Synthesis of PLGA Nanoparticles Encapsulated with Immunodominant $MOG_{35–55}$ Peptide Analogues for the Treatment of Multiple Sclerosis

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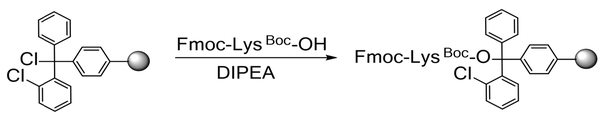
https://doi.org/10.17952/38EPS.2026.P357

Introduction

Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system (CNS), characterized by inflammation and demyelination[1]. $MOG_{35–55}$ is an immunodominant myelin epitope widely used in experimental autoimmune encephalomyelitis (EAE), a principal animal model of MS[1, 2]. In this study, our aim was to modulate the pathogenic T-cell response, the TCR-interacting residues **Arg^{41} and Arg^{46} of $MOG_{35–55}$ were replaced with Ala**, generating **$[Ala^{41}]MOG_{35–55}$** and **$[Ala^{41,46}]MOG_{35–55}$**, respectively[3]. The peptide analogues were **encapsulated in PLGA nanoparticles** to protect the peptides from degradation and enable their sustained and controlled release, providing a suitable delivery strategy for subsequent *in vivo* evaluation in the EAE model[4].

1 Solid Phase Peptide Synthesis on 2-CLTR-Cl



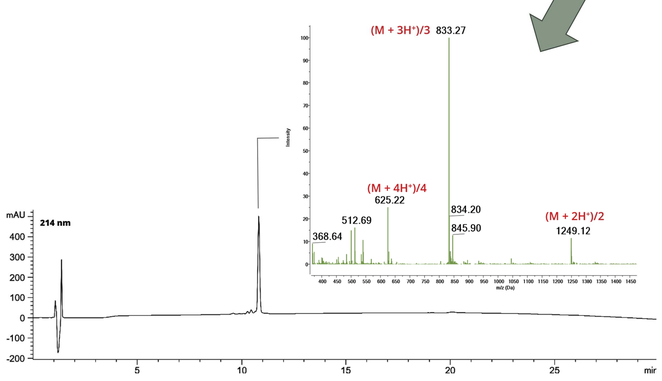
1) 25% 4-Methylpiperidine/DMF — 2) Fmoc-AA-OH, HOBt, DIC

Met-Glu tBu-Val-Gly-Trp Boc-Tyr tBu-X_{AA}-Ser tBu-Pro-Phe-Ser tBu-Y_{AA}-Val-Val-His Trt-Leu-Tyr tBu-Arg Pbf-Asn Trt-Gly-Lys Boc-O

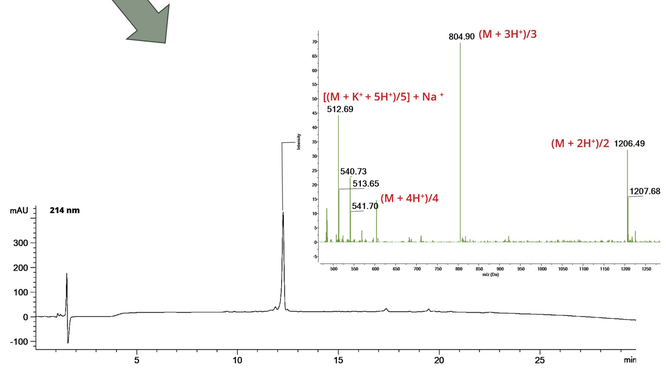
1) DCM/TFE, (7: 3), 1 h
2) TFA/DCM/EDT, (95: 4: 1), 5 h

H_2N-Met-Glu-Val-Gly-Trp-Tyr- X_{AA}-Ser-Pro-Phe-Ser- Y_{AA}-Val-Val-His-Leu-Tyr-Arg-Asn-Gly-Lys-COOH

