Crosslink reaction of α-/ω-substituted diacrylate polyethylene-glycol in Fmoc-FF hydrogel matrices

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TOPIC: **Peptide materials**

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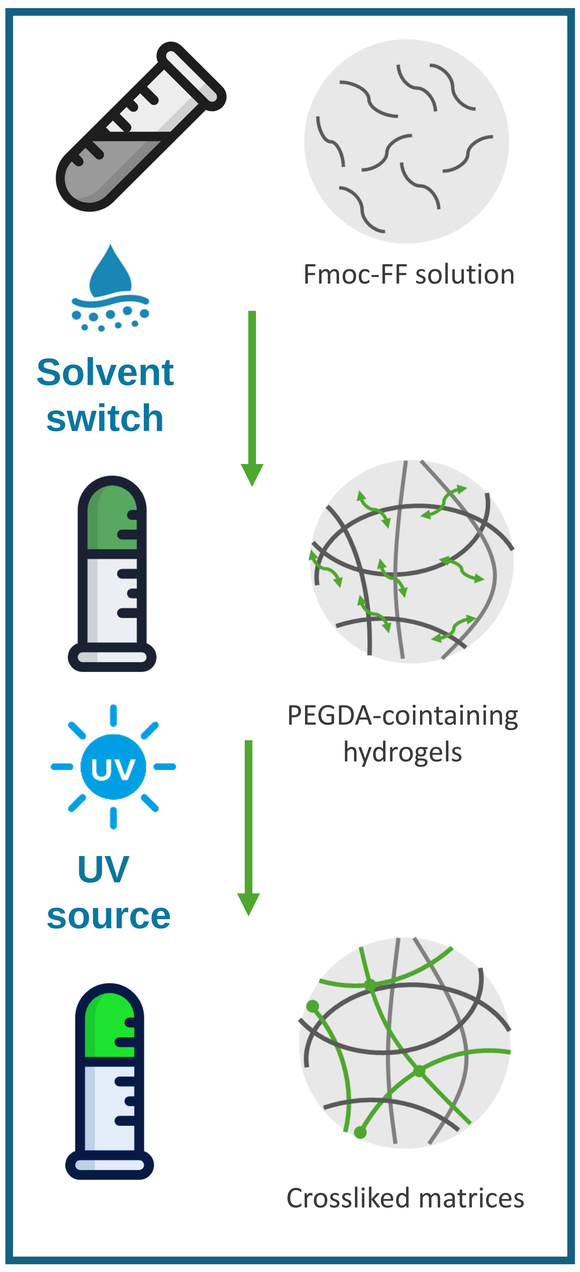
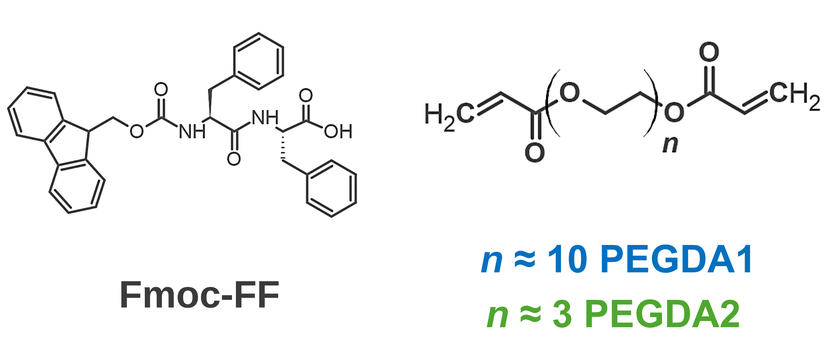
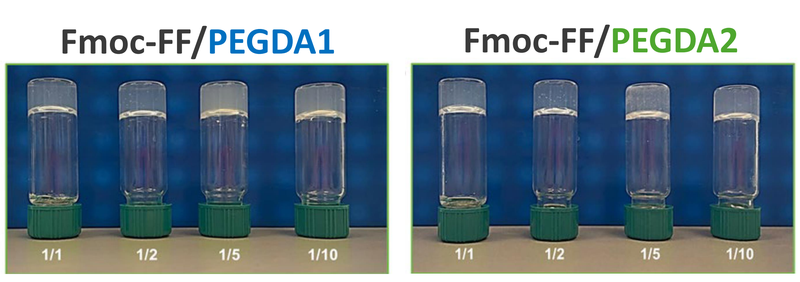
Abstract: Peptides can form **supramolecular gels,** as N$^{\alpha}$-9-fluorenylmethoxycarbonyl protected diphenylalanine (**Fmoc-FF).** [1] The Fmoc-FF hydrogel functional properties are modified incorporating additional entity. Multicomponent matrices of Fmoc-FF and diacrylate **α-/ω-substituted polyethylene glycol derivatives (PEGDAs)** were formulated, by using **two different PEGDA** molecular weight (575 and 250 Da for **PEGDA1** and **PEGDA2**, respectively) at **different molar peptide/polymer ratio (1/1, 1/2, 1/5 ,1/10).**[2] The acrylate moieties were **cross-linked by UV irradiation at 365 nm**, thus production no-covalent/covalent interpenetrated networks (IPNs). The properties of final materials (in terms of permeability, rheological response, and topography) were modulated by tuning the polymerization time. [3]





