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### **Apolipoprotein E4 mediated targeting of blood brain barrier using nano-micellar metal chelators for treatment of Alzheimer disease**

**Fatemeh Bahadori, Burak Celik, Fatma Kazdal and Tuba Kusman**  
Bezmialem Vakif University, Turkey

Alzheimer Disease (AD) is one of the most important disorders of current century. Many pathological factors are contributed in the progress of this disease, the most important one being aggregation of Amyloid  $\beta$  ( $A\beta$ ) in brain. Thus, prevention of  $A\beta$  aggregation could have an important role in the treatment of AD. It is well-defined that some divalent metals namely iron, copper and zinc play role in  $A\beta$  aggregation. Thus, formulations with metal-protein attenuating (MPA) and metal chelating activity (metal chelators (MCs)) could play a possible role as co-treatment agents for AD. However, MCs are generally neurotoxic and more importantly, they are hydrophilic which means they wouldn't pass through Blood Brain Barrier (BBB). Since the structure-activity relationship of MCs is defined as carrying oxygen bearing functional groups in ortho position, we chose series of plants which are rich in poly-phenolic compounds with this special property. We also chose a series of synthetic compounds with high MC activity. Plant extracts were prepared and screened for their MC and MPA activity by incubating with  $A\beta$  aggregates. The methanolic extract of *Rosmarinus officinalis* (RO) showed the highest metal chelating and metal protein attenuating activity while Pyrrolidine Dithiocarbamate (PDTC) was the most active and non-toxic synthetic material. Nano-micellar Poly Lactic-co-Glycolic Acid (PLGA) formulation of RO and PDTC was prepared and surface modified with Apolipoprotein E4. Both formulations showed satisfying MPA and MC activity with a hydrodynamic size less than 200 nm while Apo E4 provided targeting property using its specialized receptors on BBB.

#### **Biography**

Fatemeh Bahadori has completed his PhD from Istanbul Technical University. He is Assistant Professor at Faculty of Pharmacy, Department of Pharmaceutical Biotechnology, Bezmialem Vakif University. He has published more than 11 papers in reputed journals and has been serving as Vice Director of Institute of Health Sciences, Bezmialem Vakif University since 2014.

[fatemehbahadori@hotmail.com](mailto:fatemehbahadori@hotmail.com)

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