Protective Effects of Troxerutin on β-Amyloid (1-42)-Induced Impairments of Spatial Learning and Memory in Rats

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In our study, we examined the protective effect of troxerutin, a natural bioflavonoid, on β-amyloid, Aβ (1-42)-induced impairments of learning and memory. Male Wistar rats (300-350 g) were divided into six groups, sham, Aβ (1-42)-, Aβ (42-1)-injected, and three groups Aβ (1-42)-injected plus treatment with three different doses of troxerutin (50, 150, and 300 mg/kg) for 8 consecutive days. The Aβ peptides were injected intracerebroventricularly (i.c.v.) into the right lateral ventricle; 8 days later, the Morris water maze test was performed to assess spatial learning and memory. Our results showed that troxerutin at lower doses (50 and 150 mg/kg) exerted no significant effect on Aβ-induced impairment of memory performance, but the dose of 300 mg/kg significantly protected against the above impairment of spatial learning and memory in Aβ (1-42)-treated animals. The beneficial effects of troxerutin may partly be due to its antioxidant and anti-inflammatory activities and to modifications in the cholinergic system.

Keywords: troxerutin, spatial learning and memory, Morris water maze, β-amyloid, Alzheimer's disease.

INTRODUCTION

Alzheimer’s disease (AD) is a frequent cause of dementia in elderly peoples; it is accompanied by progressive cognitive decline and memory loss. Pathologic hallmarks of this disease include the formation of senile plaques, neurofibrillary tangles (NFTs), synapse loss, and neuronal dysfunction in different sites of the brain, in particular in the hippocampus [1-3]. Accumulation of amyloid β protein, Aβ, a main component of the senile plaques, in the brain initiates a cascade of events that ultimately lead to neuronal dysfunction and cognitive deficits. Other proposed mechanisms for AD include impairment of cholinergic transmission, oxidative stress, action of inflammatory agents, and glutamate-mediated excitotoxicity [4-6].

Troxerutin has been recognized as a trihydroxyethylated derivative of the natural bioflavonoid rutin; it has been found in tea, coffee, cereal grains, and a variety of fruits and vegetables. Troxerutin possesses a number of biological activities, such as anti-oxidative, anti-inflammatory, and nephroprotective, and is considered an effective agent in the treatment of cardiovascular diseases [7-9]. It was also demonstrated that troxerutin enhances the expression of nicotinic acetylcholine receptors and inhibits cholinesterase (AChE) activity in the brain [10].

Our earlier studies demonstrated that troxerutin alleviates Aβ-induced impairment of hippocampal long-term potentiation (LTP), an important mechanism involved in learning and memory, and reduces the amount of oxidative stress markers in the hippocampus of Aβ-treated rats (unpublished). According to these findings, we hypothesized that if some probable pathologic mechanisms involved in neurodegenerative diseases are suppressed by troxerutin, it may also manifest some protective action against AD. Therefore, in our behavioral study, we examined for the first time a protective effect of troxerutin on spatial learning and memory deficits in the Morris water maze (MWM) test in an Aβ-induced rat model of AD.

METHODS

Animals and Treatments. Adult male Wistar rats (body mass 300-350 g) were obtained from the Pasteur Institute of Iran. They were maintained at an