asih et al. (eds.), *Proceedings of the 19th International Conference on Quality in Research (QiR 2025)*, Advances in Engineering Research 303,
https://doi.org/10.2991/978-94-6239-717-0_24

fatalities [1–3]. Globally, trauma is responsible for over four million deaths annually, with uncontrolled bleeding being a primary contributor to this mortality [4,5]. These statistics underscore the critical need for effective hemostatic interventions to manage bleeding promptly and improve survival outcomes in trauma care. The increasing incidence of such injuries underscores the urgent demand for effective hemostatic materials that not only stop bleeding rapidly but also support the healing process and minimize complications.

Among the commercially available hemostatic agents, polypeptide-based (such as collagen [6,7] and gelatin [8–10]) and polysaccharide-based (such as chitosan [11]) sponges are extensively used in clinical settings due to their biodegradability, porosity, and ease of application [12,13]. These sponges function primarily by absorbing blood, concentrating platelets and clotting factors, and accelerating the intrinsic coagulation cascade [14]. Nevertheless, their utility remains limited in the context of high-pressure arterial bleeding or in confined anatomical regions, such as in deep trauma or dental sockets. Furthermore, the rapid swelling behavior of gelatin sponges can cause mechanical compression on surrounding tissues, potentially exacerbating damage or inducing nerve pressure [15].

To address these challenges, various studies have incorporated bioactive inorganic materials—especially calcium-based additives—into biopolymer matrices to create hemostatic materials with active functionality. Calcium ions (Ca^{2+}) play a central role in activating coagulation factors and thrombin generation, and their sustained release from materials such as calcium carbonate or calcium phosphates has been shown to improve clotting efficiency and wound healing [16–18]. Monetite ($CaHPO_4$), a metastable and resorbable phase of calcium phosphate [19], offers several advantages as a functional additive in gelatin matrices. It not only releases calcium ions [20] to enhance coagulation but also demonstrates high biocompatibility and acts as a modulator of keratinocyte proliferation and differentiation—both essential for effective wound closure and re-epithelialization [21].

In addition to its hemostatic potential, monetite has been widely studied for its osteoconductive properties, making it particularly advantageous in dental and maxillofacial applications where both bleeding control and bone regeneration are required. Monetite has shown the ability to support osteoblast attachment, proliferation, and mineralization, thereby facilitating bone tissue integration and regeneration [22–24]. This dual functionality presents a promising approach for post-extraction sockets, periodontal surgeries, or bone defect management, where bleeding and bone loss occur simultaneously.

Despite these promising attributes, there is a clear lack of research integrating monetite into gelatin-based hemostatic sponges. This study aims to bridge that gap by synthesizing and characterizing a novel gelatin-monetite composite sponge via freeze-drying and thermal cross-linking methods. The research objectives are: (1) to evaluate the morphological and chemical properties of the composite, (2) to assess its swelling behavior, degradation rate, and calcium ion release profile under physiological conditions, and (3) to verify its cytocompatibility for potential biomedical use.

Through this study, we propose a multifunctional hemostatic material that combines the passive blood absorption of gelatin with the active calcium-releasing and osteoconductive properties of monetite, making it especially relevant for applications in surgery, trauma, and dental care. The methodology includes sponge fabrication via freeze-drying, followed by comprehensive characterization using SEM, FTIR, swelling and degradation tests, ion release studies, and biocompatibility evaluation.

2 Materials and Methods

2.1 Materials

The main materials used in this study were gelatin (from bovine skin, Type B, Sigma-Aldrich, USA) and monetite ($CaHPO_4$, Himedia, India). Distilled water and deionized water were used as solvents throughout the preparation process.

2.2 Preparation of Gelatin-Monetite Sponge

For each formulation, 9 grams of total solids (gelatin and monetite combined) were dissolved in 150 mL of distilled water to obtain a 6% (w/v) solution. Gelatin was weighed and dissolved in distilled water using a magnetic stirrer in a beaker glass at 50–60 °C until completely solubilized. The gelatin solution was cooled to 50 °C and transferred to a mixing bowl. Separately, monetite was dispersed in 50 mL of deionized water and stirred using a magnetic stirrer for 2 hours to ensure uniform dispersion. The monetite suspension was then added to the gelatin solution and thoroughly mixed. The resulting mixture was vigorously stirred for 2 minutes to form a stable foam, expanding to approximately 6–8 times its original volume. This foam was immediately transferred into silicone molds (1 cm × 1 cm × 1 cm). The molds were placed at 4 °C for 1 hour to stabilize the foam structure, followed by deep freezing at –80 °C for 24 hours. Freeze-drying was performed using a freeze dryer set to –50 °C and 0.300 mbar for 48 hours. After freeze-drying, the samples were subjected to thermal cross-linking in a vacuum drying oven at 160 °C under atmospheric pressure for 3 hours. The final gelatin-monetite sponges were stored in a dry box at room temperature until further characterization.

