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Original Article

Activity of Alginate-Gelatin Hydrogels Containing Metal-Organic Frameworks Against *Escherichia coli* and *Staphylococcus aureus* for Wound Dressing Application

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Abstract

Bacterial infections, such as *S. aureus* and *E. coli,* remain a global health issue, particularly concerning bacterial resistance, which often leads to serious complications. One approach to address this problem is the development of Metal Organic Frameworks (MOFs), known for their high conductivity and antibacterial activity. Zn-based MOFs are known to possess strong antibacterial activity because Zn^{2+} ions can damage bacterial cell membranes, disrupt enzymatic processes, and induce oxidative stress. In comparison, Zr-based MOFs are well known for their excellent chemical stability and biocompatibility. In this study, hydrogels containing three types of MOFs-Zn-BDC, Zn-Fer, and Zr-BDC were developed. This research aims to synthesize and characterize alginate-gelatin hydrogels containing MOFs and evaluate their antibacterial activity. The results indicate that the modification of alginate-gelatin hydrogels with MOFs has been successfully synthesized, as evidenced by FTIR, XRD, and SEM-EDS analyses. The materials successfully produced include Hy/Zn-BDC, Hy/Zn-Fer, and Hy/Zr-BDC. Antibacterial activity testing shows that adding MOF into the hydrogel matrix significantly increases the inhibition against *S. aureus* and *E. coli* compared to the hydrogel without MOF. Among the three MOF variants, Hy/Zn-BDC showed the highest antibacterial activity, followed by Hy/Zn-Fer and Hy/Zr-BDC. Specifically, Hy/Zn-BDC inhibited *S. aureus* growth by 95% and *E. coli* by 100%, accompanied by the lowest effective inhibitory concentration values (2.0 mg/mL and 2.4 mg/mL, respectively). These results demonstrate the high effectiveness of Zn-based MOF in enhancing the antibacterial performance of the hydrogel as well as its potential development for wound dressing applications.

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INTRODUCTION

Indonesia is a tropical country with consistently high temperatures and humidity (27–32 °C; humidity >70%), which promotes the growth and survival of pathogenic bacteria, the primary cause of various infections.[1,2] According to ecological theory, the high biodiversity in tropical regions contributes to greater diversity and transmission of pathogens, which is further exacerbated by inadequate sanitation and dense populations.[3–5] The tropical environment tends to promote the growth of pathogenic bacteria, particularly Escherichia coli (E. coli) and Staphylococcus aureus (S. aureus), which are common causes of skin, urinary, and gastrointestinal infections, as well as open wounds.[6]

Moreover, the increase in Anti Microbial Resistance (AMR) has become a global health issue that needs to be addressed urgently. A review by Murray et al. (2022) reported six main types of pathogenic bacteria responsible for 3.57 million deaths due to AMR, with the two most prevalent bacteria being Escherichia coli, followed by *S. aureus*.[7] In wound infections, resistance to these bacteria often leads to delayed healing, recurrent infection, and in severe cases, systemic infection, sepsis, or death, making AMR a serious threat in wound management.[8] This situation drives new strategies to address the AMR problem, one of which is the utilization of Metal-Organic Frameworks (MOF).

MOF is a porous material with a three-dimensional framework structure composed of metal ions and organic ligands, featuring a high surface area and porosity.[9] The mechanism of MOF as an antibacterial agent generally involves the release of metal ions that can damage bacterial cell membranes, disrupt bacterial metabolic activity, and produce reactive oxygen species (ROS) that cause oxidative stress in bacteria.[10] The advantage of MOF is its flexibility in selecting types of metals and ligands, allowing for the modification of the physicochemical properties of MOF according to its application needs.

Various studies indicate that the type of metal and ligand used in synthesizing Metal-Organic Frameworks (MOF) can affect the effectiveness of antibacterial activity. The research results of Lopez et al. (2022) show that zinc-based MOFs with different ligands, namely MOF-74 and MOF-5, can inhibit the growth of *E.coli* and *K. pneumoniae* by 90% to 99.9%, respectively.[11] The study conducted by Mulyati et al. (2025) reveals that zinc-based MOF, specifically Zn-BDC (MOF-5), has inhibition zones against *E.coli* and *S. aureus* of 36.2±1 mm and 38.9±1 mm, respectively, while the zirconium-based MOF, Zr-BDC (UiO-66), shows inhibition zones of 11.4±1 mm against *E.coli* and 17.3±1 mm against *S. aureus*.[12] On the other hand, the direct application of MOF to wound tissue presents several disadvantages, including low bioavailability and biocompatibility, leading to reduced therapeutic effects.[13] One of the strategic approaches that can be undertaken to address this issue is to develop MOF in hydrogel formulations.

Hydrogel is a hydrophilic polymer with a porous structure and the ability to absorb wound fluids (exudates) while maintaining moisture, thus accelerating the wound healing process.[14] The selection of the hydrogel matrix is crucial as it determines the mechanical properties and biocompatibility. One type of hydrogel matrix frequently used is gelatin and sodium alginate. Gelatin is a derivative of collagen obtained from partial hydrolysis, known for its biocompatible, biodegradable properties, and its ability to form a gel at body temperature.[15] On the other hand, pure gelatin tends to have limitations such as low mechanical stability and rapid degradation. To address this issue, gelatin is often combined with other natural polymers, such as sodium alginate. Sodium alginate is an anionic polysaccharide that possesses biocompatible and non-toxic properties, as well as high swelling capacity and good permeability, making it widely used in biomedical applications such as wound dressings and drug delivery systems.[16] The combination of alginate-gelatin improves mechanical stability and swelling capacity and provides a suitable porous environment for the controlled loading and release of various bioactive agents.[17]

