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

Georgia Biniari ‡, Iro Triantafyllakou ‡, Carmen Simal, Spyridon Mourtas, Theodore Tselios

Department of Chemistry, University of Patras, 26504 Rion, Greece

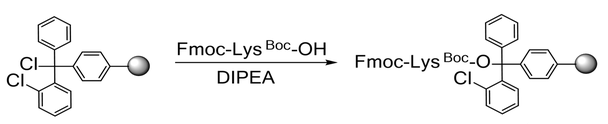
‡ These authors contributed equally to this work.

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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



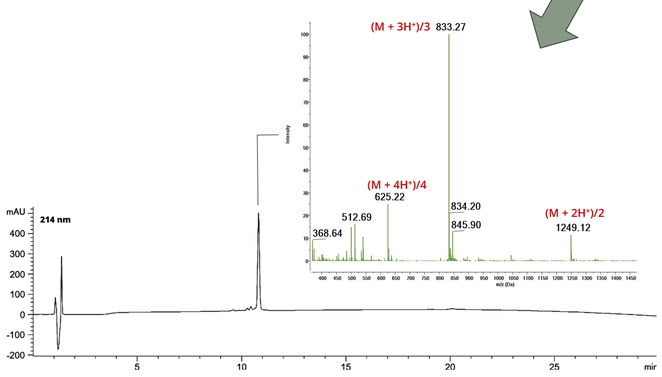
1) 25% 4-Methylpiperidine/DMF ⟲ 2) Fmoc-AA-OH, HOBt, DIC

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-

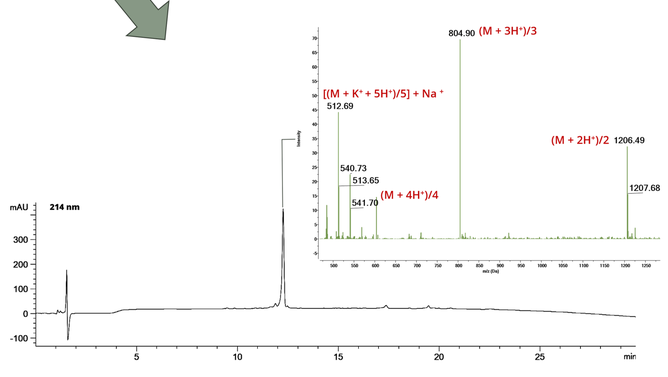
1) DCM/TFE, (7: 3), 1 h
2) TFA/DCM/EDT, (95: 4: 1), 5 h

