Phosphate and HEPES buffers potently affect the fibrillation and oligomerization mechanism of Alzheimer's Aβ peptide.

Garvey M, Tepper K, Haupt C, Knüpfer U, Klement K, Meinhardt J, Horn U, Balbach J, Fändrich M (2011) Phosphate and HEPES buffers potently affect the fibrillation and oligomerization mechanism of Alzheimer's Aβ peptide. *Biochem Biophys Res Commun* 409(3), 385-388.

Details

PubMed

Abstract

The oligomerization of Aβ peptide into amyloid fibrils is a hallmark of Alzheimer's disease. Due to its biological relevance, phosphate is the most commonly used buffer system for studying the formation of Aβ and other amyloid fibrils. Investigation into the characteristics and formation of amyloid fibrils frequently relies upon material formed in vitro, predominantly in phosphate buffers. Herein, we examine the effects on the fibrillation and oligomerization mechanism of Aβ peptide that occur due solely to the influence of phosphate buffer. We reveal that significant differences in amyloid fibrillation are observed due to fibrillation being initiated in phosphate or HEPES buffer (at physiological pH and temperature). Except for the differing buffer ions, all experimental parameters were kept constant. Fibril formation was assessed using fluorescently monitored kinetic studies, microscopy, X-ray fiber diffraction and infrared and nuclear magnetic resonance spectroscopies. Based on this set up, we herein reveal profound effects on the mechanism and speed of Aβ fibrillation. The three histidine residues at positions 6, 13 and 14 of Aβ(1-40) are instrumental in

these mechanistic changes. We conclude that buffer plays a more significant role in fibril formation than has been generally acknowledged.

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Identifier

doi: 10.1016/j.bbrc.2011.04.141

PMID: 21575606