

Curcumin-Loaded Gellan Gum Hydrogels Crosslinked with Gallium (III) Nitrate for Bioactive Wound Dressing Applications

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INTRODUCTION

Effective wound management is crucial for protecting wounds from trauma and infection while promoting optimal healing. Hydrogels are highly suitable for this purpose due to their high-water content, biocompatibility, biodegradability, and ability to support gas exchange (1). Gellan gum (GG) is a natural polymer with excellent gel-forming properties; however, its weak mechanical strength and lack of antibacterial and antioxidant activities limit its applications (2). Gallium (III) ions (Ga) can serve as crosslinkers to improve structural stability while providing intrinsic antibacterial effects, whereas curcumin, a natural polyphenol, offers potent antioxidant and antimicrobial properties but suffers from poor solubility and bioavailability (3–5). Therefore, combining GG with Ga and curcumin provides a rationale for developing a multifunctional hydrogel capable of enhancing wound healing.

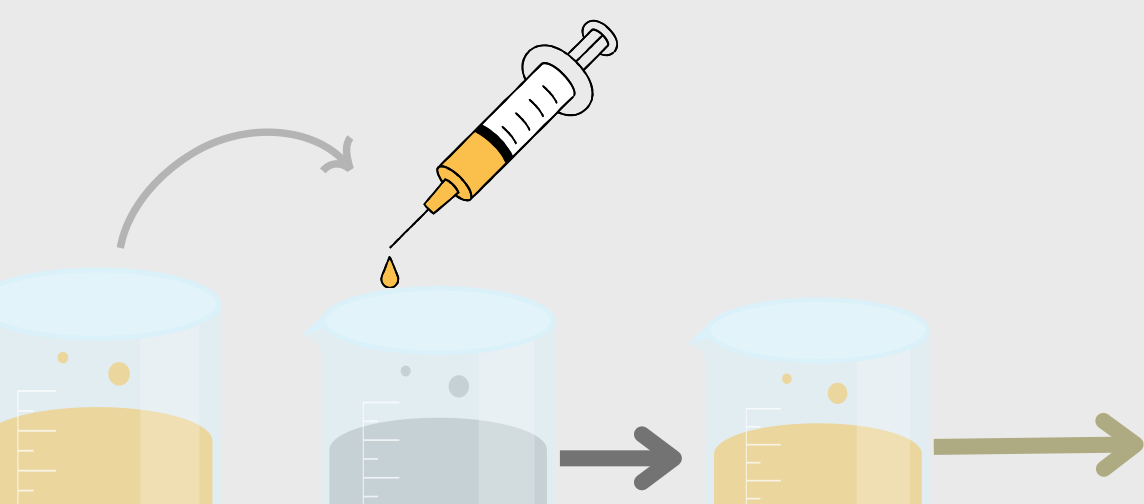
OBJECTIVES

- Formulate GG-based hydrogels loaded with curcumin through ionic gelation and lyophilisation
- Evaluate the physicochemical properties, antioxidant activity, antibacterial activity and biocompatibility of curcumin-loaded GG hydrogels.

METHODOLOGY

Part 1: Optimisation and synthesis of curcumin-loaded Ga-GG hydrogels

- Optimisation with different concentrations of GG (1.0% and 1.5%) and Ga (0.3% and 0.5%)
- Synthesis with different concentrations of curcumin (1 to 5%) in GG 1.5% Ga 0.3%



Part 2: Characterisation of curcumin-loaded Ga-GG hydrogels

- Encapsulation Efficiency
- In vitro* Release Study (in PBS medium over 5 days)
- Attenuated Total Reflectance– Fourier Transform Infrared (ATR-FTIR) spectroscopy
- Scanning Electron Microscopy (SEM)
- Gel Fraction Determination
- Swelling Analysis (in PBS medium over 24 hours)
- Degradation Analysis (in PBS with lysozyme for 10 days)
- Antioxidant Activity (DPPH assay)
- Antibacterial Activity (Colony-counting using MRSA and *P.aeruginosa*)
- Cell Viability Test (MTT assay)
- Statistical Analysis (One-way ANOVA)