The combination of alginate-gelatin hydrogel with Metal-Organic Frameworks (MOF) has the potential to produce synergistic effects, where the physicochemical characteristics and antibacterial activity of the MOF integrate with the mechanical stability and fluid absorption properties of the hydrogel.[13] This is consistent with the research conducted by Maghsoudi et al. (2025), which reported that alginate-gelatin hydrogel loaded with 4% ZIF 8 demonstrated an increase in antibacterial activity of up to 99% against *Escherichia coli* and *Staphylococcus aureus*.[18] On the other hand, studies on alginate-gelatin hydrogel containing different types of MOFs are still quite limited. This study will synthesize alginate-gelatin hydrogel combined with various MOFs, namely Zn-BDC, Zn-Fer, and Zr-BDC, and will examine their antibacterial activity.

MATERIALS AND METHODS

Materials

The materials used in this research are Zinc (II) nitrate hexahydrate ($Zn(NO_3)_2 \cdot 6H_2O$), Zirconium tetrachloride ($ZrCl_4$), Ferulic Acid ($C_{10}H_{10}O_4$), and 1,4-benzenedicarboxylic acid (H_2BDC) with a purity of 99.0%, supplied by Sigma-Aldrich; as well as N, N-dimethylformamide (DMF), chloroform ($CHCl_3$), methanol (CH_3OH), gelatin, sodium alginate, phosphate-buffered saline (PBS), Luria-Bertani (LB), and Nutrient Agar (NA), also with a purity of 99.0% provided by Merck, German. The test bacterial strains used are *S. aureus* ATCC 33591 (Gram-positive) and *E. coli* ATCC 25922 (Gram-negative), obtained from the "Balai Besar Laboratorium Kesehatan" in Yogyakarta.

Methods

MOF Synthesis

The synthesis of MOF was conducted by modifying the research of Mulyati et al. (2025), Zulfa et al. (2024), and Zeraati (2022).[12,19,20] At this stage, three types of MOF were synthesized, namely Zn-BDC, Zn-Fer, and Zr-BDC, using two different metal centers: zinc (Zn) or zirconium (Zr), as well as using the ligands 1,4-benzenedicarboxylic acid (H_2BDC) or ferulic acid. In the synthesis of Zn-MOF, 1.08 grams of $Zn(NO_3)_2.6H_2O$ and 0.198 grams of H_2BDC were dissolved in 30 mL of dimethylformamide (DMF). In the synthesis of Zn-Fer, 0.522 grams of $Zn(NO_3)_2.6H_2O$ were dissolved in 10 mL of DMF, and 0.388 grams of ferulic acid were dissolved in 10 mL of ethanol. Meanwhile, the synthesis of Zr-MOF involved reacting 0.53 grams of zirconium tetrachloride ($ZrCl_4$) and 0.34 grams of H_2BDC in 30 mL of DMF. Each solution was heated at a temperature of 120°C for 24 hours. The resulting mixture was decanted, and the solid was washed using 30 mL of DMF and 30 mL of chloroform twice every 24 hours. The product was dried at 60°C for 24 hours. The result is dried at a temperature of 60°C for 24 hours. The solid formed is subsequently called Zn-BDC, Zn-Fer, and Zr-BDC.

Modification of Alginate-Gelatin Hydrogel with MOF

The synthesis of Alginate-Gelatin Hydrogel/MOF is carried out by modifying the research of Maghsoudi et al. (2025), which involves dissolving sodium alginate powder in distilled water to achieve a concentration of 12% weight/volume (w/v), and the solution is stirred at 80°C for one hour.[18] Simultaneously, a 6% w/v gelatin solution is prepared by dissolving gelatin in distilled water and stirring it at 50°C. Once completely dissolved, both solutions are mixed in a 1:1 ratio and stirred at 50°C until a uniform polymer is obtained, referred to as hydrogel (Hy). The Alginate–Gelatin Hydrogel/MOF was prepared by incorporating Zn-BDC, Zn-Fer, and Zr-BDC into the hydrogel matrix at a fixed concentration of 5% using a sterile syringe, followed by centrifugation at 1000 rpm for 1 minute. The 5% concentration was selected to minimize particle aggregation and maintain hydrogel homogeneity, as previously reported by Maghsoudi et al. (2025). The MOF-modified alginate-gelatin hydrogel is subsequently referred to as Hy(Zn-BDC), Hy(Zn-Fer), and Hy(Zr-BDC).

Characterization of MOF and Alginate-Gelatin/MOF Hydrogel

The materials were characterized to confirm the formation of MOF and alginat-gelatin/MOF hydrogel as per the studies by Xiong et al. (2023) and Maghsoudi et al. (2025).[15,18] Confirmation of the formation of Zn-BDC, Zn-Fer, and Zr-BDC was carried out through diffractogram analysis using a JEOL XRD diffractometer with Cu Ka radiation (λ = 1.54056 Å) on a scale of 5–50°. Confirmation of the formation of Hy(Zn-BDC), Hy(Zn-Fer), and Hy(Zr-BDC) was performed through functional group analysis using ATR FTIR from Shimadzu Corporation, Japan, within a wavenumber range of 400–4000 cm^{-1}. Moreover, the material's surface morphology and elemental composition were analyzed using SEM-EDX (Zeiss EVO MA10) with gold coating.

Swelling and biodegradation tests of Alginate-Gelatin/MOF hydrogels.

