https://doi.org/10.17952/37EPS.2024.P2175

Use of Green Solid Phase Peptide Synthesis to Obtain Tripeptide-85

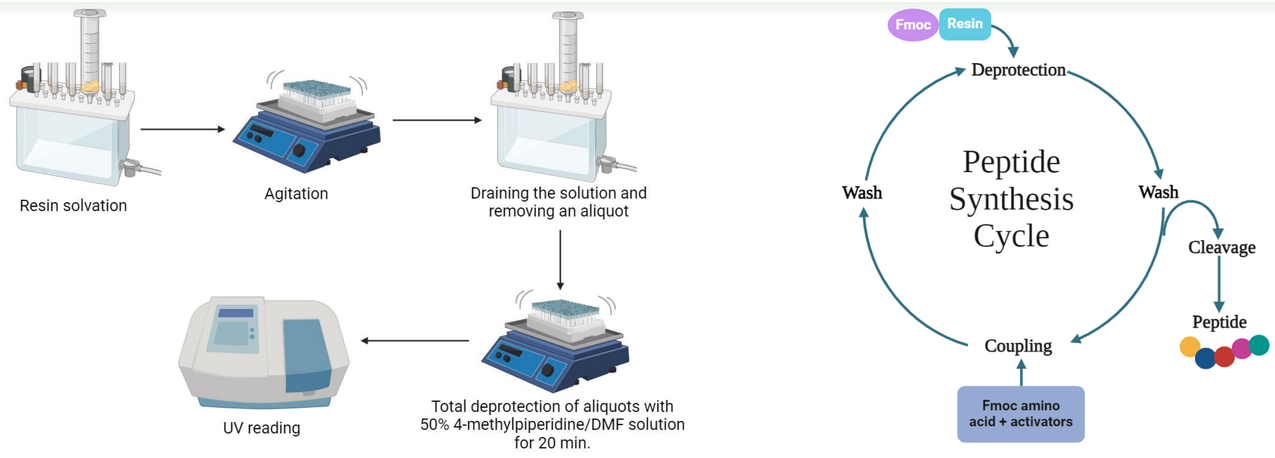
Brasil, M. C. O. A.[1]; Principal, C. R.[2]; Kuchenbecker, V.[2]; Katekawa, E.[2]; Magalhães, W. V.[2]; Cilli, E. M.[1]

mcoa.brasil@unesp.br; eduardo.cilli@unesp.br

[1]São Paulo State University (UNESP), Institute of Chemistry, Araraquara; [2]R&D, Chemyunion (Brasil)

ABSTRACT

Peptides have increasingly attracted the attention of the industry due to their applicability, safety profile, and possibility of conjugation with other molecules. Most peptides currently produced are obtained through solid phase peptide solid phase peptide synthesis (SPPS), but this methodology still uses solvents that are considered problematic from an ecological point of view, such as dimethylformamide (DMF)[1-3]. The objective of this study was to test green solvents in the SPPS protocol.



RESULTS

Deprotection analysis

Table 1: First amino acid deprotection analysis

Solvent	Temperature	% Deprotection Time						
		5	25	45	65	85	105	125
20% 4-methylpiperidine/DMF	Room temperature	100	-	-	-	-	-	-
50% Morpholine/ 2-MeTHF	Room temperature	63	83	96	100	-	-	-
	50°C	89	100	-	-	-	-	-
30% Imidazole/ DMF	Room temperature	18	36	52	66	78	90	100
	50°C	21	40	57	72	82	92	100
30% imidazole/ DMF	Room temperature	18	36	52	66	78	90	100
	50°C	21	40	57	72	82	92	100
25% Aminoethanol/ DMF	Room temperature	79	100	-	-	-	-	-
	50°C	100	-	-	-	-	-	-
25% 2-amino-2-methyl-1-propanol/ DMF	Room temperature	88	100	-	-	-	-	-
	50°C	79	91	100	-	-	-	-
25% 2-amino-2-methyl-1-propanol/ 2-MeTHF	Room temperature	26	46	62	75	85	93	100
	50°C	73	90	97	99	100	-	-

Peptide synthesis

Figure 1: Synthesis of the EVF peptide using the standard SPPS protocol.

