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Development of chitosan-pectin cryogels for controlled drug release

Ana Isabel Ribeiro[1], Andreia Romeiro[2], Patrícia Alves[1,3], Mariana Emilia Ghica[1]

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

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

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

INTRODUCTION & AIM

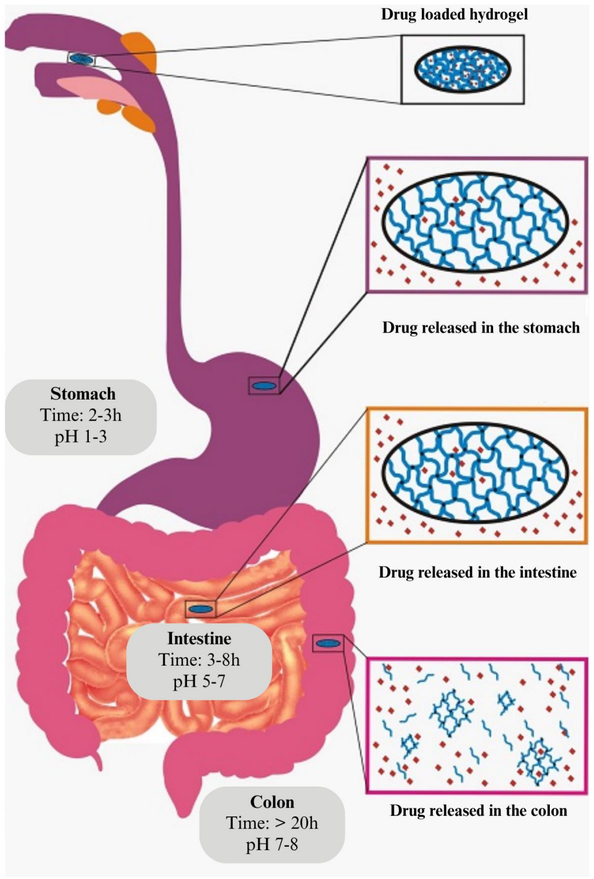

Figure 1. Schematic representation of an oral SDDS along the gastrointestinal tract. (Adapted from Rizwan et al., 2017)

Treatments for inflammatory bowel diseases require the ability to deliver drugs specifically to the intestinal tract in order to minimize systemic side effects. Hydrogels are promising materials for smart drug delivery systems (SDDS) due to their biocompatibility, high water absorption capacity, and similarity to biological tissues, enabling controlled and localized drug release.

In this study, cryogels of chitosan (Chit) and pectin (Pec) with physical crosslinking were developed at different volume ratios (1:1, 2:1, and 1:2) and pectin concentrations (1%, 2.5%, and 5% w/v), incorporating the drug sulfasalazine (SSZ) used in the treatment of inflammatory bowel diseases.

METHODS

Cryogel Preparation

- Chitosan (2.5% w/v) and pectin (1-5% w/v) dissolved separately in acetic acid (2% v/v) at 40 °C.
- Polymer solutions mixed at volume ratios 1:1, 2:1, 1:2 (Table 1).
- Sulfasalazine (SSZ, 10 mg) incorporated under light protection.
- Samples frozen and freeze-dried to obtain cryogels.

Preparation of Release Media

- Phosphate-Buffered Saline (PBS), Simulated gastric fluid (SGF) and Simulated intestinal fluid (SIF)
- PBS pH 7.4, SGF pH 2 (NaCl 0.2% w/v; HCl 1 M), SIF pH 7 (KH_2PO_4 0.05 M; KOH 0.2 M).
- Media mimic stomach, intestine and colon physiological pH.

Hydrogel Characterization

- SEM: morphology and pore structure.
- Porosity: ethanol intrusion method.
- Swelling: in PBS (pH 7.4).

In vitro Drug Release

- Cryogels immersed in SGF, SIF or PBS at 37 °C, 100 rpm.
- Sampling up to 240 min (SGF/SIF) and 24 h (PBS).
- Absorbance measured by UV-Vis at 359 nm.
- Cumulative release calculated with dilution correction factor.
- Release profiles fitted to kinetic models (Zero-order, First-order, Higuchi, Korsmeyer-Peppas).

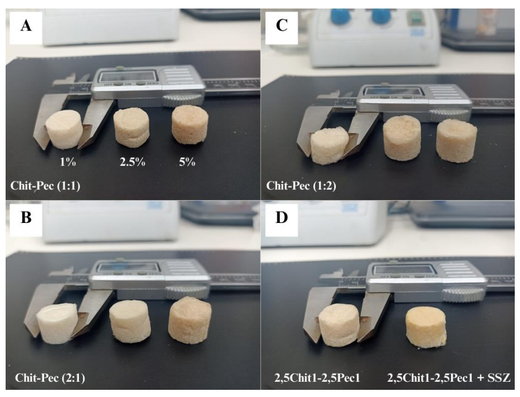

Figure 2. Chitosan-pectin cryogels: (A – volume ratio 1:1, B – volume ratio 2:1, C – volume ratio 1:2, and D – Cryogel 2.5Chit1-2.5Pec1 with and without SSZ).