The measurement of the swelling ratio and biodegradation rate of the three types of hydrogels, namely Hy(Zn-BDC), Hy(Zn-Fer), and Hy(Zr-BDC), was conducted according to the procedure by Maghsoudi et al. (2025), which involves immersing the samples in a phosphate-buffered saline (PBS) solution.[18] In the initial stage, the dry weight of the sample was measured and recorded as W_0. Subsequently, the sample was immersed in 3 mL of PBS at 37 °C until it reached equilibrium, after which its weight was measured again and recorded as W_t. The weight change reflects fluid absorption (swelling) or mass loss due to degradation. The swelling or degradation ratio value at a specific time is calculated using the equation:

$$\text{Swelling Ratio} = \frac{W_t - W_0}{W_0}$$

$$\text{Degradation ratio (\%)} = \frac{W_0 - W_t}{W_0} \times 100\%$$

Antibacterial Activity

Antibacterial activity was evaluated using two complementary approaches, which included quantification of bacterial growth inhibition via optical density at 600 nm (OD600) and determination of the effective inhibitory concentration and effective bactericidal concentration assay using the broth Effective inhibitory concentration method, following a modified method of Li et al. (2023).[21] Gram-positive *S. aureus* (ATCC33591) and Gram-negative *E. coli* (ATCC25922) were used as test organisms.

Bacterial suspensions were adjusted to 1×10^6 CFU/mL. In the experimental groups, 5 mL of bacterial suspension was combined with hydrogel samples (Hy, Hy(Zn-BDC), Hy(Zn-Fer), or Hy(Zr-BDC)) in sterile 15 mL centrifuge tubes. Control groups contained only bacterial suspension without hydrogel, while the positive control contained an amoxicillin solution. All tubes were sealed with breathable membranes and incubated at 37 °C for 24 h. Following incubation, OD600 was measured using a UV–Vis spectrophotometer. The relative bacteriostatic rate (%) was calculated as:

$$\text{Relative bacteriostatic rate} = \frac{A-B}{A} \times 100\%$$

where *A* is the OD value of the control group, and *B* is the OD value of the hydrogel-treated group.

Effective inhibitory concentration and effective bactericidal concentration assays were determined using the broth method. Hydrogel samples were prepared as extracts by dissolving the gel in LB medium prior to testing. Serial dilutions of the bacterial suspension (10^3–10^6 CFU/mL) were prepared in the nutrient broth. For effective inhibitory concentration determination, 100 µL of each dilution was added to hydrogel extract and incubated at 37 °C for 24 h. Effective inhibitory concentration was defined as the lowest concentration showing no visible growth (OD ≤ 0.05 at 600 nm). For an effective bactericidal concentration assay, aliquots from wells without visible growth were plated on nutrient agar, incubated at 37 °C for 24 h, and examined for colony formation. The Effective bactericidal concentration was the lowest concentration that achieved ≥ 99.9% bacterial killing. All experiments were performed in triplicate (n = 3) to ensure reproducibility.

RESULTS AND DISCUSSION

Synthesis of MOF and Alginate-Gelatin Hydrogel/MOF

Using a solvothermal method, the MOF has been successfully synthesized by reacting metals and organic ligands. The successful formation of Zn-BDC and Zr-BDC is indicated by the appearance of a white solid, in line with the report by Mulyati et al. (2025) that the reaction between Zn^{2+} or Zr^{4+} ions with H_2BDC generally yields a white-colored MOF.[12] Additionally, the successful formation of Zn Fer is evidenced by the emergence of a yellowish-brown solid, which is associated with the property of ferulic acid that possesses a longer π conjugation system, allowing it to absorb visible light, consistent with the findings of Zeraati et al. (2022).[19]

Alginate-gelatin hydrogel is produced by mixing alginate and gelatin solutions in a 1:1 ratio. This composition is chosen because it results in a gel with a sufficiently dense yet elastic consistency suitable for combination with active materials. The intermolecular interaction between the polymer chains of alginate and gelatin, which plays a crucial role in the consistency of the gel, is through the formation of hydrogen bonds and electrostatic interactions between the carboxylate groups of alginate and the amine groups of gelatin.[22] The resulting alginate-gelatin hydrogel is then supplemented with Zn-BDC, Zn-Fer, and Zr-BDC.

In this study, the control hydrogel without MOF is a milky white gel with a smooth texture. Adding MOF (Zn-BDC, Zr-BDC, Zn-Fer) to the alginate-gelatin hydrogel results in gels with different color changes and levels of turbidity. The incorporation of Zn-BDC and Zr-BDC yields gels that remain white but become more opaque, while the addition of Zn-Fer produces a gel with a yellowish-brown color. The phenomenon of color change in the hydrogel after the addition of MOF indicates that the optical properties of the active substances (MOF) can affect the visual appe-

-ance of the hydrogel matrix, as well as providing preliminary evidence that the modification of the hydrogel with MOF has been successfully conducted.[23] An illustration of the formation of the alginate-gelatin hydrogel/MOF is shown in Figure 1.