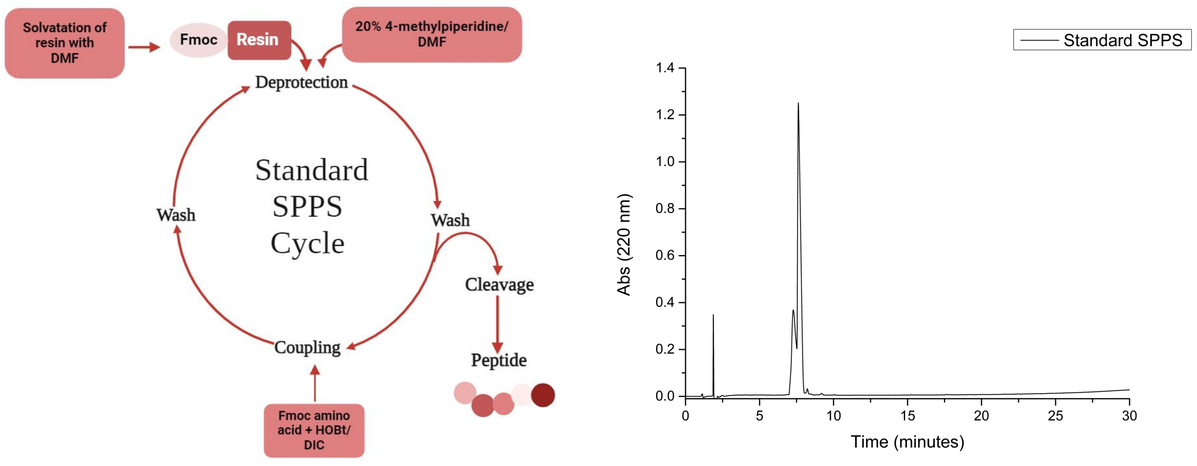


Figure 2: Synthesis of the EVF peptide using the partial GSPPS protocol with aminoethanol.

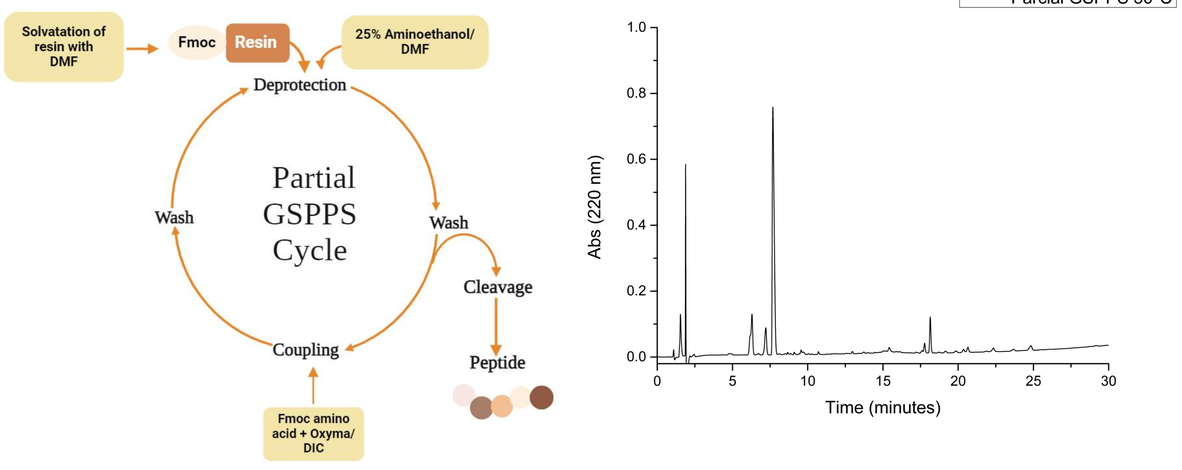


Figure 3: Synthesis of the EVF peptide using the partial GSPPS protocol with 2-amino-2-methyl-1-propanol.