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

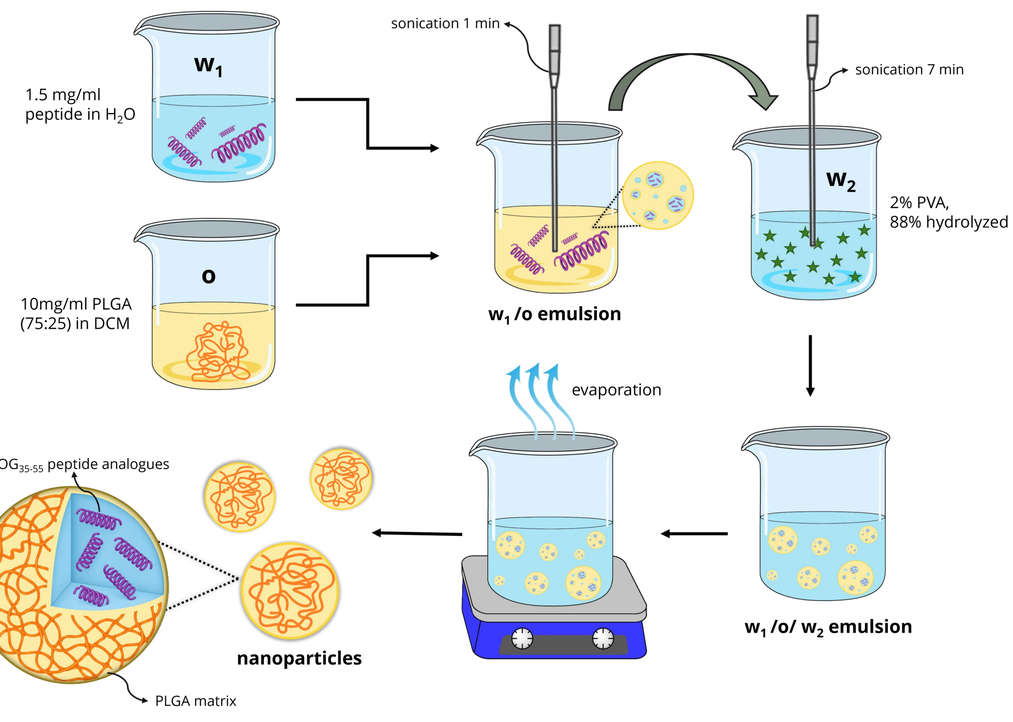


X_{AA}: Ala , Y_{AA}: Ala



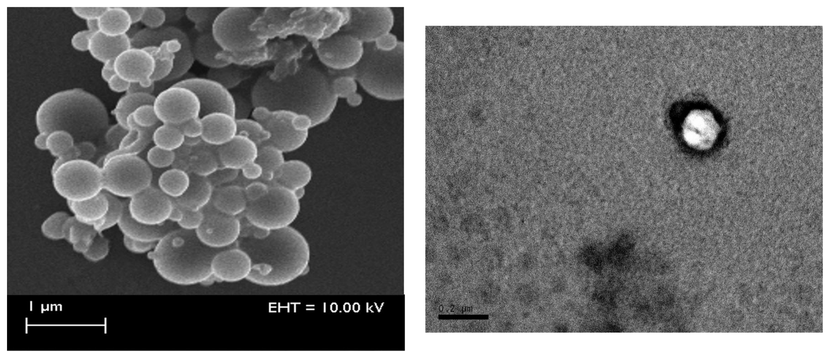
2 Preparation of PLGA Nanoparticles

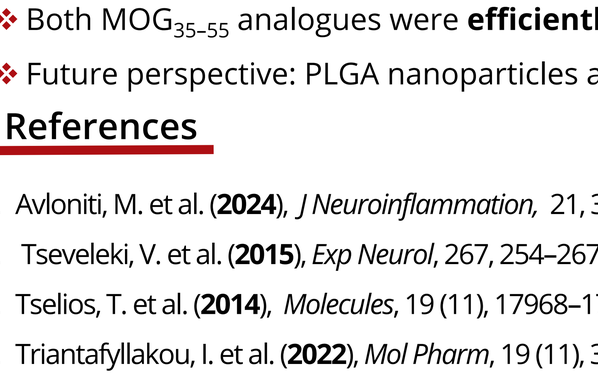
❖ Double emulsion technique: water - in – oil - in - water



3 Characterization of PLGA Nanoparticles

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





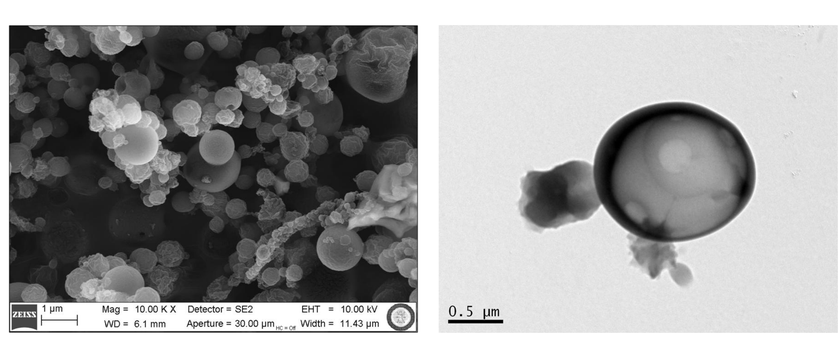
Particle size (average): **378.4 nm**

PDI: **0.4**

ζ-potential: **-34.8V**

Encapsulation efficiency: **84%**

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

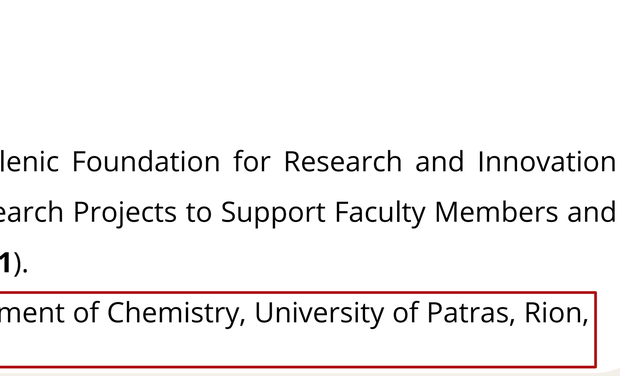


Particle size (average): **442.9 nm**

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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Contact details: Theodore Tselios, Department of Chemistry, University of Patras, Rion, Greece. **ttselios@upatras.gr**