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Development of novel chitosan–gelatin-based hydrogels for drug delivery applications

Sara Beatriz Cardoso[1], Patrícia Alves[1,2], Andreia Romeiro[3], Mariana Emilia Ghica[1]

[1]University of Coimbra, CERES, Department of Chemical Engineering, Coimbra, Portugal

[2]University of Coimbra, CEMMPRE, ARISE, Department of Mechanical Engineering, Coimbra, Portugal

[3]University of Coimbra, CEMMPRE, ARISE, Department of Chemical Engineering, Coimbra, Portugal

INTRODUCTION & AIM

- Chitosan (CH) is a biodegradable natural polymer with unique properties, allowing to substitute other materials in packaging, tissue engineering, wound dressing, controlled drug release applications.
- Chitosan hydrogels may not have the best physicochemical characteristics for certain applications.
- Crosslinking agents and blends with other (bio)materials is a useful strategy to improve chitosan hydrogel properties.
- Gelatin (GEL) forms a polyelectrolyte complex with chitosan due to electrostatic interactions between chitosan's amino groups and gelatin's carboxyl groups.
- Glyoxal (GLY) helps stabilize the hydrogel's structure, increasing mechanical strength.
- The aim of this work was to synthesize a hydrogel consisting of chitosan and gelatin without and with crosslinking with glyoxal having a good balance between porosity, durability and release ability for the oral delivery of paracetamol.

METHOD

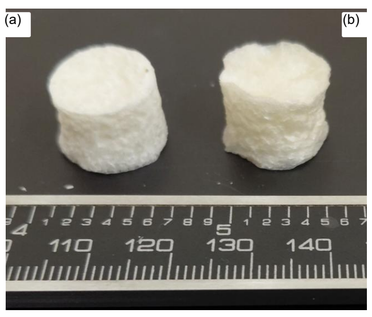

Figure 1. Images of CH:GEL 1:1 cryogels with glyoxal, with (a) and without (b) paracetamol.

Figure 2. Images of CH:GEL 1:2 cryogels with glyoxal, with (a) and without (b) paracetamol.

- Preparation of low molecular weight chitosan solution (2.5% w/v) and gelatin type B solutions (1%, 2.5% and 5% w/v) using 2% v/v acetic acid.
- Mixing of the solutions (CH:GEL ratios of 1:1, 1:2 and 1:3) in open syringes, which were then left in the fridge for 24h, followed by 48h in the freezer, then freeze-dried for 72h at -80 ºC and 0.2 mbar.
- Preparation of CH:GEL samples (ratios of 1:1 and 1:2 with 2.5% w/v gelatin) using 2.5% v/v glyoxal.
- Chemical bonding and surface morphological characterization by FTIR and SEM, respectively, and investigation regarding porosity, swelling and degradation behavior.
- The systems with best performance were loaded with 10 mg/mL paracetamol (PCT).
- Release of paracetamol was carried out under simulated digestion conditions, including successive release in simulated oral fluid (SOF), simulated gastric fluid (SGF) and simulated intestinal fluid (SIF).

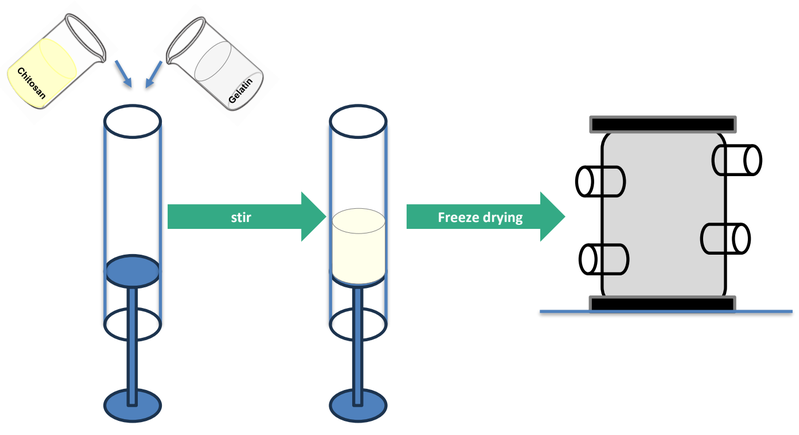

Figure 3. Preparation of the CH:GEL cryogels.