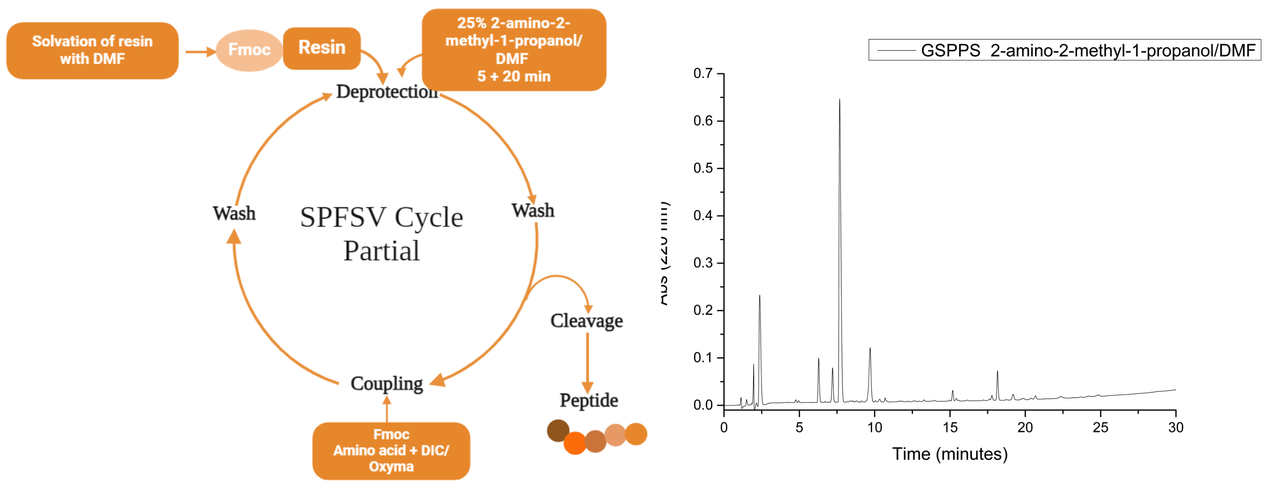


Figure 4: Synthesis of the EVF peptide using the GSPPS protocol with 2-amino-2-methyl-1-propanol in 2-MeTHF.