Table 1. Chitosan-pectin formulations.

Cryogels	Volume Ratio	Chitosan (% w/v)	Pectin (% w/v)
2.5Chit1-1Pec1	1:1	2.5	1
2.5Chit1-2.5Pec1	1:1	2.5	2.5
2.5Chit1-5Pec1	1:1	2.5	5
2.5Chit2-1Pec1	2:1	2.5	1
2.5Chit2-2.5Pec1	2:1	2.5	2.5
2.5Chit2-5Pec1	2:1	2.5	5
2.5Chit1-1Pec2	1:2	2.5	1
2.5Chit1-2.5Pec2	1:2	2.5	2.5
2.5Chit1-5Pec2	1:2	2.5	5

RESULTS & DISCUSSION

Porosity and Swelling

Table 2. Porosity and density values of different cryogels.

Cryogels	Porosity ($\bar{\varepsilon}$)	Density (g/cm³)
2.5Chit1-1Pec1	79.0%	0.035
2.5Chit1-2.5Pec1	79.0%	0.072
2.5Chit1-5Pec1	72.0%	0.046
2.5Chit2-1Pec1	90.0%	0.089
2.5Chit2-2.5Pec1	96.0%	0.043
2.5Chit2-5Pec1	87.0%	0.043
2.5Chit1-1Pec2	77.0%	0.055
2.5Chit1-2.5Pec2	77.0%	0.052
2.5Chit1-5Pec2	81.0%	0.042

- Average porosity values ranged from 72% to 96%
- Densities from 0.035 to 0.089 g/cm³.
- Cryogels with a higher content of chitosan showed higher porosity, with 2.5Chit2-2.5Pec1 standing out at 96%.
- Effect on porosity depends on the molar ratio of each polymer.

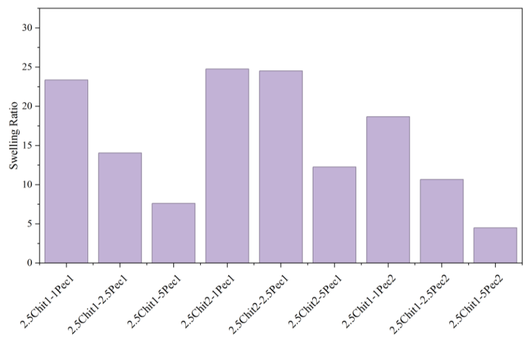

Figure 3. Swelling ratio variation of the studied cryogels when immersed in PBS at pH 7.4 during the first hour.

- Chit-Pec (2:1) cryogels had higher values
- Chit-Pec (1:2) cryogels had lower swelling.

In Vitro Drug Release

SSZ release is pH-dependent.

Chit-Pec (1:1)

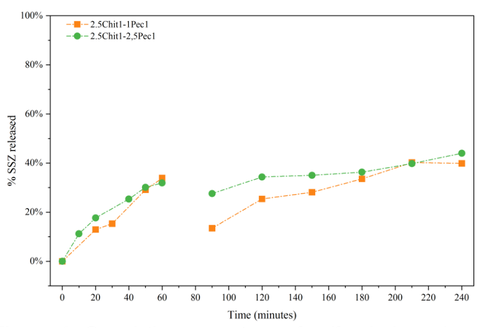

Figure 4. Cumulative percentage of sulfasalazine released over time in SGF solution (0-60 min) and SIF (up to 240 min) at 37 °C from the Chit-Pec (1:1) cryogels.

Table 3. Kinetic parameters obtained from the linearization of the kinetic models applied to the SSZ release profile from Chit-Pec (1:1) cryogels in SGF and SIF.

Kinetic Models	Parameters	1st Release – pH 2		2nd Release – pH 7	
		2.5Chit1-1Pec1	2.5Chit1-2.5Pec1	2.5Chit1-1Pec1	2.5Chit1-2.5Pec1
Zero Order	K_0 / min^{-1}	0.56	0.50	0.17	0.09
	R^2	0.9918	0.9458	0.9223	0.9290
First Order	K_1 / min^{-1}	0.007	0.004	0.002	0.001
	R^2	0.9798	0.9879	0.9398	0.8908
Higuchi	K_H / min$^{-0,5}$	4.24	4.22	0.04	2.38
	R^2	0.9143	0.9948	0.9482	0.9301
Korsmeyer -Peppas	K / min^{-n}	0.13	0.47	0.89	0.64
	n	0.92	0.59	1.0	0.41
	R^2	0.9627	0.9967	0.9158	0.9290

Kinetic modeling:

- Higuchi model pH 7 (Fickian diffusion).
- pH2: zero-order and Korsmeyer–Peppas models (polymer matrix relaxation also contributed to the release)

Chit-Pec (2:1)