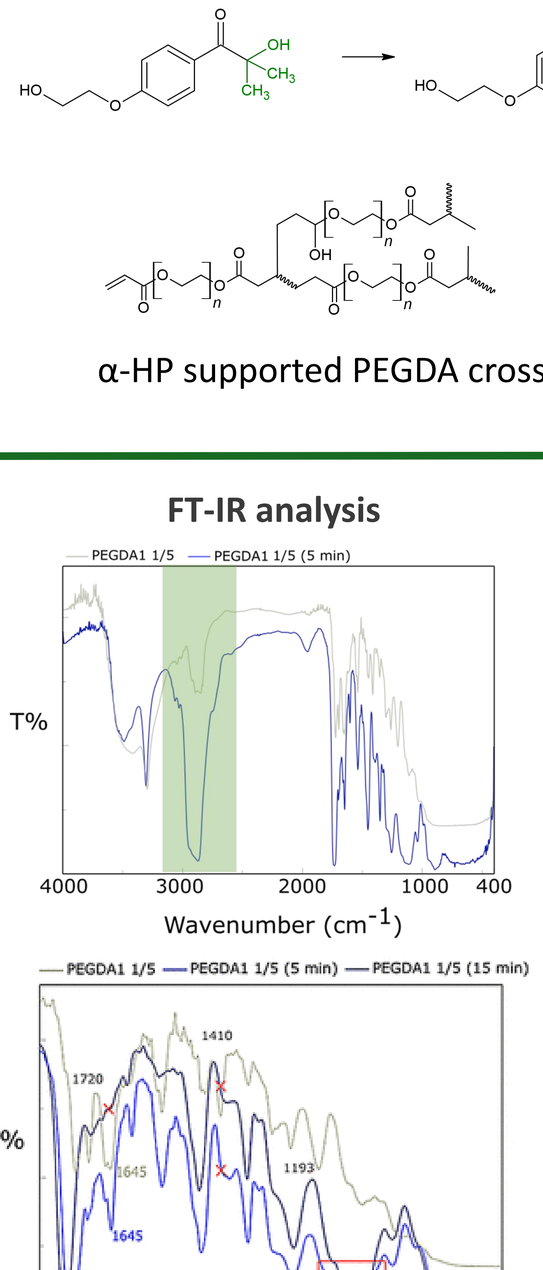
Chemical structures of hydrogel components

Hydrogel components: Fmoc-FF and α-/ω-substituted polyethylene glycol derivatives (PEGDAs, Mw 575 and 250 Da for **PEGDA1** and **PEGDA2**, respectively). Different molar peptide/polymer ratio (1/1, 1/2, 1/5 ,1/10) were tested Fmoc-FF was dissolved in DMSO at 100 mg/mL. PEGDA solution were obtained in water.



Inverted test tube for mixed matrices

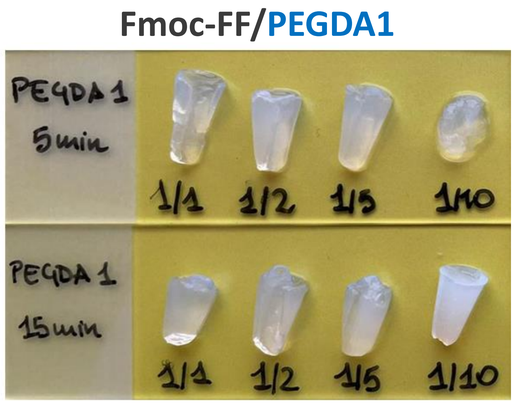
Multicomponent hydrogel formulation: For all the tested experimental conditions, self-supporting hydrogels are formed, using a **solvent switch** approach (dilution of Fmoc-FF stock with PEGDA solutions in water at 0.5 wt%). Both PEGDAs are quantitatively included (no syneresis effects). Gelation kinetics are not affected



α-HP supported PEGDA crosslink reaction

Crosslinking PEGDAs: acrylic groups can cross-link under **UV–vis irradiation (365 nm)** *via* a radical mechanism favored by a photoinducer (α-HP, Irgacure 2959). Two **irradiation times (5 and 15 min)** were tested. The cross-linked matrices have been characterized from different points of view to emphasize the emergent properties of the proposed materials, expanding their possible applicative scenario.