2.3 Scanning Electron Microscopy (SEM)

The morphology and internal pore structure of the gelatin-monetite sponges were observed using Scanning Electron Microscopy (SEM). Prior to analysis, the samples were mounted on aluminum stubs using carbon tape and coated with a thin layer of gold-palladium (Au-Pd) using a sputter coater to enhance electrical conductivity and image clarity. SEM imaging was used to examine pore size distribution and the dispersion of monetite particles within the gelatin matrix.

2.4 Fourier Transform Infrared Spectroscopy (FTIR)

FTIR was used to investigate the chemical interactions between gelatin and monetite. Spectra were recorded in the range of 4000–500 cm^{-1} to identify functional groups and potential bonding changes due to composite formation.

2.5 Porosity Measurement

Porosity was assessed using the liquid displacement method with hexane as the non-swelling, non-reactive displacement liquid. Sponges (1 cm × 1 cm × 1 cm) were weighed before and after immersion in hexane under vacuum conditions to ensure complete pore penetration. Porosity was calculated using the following equation :

$$\text{Porosity } (\%) = 100 \text{ x } \frac{W_f - W_i}{\rho \text{ x } V_t} \quad (1)$$

Where Wf = weight after hexane saturation, Wi = initial dry weight, ρ = density of hexane, and Vt = total volume (1 cm^3).

2.6 Swelling test

Swelling tests were performed by immersing dried sponge samples in phosphate-buffered saline (PBS) at room temperature. The swelling ratio was calculated at various time intervals by measuring the weight difference before and after immersion.

2.7 Calcium (Ca) Ion Release

The release of calcium ions (Ca^{2+}) from the sponges was quantified at selected time points (15, 30, and 60 minutes) using a calcium ion-selective method. The release profile was used to evaluate the ability of monetite to provide sustained calcium ion delivery.

2.8 Degradation Test

To assess biodegradability, samples were immersed in PBS within multiwell plates and incubated at 37 °C. Measurements were taken at 2, 4, 8, 16, 24, and 48 hours. After each time point, samples were removed, transferred to dry multiwell plates, and freeze-dried for 48 hours. The final dry mass was then recorded to evaluate the extent of degradation over time.

2.9 Cytotoxicity Test

The cytotoxicity of the gelatin-monetite sponges was evaluated using the MTT assay on HEK293 cells (ATCC CRL-3216). Cells were seeded into a 96-well plate at a density of 4000 cells per well in 100 µL of growth medium consisting of Dulbecco's Modified Eagle Medium (D-MEM) supplemented with 10% fetal bovine serum (FBS), 100 U/mL penicillin, and 100 µg/mL streptomycin. After 24 hours of incubation at

37 °C and 5% CO_2, the cells reached approximately 50% confluency, and material extracts were added to each well. The MTT assay was performed on day 3 following extract exposure. A volume of 10 µL of MTT solution (5 mg/mL) was added to each well, and the plate was incubated for 4 hours at 37 °C to allow the formation of formazan crystals. Subsequently, the medium was removed, and the resulting crystals were dissolved in ethanol. The absorbance was measured at 595 nm using a microplate reader. Cell viability was calculated as a percentage relative to untreated control cells.

3 Results and Discussion

3.1 Morphological Analysis

SEM images, as shown in Fig.1, revealed a highly porous, interconnected sponge-like structure in the control sample (pure gelatin), with pore sizes ranging from 350 to 700 µm. The smooth surface of the pore walls confirmed the absence of inorganic filler, reflecting a typical morphology of freeze-dried gelatin [25,26]. In contrast, the incorporation of monetite at concentrations of 3%, 5%, and 10% resulted in visible microstructural changes. Monetite particles, sized between 5 and 20 µm, were clearly distributed within the gelatin matrix and appeared to be well-integrated in the polymer network. At higher concentrations, monetite tended to cluster, resulting in a denser microstructure and a slight reduction in average pore size. These changes are indicative of the space-filling effect of monetite and its influence on the internal architecture of the sponge.

Elemental composition analysis using EDS (Fig.1) further confirmed the successful incorporation of monetite. While the control sponge showed dominant peaks corresponding to carbon (C), oxygen (O), and minor nitrogen (N)—attributable to the organic nature of gelatin[26]—the presence of monetite was validated by increasing intensity of calcium (Ca) and phosphorus (P) peaks in the modified samples. The Ca and P signals, which intensified progressively from 3% to 10% monetite, are consistent with the elemental signature of monetite ($CaHPO_4$) [24,27] and support its dose-dependent distribution within the composite. The Ca/P ratio observed remained within the theoretical range for monetite, suggesting that no phase transformation occurred during the fabrication process.