RESULTS

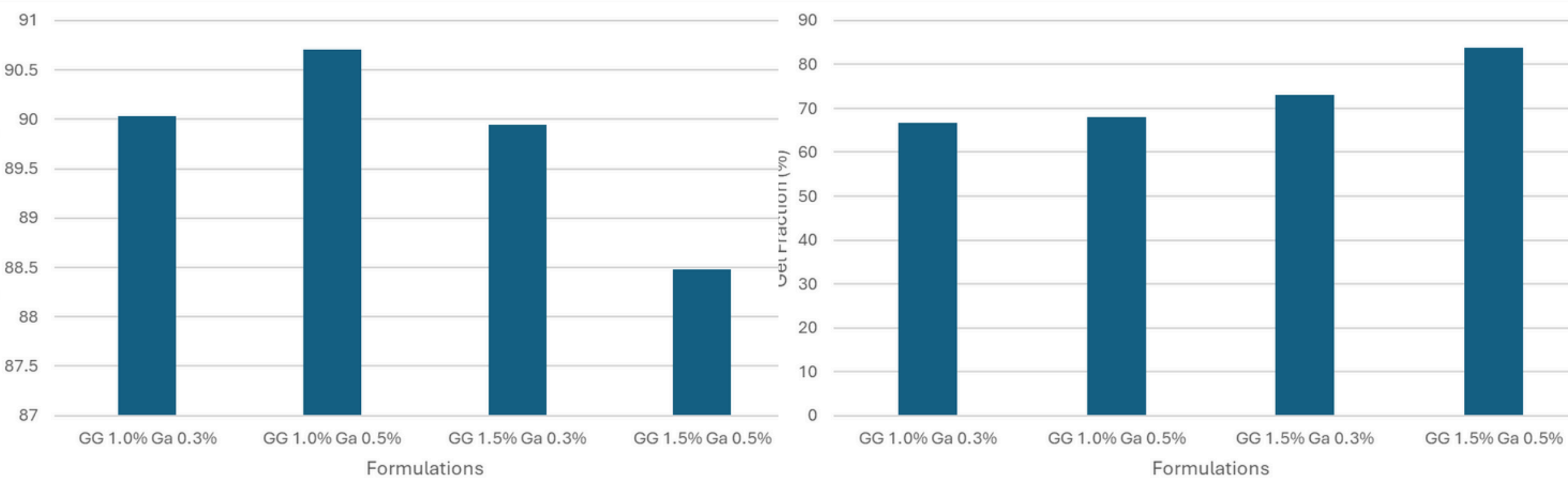


Figure 1 & 2: Encapsulation efficiency (%) (Figure 1) and gel fraction (%) (Figure 2) of hydrogels with different concentration of GG and Ga.

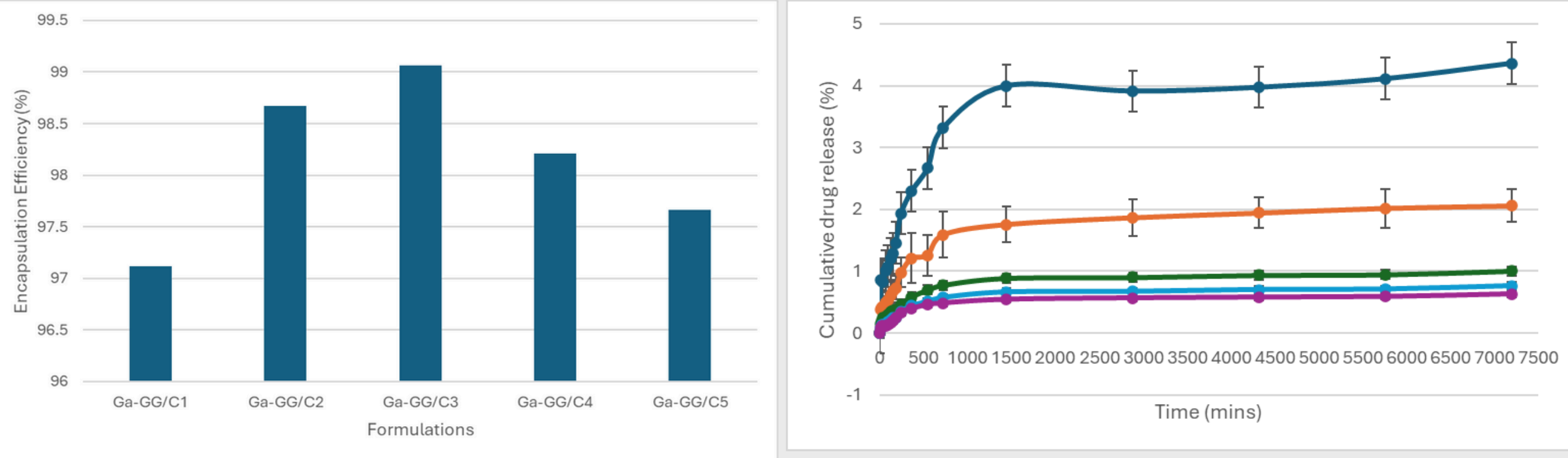


Figure 3: Encapsulation efficiency (%) of Ga-GG hydrogels with different curcumin concentrations, ranging from 97.12% to 99.06%

Figure 4: Cumulative curcumin release profile of Ga-GG hydrogels in PBS (pH 7.4) over 7500 min. All formulations showed an initial burst followed by sustained release and plateau.

