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## Effect of magnetic tacrine-loaded chitosan nanoparticles on spatial learning, memory, amyloid precursor protein and seladin-1 expression in the hippocampus of streptozotocin-exposed rats

**Golamreza Hassanzadeh**

Tehran University of Medical Sciences, Iran

Alzheimer's disease (AD) is a progressive neurodegenerative disease characterized by memory and cognitive dysfunction due to neuronal cell loss in higher brain centers. Senile plaques containing amyloid  $\beta$  ( $A\beta$ ) are associated with this disease as well as a reduction in cholinergic neuron numbers. Tacrine is a reversible cholinesterase inhibitor in clinical use to treat moderate forms of AD. Chitosan nanoparticles represent an effective systemic delivery system for drugs. The application of tacrine-loaded chitosan nanoparticles has been shown to selectively increase tacrine concentrations in the brain tissue. In this study, we compared magnetic and non-magnetic tacrine-loaded chitosan nanoparticles for their bioactivity and neuroprotective potency in streptozotocin (stz)-induced neurodegeneration, an accepted animal model for AD. Male rats received a single injection of stz via an implanted cannula into the lateral brain ventricle. Tacrine (tac)-loaded chitosan nanoparticles were delivered into the tail vein. Spatial learning and memory were analyzed using the Morris water maze task. Amyloid precursor protein gene (APP) and seladin-1 gene expression were studied in the hippocampus by real time-PCR. Tac-loaded non-magnetic and tac-loaded magnetic chitosan nanoparticles improved spatial learning and memory after stz treatment with magnetic nanoparticles being most effective. Similarly, tac-loaded chitosan nanoparticles increased seladin-1 and reduced APP gene expression. Again, magnetic nanoparticles were more effective. These data reveal that tac-loaded non magnetic and tac-loaded magnetic chitosan nanoparticles to a higher extent improve brain deficits related to stz application. We conclude that the magnetic target drug delivery system is a promising therapeutic strategy to protect AD-related degenerating in the CNS.

hassanzadeh@tums.ac.ir

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