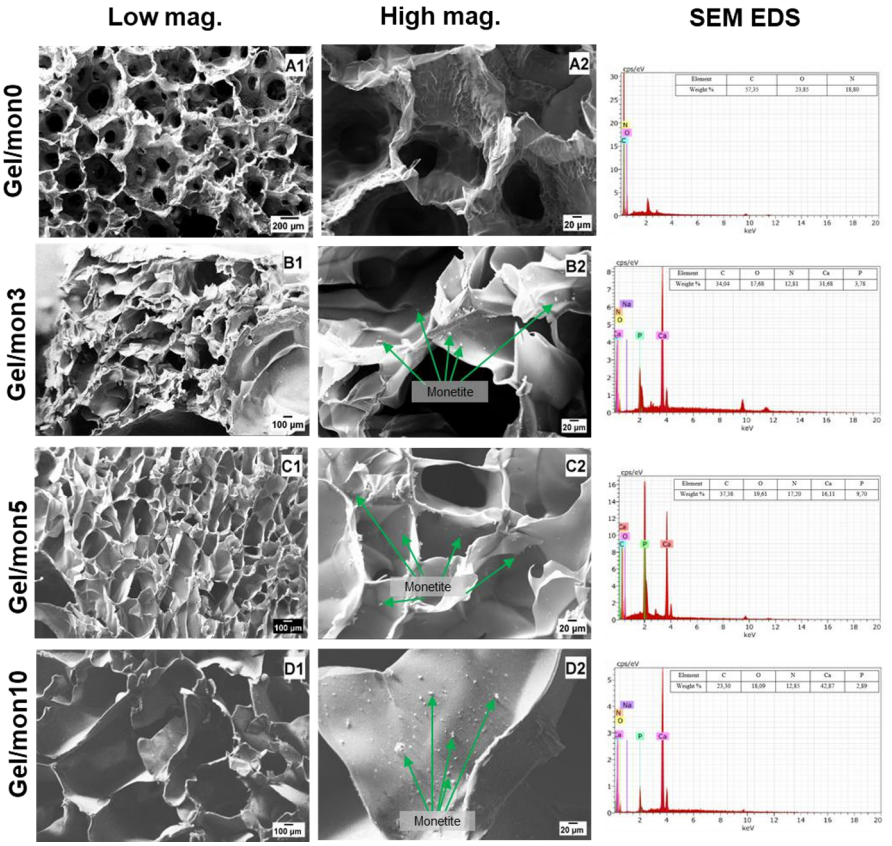

Fig. 1. SEM micrographs and EDS spectra of gelatin-monetite sponges at different monetite concentrations.

3.2 Porosity

The graph in Fig.2 showed the relationship between monetite concentration and the porosity of gelatin-monetite sponges. As shown, porosity decreases with increasing monetite content. The pure gelatin sponge exhibits the highest porosity at approximately 40%. Upon the incorporation of 3% and 5% monetite, porosity drops to around 35% and 32%, respectively. Interestingly, at 10% monetite, the porosity appears to stabilize, showing a slight increase to about 33%, but remains lower than the control.

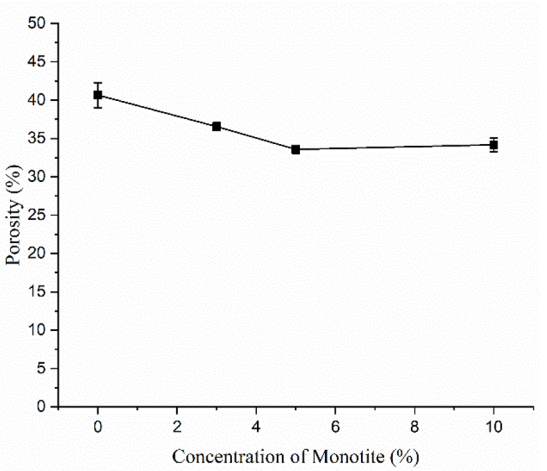

Fig. 2. Porosity of gelatin-monetite sponges as a function of monetite concentration.

This trend is consistent with the SEM observations, which revealed a transition from highly open, interconnected porous structures in the control sample to denser microstructures in monetite-containing composites. The monetite particles, observed to be evenly dispersed at lower concentrations and increasingly clustered at higher concentrations, occupy the pore spaces within the gelatin matrix. This occupation likely reduces the void volume, explaining the corresponding decline in porosity.

Furthermore, the slight increase in porosity at 10% monetite may result from the non-uniform packing and agglomeration of monetite particles, as seen in the SEM micrographs (D2). These clusters may create irregular voids or microgaps at higher loadings, contributing to the minor increase in porosity despite overall densification.

3.3 Chemical Characteristics

The FTIR spectra (Fig.3) show that pure gelatin displays characteristic peaks at ~3280 cm^{-1} (N–H stretching), ~2930 cm^{-1} (C–H stretching), ~1640 cm^{-1} (amide I), ~1540 cm^{-1} (amide II), and ~1230 cm^{-1} (amide III) [28]. After thermal crosslinking, these peaks remain with slight intensity reduction, indicating preservation of gelatin's structure. In the gelatin-monetite composites (GelMon3, GelMon5, and GelMon10), additional peaks appear around 1040–1120 cm^{-1}, 960 cm^{-1}, and 560–600 cm^{-1}, corresponding to phosphate (PO_4^{3-}) vibrations from monetite [29]. The increasing intensity of these peaks with higher monetite content confirms successful incorporation.

No significant shifts in the amide bands were observed, suggesting that the interaction between gelatin and monetite is physical rather than chemical. These results indicate that monetite is embedded within the gelatin matrix without altering its backbone, contributing phosphate functionality while maintaining the original properties of gelatin.