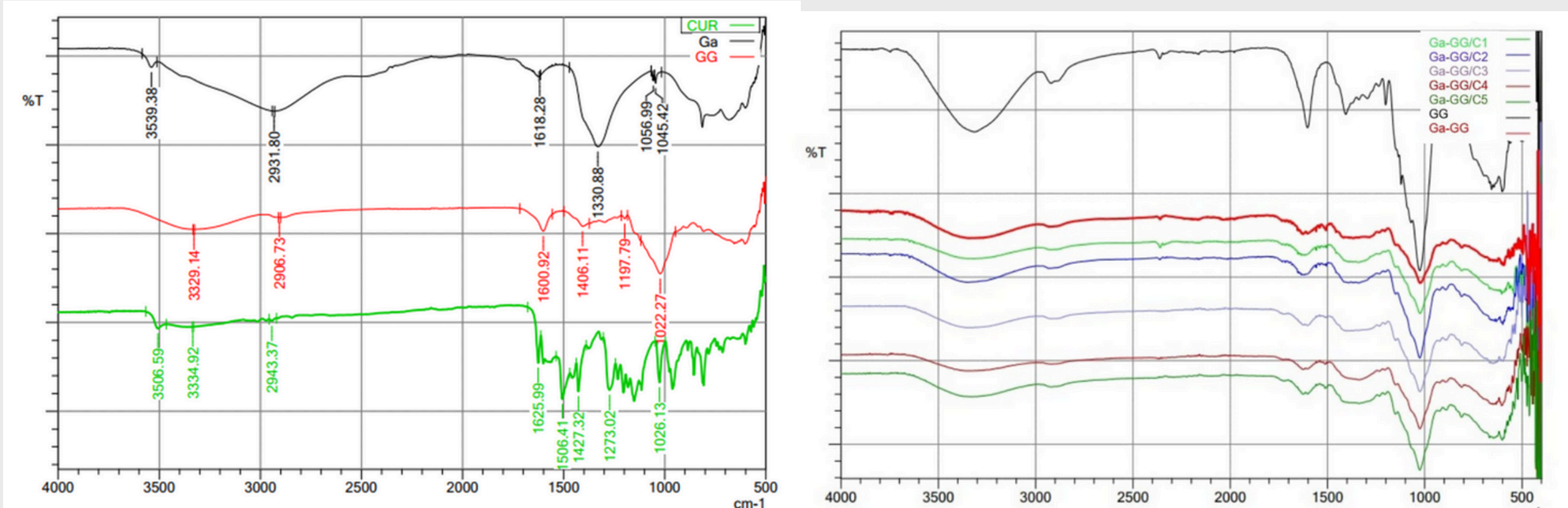


Figure 5&6: FTIR spectra for GG, Ga and curcumin powder (Figure 5) and FTIR spectra for GG, Ga-GG, Ga-GG/C1, Ga-GG/C2, Ga-GG/C3, Ga-GG/C4 and Ga-GG/C5 hydrogels (Figure 6)

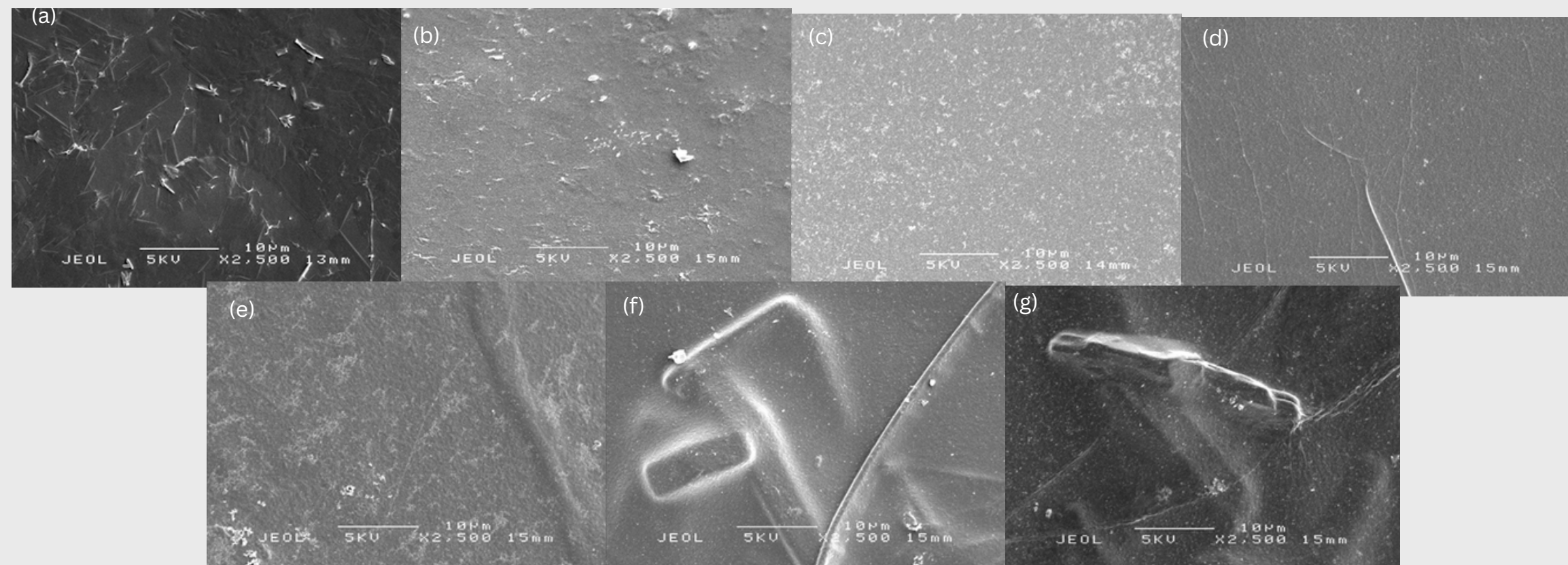


Figure 7: Scanning electron micrograph of GG (a), Ga-GG (b), Ga-GG/C1 (c), Ga-GG/C2 (d), Ga-GG/C3 (e), Ga-GG/C4 (f), Ga-GG/C5 (g) under 2500x magnification

