Solvent-Driven Control of Structure in Short Fmoc Peptide Hydrogels: A SAXS Study

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Antimicrobial peptides (AMPs) hold strong potential in combatting microbial resistance [1,2]. However, their limited shelf-life, susceptibility to degradation, and costs of synthesizing larger peptide structures remain major obstacles to clinical translation [2]. Short Fmoc-phenylalanine-based peptides have recently gained attention for their intrinsic antimicrobial activity and their ability to self-assemble into hydrogels under physiological conditions [3,4]. Nevertheless, the mechanisms governing their self-assembly, particularly in complex solvent environments, remain poorly understood, limiting their rational design as functional biomaterials.

The aim of this work is to establish structure-function relationships in Fmoc-dipeptide systems by investigating how solvent conditions direct self-assembly and macroscopic material properties. We systematically vary peptide concentration, pH, ionic strength and the fraction of dimethyl sulfoxide (DMSO) as co-solvent in buffer. DMSO modifies peptide self-assembly by altering solvation and weakening hydrogen bonding, making it a powerful handle to tune supramolecular structure.
Small-angle X-ray scattering (SAXS), combined with rheology and electrophoretic mobility analysis, reveals the formation of nanostructured Fmoc-dipeptide hydrogels with tunable pH-dependent structural and viscoelastic properties. These structural transitions shift as a function of pH, ionic strength and DMSO fraction.

This work establishes a direct link between solvent-controlled self-assembly and material function, providing a basis for designing tunable peptide hydrogels as platforms for AMP incorporation and stabilization in biologically relevant environments.

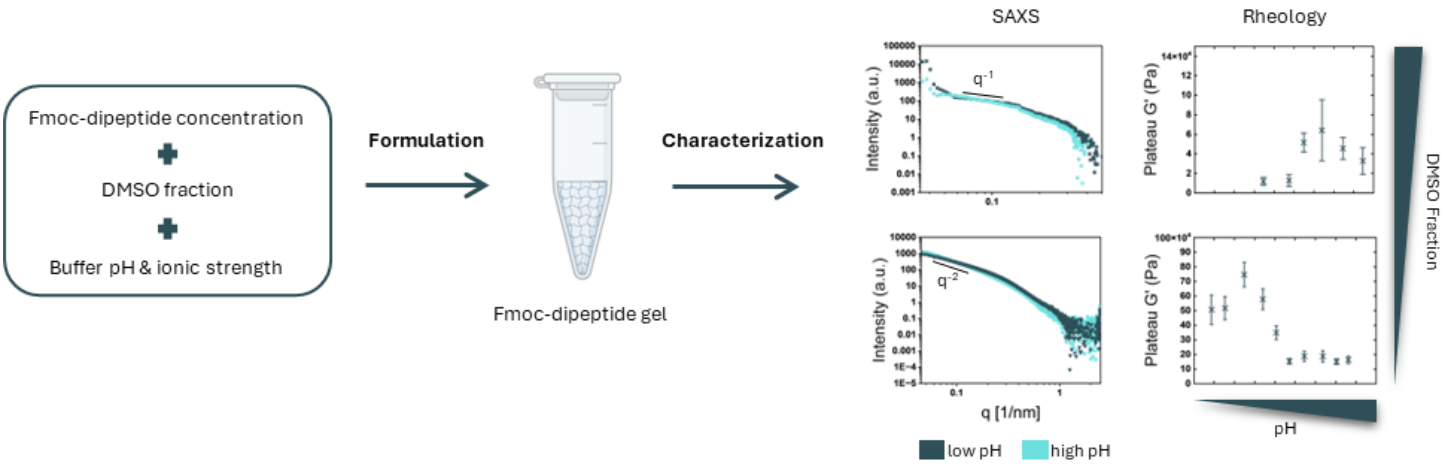


***Figure 1**. From formulation to Fmoc-dipeptide gel structure and viscoelastic properties. Created with https://BioRender.com*

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