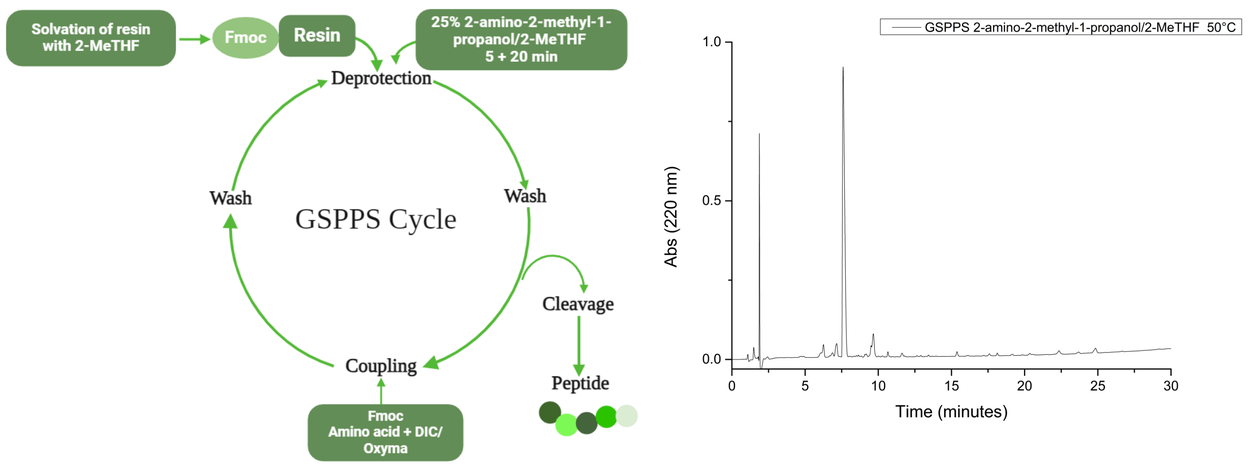
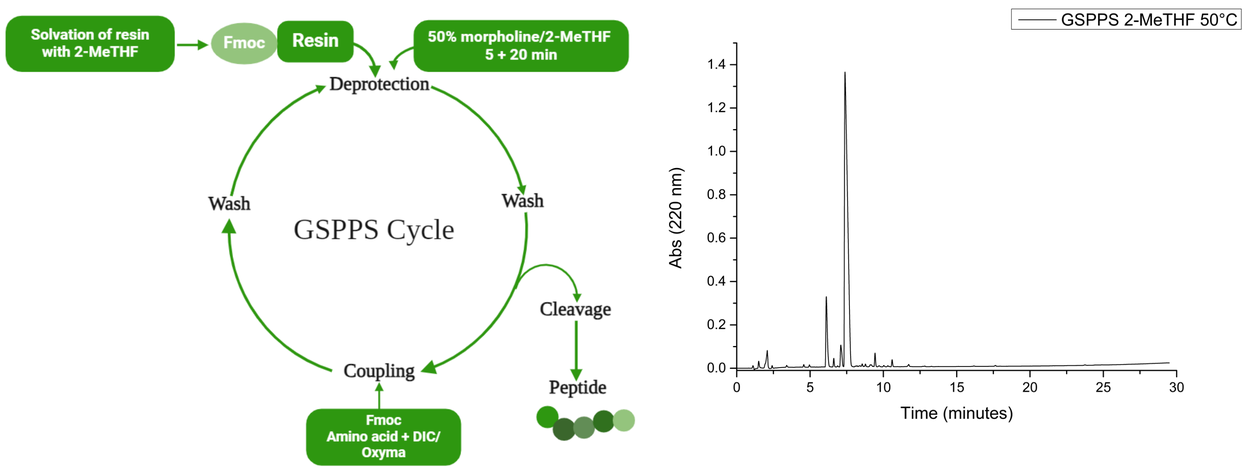


Figure 5: Synthesis of the EVF peptide using the GSPPS protocol with morpholine in 2-MeTHF.



CONCLUSION

The deprotection methods evaluated were efficient in deprotecting the Fmoc group, and the peptides obtained from the new protocols applied for synthesis presented a higher degree of purity than the peptide synthesized by the standard SPPS protocol.

REFERENCE

(1) AL MUSAIMI, O.; JAD, Y. E.; KUMAR, A.; EL-FAHAM, A.; COLLINS, J. M.; BASSO, A.; LA TORRE, B. G.; ALBERICIO, F. Greening the solid-phase peptide synthesis process. 2-methf for the incorporation of the first amino acid and precipitation of peptides after global deprotection. **Organic Process Research & Development**, v. 22, n. 12, p. 1809-1816, 2018.

(2) AL MUSAIMI, O.; TORRE, B. G.; ALBERICIO, F. Greening Fmoc/t Bu solid-phase peptide synthesis. **Green Chemistry**, v. 22, n. 4, p. 996-1018, 2020.

(3) FERRAZZANO, L.; CATANI, M.; CAVAZZINI, A.; MAETELLI, G.; CORBISIERO, D.; CANTELMI, P.; FANTONI, T.; MATTELLONE, A.; DE LUCA, C.; FELLETI, S.; CABRI, W. TOLOMELLI, A. Sustainability in peptide chemistry: current synthesis and purification technologies and future challenges. **Green Chemistry**, v. 24, n. 3, p. 975-1020, 2022.

ACKNOWLEDGMENTS

FAPESP · CNPq Conselho Nacional de Desenvolvimento Científico e Tecnológico · LASEBio Laboratório de Síntese e Estudos de Biomoléculas · CHEMYUNION Inspiring Innovation