RESULTS & DISCUSSION

Swelling tests

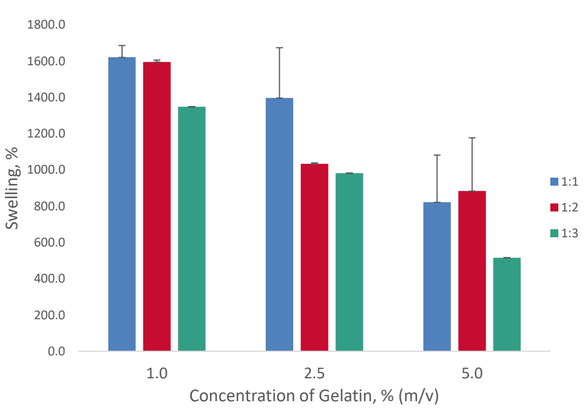

Figure 4. Swelling of the CH:GEL samples without GLY in PBS.

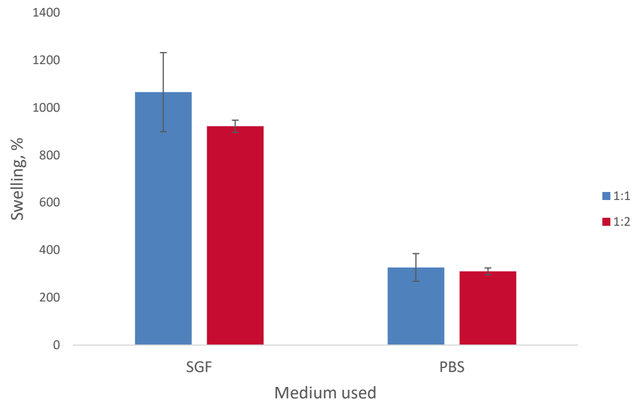

Figure 5. Swelling of the CH:GEL samples with GLY in PBS and SGF.

- CH:GEL samples without glyoxal were almost immediately degrading in acidic media. With glyoxal, the samples can withstand low pH values, however, in PBS less swelling occurred.
- At a lower pH (SGF), chitosan's amino groups are more protonated allowing more free water to enter the hydrogel matrix, resulting in higher swelling in this media compared with PBS [1].
- With the increase of the GEL:CH ratio, there is an increase of the bonds formed, leading to the decrease of the flexibility of the matrix chains, thus less swelling.is observed [2] indifferently if using glyoxal or not.

Degradation tests

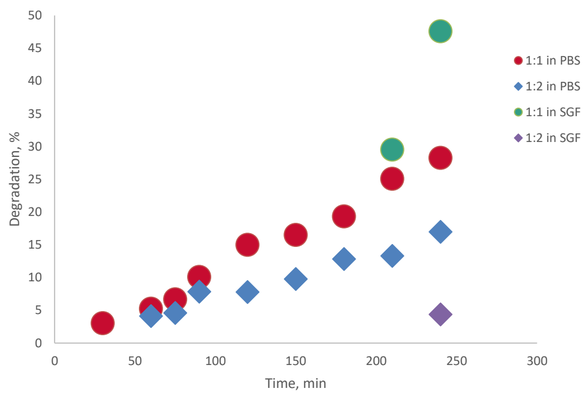

Figure 6. Degradation of the 1:1 and 1:2 CH:GEL samples with GLY in PBS and in SGF

- With the increase in gelatin content, more sites for CH-GEL interaction are provided, which stiffens the material, thus being less prone to break. Therefore, lower degradation is observed, compared with the samples with lower content of gelatin.
- At lower pH, the protonation of chitosan's amino groups allows the samples to have a bigger swelling capacity, which makes them last longer than when tested at higher pH.
- Glyoxal plays a crucial role, since the samples without a crosslinking agent couldn't withstand the pH of the SGF.

SEM analysis

- The introduction of glyoxal in the matrix, led to the formation of a more compact surface with almost closed pores for the CH:GEL system with 1:1 ratio.
- The increase in gelatin content allowed the formation of bigger and better-defined pores.