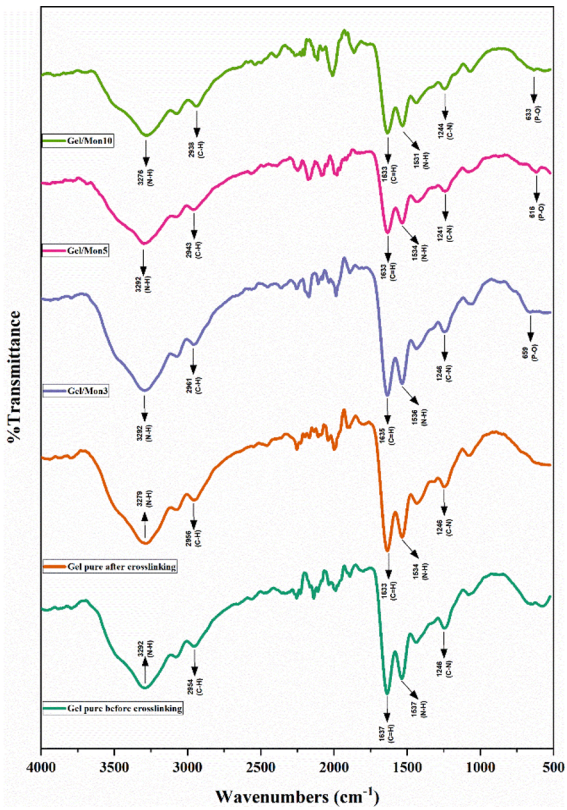

Fig. 3. FTIR spectra of gelatin before and after crosslinking, and gelatin-monetite composites with varying monetite concentrations (3%, 5%, and 10%).

3.4 Swelling behaviour

The swelling behavior of the gelatin and gelatin-monetite sponges shows a clear trend within the first 10 minutes of immersion (see Fig.4). The pure gelatin sponge exhibits a rapid swelling response, reaching a swelling degree equivalent to 10 times its original weight (~1000%). However, the incorporation of monetite leads to a progressive decrease in swelling capacity. At monetite concentrations of 3%, 5%, and 10%, the swelling degrees decrease to approximately 700%, 600%, and 400%, respectively.

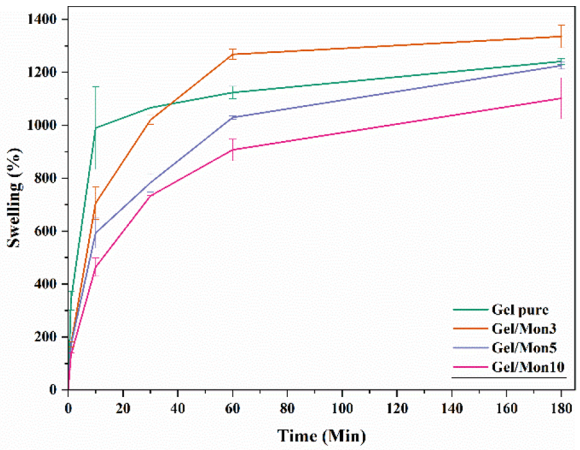

Fig. 4. Swelling behavior of gelatin and gelatin-monetite sponges over 180 minutes.

This decreasing trend is strongly associated with the reduction in porosity, as previously observed in the porosity measurements and SEM images. Monetite particles occupy part of the internal pore space, reducing the free volume available for water uptake and restricting the material's ability to expand. The denser morphology and reduced pore interconnectivity hinder rapid fluid infiltration, which is essential for the initial swelling phase [30].

While pure gelatin offers high swelling due to its open porous structure, the controlled swelling introduced by monetite provides mechanical advantages in biomedical applications where excessive expansion may be detrimental—such as in confined tissue environments or surgical sites.

3.5 Calcium Ion Release

The calcium ion (Ca^{2+}) release profile of gelatin-monetite sponges was monitored at time intervals of 15, 30, 45, and 60 minutes. As shown in Fig. 5, all formulations (GelMon3, GelMon5, and GelMon10) exhibited a gradual and sustained release of calcium ions over time, beginning with an initial burst followed by a slower incremental increase. This release behavior corresponds to the swelling dynamics of the gelatin matrix, as water uptake facilitates the diffusion of calcium ions from embedded monetite particles into the surrounding medium.

At the early stage (15 minutes), Ca^{2+} content reached approximately 1.3 ppm across all samples, indicating a rapid onset of ion diffusion initiated by water absorption. By 60 minutes, the Ca^{2+} concentration increased progressively: GelMon3 and GelMon5 reached ~1.9 ppm, while GelMon10 exhibited the highest release (~2.1 ppm). This trend aligns with the increasing monetite content, as a higher amount of monetite provides a greater reservoir for calcium ion release.

