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FORMULATION STRATEGIES FOR PHARMACEUTICAL USE OF pNIPAM MICROGEL

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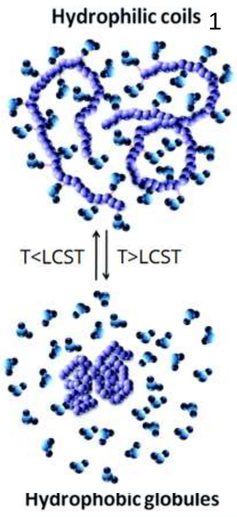
Università degli Studi di Ferrara



INTRODUCTION

Poly-N-isopropylacrylamide (pNIPAM) is a thermoresponsive synthetic polymer capable of undergoing a reversible phase transition from a hydrophilic swollen (inflated) state to a hydrophobic collapsed (globular) state upon exceeding the lower critical temperature (LCST), located around 32–33°C. This property makes it a promising candidate for topical controlled-release applications. However, the use of pNIPAM is limited by its low encapsulation efficiency, necessitating the development of alternative strategies to improve its yield while maintaining its thermoresponsiveness.

In this study, pNIPAM microgel was evaluated as a carrier system for caffeic acid (CA), chosen as a molecular model due to its relatively simple structure. Three different possible strategies were considered to optimize the encapsulation of the active ingredient: hybrid microgel with keratin, β-cyclodextrin and liposomes.

METHOD

FORMULATION SET UP

Loading CA	
Microgel and Hybrid Microgel pNIPAM-keratin	➢ Loading Microgel with CA: 1 h at 40°C under agitation. ➢ Partitioning study with Eppendorf filter
pNIPAM-β-cyclodextrin	➢ CD-CA complex to the microgel ➢ Orbiatl shaking for 24 hours
Liposomes-pNIPAM PC:CH 2:1 mol/mol (20 mg/mL)	➢ Loading pNIPAM with CA ➢ *Ethanol injection* (EI) method

CHARACTERIZATION

Morphological characterization

TEM Analysis (*Transmission Electron Microscopy*)

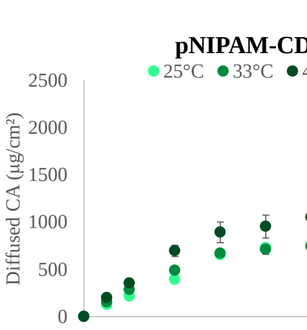
Quantitative determination of CA

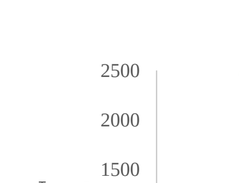
UV-visible, λ=321 nm

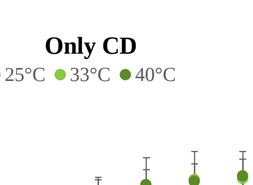
Dimensional analysis

PCS (*Photon Correlation Spectroscopy*): size (nm) and PdI

In vitro diffusion of CA



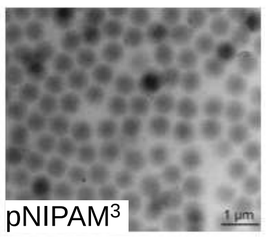

Cellulose esters

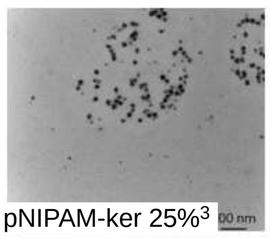

Lipid-functionalized cellulose esters

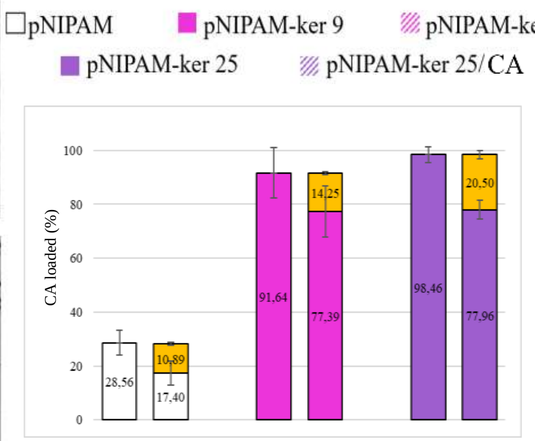
- Receiving phase: HPLC water
- Membrane: Lipid-functionalized cellulose esters
- Withdrawals 30 min, 1, 2, 3, 4, 5, 6, 7, 8 hours after loading
- UV-visible analysis at 321 nm

