Effect of Alzheimer Peptide Aβ(1-40) on Membrane Structure

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Introduction

Amyloid plaques are a hallmark of central nervous systems affected by Alzheimer's disease. These plaques are formed by fibrils in which the main component is the so called β-amyloid peptide Aβ(1-40) (1). The aggregation capacity of amyloid peptides depends on a conformational change which implies the conversion of α-helical structure into β structures. The toxicity of the amyloid aggregates is related to the existence of low molecular weight oligomers present during the aggregation process. The presence of biological membranes, could play an important role in amyloid aggregation (2). In the present work we have studied, using Small Angle X-Ray scattering (SAXS), the influence of Alzheimer's amyloid peptide Aβ(1-40) on the structure of model biological membranes of different lipid composition.

Results

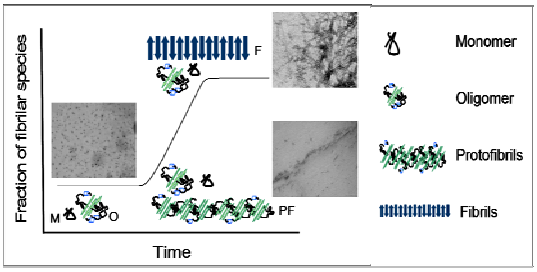

Fig 1: Fibril formation following sigmoidal kinetics, usually interpreted as a nucleation-dependent polymerization processes. Such processes evolve through two distinct phases: formation of β-sheet oligomers from unordered monomers (lag phase) and oligomers assembly to form fibrils (elongation phase). In the latter, the oligomers β-sheet converts into fibrilar β-sheet (3).

Lipid composition	Charge (mV)	Anisotropy
PC	- 7.0	0.0736 ± 0.0139
PC:PA (9:1)	- 55.0	0.0712 ± 0.0044
Raft like, PC:SM:Chol (2:1:1)	-9.4	0.1939 ± 0.0248

Table I. Z-potential (dependant on the surface charge density) and DPH anisotropy (as an estimation of membrane fluidity) of the model membrane systems used in the present study.

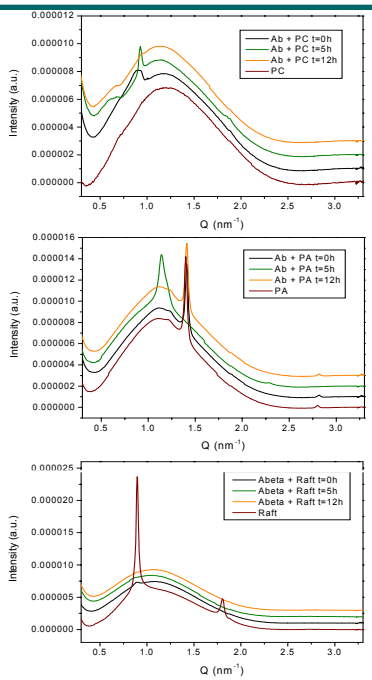

Fig 2. SAXS patterns of liposomes of different lipid composition in the presence and absence of the Aβ(1-40) peptide. SAXS patterns have been offset for the sake of clarity.

Discussion

The results show that the presence of the peptide during the formation of PC liposomes (zwitterionic and fluid) causes the formation of multilamellar structures (appearance of Bragg reflections in the SAXS pattern). Bragg reflections are not observed when PC liposomes are formed in the absence of peptide.

In negatively charged liposomes (10% of PA) the presence of the peptide implies a shift of the Bragg reflections already present in the absence of peptide.

Finally, in rigid membranes (raft-like) the peptide seems to hamper the formation of multillamelar liposomes, observable in the absence of peptide.

In conclusion, it is apparent from the work that the influence of Aβ(1-40) on membrane structure depends on the liposomes surface charge and fluidity.

References

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