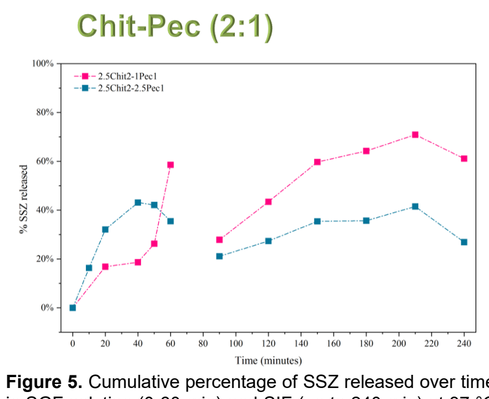

Figure 5. Cumulative percentage of SSZ released over time in SGF solution (0-60 min) and SIF (up to 240 min) at 37 °C from the Chit-Pec (2:1) cryogels.

Table 4. Kinetic parameters obtained from the linearization of the kinetic models applied to the SSZ release profile from Chit-Pec (2:1) cryogels in SGF and SIF.

Kinetic Models	Parameters	1st Release – pH 2		2nd Release – pH 7	
		2.5Chit2-1Pec1	2.5Chit2-2.5Pec1	2.5Chit2-1Pec1	2.5Chit2-2.5Pec1
Zero Order	K_0 / min^{-1}	0.78	0.85	0.36	0.16
	R^2	0.7687	0.7956	0.9493	0.9440
First Order	K_1 / min^{-1}	0.006	0.01	0.004	0.004
	R^2	0.7713	0.8166	0.7114	0.9173
Higuchi	K_H / min$^{-0,5}$	5.58	0.07	8.66	3.96
	R^2	0.6499	0.9288	0.9637	0.9584
Korsmeyer -Peppas	K / min^{-n}	0.41	0.89	1.1	0.031
	n	0.54	0.41	0.68	0.68
	R^2	0.7093	0.6643	0.9401	0.9066

Kinetic modeling:

- pH 2: released more SSZ
- pH 7: release was more linear, likely due to the lower solubility of chitosan.

- pH 2: Higuchi model fit 2.5Chit2-2.5Pec1; no model fit 2.5Chit2-1Pec1.
- pH 7: Higuchi model best fit for both cryogels.

Morphology

Chit-Pec (1:1)

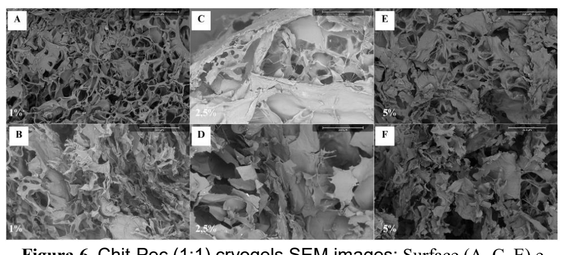

Figura 6. Chit-Pec (1:1) cryogels SEM images: Surface (A, C, E) e transversal (B, D, F). Pectin concentrations of 1%, 2.5% e 5% (in figure).

Chit-Pec (2:1)

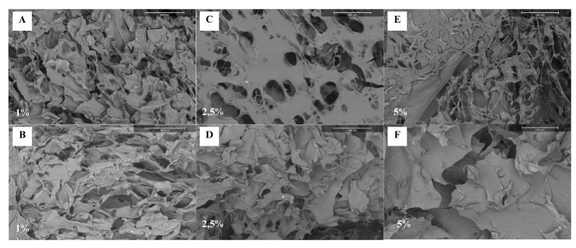

Figura 7. Chit-Pec (2:1) cryogels SEM images: Surface (A, C, E) e transversal (B, D, F). Pectin concentrations of 1%, 2.5% e 5% (in figure).

- Pectin increase leads to more compact and less porous structures

REFERENCES

Rizwan, M., Yahya, R., Hassan, A., Yar, M., Azzahari, A. D., Selvanathan, V., Sonsudin, F., & Abouloula, C. N. (2017). pH Sensitive Hydrogels in Drug Delivery: Brief History, Properties, Swelling, and Release Mechanism, Material Selection and Applications. Polymers, 9(4), 137. https://doi.org/10.3390/polym9040137

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CONCLUSION AND FUTURE WORK

- *In vitro* release studies of SSZ in different media (pH 2, 7 and 7,4) showed that Higuchi and zero-order kinetic models best fitted the release profiles. This indicates that diffusion and polymer matrix relaxation are the main rate-limiting mechanisms in drug release. The release profiles of cryogels 2.5Chit1-1Pec1 and 2.5Chit2-1Pec1 approximate zero-order kinetics. These results suggest that process optimization is required to achieve a controlled drug release.
- Future steps to complement this study include repeating *in vitro* sulfasalazine release tests at different pH values (1.2; 6.8 and 7.4), performing *in vitro* degradation tests in the presence of enzymes and exploring the application of enteric coatings on the hydrogels and chemical crosslinking to enhance hydrogel stability.