Reaction Calorimetry-Guided Synthesis of Hydrogels for Safe Pharmaceutical Applications

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Hydrogels (HGs), polymeric materials capable of absorbing significant amounts of water, are of growing interest for biomedical applications, especially in drug delivery systems. Their performance is largely dictated by parameters such as swelling capacity, mesh size, and viscoelastic behaviour. This work focuses on the synthesis and characterization of acrylic acid-based hydrogels optimized for topical drug delivery, with particular emphasis on process safety, material functionality, and formulation tunability.

The hydrogels were synthesized via free-radical polymerization of acrylic acid (AA), partially neutralized with sodium hydroxide to enhance hydrophilicity, in the presence of N,N′-methylenebisacrylamide (MBA) as a covalent crosslinker. Sodium persulfate was used as a thermal initiator. The synthesis was performed using a reaction calorimeter (MT EasyMax 102) equipped with a pH probe, allowing precise control over reaction conditions and enabling the assessment of exothermicity for safe scale-up.

A design of experiments (DoE) approach was adopted, varying key parameters such as initial water content, neutralization degree, and crosslinker concentration. The calorimetric analysis revealed that higher neutralization degrees reduced the thermal demand of the reaction, likely due to altered monomer reactivity. Rheological testing and swelling studies provided insight into the mechanical and absorptive properties of the resulting materials. Sol–gel transitions were clearly distinguishable through linear viscoelastic region (LVER) determination, and frequency sweeps enabled the calculation of mesh size and crosslink density via the generalized Maxwell model.

The results indicate that synthesis parameters strongly influence the final gel properties. Specifically, the degree of AA neutralization and the water content during synthesis were critical in defining the gel’s swelling capacity and mechanical behaviour. One formulation demonstrated a favourable balance of drug loading potential, swelling behaviour, and manageable viscosity—making it ideal for further development in topical drug delivery applications.

In conclusion, the experimental protocol allowed for the rapid screening and evaluation of multiple hydrogel formulations. Future work will focus on recipe optimization, exploring alternative crosslinkers, and transitioning to continuous processing. This study provides a solid foundation for the safe and efficient development of functional hydrogels for pharmaceutical use.