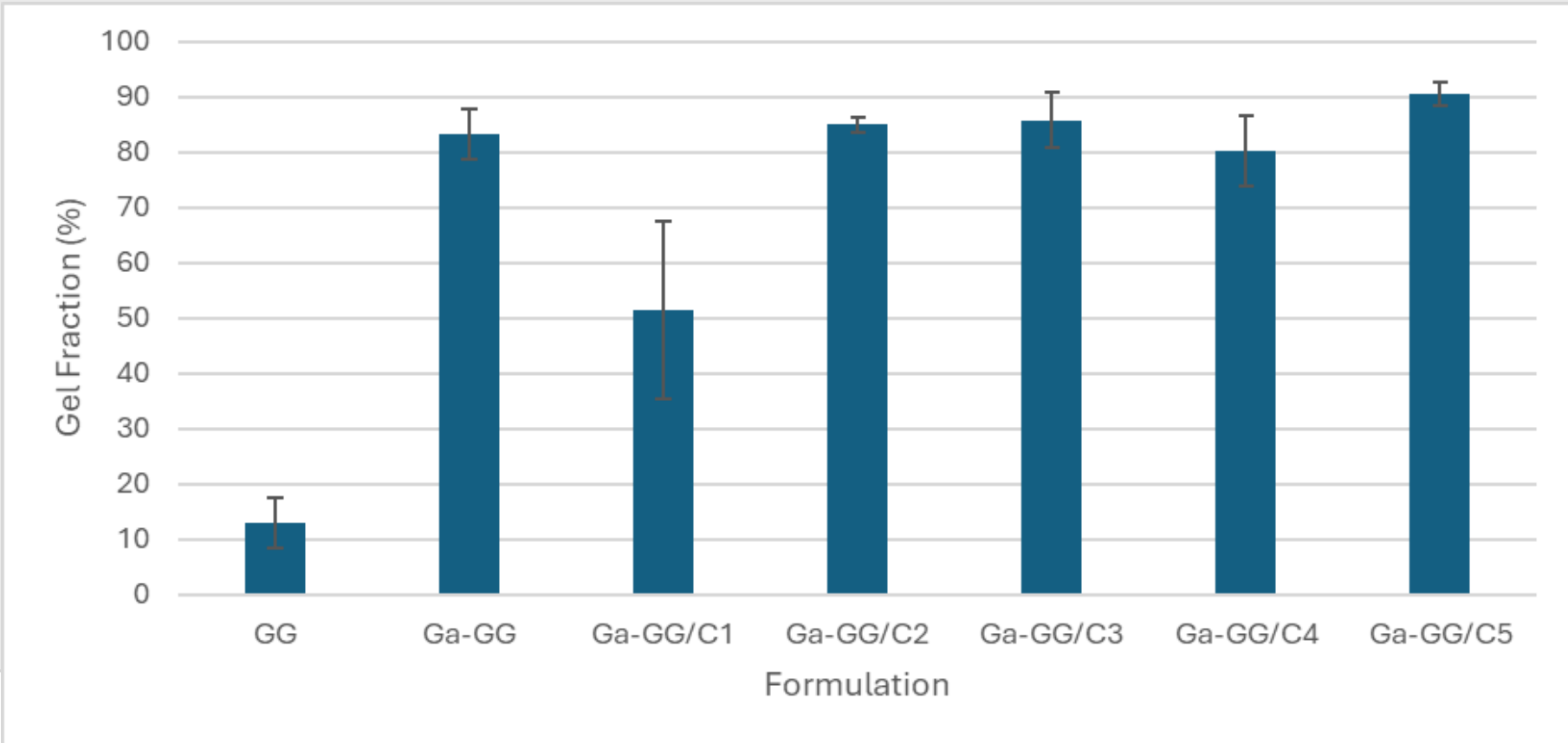


Figure 8: Gel fraction (GF) of GG, Ga-GG, and Ga-GG/C hydrogels. GG-only hydrogel showed the lowest GF (12.87%). Ga crosslinking significantly improved GF (85.3%, $p < 0.05$). Among curcumin-loaded formulations, C1 had the lowest GF (51.4%), while C2–C5 were comparable to Ga-GG with no significant differences.