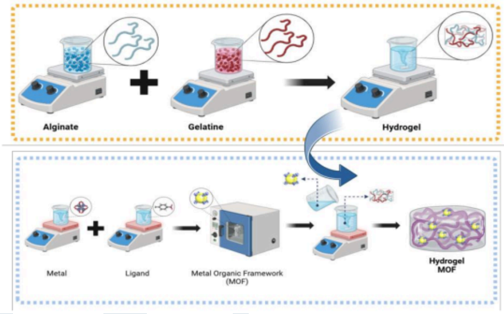

Figure 1. Schematic Illustration of the Formation of Alginate–Gelatin Hydrogel Containing MOF

Characterization of MOF and Alginate-Gelatin Hydrogel/MOF

The characterization of the samples was conducted by analyzing functional groups through diffraction patterns through PXRD, ATR-FTIR, surface analysis, and elemental distribution through SEM-EDS. Figure 2a shows that Zn-BDC has characteristic peaks of Zn-BDC similar to the study by Wu et al. (2018), which presents characteristic peaks at 6°, 9°, and 13°, while other characteristic peaks are at 20°, 34°, and 42°.[24] On the other hand, Zr-BDC displays characteristic peaks of Zr-BDC in accordance with the study by Strauss et al. (2020), with characteristic peaks at 7° and 8°, while other characteristic peaks are at 25°, 30°, and 43°.[25] Additionally, Zn-Fer shows characteristic peaks of Zr-Fer consistent with the research conducted by Demir et al. (2015), namely at 8°, 12°, and 15°, while other characteristic peaks are at 26° and 29°.[26]. This result confirms that the MOFs, including Zn-BDC, Zn-Fer, and Zr-BDC, have been successfully formed. The resulting MOFs were then used to synthesise alginate-gelatin/ MOF hydrogels, which were subsequently characterised using ATR-FTIR and SEM-EDS to ensure the integration of the MOFs within the hydrogel matrix.

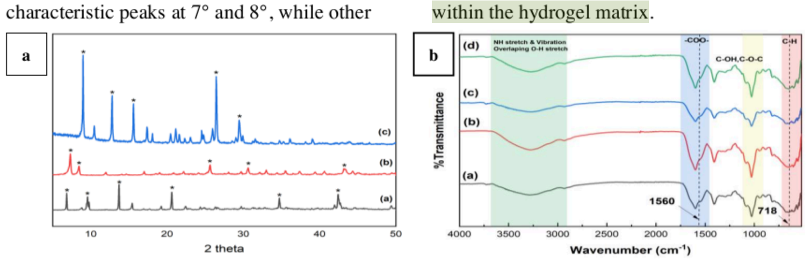

Figure 2a. XRD diffractogram patterns of (a) Zn-BDC, (b) Zr-BDC, and (c) Zn-Fer;
2b. ATR-FTIR spectra of (a) Hy, (b) Hy/Zn-BDC, (c) Hy/Zn-Fer, (d) Hy/Zr-Fer

Figure 2b shows that the spectra of the hydrogel have specific peaks, namely a broad peak at 3600-3000 cm^{-1} indicating the presence of –OH and –NH groups, while at 1600 cm^{-1} indicates the C=O groups, and at 1560 cm^{-1} indicates the amide group. Additionally, the peaks at 1080 cm^{-1} and 1030 cm^{-1} indicate the presence of C-OH and C-O-C groups, respectively, while the peak at 718 cm^{-1} indicates the C-H group as noted in the studies by Maghsoudi et al. (2025) and Wang et al. (2022).[18,27] On the other hand, the hydrogel that has been modified by Metal Organic Frameworks (Hy/Zn-BDC, Hy/Zn-Fer, and Hy/Zr-BDC) shows a decrease in peak intensity at 1560 cm^{-1} and 718 cm^{-1}, indicating conformational changes in the polymer chain due to the presence of MOF[27]. The change was caused by forming a bridge between the Metal Organic Framework and the hydrogel.[28,29] The observed differences in the MOF-modified hydrogel based on ATR-FTIR are further confirmed through SEM analysis to examine the surface morphology and EDS to identify the constituent elements.

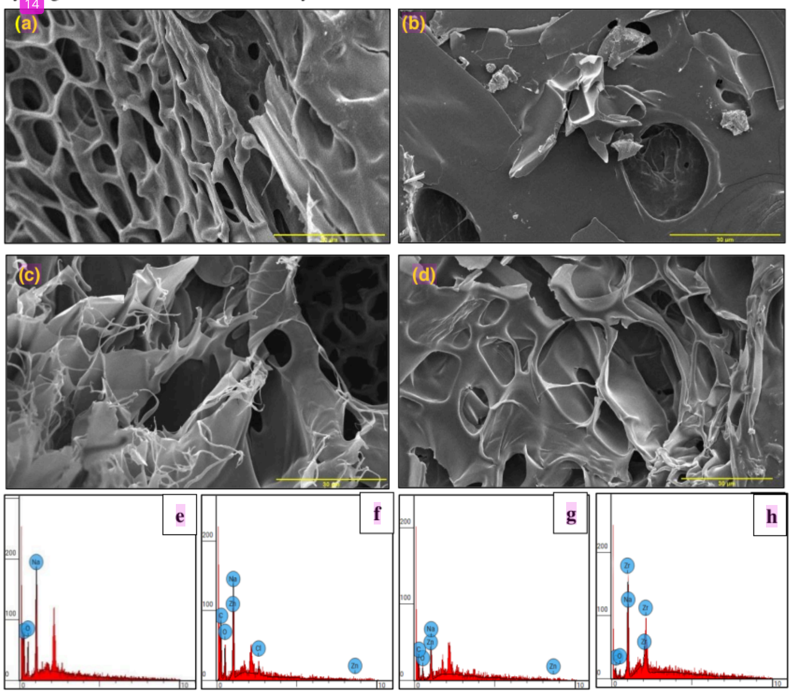

Figure 3. SEM morphology of (a) Hy, (b) Hy/Zn-BDC, (c) Hy/Zn-Fer, and (d) Hy/Zr-BDC; EDS spectra of (e) Hy, (f) Hy/Zn-BDC, (g) Hy/Zn-Fer, and (h) Hy/Zr-BDC

Figure 3 shows that the morphology observed in the SEM results of the hydrogel (Figure 3a) reveals small cavities of irregular sizes. Furthermore, the morphology of the hydrogel modified with Zn-BDC (Figure 3b) presents larger cavities than the hydrogel with a regular size. Conversely, the morphology of the hydrogel modified with

Zn-Fer (Figure 3c) demonstrates even larger cavities than the hydrogel with a regular size, shaped like curtains. The SEM morphological results of the hydrogel modified with Zr-BDC (Figure 3d) indicate larger cavities with a regular size resembling peeling skin.

