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Metal ion binding to amyloid peptide fragments: Biochemical and biomedical involvement

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Biochemistry of Alzheimer's disease (AD) is related to the conformational changes of amyloid-β peptides, which result in peptide oligomerization and fibril formation and, finally, in the appearance of senile plaques and extensive neuronal loss. Unfortunately, the factors regulating the process of plaque-associated beta-amyloid peptide (Aβ) aggregation are only partly understood. β-Amyloid peptide fragments have been synthesized by SPPS according to Boc/Bzl strategy. Binding of metal ions to β-amyloid peptides was studied at pH 7.4 or 6.6. It was found that Aβ(1-10) peptide binds only one Cu(II) ion at pH 7.4. However, the intensity of peak corresponding to the doubly charged ion $[M+Cu]^{2+}$ increases significantly with time and copper concentration. Aβ(1-16) peptide may bind one Cu(II) at 1:1 and 1:2 peptide-Cu ratio, and one and two Cu(II) at a peptide-Cu ratio of 1:10. Copper binding to Aβ fragments changed much the peptide conformation. MS spectra showed metal-induced aggregation, especially at pH 7.4. During the binding of Cu(II) to N-terminal truncated β-amyloid peptides, no copper ion was found to bind to Aβ(31-40) at 1:1 and 1:2 peptide: Cu(II) ratios. At 1:10 peptide-metal ion ratio, a low intense peak corresponding to $[M+Cu]^{2+}$ ion was detected by ESI-MS after 7-8 min incubation of peptide-metal ion. A close relationship between pH, metal concentration and the proportion of conformers of Aβ fragments was found, as well. Copper ions bind strongly and specifically to β-amyloid(1-40) peptide and to its N- and C-terminal truncated versions. Our ESI-MS investigation showed that the C-terminal 31-40 sequence is not involved in copper binding. Our results also prove that Zn(II) has lower affinity toward Aβ-peptides as compared to Cu(II). At 1:10 peptide-Zn(II), no peaks corresponding to the Aβ-peptides was detected by ESI-MS, were an aggregation process was suspected. Our data is discussed in the light of recent literature on neurodegeneration biochemistry.

Biography

Marius Closca is a PhD student of Alexandru Ioan Cuza University of Iasi, Romania, department of chemistry in the field of biochemistry 2017 to present. The short scientific experience is confirmed by the scientific results obtained in the field of organic chemistry and biochemistry, results included in one paper in Journals accredited by CNCSIS (category B and C) and a participation at the conference of faculty of chemistry Iasi CHEM 2017, Iași, Romania, 26-28 October 2017.

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