Cellulose acetate phthalate-chitosan based nanoparticles for transdermal delivery of captopril in pediatric patients

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INTRODUCTION

The Pediatric Committee at the European Medicines Agency identified the need for the development of age-appropriate formulations of captopril in the pediatric population for the treatment of cardiovascular diseases and diabetic nephropathy (1). Captopril (CAT) is currently administered by extemporaneous liquid formulation or tablet due to its limited water stability (2). The aim was to develop polymeric nanoparticles for transdermal delivery of CAT to obtain a prolonged CAT release as well as an easy dosage control with high compliance of pediatric patients. Cellulose acetate phthalate (CAP) and chitosan (CH) were used to prepare nanoparticles without using surfactants.

EXPERIMENTAL METHODS

Nanoparticle preparation

CAP nanoparticles (A) and CAP nanoparticles combined with CH (B) in different concentrations were prepared. The CAP:CH ratio was 1:1 w/w (B1) and 1:3 w/w (B2). Polymeric nanoparticles were obtained by nanoprecipitation method-dropping technique (3) (Figure 1).

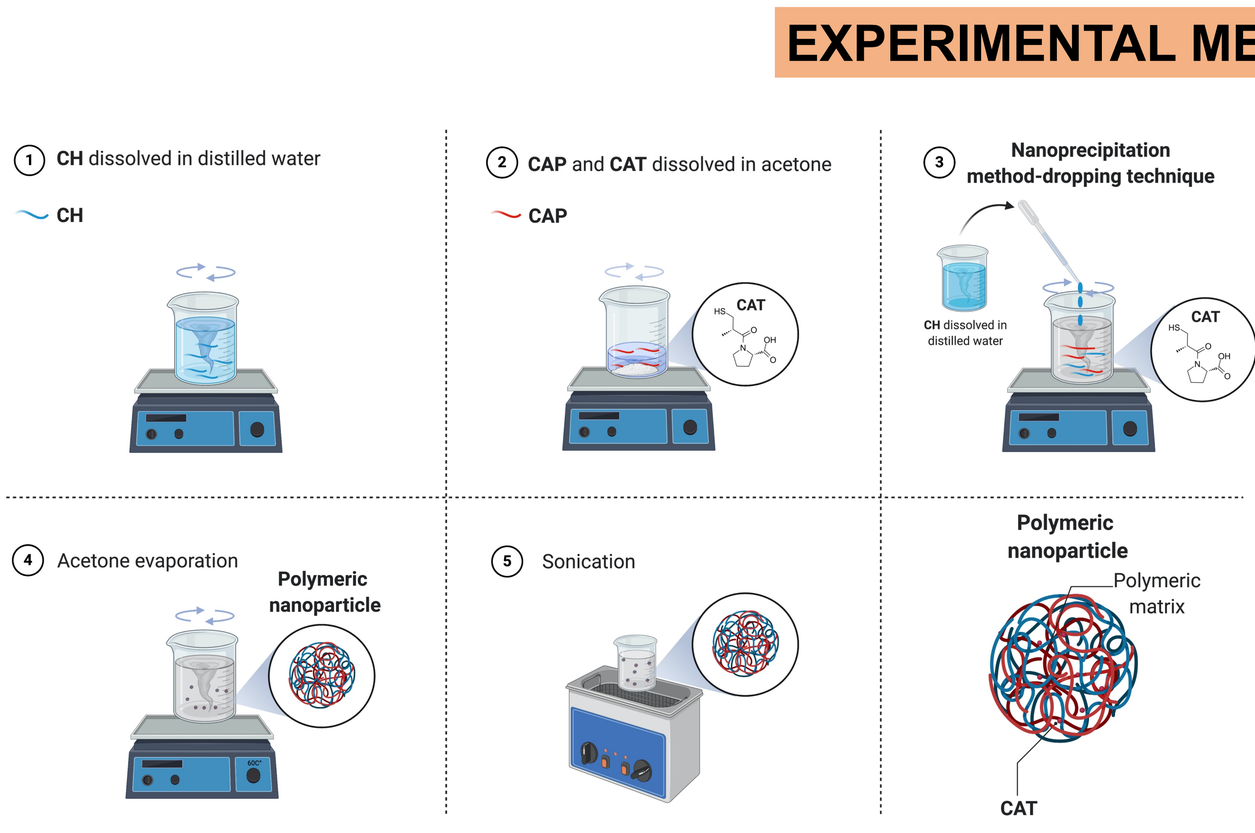

Figure 1. Nanoprecipitation method-dropping technique

Nanoparticle characterization

- Size and Polydispersity Index (PDI)
- Physical stability after 1, 7, 14 and 28 days
- Drug loading
- FTIR