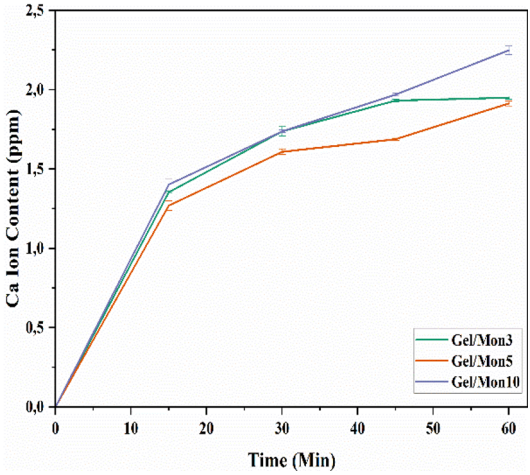

Fig. 5. Calcium ion (Ca^{2+}) release from gelatin-monetite sponges measured at 15, 30, 45, and 60 minutes

However, the difference between GelMon5 and GelMon10 was not statistically significant, suggesting that beyond a certain concentration, the release rate may plateau due to saturation effects or limited diffusion through the denser matrix. This phenomenon is further explained by the swelling data, which showed that higher monetite concentrations corresponded to reduced porosity and lower swelling ratios. Specifically, GelMon10 exhibited lower swelling (~400%) compared to GelMon3 (~700%), which may restrict water penetration and limit ion diffusion despite higher monetite content.

The observed sustained release of calcium ions (Ca^{2+})—rising from 1.3 ppm at 15 minutes to 2.0 ppm at 60 minutes—is a critical feature in activating the intrinsic pathway of the blood coagulation cascade [31]. Calcium ions serve as essential cofactors in several stages of clot formation, particularly in the activation of factors II (prothrombin), VII, IX, and X [32,33]. The controlled release ensures that clotting is not only initiated quickly but also sustained, which is particularly important in cases of severe or diffuse bleeding.

Beyond hemostasis, the release of calcium ions also plays a key role in bone regeneration. Calcium signaling is known to stimulate osteoblast differentiation and bone matrix mineralization [34,35]. Monetite itself, being a resorbable calcium phosphate, can support osteoconduction, acting as a scaffold that promotes bone ingrowth.

3.6 Degradation Behaviour

The degradation profile of the gelatin and gelatin-monetite sponges over 48 hours reveals a clear trend influenced by monetite concentration, as shown in Fig. 6. The pure gelatin sponge (Gel/Mon0) and the composite containing 3% monetite (Gel/Mon3) exhibited rapid degradation, reaching complete weight loss (~100%) within 24 hours of immersion. This rapid breakdown aligns with the inherently high hydrophilicity and

loose network structure of gelatin, which facilitates water infiltration and matrix disintegration.

In contrast, sponges containing 5% and 10% monetite (Gel/Mon5 and Gel/Mon10) demonstrated significantly slower degradation, with residual weights of approximately 10% and 30%, respectively, even after 48 hours. The prolonged degradation observed in these composites is likely attributed to the increase in material density and reduced porosity, as previously confirmed through SEM and porosity measurements. Higher monetite content results in a denser matrix, which limits water penetration and delays hydrolytic breakdown of the gelatin network.

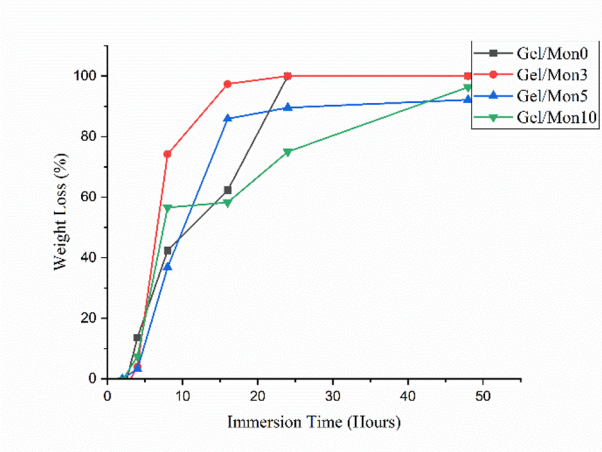

Fig. 6. Degradation profile of gelatin and gelatin-monetite sponges over 48 hours of immersion.

3.7 Calcium ion release mechanism: Interplay between Swelling and Degradation

The release of calcium ions (Ca^{2+}) from the gelatin-monetite sponge might be primarily governed by the matrix's swelling and subsequent degradation behavior. Upon immersion in an aqueous environment, the gelatin sponge rapidly absorbs water, triggering an expansion of the polymer network—a process known as swelling [36]. This swelling increases the mobility of water molecules within the matrix and creates diffusion channels through which calcium ions, originally embedded in the monetite phase, can begin to migrate out of the scaffold [37] and into the surrounding medium.

As illustrated in Fig.7, this initial swelling phase enables the onset of Ca^{2+} release, which continues progressively over time. The rate and extent of ion release are influenced by the degree of swelling, which in turn is modulated by porosity and monetite content. In the early stages (within the first hour), the gelatin network remains structurally intact but hydrated, allowing for a sustained release of calcium ions.

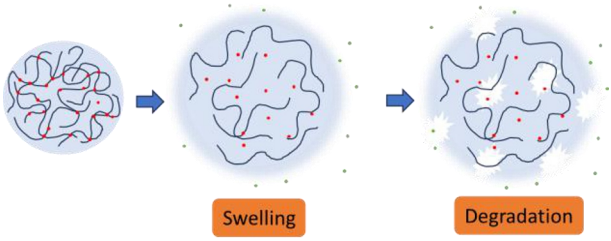

Fig.7. Schematic representation of the mechanism of calcium ion release from gelatin-monetite sponges, governed by the swelling and degradation behavior of the gelatin matrix.

