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FORMULATION STRATEGIES FOR PHARMACEUTICAL USE OF pNIPAM MICROGEL

I*ntroduction*

Poly-N-isopropylacrylamide (pNIPAM) is a thermoresponsive synthetic polymer that undergoes a reversible phase transition from a swollen to a collapsed state when the lower critical solution temperature (LCST) is exceeded (around 32–33 °C). This property makes it a promising candidate for controlled-release topical delivery.

However, its poor drug-loading capacity necessitates the development of alternative strategies to enhance its effectiveness. In this study, a pNIPAM microgel was evaluated as a carrier for caffeic acid (CA), selected as a model molecule due to its relatively simple structure.

Three approaches were explored:

1. Hybrid pNIPAM–keratin microgel: Keratin was selected for its biocompatibility with topical use. It reduced the particle size without affecting the thermoresponsiveness of the polymer.
2. Use of β-cyclodextrins within pNIPAM: β-cyclodextrins can form inclusion complexes with CA, improving its aqueous solubility (CA has poor solubility, LogP ≈ 1.2).
3. Liposomes embedded in the pNIPAM microgel: Liposomes composed of phosphatidylcholine and cholesterol (2:1 molar ratio) were used to enhance CA encapsulation.

Methods

Formulations were characterized by morphology, particle size and surface charge. Stability and loading efficiency were monitored. In vitro diffusion was tested using Franz cells and lipid-functionalized cellulose membranes mimicking the skin barrier.

Results

All strategies improved CA loading efficiency (>90%). Only keratin and liposome formulations 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.

Conclusions

The three approaches explored represent promising strategies for the topical application of pNIPAM, improving its functional properties. However, further studies are needed to evaluate the stability of the systems, as well as their toxicity and rheological profiles.