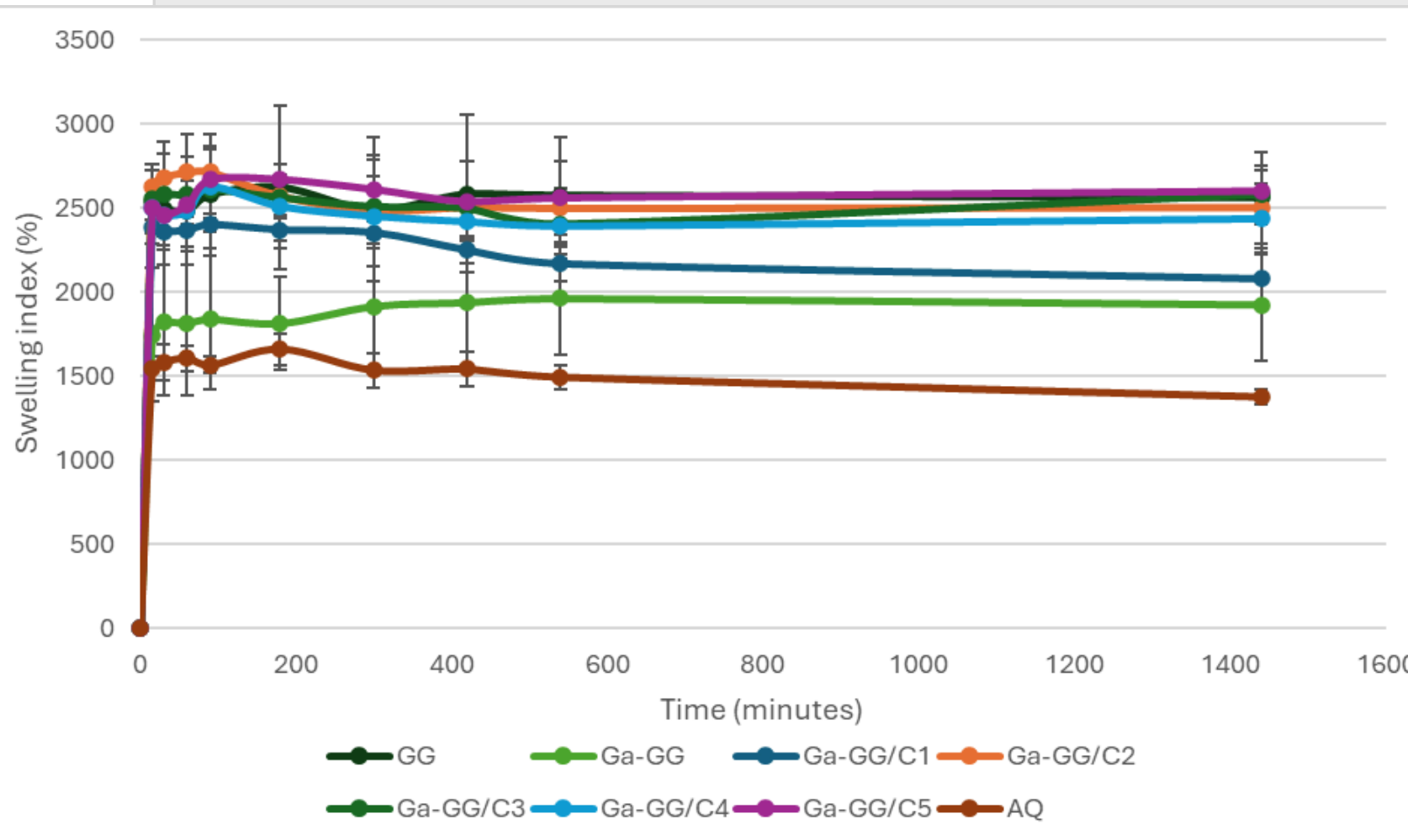


Figure 9.: Swelling index of GG, Ga-GG, Ga-GG/C hydrogels, and AQ dressing in PBS (pH 7.4). All samples swelled rapidly within 15 min, then plateaued by 300–540 min.

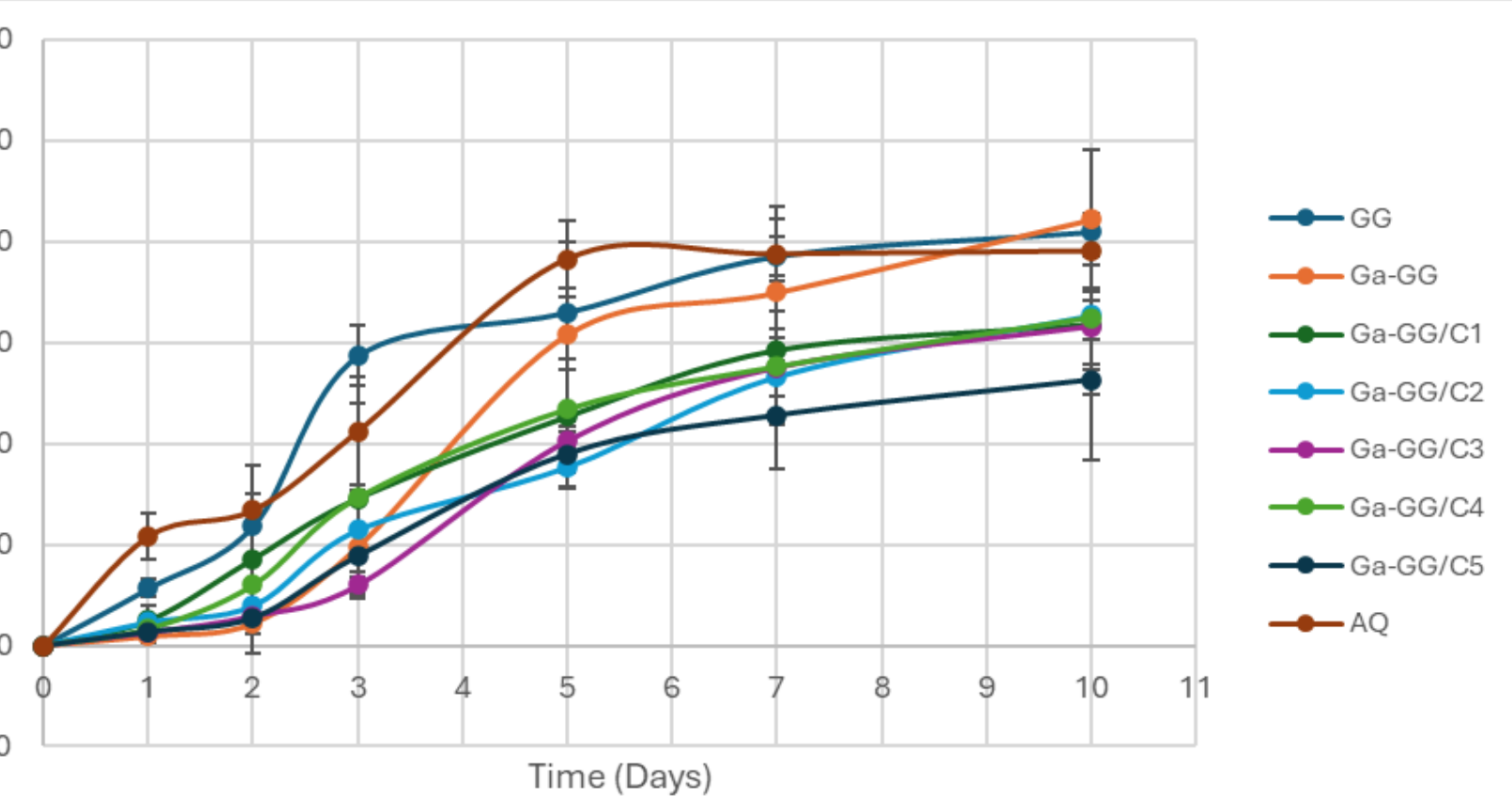


Figure 10: Weight loss (%) of GG, Ga-GG, Ga-GG/C, and AQ hydrogels in lysozyme over 10 days. All showed progressive degradation.

