Research Paper

Anti-inflammatory Potential of Dapsone Loaded Chitosan Nanoparticles in Streptozotocin-Induced Experimental Dementia

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ABSTRACT: The potential of dapsone loaded characterized chitosan nanoparticles (CSNP) as a targeted delivery was investigated in memory deficits associated with dementia of Alzheimer disease type. Streptozotocin (STZ) in two doses (3 mg/kg on 1st and 3rd day) via intracerebroventricular route was used to induce dementia in swiss albino mice. The results showed that administration of STZ significantly impaired learning and memory based on Morris water-maze (MWM) test and raised myeloperoxidase (MPO) level along with neutrophils infiltration density (based on brain myeloperoxidase activity along with histological studies). Dapsone (1 mg/kg & 2 mg/kg for 11 days) loaded CSNP significantly attenuated STZ induced memory impairment as well as brain MPO activity along with increased neutrophils infiltration.

KEYWORDS: Chitosan nanoparticles; dementia; streptozotocin; dapsone; myeloperoxidase activity

Introduction

Several causes of memory impairment are known out of which more than 50% accounts for Alzheimer’s disease (AD) (Maslow 2010; Brookmeyer et al., 2007; Liana and Paul 2008). The identification of compounds that have disease modifying properties along with targeted delivery system is an active area of research to alter the progression of AD (Jeffrey 2009). Cholinesterase inhibitors employed for AD therapy are only modestly effective, as earlier stages of AD might not be characterized by impaired function of the cholinergic system (DeKosky et al., 2002). Advances in understanding of the etiologies and pathogenesis of AD highlights that inflammatory changes play an important role. (Fuller et al., 2010; Antero et al., 2009; Camerib and Landreth 2010; McGeer and McGeer 2003; Magdalena et al., 2006; Michael and Kerry 2007; Leonel et al., 2008). Anti-inflammatory therapy has attracted much attention as a strategy for reducing the risk or slowing the progression of AD (Aisen et al. 2002; McGeer and McGeer 2010; McGeer and McGeer 2007; Szekely et al., 2004; Curtis et al., 2009), as these proved effective at an early stage of AD (McGeer et al., 1996; Veld et al., 2001).

Several reports indicated association of lower prevalence of AD, in aged leprosy patients with the anti-inflammatory action of dapsone (Zhu et al., 2001; Kettle and Winterbourn 1991; McGeer et al., 1992; Chui et al., 1994; Cgui et al., 1994). Further dapsone has been demonstrated to be an irreversible inhibitor of myeloperoxidase (Kettle and Winterbourn 1991), interfere with neutrophil chemotactic migration (Harvath et al., 1986), suppression of neutrophil recruitment (Debol et al., 1997), inhibition of eosinophil peroxidase activity (Debol et al., 1992) and inhibition of 5-lipoxygenase products generation (Wozel and Lehmann 1995). However, the preventive effect of dapsone in Alzheimer’s disease is still controversial probably due to poor ability to reach target site in sufficient concentration at the employed doses (Mannila et al., 2005; Goto et al., 1995; Masumi et al., 1999; Guenther et al., 2001).

Chitosan (a natural cationic polysaccharide) accumulation in neuronal cells, more preferably in pyramidal neurons of the hippocampus, as well as accumulation at extracellular structure (preferably at