X_{AA}: Ala , Y_{AA}: Arg

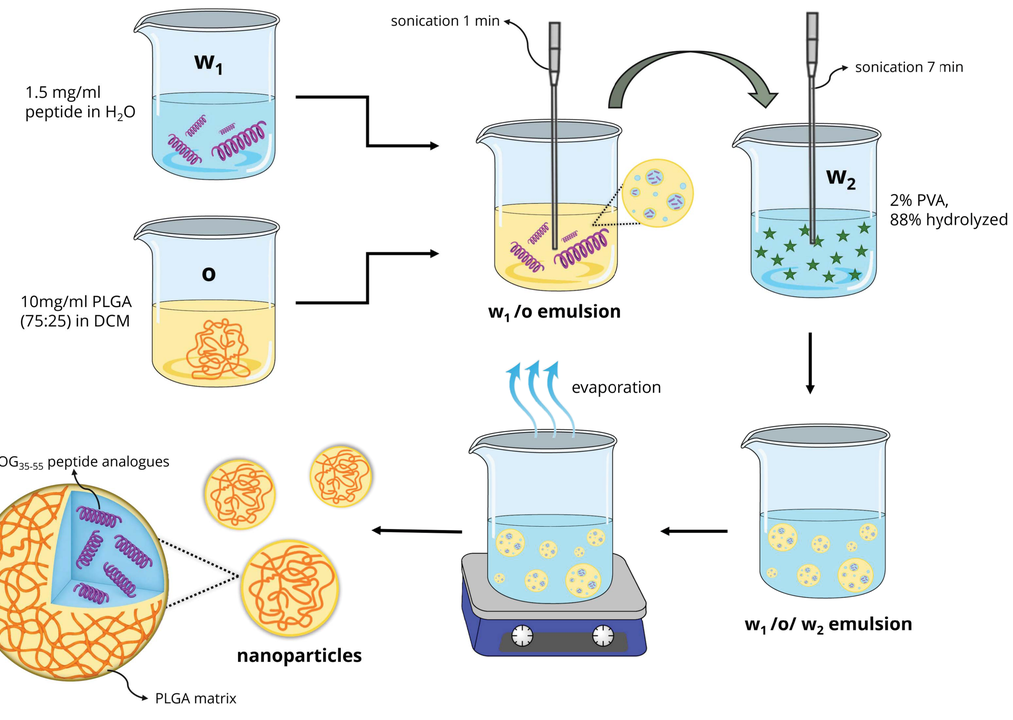


X_{AA}: Ala , Y_{AA}: Ala



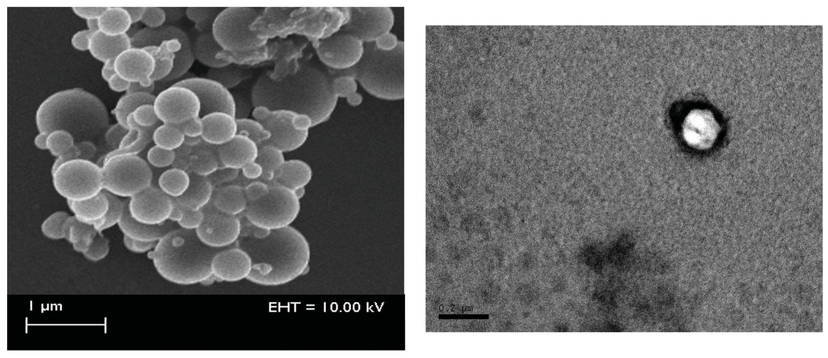
2 Preparation of PLGA Nanoparticles

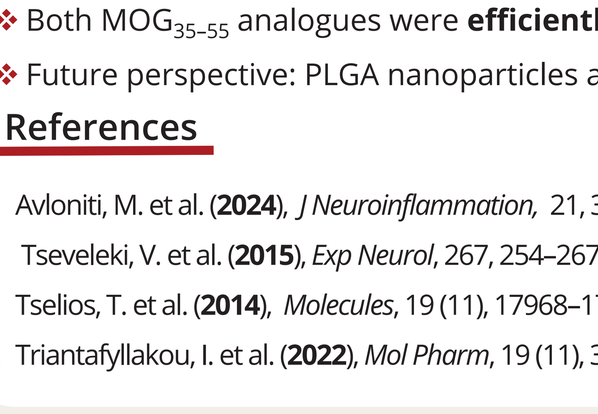
❖ Double emulsion technique: water - in – oil - in - water



3 Characterization of PLGA Nanoparticles

$[Ala^{41}]MOG_{35-55}$





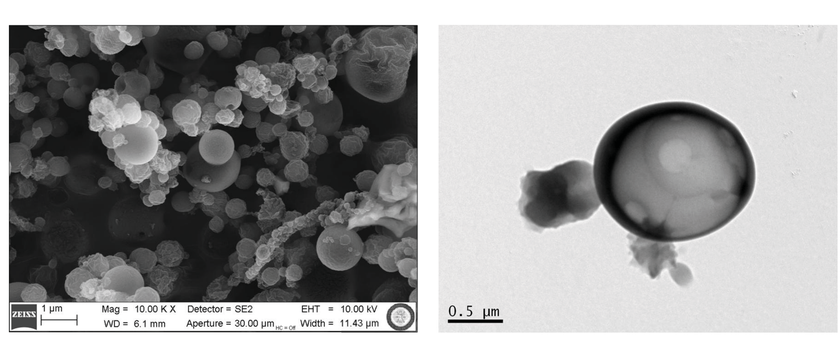
Particle size (average): **378.4 nm**

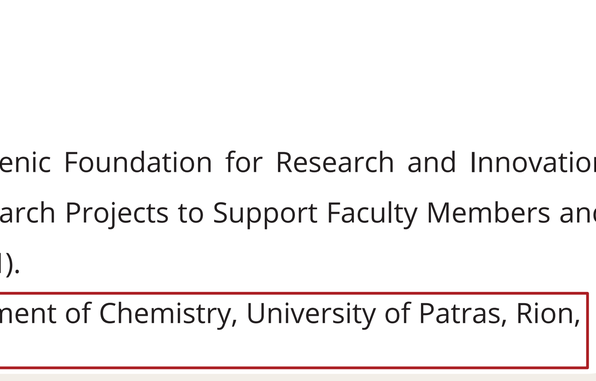
PDI: **0.4**

ζ-potential: **-34.8V**

Encapsulation efficiency: **84%**

$[Ala^{41, 46}]MOG_{35-55}$





Particle size (average): **442.9 nm**

PDI: **0.45**

ζ-potential: **-33.5V**

Encapsulation efficiency: **79%**

Both nanoparticle formulations showed heterogeneous particle size distributions within the **300–500 nm range**, with a minor population of larger particles.

Conclusions

❖ Successful synthesis of **$[Ala^{41}]MOG_{35–55}$** and **$[Ala^{41,46}]MOG_{35–55}$** peptide analogues

❖ **PLGA nanoparticles** were successfully prepared using a **W/O/W double-emulsion** approach, although further optimization of the particle size is required.

❖ Both $MOG_{35–55}$ analogues were **efficiently encapsulated** within PLGA nanoparticles

❖ Future perspective: PLGA nanoparticles are a **promising delivery strategy** for *in vivo* evaluation in the EAE model

References

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Acknowledgments

The research project is funded by the Hellenic Foundation for Research and Innovation (H.F.R.I.) under the "3rd Call for H.F.R.I. Research Projects to Support Faculty Members and Researchers" (H.F.R.I. Project Number: **25251**).

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