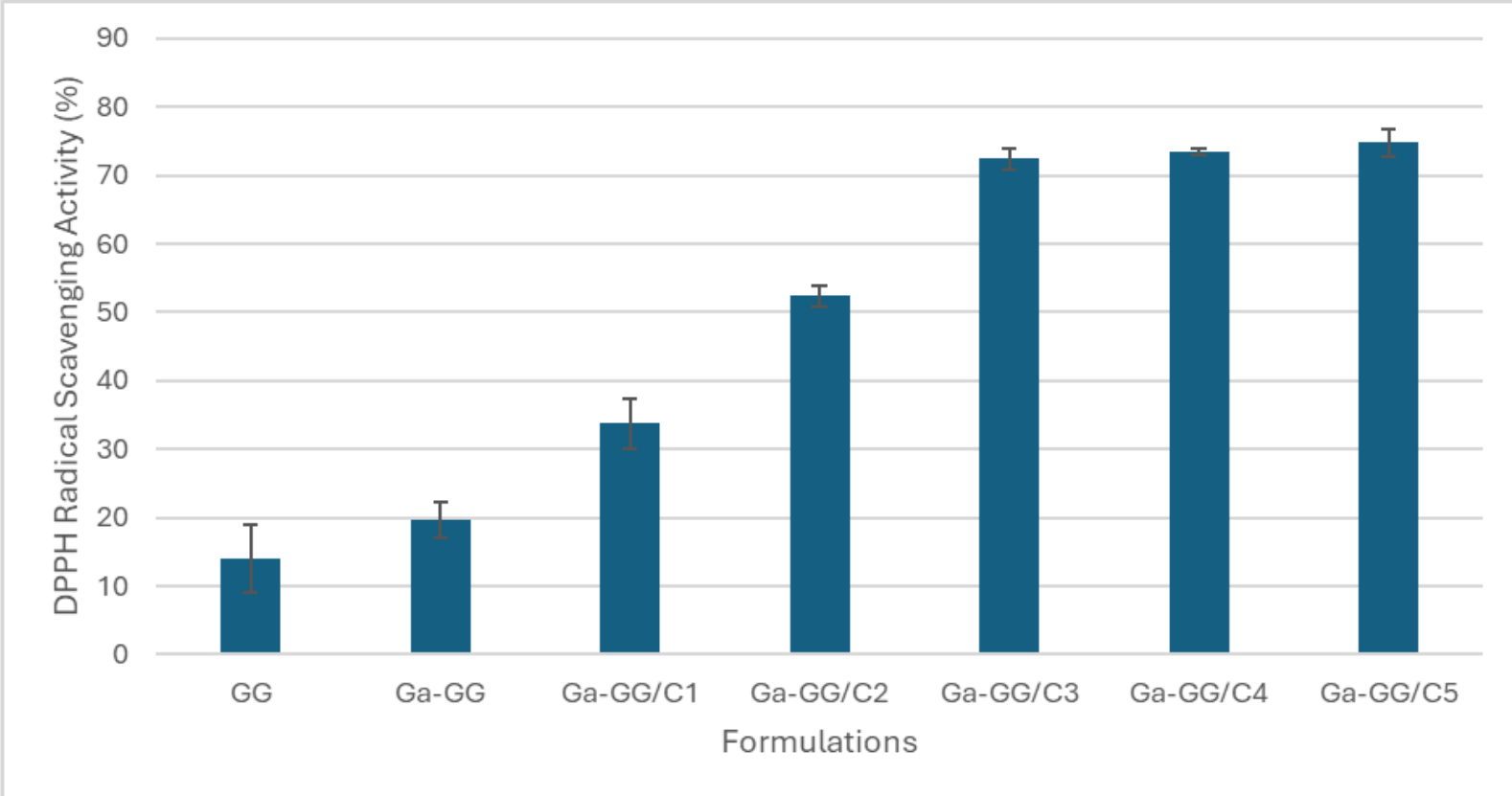


Figure 11: Antioxidant activity (DPPH assay) of GG, Ga-GG, and curcumin-loaded Ga-GG hydrogels. GG and Ga-GG showed minimal scavenging. Curcumin incorporation significantly enhanced activity ($p < 0.05$) in a dose-dependent manner from C1 to C3 (~34–72%). Further increases from C3 to C5 (~75%) were not statistically significant.

