Modulation of Lipopolysaccharide Stimulated Nuclear Factor kappa B Mediated iNOS/NO Production by Bromelain in Rat Primary Microglial Cells

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ABSTRACT

Background: Microglial cells act as the sentinel of the central nervous system. They are involved in neuroprotection but are highly implicated in neurodegeneration of the aging brain. When over-activated, microglia release pro-inflammatory factors, such as nitric oxide (NO) and cytokines, which are critical in eliciting neuroinflammatory responses associated with neurodegenerative diseases. This study examined whether bromelain, the pineapple-derived extract, may exert an anti-inflammatory effect in primary microglia and may be neuroprotective by regulating microglial activation. Methods: Following the isolation of neonatal rat primary microglial cells, the activation profile of microglia was investigated by studying the effects of bromelain (5, 10, 20, and 30 µg/ml) on the levels of NO, inducible nitric oxide synthase (iNOS), and nuclear factor kappa B (NF-κB) in microglia treated with lipopolysaccharide (LPS) (1 µg/ml). Data were analyzed using Student’s t-test. P values less than 0.05 were considered to be statistically significant, compared with the LPS-treated group without bromelain. Results: Results showed that pretreatment of rat primary microglia with bromelain, decreased the production of NO induced by LPS (1 µg/ml) treatment in a dose-dependent manner. Bromelain (30 µg/ml) also significantly reduced the expression of iNOS at mRNA level and NF-κB at protein level. Moreover, the study of mitochondrial activity in microglia indicated that bromelain had no cytotoxicity at any of the applied doses, suggesting that the anti-inflammatory effects of bromelain are not due to cell death. Conclusion: Bromelain can be of potential use as an agent for alleviation of symptoms in neurodegenerative diseases.

Keywords: Microglia, Nitric oxide, NF-kappa B, Neuroimmunomodulation, Ananas

INTRODUCTION

Microglia are the innate immune cells or resident macrophages that can exist in activated and inactivated forms and are believed to regulate inflammatory responses in the central nervous system (CNS) 1,2. In response to a plethora of stimuli, microglia become activated and then initiate an inflammatory cascade in the CNS that contributes to the pathogenesis of Alzheimer’s disease, Parkinson’s disease, multiple sclerosis, AIDS dementia complex, and ischemia 3-5. Activated microglia have been shown to produce inflammatory mediators including NO and cytokines such as the tumor necrosis factor-α (TNF-α) 6,7.

Although microglia play a protective role by releasing trophic factors and removing dead cells, chronic microglial activation and consequent over-production of pro-inflammatory mediators lead to the initiation and progression of several neurodegenerative diseases 8-10.

A number of anti-inflammatory reagents can prevent...