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High-Loading Seplife Fmoc-RinkAmide-PS-PEG Resin: A Robust Solid Support for the Synthesis of Complex Peptides and Tirzepatide

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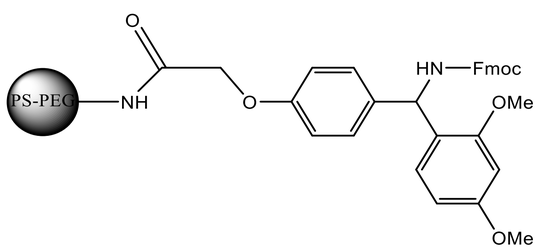
Reference: A. Kumar, P.K. Kabwe, M. Alhassan, W. Hou, C. Wang, C. Zhang, Y. Li, XK. Kou, S. Serban, A. Basso, A. Sharma, BG. De La Torre, F. Albericio. "An Original PEG-Functionalized PS Resin Enables Synthesis of Difficult Peptides: Application to Tirzepatide." ChemistrySelect11, no. 6 (2026): e06541

01 Introduction

- **The Problem**: Standard Polystyrene (PS) is hydrophobic, causing poor swelling in solvents like DMF. This leads to peptide aggregation, incomplete reactions, and low purity, especially in complex sequences.
- **The Trade-off:** While existing PEG-modified resins improve solvation, they typically suffer from significantly reduced loading capacity.
- **Solution**: Seplife® Fmoc-RinkAmide-PS-PEG resin uses a PS matrix cross-linked with 1% divinylbenzene. A proprietary PEG grafting process achieves high loading while maintaining excellent swelling in polar and non-polar solvents.
- **Validation**: Performance was confirmed via successful synthesis of a diverse library, including small pentapeptides, the ACP decapeptide, Afamelanotide (13-mer) and Tirzepatide (39-mer).

02 Seplife® Fmoc-RinkAmide-PS-PEG Resin general characteristics

Product	Seplife® Fmoc-RinkAmide-PS-PEG Resin
Matrix	Crosslinked polystyrene grafted with polyethylene glycol
Substitution (mmol/g)	<0.2; 0.2-0.3; 0.3-0.4; 0.4-0.5
Particle size range (micron)	100-250



Properties

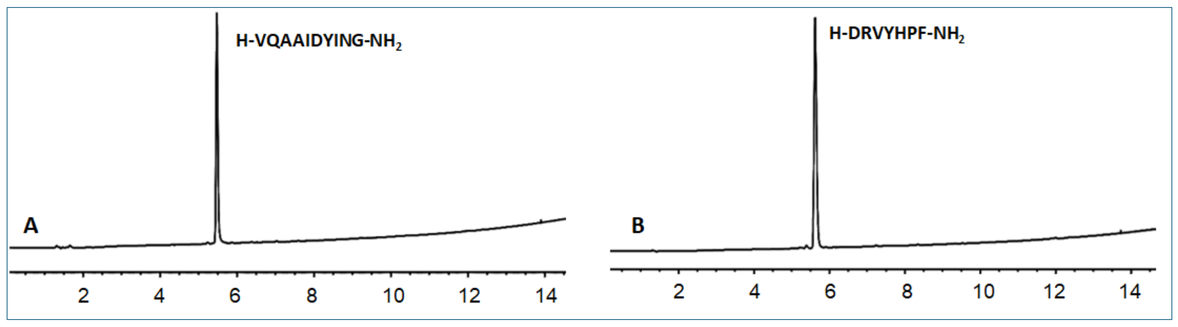
- **Enhanced Stability**: PEG is grafted onto a low crosslinked polystyrene (PS) matrix via an ethyl ether group, which increases acid treatment stability and minimizes PEG leaching.
- The grafted copolymer shows modified physicochemical properties driven by the PEG moiety, combining hydrophobic and hydrophilic characteristics.
- **Fmoc SPPS Ready**: Functionalized with a modified Rink Amide linker, ideal for the Fmoc SPPS of peptide amides. Cleavage from this support is achieved by 95% TFA.

03 Short peptide synthesis using Seplife® Fmoc-RinkAmide-PS-PEG Resin

Short Peptide Synthesis Performance, using a standard Fmoc strategy with DMF as a solvent

- **High Efficiency**: Successfully synthesized a library of 5 to 20-mer peptides with crude purities up to 98%.
- **Performance Parity**: Demonstrated results equivalent or superior to leading commercial PEG-resins across various sequences.
- **Consistency**: Maintains high purity, proving the robustness of the Seplife® PS-PEG matrix.