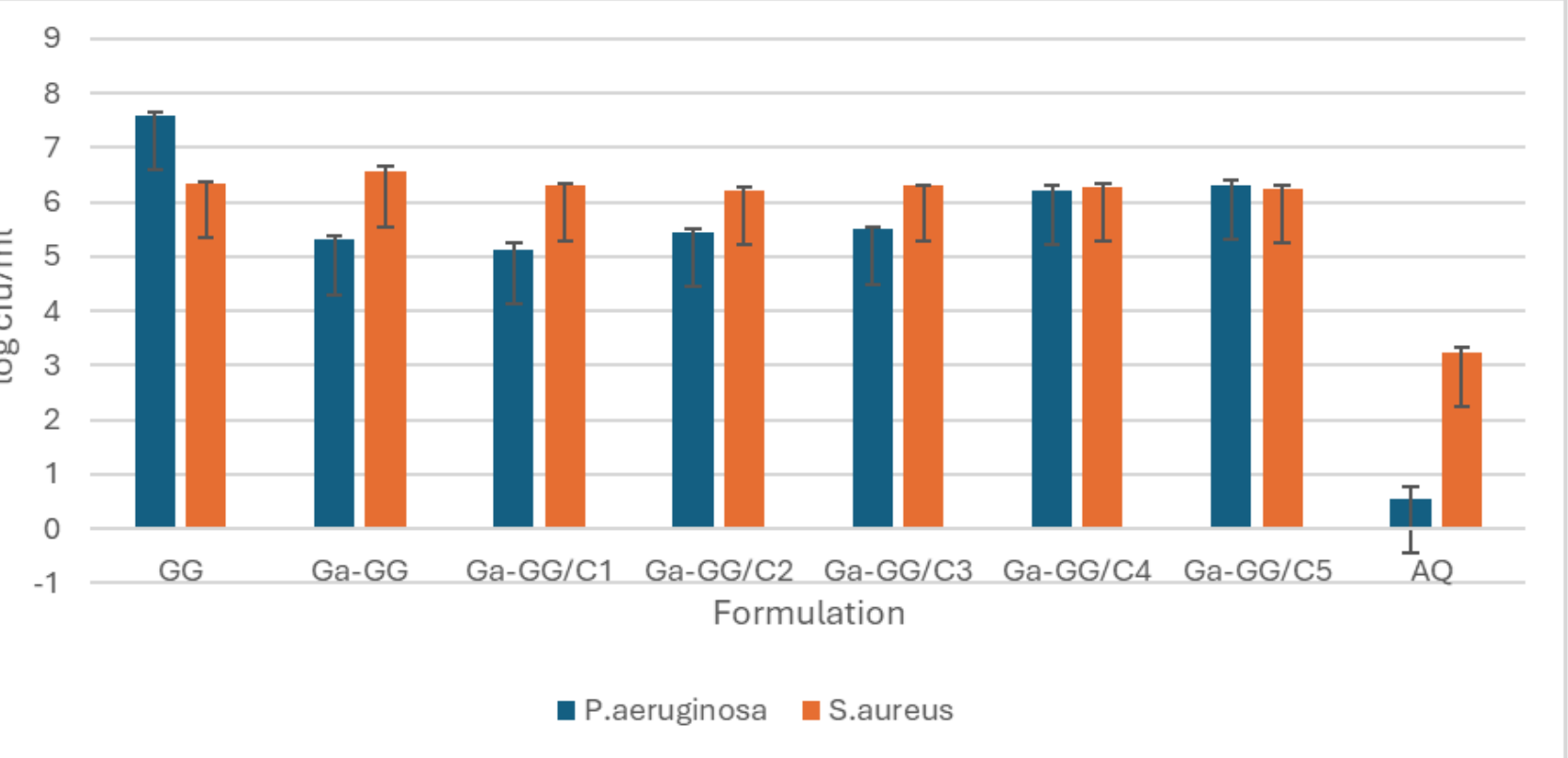


Figure 12: Antibacterial activity of GG, Ga-GG, curcumin-loaded Ga-GG, and AQ dressings against *P. aeruginosa* and MRSA. Ga incorporation significantly reduced *P. aeruginosa* growth (7.6 → 5.3 log CFU/mL, $p < 0.05$) but showed no effect on MRSA. Curcumin loading did not further enhance activity ($p > 0.05$) and higher concentrations slightly increased *P. aeruginosa* viability. AQ demonstrated the strongest effect, reducing counts to 0.5 (*P. aeruginosa*) and 3.2 (MRSA).