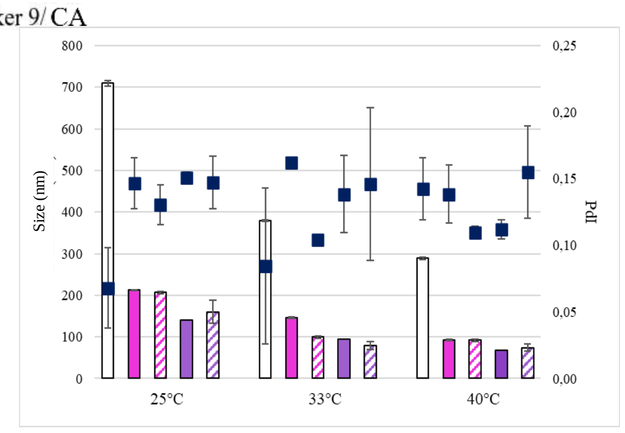
RESULTS & DISCUSSION

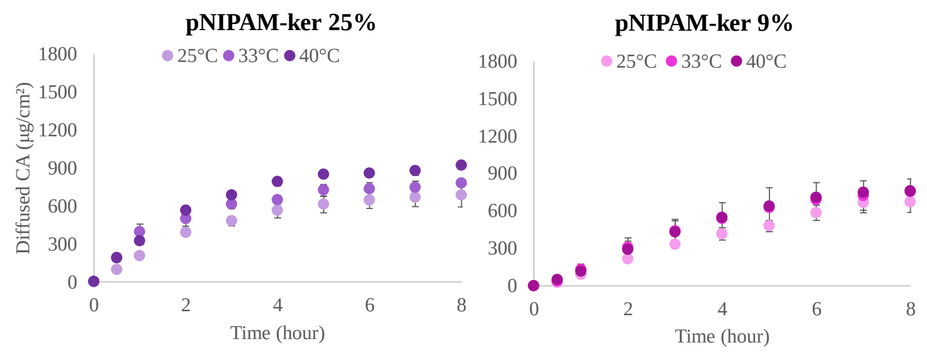
Hybrid Microgel pNIPAM-keratin



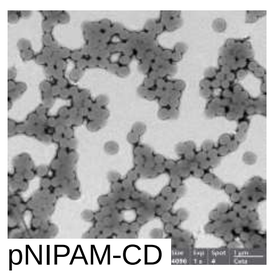


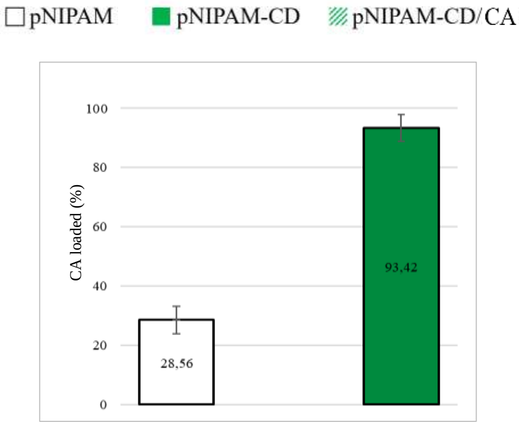


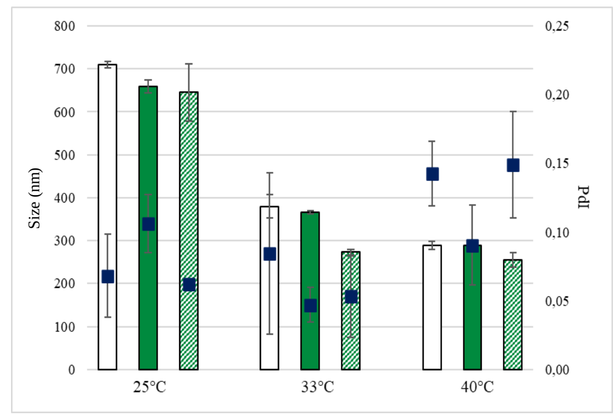




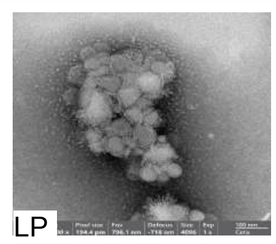
pNIPAM-β-cyclodextrin

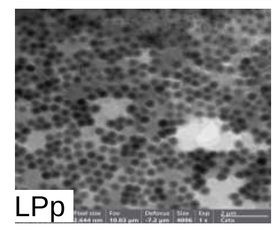


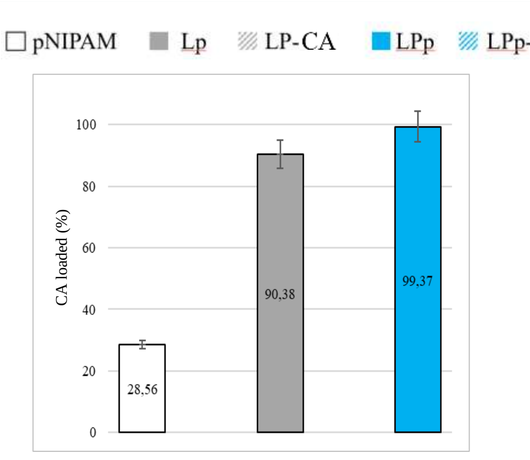


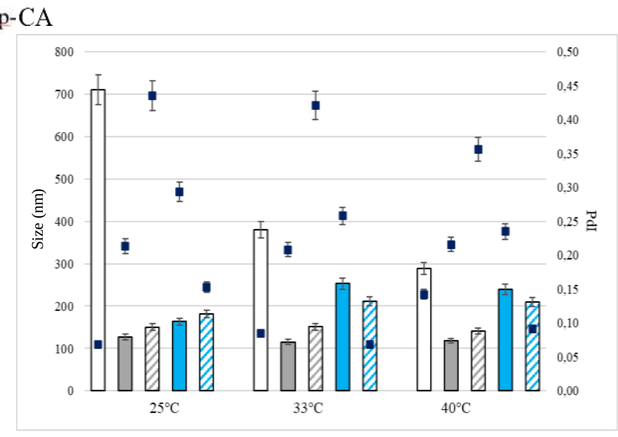


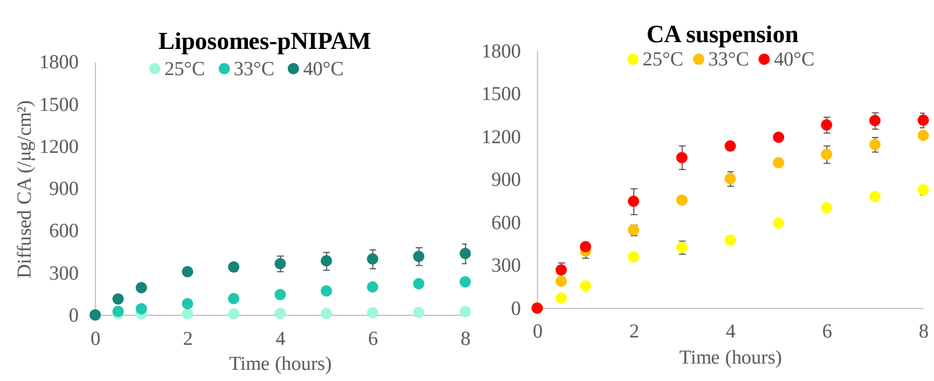
Liposomes-pNIPAM











CONCLUSION

The present preliminary study shows that the three formulation strategies led to an increase caffeic acid loading efficiency compared to the sole polymer and provided controlled drug release. Only keratin and liposome formulation strategies reduced particle size. Thermoresponsive behavior was retained with keratin and cyclodextrins, but not with liposomes. *In vitro* diffusion showed that pNIPAM–keratin released CA in a temperature-independent manner, while the other systems displayed temperature-dependent release. Therefore, the three approaches explored represent promising strategies for the topical application of pNIPAM.

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2. https://permegear.com/franz-cells/
3. Buratti E, Sguizzato M, Sotgiu G, Zamboni R, Bertoldo M. *Keratin-PNIPAM Hybrid Microgels: Preparation, Morphology and Swelling Properties.* Gels. 2024 Jun doi: 10.3390/gels10060411.