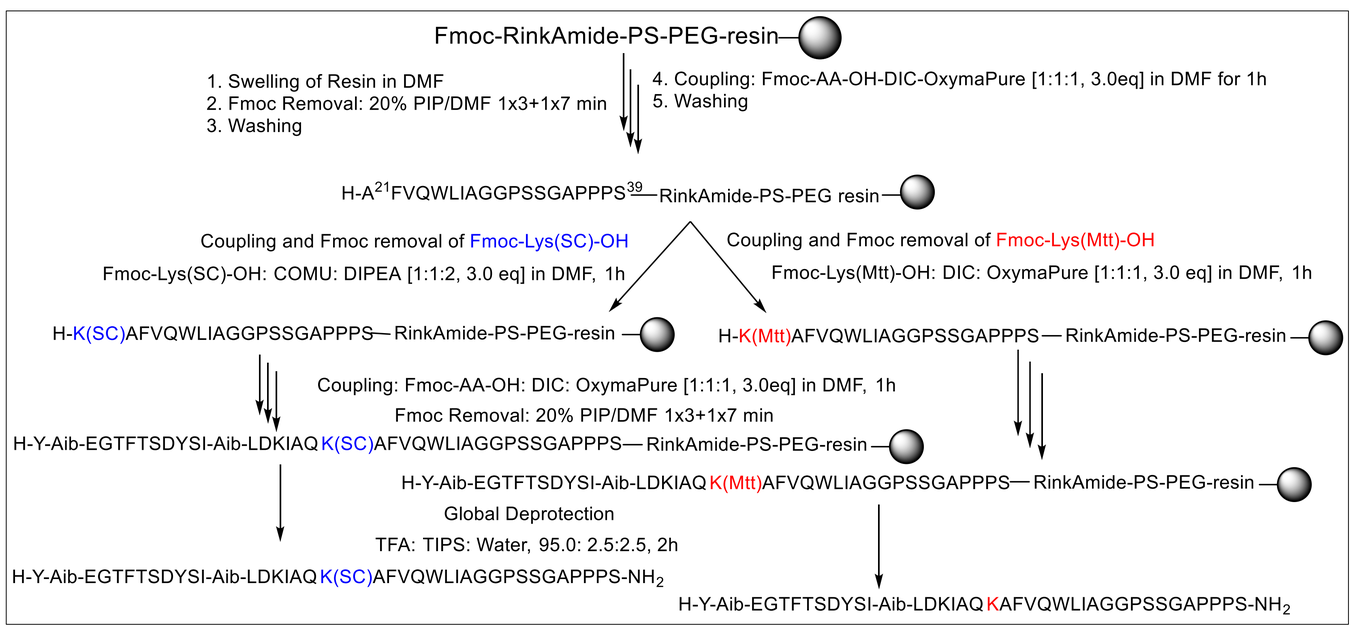
Peptide Sequence	Crude purity of peptides (%)	
	Seplife® Fmoc-RinkAmide-PS-PEG	Competitor PEG-resin
H-Tyr-Sar-Sar-Phe-Leu-NH2	98%	98%
H-Tyr-Ser-Ser-Phe-Leu-NH2	95%	NA
H-Asp-Arg-Val-Tyr-His-Pro-Phe-NH2	97%	97%
H-Val-Gln-Ala-Ala-Ile-Asp-Tyr-Ile-Asn-Gly-NH2	97%	97%
Ac-Ser-Tyr-Ser-Leu-Glu-His-Phe-Lys-Trp-Gly-Lys-Pro-Val-NH2	95%	97%

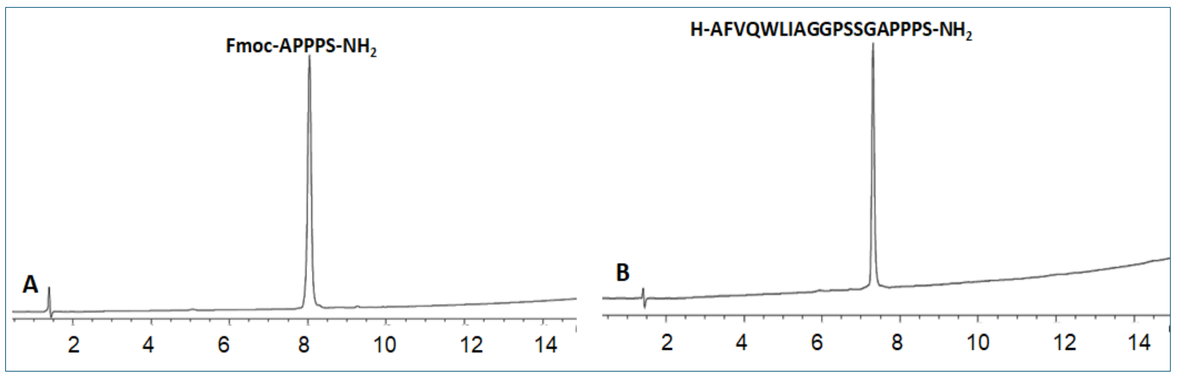


Representative analytical HPLC chromatograms of crude peptides,
A) ACP Decapeptide (H-VQAAIDYING-NH2), **(B)** H-DRVYHPF-NH2,
Method: (5-95 % B into A) in 15 min; flow rate: 1 mL/min; detection at 220 nm.