The elemental composition on the surface of each sample was further analyzed using Energy Dispersive X-Ray Spectroscopy (EDS) as shown in Figures 3e-h. The Hy sample (Figure 3e) shows peaks in the elemental spectrum for C and O, characteristic of the alginate gelatin matrix. After modification, the Hy/Zn-BDC and Hy/Zn-Fer samples (Figures 3f and 3g) exhibited additional peaks in the elemental spectrum for Zn. In contrast, the Hy/Zr-BDC sample (Figure 3h) displayed a peak for the elemental Zr. These results confirm the successful modification of MOFs within the alginate gelatin hydrogel matrix.[30] The presence of Na and Cl in the samples is likely attributed to residual salts from the synthesis process. These results also strengthen the ATR-FTIR analysis, which showed a decrease and shift in absorption as initial indicators of the successful modification of gelatin alginate-gelatin with MOF.

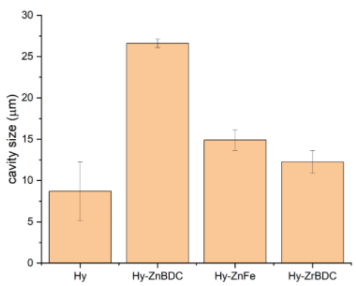

Figure 4. Cavity Size distribution of hydrogel

Analyzing the distribution of cavity sizes measured with ImageJ (Figure 4) shows that the hydrogel has small cavity sizes, but with variable sizes indicated by the longest error bars. After the modified hydrogel, however, it exhibited larger cavity sizes, although with more regular dimensions. The formation of these more regular cavities is due to the incorporation of MOF into the hydrogel network, which fundamentally alters the porous architecture through enhanced cross-linking, resulting in a denser and more interconnected network.[31]

The successful integration of MOFs into the alginate–gelatin hydrogel matrix was confirmed by FTIR, XRD, and EDS analyses, indicating the presence of active metal centers (Zn^{2+} or Zr^{4+}) that can be gradually released from the hydrogel network. The porous and interconnected morphology observed in the SEM images facilitates the diffusion of these ions and their interaction with bacterial cell membranes. These structural features contribute to the enhanced antibacterial activity observed against *E. coli* and *S. aureus*, demonstrating the potential of the composite hydrogel as an effective antibacterial wound dressing.

Swelling and Biodegradation Tests.

The results of the swelling and biodegradation tests indicate that adding MOF to the alginate-gelatin hydrogel can reduce the swelling ratio and the percentage of biodegradation over time during immersion in PBS solution at 37°C. (Figure 5). These results align with the study by Maghsoudi et al. (2025), which reported that adding 4% ZIF-8 in the alginate-gelatin matrix could decrease the swelling ratio to 3.5 and biodegradation to 30%.[18] In this study, the alginate-gelatin hydrogel (Hy) experienced the highest degradation of 62% on day 27, attributed to its looser matrix structure, making it easier to degrade. When comparing the alginate-gelatin hydrogel/MOF, the Hy/Zn-BDC sample had a biodegradation percentage of 36% on day

27, while Zn-Fer and Zr-BDC exhibited 34% and 25%, respectively. This may be due to differences in the chemical properties and stability of the MOF.

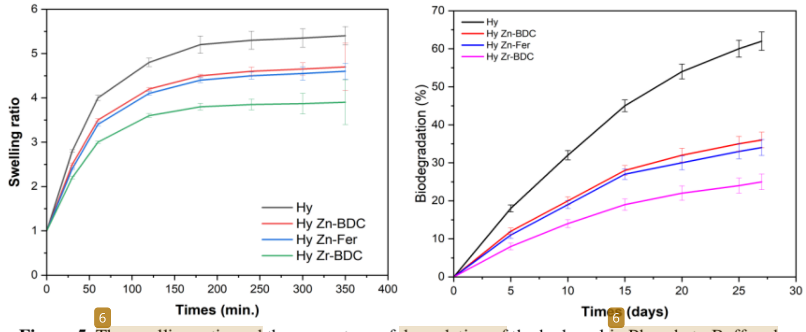

Figure 5. The swelling ratio and the percentage of degradation of the hydrogel in Phosphate-Buffered Saline (PBS) solution.

Hydrogels combined with metal-based Zn MOFs enhance the hydrogel matrix, whereas Zr BDC is very stable and further inhibits water penetration. Additionally, the incorporation of MOFs into the alginate-gelatin hydrogel can reduce the swelling ratio as the MOF particles fill the internal pores, limiting the space for water absorption.[18,32] The Hy/Zn-BDC sample has the highest swelling ratio of 4.7; Hy/Zn-Fer is slightly lower at 4.6; while Hy/Zr BDC has the lowest at 3.9.