Fmoc-FF/PEGDA1



Fmoc-FF/PEGDA2

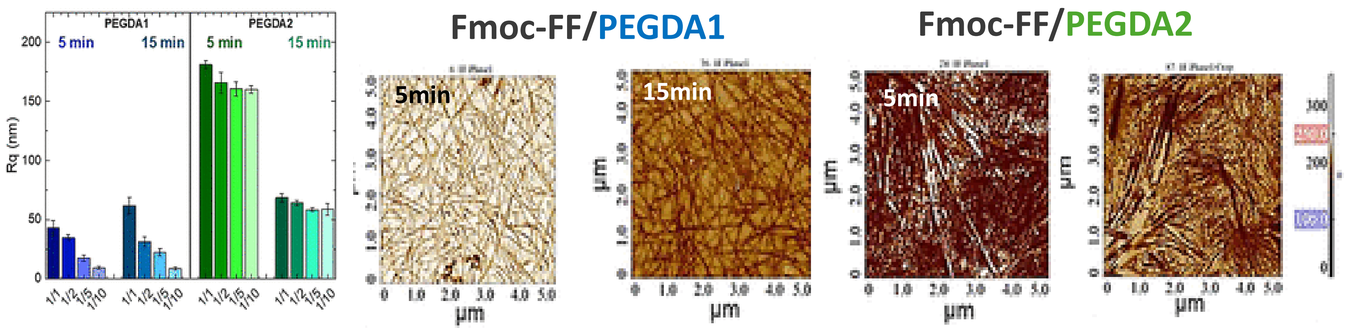
Macroscopical PEGDAs gels. A progressive transparency decreases with the increase in time exposure is detected (UV–vis). This evidence was correlated with the formation of light scattering supramolecular elements mainly resulting from the density of acrylic mesh.

FT-IR analysis

FT-IR analysis. Increase band at 2920–2880 cm^{-1} (green region C–H stretching); modification of 1410 cm^{-1} band (deformation C═CH_2) and the decrease in the intensity of acylic C═O signal (1193 cm^{-1}). Broad band (1190–1050 cm^{-1}) of primary alcohols post-reaction.

Rheological characterization: Extrapolated storage modulus (G') and loss modulus (G") from oscillation strain sweeps, tan δ (G"/G'), breakage point of strain (ω*c*), and frequency (ν*c*).

		5min					*15 min*				
	Ratio	**G'(Pa)**	**G''(Pa)**	**tanδ**	**ωc (%)**	**νc (Hz)**	**G'(Pa)**	**G''(Pa)**	**tanδ**	**ωc (%)**	**νc (Hz)**
PEGDA1	1/1	3224	560	0.173	16	32	3600	620	0.172	20	35
	1/2	2172	334	0.154	17	35	2460	380	0.154	28	35
	1/5	1660	225	0.135	9	39	1760	236	0.134	11	43
	1/10	960	114	0.118	26	49	1476	179	0.121	30	60
PEGDA2	1/1	5380	782	0.145	16	-	5941	855	0.144	27	-
	1/2	4590	605	0.132	18	-	8321	812	0.117	31	-
	1/5	2160	263	0.122	14	-	5590	1255	0.224	43	-
	1/10	4060	45	0.100	38	-	9390	1428	0.152	54	-



AFM analysis. R*q* roughness histograms (left). AFM semicontact phase-contrast mode images. The number of fibers decreases with the increase of PEGDA1 ratio, independently from the UV exposure time. A similar trend was found in the PEGDA2 samples. However, in all the PEGDA2 samples, an increase in the fiber number, as well as in the fiber dimension, was detected. OrientationJ tool analysis showed also a preferential orientation for all the PEGDA2-cointaining gels (θ~0 deg). **Topography is influenced by PEGDA molecular weight and UV-exposure.**

References: [1] Diaferia C. *et al.* J. Mater. Chem. B, 2019,7, 5142-5155. [2] Rosa E. *et al* Gels, 2022, 8(12), 831. [3] Rosa E. *et al* ACS Appl. Polym. Mater. 2024, 6, 12, 7197–7208