After approximately 2 hours, the gelatin matrix begins to undergo and hydrolytic degradation, as evidenced in the degradation study. This breakdown of the polymer chains further facilitates the liberation of any remaining Ca^{2+} ions by dismantling the physical barriers within the matrix. The degradation not only completes the ion release process but also contributes to the material's resorbability—an important characteristic for biomedical applications.

The findings highlight a two-phase release mechanism: (1) diffusion-driven Ca^{2+} release during swelling, and (2) degradation-enhanced release as the matrix disintegrates. This controlled release behavior, coupled with rapid fluid uptake and bioactive ion delivery, underscores the potential of monetite-incorporated gelatin sponges as effective hemostatic agents, particularly in applications requiring both hemostasis and bioactivity for wound healing.

3.8 Cytotoxicity Evaluation

The cytotoxicity results, evaluated via cell viability assays, demonstrate that all sponge formulations—both pure gelatin (Gel/Mon0) and those incorporated with monetite (Gel/Mon3, Gel/Mon5, Gel/Mon10)—exhibited cell viability above 70%, with values ranging from 74.23% to 79.23%, as shown in Fig. 8. These results indicate that all tested samples fall within the range considered non-cytotoxic and safe for cell proliferation, according to ISO 10993-5 standards [28]. Notably, the highest viability was observed in Gel/Mon10 (79.23%), suggesting that the presence of monetite does not induce toxic effects and may even promote a favorable environment for cell growth, potentially due to the release of bioactive calcium ions. The data affirm that the gelatin-monetite sponges are biocompatible and suitable for further biomedical applications, particularly for wound-contact materials such as hemostats.

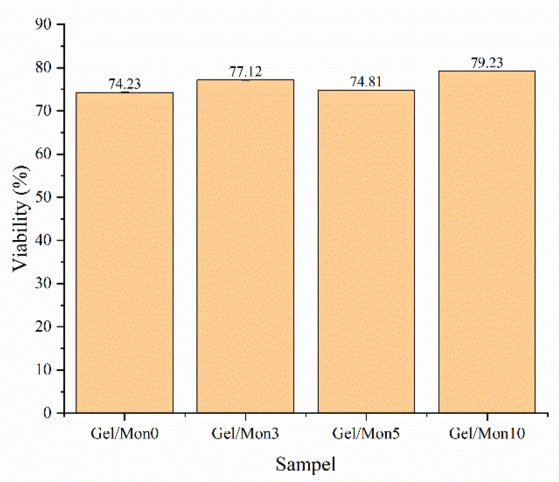

Fig. 8. Cell viability (%) of gelatin and gelatin-monetite sponges as determined by cytotoxicity assay.

4 Conclusions

This study successfully developed and characterized gelatin-based hemostatic sponges incorporated with varying concentrations of monetite ($CaHPO_4$). The incorporation of monetite was shown to significantly influence the physicochemical and biological properties of the composite sponges. SEM and EDS analyses confirmed the uniform distribution of monetite particles within the gelatin matrix, while FTIR spectra demonstrated that the interaction between gelatin and monetite was physical, preserving the functional groups of both components. Porosity measurements revealed a decline in porosity with increasing monetite content, which correlated with reduced swelling capacity and slower degradation rates.

Swelling tests showed that gelatin-monetite sponges absorbed water rapidly, with the highest swelling ratio observed in GelMon3. However, higher monetite content (GelMon5 and GelMon10) led to reduced swelling due to increased material density. Calcium ion release studies indicated that Ca^{2+} diffusion was governed by the swelling behavior of the gelatin matrix and further enhanced during matrix degradation, which began after approximately 2 hours of immersion. This two-phase release mechanism supports the material's potential as a bioactive hemostat. Degradation profiles confirmed that higher monetite content extended the material's structural integrity, with GelMon10 exhibiting 30% residual mass after 48 hours. Cytotoxicity evaluation revealed that all samples, including those containing monetite, maintained cell viability above 70%, indicating non-toxicity and confirming their biocompatibility.Taken together, these findings demonstrate that gelatin-monetite sponges possess a combination of rapid fluid uptake, sustained calcium ion release, controlled degradation, and cytocompatibility—properties essential for an effective hemostatic material. Therefore, the

gelatin-monetite composite sponge represents a promising candidate for further development as a multifunctional hemostat for surgical and dental applications.

Acknowledgements. The research is supported by Faculty of Engineering Universitas Indonesia under Hibah Seed Funding Lektor Skema Riset Tahun Anggaran 2024/2025.

Disclosure of Interests. The authors declare no conflicts of interest.