The decreased swelling value following the addition of MOF indicates a denser hydrogel structure while still maintaining optimal fluid absorption, thereby facilitating the diffusion of active metal ions (Zn^{2+} or Zr^{4+}) into the surrounding wound environment. Furthermore, the reduced biodegradation rate suggests a more controlled degradation process, where the release of metal ions occurs gradually, maintaining the stability of antibacterial activity against *E. coli* and *S. aureus* over a certain period. Accordingly, these physicochemical properties play a crucial role in the effectiveness of alginate–gelatin/MOF hydrogels as antibacterial wound dressing materials.[18]

Antibacterial Activity

The antibacterial activity of modified MOF alginate-gelatin hydrogel against Gram-positive *S. aureus* (ATCC 33591) and Gram-negative *E. coli* (ATCC 25922) was analyzed using the parameters of OD_{600}, effective inhibitory concentration, and effective bactericidal concentration assay. The OD values were obtained from measuring the turbidity of the bacterial suspension at a wavelength of 600 nm after 24 hours of incubation. The results of the OD test indicate that adding MOF into the hydrogel matrix can enhance the ability to inhibit bacterial growth MOF in hydrogel matrices inhibits *S. aureus* and *E. coli* through the release of metal ions, the formation of reactive oxygen species (ROS), and disruption of bacterial cell membranes compared to hydrogels without MOF (Hy).[33]

In the OD test against *S. aureus* (Figure 6a), Hy/Zn-BDC (0.2726) showed the highest inhibitory effect, followed by Hy/Zn-Fer (0.3420), Hy/Zr-BDC (0.3837), and Hy (0.4085). The positive control (amoxicillin) had an OD value of 0.2614, while the negative control (bacteria without treatment) displayed the highest OD value of 0.5810.

A similar pattern was observed in *E.coli* (Figure 6b), where Hy/Zn-BDC exhibited the lowest OD (0.1678), followed by Hy/Zn-Fer (0.2251), Hy/Zr-BDC (0.3352), and Hy (0.6156). The OD value in the positive control (ampicillin) was relatively high, indicating that *E.coli* in this study was resistant to the antibiotic. *E.coli* have a lipopolysaccharide (LPS) layer on their outer membrane that limits the penetration of antibiotic molecules.[34] These results indicate that alginate-gelatin hydrogels with Zn-based MOFs, particularly Hy/Zn-BDC, possess the strongest antibacterial potential against Gram-positive and Gram-negative bacteria.

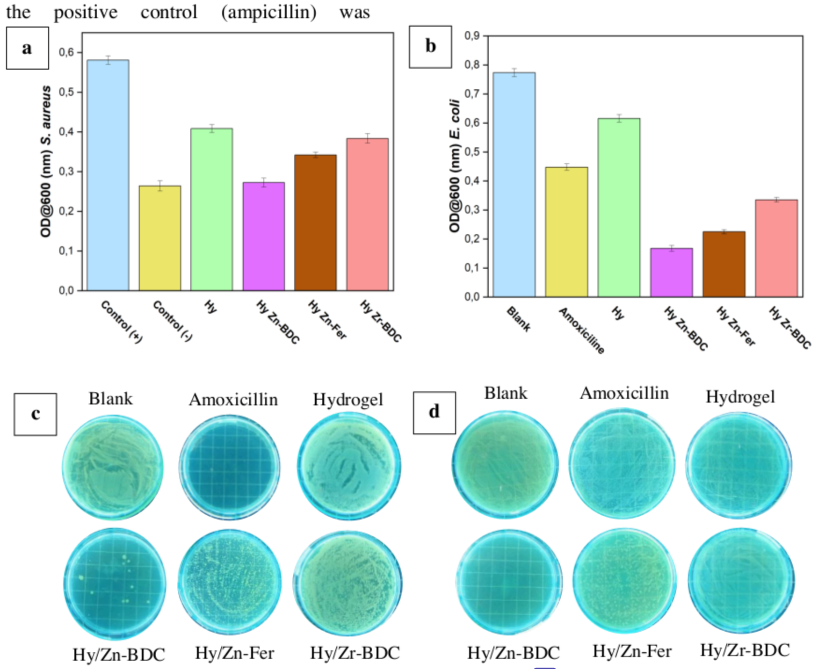

Figure 6. Antibacterial evaluation of alginate–gelatin/MOF hydrogels against *Staphylococcus aureus* and *Escherichia coli*. Panels (a) and (b) show the optical density (OD_{600}) of *S. aureus* and *E. coli* cultures, respectively, after 24 h incubation with hydrogels. Panels (c) and (d) depict the bacterial inhibition ability against *S. aureus* and *E. coli*.

The total bacterial measurements after being incubated for 24 hours are shown in Figures 6c-d. No inhibition was observed against *S. aureus* or *E.coli* in the negative control. In the positive control (amoxicillin), the growth inhibition of bacteria on *S. aureus* reached 100%. At the same time, for *E.coli*, it was only 45%, indicating the existence of resistance as shown by the OD ratio. The highest antibacterial effectiveness against *S. aureus* was exhibited by Hy/Zn-BDC at 95%, followed by Zn-Fer at 50%. A similar pattern was observed in the antibacterial activity against *E.coli*, where Hy/Zn-BDC had the highest inhibition, reaching 100%, followed by Zn-Fer at 53%. The samples Hy and Hy/Zr-BDC did not show significant antibacterial activity. These results correlate with the OD ratio. This antibacterial activity was further confirmed by measuring the Effective inhibitory concentration and effective bactericidal concentration values, as shown in Figure 7. The differences in effectiveness among hydrogel materials against *S. aureus* and *E. coli* are presented in Tables 1 and Table 2.