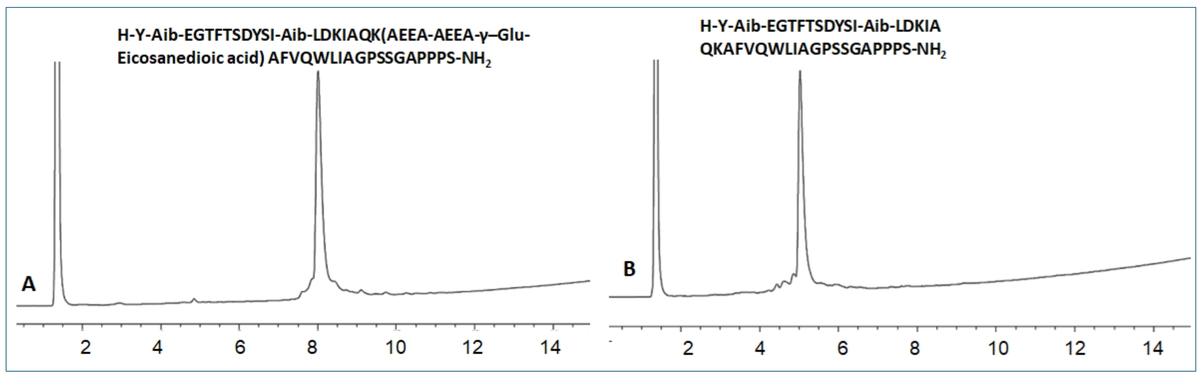
04 Tirzepatide SPPS synthesis using Seplife® Fmoc-RinkAmide-PS-PEG Resin

- **Objective**: Benchmark resin performance using a complex 39-amino acid therapeutic peptide.
- **Scale & Loading:** Synthesized at a 0.05 mmol scale using a loading of 0.37 mmol/g.
- **Dual-Route Strategy:** Validated success through both direct side-chain incorporation and on-resin modification (Fmoc-Lys(Mtt)-OH) at position 20.
- **In-Process Monitoring**: HPLC analysis of 5-mer and 19-mer fragments confirmed excellent purity throughout the assembly.
- **Final Result**: Both synthetic routes achieved a final product with 84% crude purity, demonstrating superior efficiency for long, complex sequence





HPLC analytical characterization of crude peptide 5-mer and 19-mer of Tirzepatide.
(A) Fmoc-APPPS-NH_2, Fmoc-35-39-NH_2, **(B)** H-AFVQWLIAGGPSSGAPPPS-NH_2
Method: (5-95 % B into A) in 15 min; flow rate: 1 mL/min; detection at 220 nm.



HPLC analytical characterization of crude peptide Tirzepatide
(A) H-Y-Aib-EGTFTSDYSI-Aib-LDKIAQK(AEEA-AEEA-γ–Glu-Eicosanedioic acid) AFVQWLIAGPSSGAPPPS-NH2
(B) H-Y-Aib-EGTFTSDYSI-Aib-LDKIAQKAFVQWLIAGPSSGAPPPS-NH2
Method: (30-95 % B into A) in 15 min; flow rate: 1 mL/min; detection at 220 nm

Conclusion

- **Versatile Performance**: Seplife® Fmoc-RinkAmide-PS-PEG resin where PEG is grafted onto PS is highly effective for the synthesis of long and challenging sequences, successfully producing peptides ranging from small pentapeptides to the 39-mer Tirzepatide.
- **Optimal Solvation**: The resin demonstrated excellent swelling in both DMF and DCM, ensuring efficient coupling and minimizing peptide aggregation.
- **Superior Productivity:** By modulating the PEG content, the resin achieves high loading capacities without sacrificing solvation or synthesis performance, with similar performance of other PEG-based PS resins containing more PEG and therefore inferior loading
- **High Purity Results**: Seplife® Fmoc-RinkAmide-PS-PEG-resin delivers high crude purity, proving to be a promising tool to produce complex therapeutic peptides.