

## <mark>OC n° XX</mark>

## ULTRASHORT CATIONIC PEPTIDE FMOC-FFK AS HYDROGEL BUILDING BLOCK FOR POTENTIAL BIOMEDICAL APPLICATIONS

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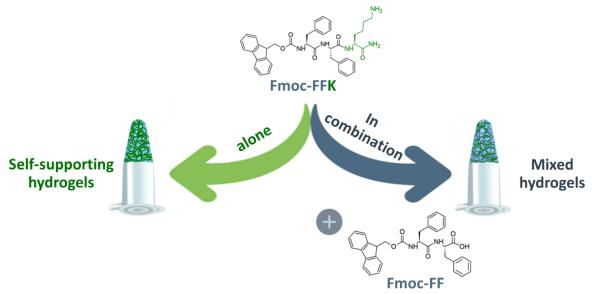
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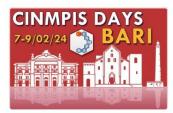
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## Abstract

Fmoc-diphenylalanine (Fmoc-FF) is a well-known low-molecular-weight peptide hydrogelator.<sup>1</sup> This simple all-aromatic peptide can generate self-supporting hydrogel materials, which have been proposed as novel materials for diagnostic and pharmaceutical applications. Our knowledge of the molecular determinants of Fmoc-FF aggregation is used as a guide to design new peptide-based gelators, with features for the development of improved tools.<sup>2</sup> Here, we enlarge the plethora of Fmoc-FF-based hydrogelated matrices by studying the properties of the Fmoc-FFK tripeptide, alone or in combination with Fmoc-FF.<sup>3</sup> For multicomponent matrices, the relative weight ratios between Fmoc-FFK and Fmoc-FF (specifically, 1/1, 1/5, 1/10, and 1/20 w/w) are evaluated. All the systems and their multiscale organization are studied using different experimental techniques, including rheology, circular dichroism, Fourier transform infrared spectroscopy, and scanning electron microscopy (SEM). Preliminary profiles of biocompatibility for the studied systems are also described by testing them in vitro on HaCaT and 3T3-L1 cell lines. Additionally, the lysine (K) residue at the C-terminus of the Fmoc-FF moiety introduces into the supramolecular material chemical functions (amino aroups) which may be useful for modification/derivatization with bioactive molecules of interest, including diagnostic probes, chelating agents, active pharmaceutical ingredients, or peptide nucleic acids.<sup>4</sup>

**Keywords:** peptide materials; hydrogels; cationic peptide; Fmoc-FF analogues; soft materials





**Figure 1.** Schematic representation of the Fmoc-FFK tripeptide alone, forming self-supporting hydrogels and the well-studied Fmoc-FF dipeptide. The latter, in combination with Fmoc-FFK, forms multicomponent Fmoc-FFK/Fmoc-FF hydrogels in which the two peptides are mixed in 1/1, 1/5, 1/10, and 1/20 (w/w) molar ratios.

[1] Diaferia, C.; Rosa, E.; Morelli, G.; Accardo, A. *Fmoc-Diphenylalanine Hydrogels: Optimization of Preparation Methods and Structural Insights.* Pharmaceuticals **2022**, *15*, 1048.

[2] Giordano, S.; Gallo, E.; Diaferia, C.; Rosa, E.; Carrese, B.; Borbone, N.; Scognamiglio, P.L.; Franzese, M.; Oliviero, G.; Accardo, A. *Multicomponent Peptide-Based Hydrogels Containing Chemical Functional Groups as Innovative Platforms for Biotechnological Applications.* Gels **2023**, *9*, 903.

[3] Gallo, E.; Diaferia, C.; Giordano, S.; Rosa, E.; Carrese, B.; Piccialli, G.; Borbone, N.; Morelli, G.; Oliviero, G.; Accardo, A. *Ultrashort Cationic Peptide Fmoc-FFK as Hydrogel Building Block for Potential Biomedical Applications.* Gels **2024**, *10*, 12.

[4] Terracciano M., Fontana F., Falanga A.P., D'Errico S., Torrieri G., Greco F., Tramontano C., Rea I., Piccialli G., De Stefano L., Oliviero G., Santos H. A., Borbone N., *Development of Surface Chemical Strategies for Synthesizing Redox-Responsive Diatomite Nanoparticles as a Green Platform for On-Demand Intracellular Release of an Antisense Peptide Nucleic Acid Anticancer Agent.* Small **2022**, *18*, 2204732.