References

[1] National Institute for Health Research. Improving outcomes after trauma and blood loss. Https://WwwNihrAcUk/Story/Improving-Outcomes-after-Trauma-and-Blood-Loss 2022.
[2] Maegel M. The european perspective on the management of acute major hemorrhage and coagulopathy after trauma: Summary of the 2019 updated European guideline. J Clin Med 2021;10. https://doi.org/10.3390/jcm10020362.
[3] Spahn DR, Bouillon B, Cerny V, Coats TJ, Duranteau J, Fernández-Mondéjar E, et al. Management of bleeding and coagulopathy following major trauma: An updated European guideline. Crit Care 2013;17. https://doi.org/10.1186/cc12685.
[4] Jones AR, Miller J, Brown M. Epidemiology of Trauma-Related Hemorrhage and Time to Definitive Care Across North America: Making the Case for Bleeding Control Education. Prehosp Disaster Med 2023;38. https://doi.org/10.1017/S1049023X23006428.
[5] Spahn DR, Rossaint R. Coagulopathy and blood component transfusion in trauma. Br J Anaesth 2005;95. https://doi.org/10.1093/bja/aei169.
[6] Shariful M, Mitsugu T. Assessment of Compressive Ratio and Sintering Temperature Effects on Mechanical Properties of Collagen/Hydroxyapatite Composite Scaffolds for Bone Tissue Engineering. Proceedings of International Exchange and Innovation Conference on Engineering & Sciences (IEICES), Interdisciplinary Graduate School of Engineering Sciences, Kyushu University; 2016. https://doi.org/10.15017/1809230.
[7] Pangesty AI, Kamila RA, Schlumbergerina ACPB, Faizurrizqi MD, Fakhri RW, Sunarso S, et al. Injectable Alginate-Collagen Hydrogel with Propolis: A Potential Cardioprotective Biomaterial. International Journal of Technology 2025;16:1019–29. https://doi.org/10.14716/ijtech.v16i3.7366.
[8] Huang Y, Zhao X, Zhang Z, Liang Y, Yin Z, Chen B, et al. Degradable Gelatin-Based IPN Cryogel Hemostat for Rapidly Stopping Deep Noncompressible Hemorrhage and Simultaneously Improving Wound Healing. Chemistry of Materials 2020;32. https://doi.org/10.1021/acs.chemmater.0c02030.
[9] Imani R, Rafienia M, Emami SH. Synthesis and characterization of glutaraldehyde-based crosslinked gelatin as a local hemostat sponge in surgery: an in vitro study. Biomed Mater Eng 2013;23. https://doi.org/10.3233/bme-130745.
[10] Kabiri M, Emami SH, Rafinia M, Tahriri M. Preparation and characterization of absorbable hemostat crosslinked gelatin sponges for surgical applications. Current Applied Physics 2011;11. https://doi.org/10.1016/j.cap.2010.08.031.

[11] Maglasang PS, McCarthy GCS, Sanchez PDC, Paglinawan FT. Effects of Chitosan and Pomelo (Citrus maxima var. Magallanes) Peel Extract on the Postharvest Quality and Shelf Life of Bitter Gourd (Momordica charantia I. var. Galaxy Max F1) under Ambient Condition. International Exchange and Innovation Conference on Engineering and Sciences, vol. 10, Kyushu University; 2024, p. 112–20. https://doi.org/10.5109/7323251.

[12] Kobatake K, Mita K, Kato M. Effect on hemostasis of an absorbable hemostatic gelatin sponge after transrectal prostate needle biopsy. International Braz J Urol 2015;41. https://doi.org/10.1590/S1677-5538.IBJU.2015.02.22.

[13] Xie X, Li D, Chen Y, Shen Y, Yu F, Wang W, et al. Conjugate Electrospun 3D Gelatin Nanofiber Sponge for Rapid Hemostasis. Adv Healthc Mater 2021;10. https://doi.org/10.1002/adhm.202100918.

[14] Nepal A, Tran HDN, Nguyen NT, Ta HT. Advances in haemostatic sponges: Characteristics and the underlying mechanisms for rapid haemostasis. Bioact Mater 2023;27. https://doi.org/10.1016/j.bioactmat.2023.04.008.

[15] Zou C-Y, Han C, Xing F, Jiang Y-L, Xiong M, Li-Ling J, et al. Smart design in biopolymer-based hemostatic sponges: From hemostasis to multiple functions. Bioact Mater 2025;45:459–78. https://doi.org/https://doi.org/10.1016/j.bioactmat.2024.11.034.

[16] Zong J, Li JM, Li N, Zhang JL, Liu Q, He Y, et al. The hemostatic property of calcium alginate sponge: An experimental study. Medical Journal of Chinese People's Liberation Army 2016;41. https://doi.org/10.11855/j.issn.0577-7402.2016.03.02.

[17] Yu X, Gao Z, Mu J, Lian H, Meng Z. Gelatin/calcium chloride electrospun nanofibers for rapid hemostasis. Biomater Sci 2023;11. https://doi.org/10.1039/d2bm01767a.

[18] Kang HJ, Park SS, Saleh T, Ahn KM, Lee BT. In vitro and in vivo evaluation of Ca/P-hyaluronic acid/gelatin based novel dental plugs for one-step socket preservation. Mater Des 2020;194. https://doi.org/10.1016/j.matdes.2020.108891.

[19] Zhou H, Yang L, Gbureck U, Bhaduri SB, Sikder P. Monetite, an important calcium phosphate compound–Its synthesis, properties and applications in orthopedics. Acta Biomater 2021;127. https://doi.org/10.1016/j.actbio.2021.03.050.