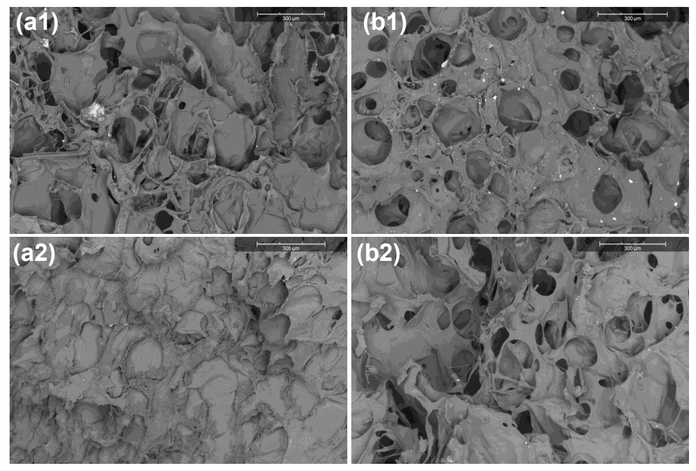

Figure 7. SEM images of the CH:GEL cryogels with PCT, ratio of 1:1 (a1, a2), and 1:2 (b1, b2), without (a1, b1), and with (a2, b2) glyoxal.

Release of paracetamol

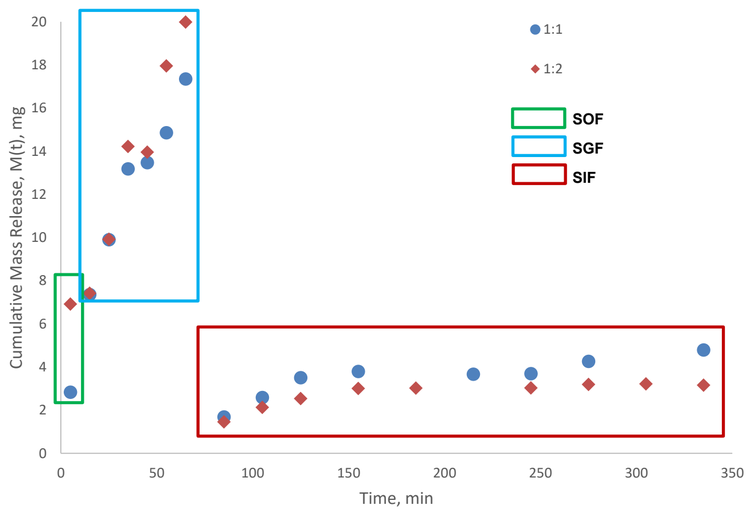

Figure 8. PCT release test from the CH:GEL samples with ratio of 1:1 (blue) and 1:2 (red) in SOF, SGF and SIF.

- At lower pH values (SGF), the samples suffer much swelling, which led to the hydrogel matrix opening, causing a higher release of the PCT loaded. This can explain the profiles observed in Figure 8 before and after the 85 minutes, where a higher content of PCT is released in SGF, compared with SIF.

CONCLUSIONS

- Hydrogels based on chitosan and gelatin were synthesized with different formulations.
- The systems with best performance were those containing the same gelatin and chitosan concentration (2.5%, w/v) mixed in two different ratios of CH:GEL, 1:1 and 1:2.
- The hydrogels could release paracetamol continuously, during 5h.

FUTURE WORK / REFERENCES

The current work is still in progress. Future works could focus on testing different concentrations of the crosslinking agent and utilize enzymes for the degradation and release of paracetamol.

[1] Kaçoğlu, H. S., Ceylan, Ö., & Çelebi, M. (2024). Determination of swelling kinetics and diffusion mechanisms of chemically crosslinked porous chitosan hydrogels. *Open Journal of Nano*, 9(2), 106–118. https://doi.org/10.56171/ojn.1488770

[2] Rohindra, D. R., Nand, A. V., & Khurma, J. R. (2004). Swelling properties of chitosan hydrogels. *South Pacific Journal of Natural and Applied Sciences*, *22*(1), 32. https://doi.org/10.1071/sp04005

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