

**International Journal of Biomedicine | June 2019 - Volume 9, Issue Suppl_1:
Abstracts From the Second Russian International Conference "Cryo-electron
microscopy 2019: achievements and prospects"**

POSTER ABSTRACT PRESENTATIONS

SESSION TITLE: APPLICATIONS OF CRYO-EM IN MEDICINE

DOI: 10.21103/IJBM.9.Suppl_1.P33

**Abstract P-33: Changes in the Structure of Amyloid Alpha-Synuclein Aggregates
under the Action of Cinnamic Acid Derivatives**

Kseniya V. Barinova¹, Mariia V. Medvedeva², Aleksandra K. Melnikova², Alexander S. Erofeev³,
Peter V. Gorelkin³, Vasily S. Kolmogorov³, Vladimir I. Muronetz^{1,2}

¹*Belozersky Institute of Physico-Chemical Biology, Lomonosov Moscow State University, Moscow, Russia;* ²*Faculty of Bioengineering and Bioinformatics, Lomonosov Moscow State University, Moscow, Russia;* ³*National University of Science and Technology «MISIS», Moscow, Russia*

Background: Alpha-synuclein is the main amyloid protein involved in the development of Parkinson's disease and other synucleinopathies. The aim of our work was to investigate the possibility of preventing alpha-synuclein amyloid aggregation using soluble curcumin analogues, known as effective antiaggregants. For this purpose, cinnamic acid derivatives were used as such analogues – ferulic (3-methoxy-4-hydroxycinnamic acid), 3-methoxy-4-acetamidoxycinnamic, and 3,4-dimethoxycinnamic acid (3,4-DMCA).

Methods: Alpha-synuclein amyloid transformation was studied in the presence of different cinnamic acid derivatives by the use of ThT fluorescence, seeding assays, resistance to proteolysis by proteinase K, circular dichroism, scanning ion conductance microscopy, and also in a cellular assay using a neuroblastoma cell line.

Results: Alpha-synuclein monomers are known to form amyloid fibrils *in vitro* at acidic pH values or at neutral pH values in the presence of the already formed fibrils of this protein, used as seeds. It was shown that the addition of all three compounds prevents the formation of fibrillar structures by alpha-synuclein. The structure of alpha synuclein fibrils formed by incubating protein monomers at pH 4.0 was investigated using scanning ion conductance microscopy. Under these conditions, large aggregates are formed, with a maximum thickness of 2.5 µm and a length of several tens of microns. In the presence of ferulic acid, the aggregates have the spherical shape and their thickness does not exceed 1.2 µm, while their diameter is several microns. In the presence of 3-methoxy-4-acetamidoxycinnamic acid, formed aggregates are slightly larger and their thickness is about 1.5 µm. 3,4-DMCA demonstrated the smallest effect, however, even in this case, the formation of extended amyloid fibrils is prevented.

Conclusion: The results show that soluble cinnamic acid derivatives, which are naturally occurring compounds found in coffee beans and other plant products, can be used to prevent pathological amyloid transformation of alpha-synuclein.

Key Words: (up to 4) alpha-synuclein • cinnamic acid derivatives

Sources of Funding: This work was supported by the Russian Foundation for Basic research (grant 19-34-80004).

International Journal of Biomedicine. 2019;9 Suppl 1: S31. doi: 10.21103/IJBM.9.Suppl_1.P33

©2019 International Medical Research and Development Corporation