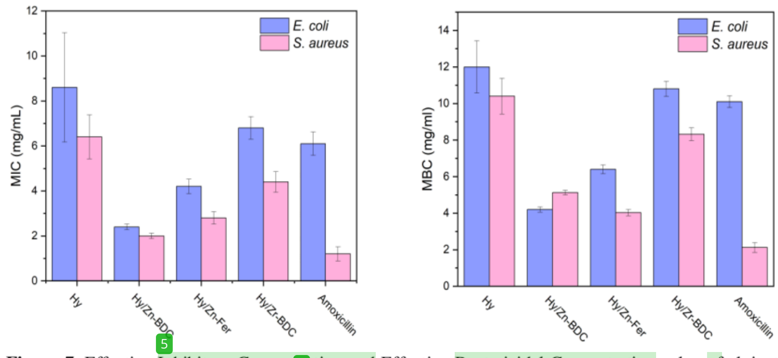

Figure 7. Effective Inhibitory Concentration and Effective Bactericidal Concentration value of alginate–gelatin/Zn-MOF hydrogels against *S. aureus* and *E. coli*

Table 1. Effective Inhibitory Concentration Values of Hydrogels against *E. coli* and *S. aureus*

Sample	Effective inhibitory Concentration (mg/mL)	
	E.coli	***S.aureus***
Hy	8.6 ± 1.4[a]	6.4 ± 1.0[a]
Hy/Zn-BDC	2.4 ± 0.1[b]	2.0 ± 0.1[bd]
Hy/Zn-Fer	4.4 ± 0.3[c]	2.8 ± 0.3[b]
Hy/Zr-BDC	6.8 ± 0.5[d]	4.4 ± 0.4[c]
Amoxicillin	6.1 ± 0.5[d]	1.2 ± 0.3[d]

Values are presented as mean ± SD (n = 3). Different superscript letters indicate significant differences (Tukey's HSD, $p < 0.05$)

Table 2. Effective Bactericidal Concentration values of hydrogels against *E. coli* and *S. aureus*

Sample	Effective Bactericidal Concentration (mg/mL)	
	E.coli	***S.aureus***
Hy	12.0 ± 1.4[a]	10.4 ± 1.0[a]
Hy/Zn-BDC	4.2 ± 0.1[b]	5.1 ± 0.1[b]
Hy/Zn-Fer	6.4 ± 0.2[c]	4.0 ± 0.2[b]
Hy/Zr-BDC	10.8 ± 0.4[d]	8.3 ± 0.3[c]
Amoxicillin	10.1 ± 0.3[d]	2.1 ± 0.3[d]

Values are presented as mean ± SD (n = 3). Different superscript letters indicate significant differences (Tukey's HSD, $p < 0.05$)

In the effective inhibitory concentration measurement for *S. aureus* bacteria, the antibacterial effectiveness of Hy/Zn-BDC and Hy/Zn-Fer is the strongest, indicated by their substantially lower significantly effective inhibitory concentration values of 2.0±0.1 mg/mL and 2.8 ± 0.3 mg/mL, respectively. The effective inhibitory concentration measurements for Hy/Zr-BDC and Hy are only 4.4 ± 0.545 mg/mL and 6.4 ± 1.0 mg/mL, respectively. A similar pattern is observed in the effective bactericidal concentration measurements, where Hy/Zn-BDC and Hy/Zn-Fer have the lowest significantly effective bactericidal concentration values of 5.1 ± 0.1 mg/mL and 4.0 ± 0.2 mg/mL, followed by Hy/Zr-BDC and Hy at 8.3 ± 0.3 mg/mL and 10.4 ± 1.0 mg/mL, respectively. Amoxicillin remains the most effective control with an effective inhibitory concentration value of 1.2 ± 0.3 mg/mL and an effective bactericidal concentration of 2.1 ± 0.3 mg/mL.

The measurement results of effective inhibitory concentration on *E.coli* bacteria also showed similar outcomes. The lowest significantly effective bactericidal concentration was obtained from Hy/Zn-BDC (2.4 ± 0.1 mg/mL), followed by Hy/Zn-Fer (4.4 ± 0.3 mg/mL), Hy/Zr-BDC (6.8 ± 0.5 mg/mL), and Hy (8.6 ± 1.4 mg/mL). The effective bactericidal concentration values for *E.coli* also exhibited a similar trend, with Hy/Zn-BDC having the smallest significant value at 4.2 ± 0.1 mg/mL, followed by Hy/Zn-Fer at 6.4 ± 0.2 mg/mL, Hy/Zr-BDC at 10.8 ± 0.4 mg/mL, and Hy at 12.0 ± 1.4 mg/mL. Amoxicillin had an effective inhibitory concentration of 6.1 ± 0.5 mg/mL and an effective bactericidal concentration of 10.1 ± 0.3 mg/mL, supporting the findings from the OD test that *E.coli* exhibits partial resistance to the antibiotic amoxicillin. These results indicate that modifying alginate-gelatin hydrogel with MOF, particularly Zn-based MOFs, effectively enhances antibacterial activity against both Gram-positive and Gram-negative bacteria.

The effective bactericidal concentration values against *E. coli* decreased in the following order: Hy > Hy/Zr-BDC > Amoxicillin > Hy/Zn-Fer > Hy/Zn-BDC, with Hy/Zn-BDC performing the best. Similarly, the effective inhibitory concentration values against *E. coli* followed the same decreasing trend: Hy > Hy/Zr-BDC > Amoxicillin > Hy/Zn-Fer > Hy/Zn-BDC, with Hy/Zn-BDC again performing best. In contrast, the effective bactericidal concentration values against *S. aureus* decreased in the order: Hy > Hy/Zr-BDC > Hy/Zn-BDC > Hy/Zn-Fer. Meanwhile, the effective inhibitory concentration values against *S. aureus* followed the order: Hy > Hy/Zr-BDC > Hy/Zn-Fer > Hy/Zn-BDC. However, both the effective bactericidal concentration and effective inhibitory concentration values against *S. aureus* were lower than those of amoxicillin, indicating that the bactericidal and inhibitory effects of the tested hydrogels were not superior to the conventional antibiotic.