[20] Medvecky L, Giretova M, Stulajterova R, Luptakova L, Sopcak T. Tetracalcium phosphate/monetite/calcium sulfate hemihdrate biocement powder mixtures prepared by the one-step synthesis for preparation of nanocrystalline hydroxyapatite biocement-properties and in vitro evaluation. Materials 2021;14. https://doi.org/10.3390/ma14092137.

[21] Tu CL, Bikle DD. Role of the calcium-sensing receptor in calcium regulation of epidermal differentiation and function. Best Pract Res Clin Endocrinol Metab, vol. 27, 2013. https://doi.org/10.1016/j.beem.2013.03.002.

[22] Ghina Imaniyyah A, Sunarso, Herda E. Monetite as a potential ideal bone substitute: A short review on fabrication and properties. Mater Today Proc, vol. 66, 2022. https://doi.org/10.1016/j.matpr.2022.06.511.

[23] Rahmawati D, Irawan B, Pangesty AI. A novel method to fabricate monetite granules for bone graft applications. Dent Mater J 2024;43:67–73.

[24] Soraya Shahnaz Tadjoedin E, Sunarso. Fabrication and mechanical properties of newly developed triphasic blocks composed of gypsum-brushite-monetite for bone graft applications. Saudi Dental Journal 2022;34. https://doi.org/10.1016/j.sdentj.2022.11.005.

[25] Al-Mofty SED, Azzazy HMES. Effect of mold shape on the microstructure of gelatin sponges for tissue engineering applications. J Mech Behav Biomed Mater 2023;142. https://doi.org/10.1016/j.jmbbm.2023.105832.

[26] Singh YP, Dasgupta S, Bhaskar R, Agrawal AK. Monetite addition into gelatin based freeze-dried scaffolds for improved mechanical and osteogenic properties. Biomedical Materials (Bristol) 2021;16. https://doi.org/10.1088/1748-605X/ac2e17.

[27] Shadanbaz S, Walker J, Woodfield TBF, Staiger MP, Dias GJ. Monetite and brushite coated magnesium: In vivo and in vitro models for degradation analysis. J Mater Sci Mater Med 2014;25. https://doi.org/10.1007/s10856-013-5059-2.

[28] Pangesty AI, Dwinovandi CS, Sunarso, Tarigan SJAP, Rahman SF, Katili PA, et al. PVA/gelatin hydrogel loaded with propolis for the treatment of myocardial infarction. Journal of Science: Advanced Materials and Devices 2024;9:100732. https://doi.org/https://doi.org/10.1016/j.jsamd.2024.100732.

[29] Salimi E, Javadpour J. Synthesis and characterization of nanoporous monetite which can be applicable for drug carrier. J Nanomater 2012;2012. https://doi.org/10.1155/2012/931492.

[30] Zhong Y, Hu H, Min N, Wei Y, Li X, Li X. Application and outlook of topical hemostatic materials: a narrative review. Ann Transl Med 2021;9. https://doi.org/10.21037/atm-20-7160.

[31] Singh S, Dodt J, Volkers P, Hethershaw E, Philippou H, Ivaskevicius V, et al. Structure functional insights into calcium binding during the activation of coagulation factor XIII A. Sci Rep 2019;9. https://doi.org/10.1038/s41598-019-47815-z.

[32] Varga-Szabo D, Braun A, Nieswandt B. Calcium signaling in platelets. Journal of Thrombosis and Haemostasis 2009;7. https://doi.org/10.1111/j.1538-7836.2009.03455.x.

[33] Bergmeier W, Stefanini L. Novel molecules in calcium signaling in platelets. Journal of Thrombosis and Haemostasis 2009;7. https://doi.org/10.1111/j.1538-7836.2009.03379.x.

[34] Octarina, Kurniawan FL, Larosa FA, Komala ON, Surboyo MDC. Physicochemical Properties of Demineralized Bone Matrix and Calcium Hydroxide Composites Used as Bone Graft Material. Crystals (Basel) 2025;15. https://doi.org/10.3390/cryst15060564.

[35] Singh YP, Mishra B, Gupta MK, Bhaskar R, Han SS, Mishra NC, et al. Gelatin/monetite electrospun scaffolds to regenerate bone tissue: Fabrication, characterization, and in-vitro evaluation. J Mech Behav Biomed Mater 2023;137. https://doi.org/10.1016/j.jmbbm.2022.105524.

[36] Verma N, Tiwari A, Bajpai J, Bajpai AK. Swelling triggered release of cisplatin from gelatin coated gold nanoparticles. Inorganic and Nano-Metal Chemistry 2022;52. https://doi.org/10.1080/24701556.2021.2025396.

[37] Ana ID, Satria GAP, Anggraeni R, Lestari A, Aprilia RD, Wigianto R, et al. Newly Developed Calcium-Enriched Hemostatic Sponge Enhanced Wound Healing and Regeneration. J Biomed Mater Res B Appl Biomater 2025;113:e35568. https://doi.org/https://doi.org/10.1002/jbm.b.35568.