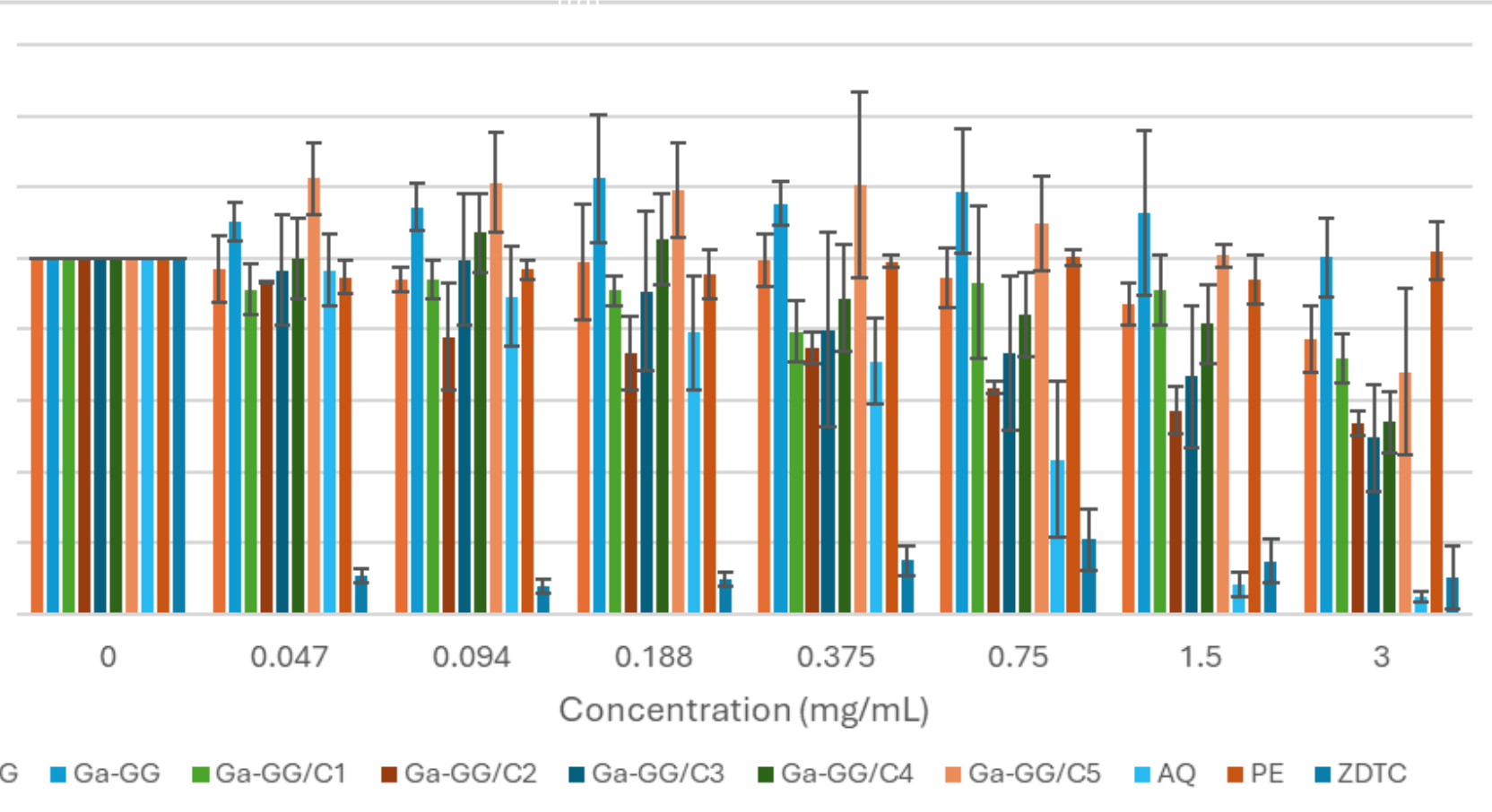


Figure 13: Cytocompatibility of GG, Ga-GG, curcumin-loaded Ga-GG, and AQ hydrogels with HaCaT cells (MTT assay). GG and Ga-GG maintained >70% viability up to 3 mg/mL. Curcumin-loaded hydrogels were generally biocompatible up to 0.375 mg/mL. C1 sustained >70% viability at 3 mg/mL, while C3–C5 preserved >80% at 1.5 mg/mL but showed cytotoxicity at 3 mg/mL. C2 and AQ reduced viability below 70% at >0.375 mg/mL. Controls: PE was non-toxic, ZDTC highly cytotoxic.

DISCUSSION

- Optimisation of the Ga-GG formulation: GG 1.5% with Ga 0.3% was identified as the optimal formulation, balancing high encapsulation efficiency (EE) with good gel fraction (GF) and bead morphology (6,7).
- Encapsulation Efficiency of curcumin: High EE achieved due to hydrogen bonding and hydrophobic interactions between GG backbone and curcumin (8).
- FTIR: Peak shifts and broadenings confirmed successful Ga crosslinking (via ionic bonding with $-\text{OH}$ and $-\text{COO}^-$ groups of GG) and curcumin encapsulation (through hydrogen bonding with GG functional groups). These interactions verified stable hydrogel formation with effective molecular entrapment (9,10).
- SEM: Incorporation of Ga and curcumin modified the hydrogel surface architecture, resulting in denser and more compact networks, thereby confirming successful crosslinking and curcumin encapsulation (11,12).
- in vitro* Drug Release: Hydrogels showed biphasic release (burst + sustained). Strong crosslinking limited curcumin diffusion, ensuring prolonged release (12,13).
- Gel Fraction & Swelling: Ga improved gel fraction and reduced swelling (8). Curcumin, especially at higher levels, increased water uptake. Compared to AQ, hydrogels absorbed more exudates (8).
- Degradation: All hydrogels showed gradual enzymatic degradation over 10 days. AQ degraded fastest (~78% by Day 10), while GG and Ga-GG displayed sharper weight loss on Day 3 and Day 5, respectively. Curcumin-loaded Ga-GG degraded more slowly (50–65%), with C5 showing the lowest degradation (~53%).
- Antioxidant Activity: Curcumin provided dose-dependent radical scavenging (11,14).
- Antibacterial Effect: Ga inhibited *P. aeruginosa* but not MRSA. Curcumin did not enhance activity; higher doses interfered with Ga's effect. AQ remained superior.
- Cytocompatibility: GG and Ga-GG were non-cytotoxic (>70% viability). Curcumin-loaded hydrogels were biocompatible at low concentrations but showed mild toxicity (15).

CONCLUSION

The curcumin-loaded Ga-GG hydrogels was successfully developed via ionic gelation method. These hydrogels exhibited controlled physicochemical properties as a wound dressing. Besides that, they showed excellent antioxidant properties, good biocompatibility and antibacterial efficacy against *P.aeruginosa* but limited activity against MRSA.

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