The antibacterial effectiveness of alginate-gelatin/MOF hydrogel is attributed to the synergistic effects between the hydrogel polymer matrix and the properties of MOF as an antibacterial agent. The alginate-gelatin hydrogel matrix plays a role in maintaining environmental moisture and supporting the diffusion process of metal ions from the MOF (Zn^{2+} or Zr^{4+}). The release of metal ions from MOFs within a hydrogel matrix can be triggered by acidic pH conditions typically found in wound areas (approximately pH 5.5–6.5).[35,36] At this pH, the metal-ligand coordination bonds in the MOF become more susceptible to degradation, leading to a faster release of metal ions (Zn^{2+} or Zr^{4+}).[37,38] Initially, the Zn^{2+} or Zr^{4+} ions gradually released from the MOF interact with the bacterial cell wall through electrostatic forces. This interaction disrupts the cell membrane structure, increasing permeability and causing leakage of intracellular contents. Subsequently, Zn^{2+} or Zr^{4+} ions will enter the cell, disrupt enzymatic functions, damage proteins and

DNA, and induce oxidative stress. The accumulation of this damage will lead to vital function failure and the death of bacterial cells.[18,21] An illustration of the antibacterial activity of alginate-gelatin hydrogel combined with MOF is shown in Figure 8.

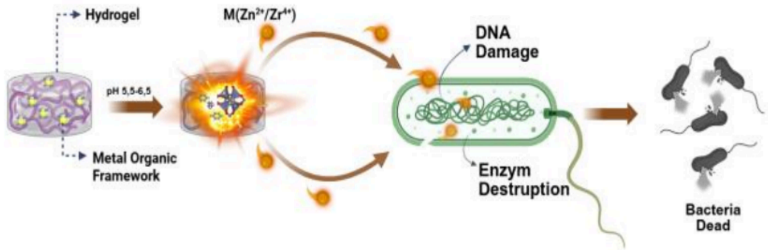

Figure 8. Schematic illustration of the antibacterial activity mechanism of alginate–gelatin hydrogel containing MOF against Gram-positive *S. aureus* and Gram-negative *E. coli*

In this study, alginate-gelatin hydrogel combined with Zn-based MOF exhibits significantly higher antibacterial activity than Zr-based MOF. Zr-based MOF tends to be more stable compared to Zn-based MOF. This results in the release of Zn^{2+} ions being relatively more straightforward, thus leading to a relatively higher antibacterial effectiveness. This is consistent with the research of Mulyani et al. (2025), which states that Zn-MOF has higher antibacterial activity against *E. coli* and *S. aureus* than Zr-MOF.[12] This finding is supported by the research of Li et al. (2023), which demonstrates that alginate modified with curcumin/Zn-MOF has antibacterial activity of up to 85% against *E.coli* through the mechanism of Zn^{2+} release that disrupts the membrane and causes bacterial cell death.[21] The results of this study indicate the potential development of alginate-gelatin hydrogels containing MOF, specifically Zn-BDC, as wound healing or wound dressing materials.

STRENGTH AND LIMITATION

The strength of this research lies in offering a new approach to enhancing antibacterial performance by modifying alginate-gelatin hydrogels with Metal Organic Frameworks (MOFs) using different metals and ligands. This study has analyzed functional groups, diffraction patterns, surface structures, element distributions, swelling, and biodegradation, thereby providing a comprehensive overview of the structure and properties of the MOF-modified hydrogel. This research also combines various quantitative antibacterial tests, such as OD-600, effective inhibitory concentration, and effective bactericidal concentration, along with illustrations and explanations of their mechanisms. The results are expected to provide a thorough discussion regarding antibacterial activity against both Gram-positive and Gram-negative bacteria. The limitation of this study is that antibacterial activity tests were only conducted on two bacterial strains, which may not fully represent the broad-spectrum antibacterial potential. In addition, in vivo testing and biocompatibility assessments have not yet been performed. Future studies will focus on validating antibacterial activity using clinical isolates and conducting biocompatibility as well as in vivo tests to ensure its potential for clinical application.

CONCLUSIONS

The alginat-gelatin hydrogel containing Zn-based MOF, namely Hy/Zn-BDC, exhibits the highest antibacterial activity, inhibiting the growth of *S. aureus* by 95% and *E. coli* by up to 100%. MOF in hydrogel matrices inhibits *S. aureus* and *E. coli* through the release of metal ions, the formation of reactive oxygen species (ROS), and the disruption of bacterial cell membranes. This outcome is superior to that of the commercial antibiotic amoxicillin. Hy/Zn-BDC can produce a synergistic effect due to the hydrogel's excess in enhancing moisture, thus allowing the Zn^{2+} ions released from the MOF to damage the bacterial membrane effectively. This finding highlights the potential for developing MOF-modified hydrogels, particularly Zn-BDC, in biomedical applications such as wound dressing for infectious wounds.

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ETHICAL CLEARANCE

The Ethics Committee of Institut Ilmu Kesehatan Bhakti Wiyata reviewed and approved the research protocol, which has the ethical clearance reference number 137/FF/EP/VI/2025.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

This research was designed and conceptualised by Tri Ana Mulyati. Tri Ana Mulyati, Juni Ekowati, Atmira Sariwati, Lia Agustina, Erawati, Siska Kusumawardani, and Aulia Krestiani conducted data collection and the implementation of the research. Tri Ana Mulyati and Fery Eko Pujiono wrote the manuscript. Fery Eko Pujiono created the illustrations. The manuscript was reviewed and revised by Tri Ana Mulyati and Juni Ekowati.

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