RESULTS

- Mean particle, PDI and drug content (%) are reported in Table 1.
- All nanoparticles have low PDI values resulting in a homogeneous system.
- CAP nanoparticles (A) have no loading capacity, whereas the cross-linking with chitosan allows the encapsulation of CAT.
- The CAP:CH ratio affects drug loading capacity that is higher in B2 than in B1.
- Polymeric nanoparticles showed good physical stability over time. A, B1 and B2 were stable for 28 days in terms of diameter size and PDI.

Formulation	Composition	Particle size (nm)	PDI	Drug loading (%)
A	CAP	515.6±5.23	0.079±0.008	-
B1	CAP:CH 1:1 w/w	279.80±2.5	0.190±0.054	29.78± 0.87
B2	CAP:CH 1:3 w/w	408.10±9.48	0.143±0.011	64.56±7.56

Table 1. Parameters for polymeric nanoparticles.

- The spectra of Figure 2 shows the interaction between CAP and CH (b) (c). The absence of S-H stretching at 2566,05 cm^{-1} of captopril in B2 (b) suggested an interaction between CAT and polymer matrix.

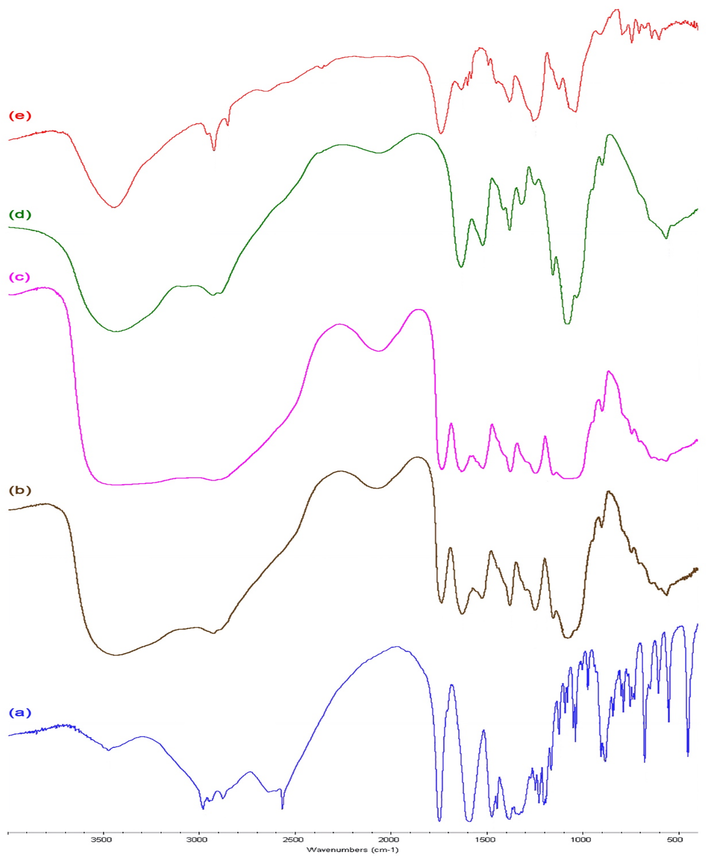

Figure 2. FTIR spectrum of captopril (a), B2 (b), blank-B2 (c), CH (d) and CAP (e).

CONCLUSION

Chitosan improved the encapsulation efficiency of CAP nanoparticles. B2 shows better results for developing suitable formulation for transdermal delivery of CAT. *In vitro* permeation studies are in progress.

REFERENCES

[1] European Medicines Agency. Needs for paediatric medicines. Available at:https://www.ema.europa.eu/en/human-regulatory/research-development/paediatric-medicines/needs-paediatric-medicines/.

[2] Pabari, R.M., McDermott, C., Barlow, J., Ramtoola, Z., 2012. Stability of an Alternative Extemporaneous Captopril Fast-Dispersing Tablet Formulation Versus an Extemporaneous Oral Liquid Formulation. Clinical Therapeutics 34, 2221–2229.

[3] Hornig, S., Heinze, T., 2008. Efficient Approach To Design Stable Water-Dispersible Nanoparticles of Hydrophobic Cellulose Esters. Biomacromolecules 9, 1487–1492.