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Protandim Protects Oligodendrocytes against an Oxidative Insult in Multiple Sclerosis (MS)

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Abstract:

Oligodendrocyte damage and loss are key features of multiple sclerosis (MS) pathology. Oligodendrocytes appear to be particularly vulnerable to reactive oxygen species (ROS) and cytokines, such as tumor necrosis factor-α (TNF), which induce cell death and prevent the differentiation of oligodendrocyte progenitor cells (OPCs). Here, we investigated the efficacy of sulforaphane (SFN), monomethyl fumarate (MMF) and Protandim to induce Nrf2-regulated antioxidant enzyme expression, and protect oligodendrocytes against ROS-induced cell death and ROS-and TNF-mediated inhibition of OPC differentiation. OLN-93 cells and primary rat oligodendrocytes were treated with SFN, MMF or Protandim resulting in significant induction of Nrf2-driven (antioxidant) proteins heme oygenase-1, nicotinamide adenine dinucleotide phosphate (NADPH): quinone oxidoreductase-1 and p62/SQSTM1, as analysed by Western blotting. After incubation with the compounds, oligodendrocytes were exposed to hydrogen peroxide. Protandim most potently promoted oligodendrocyte cell survival as measured by live/death viability assay. Moreover, OPCs were treated with Protandim or vehicle control prior to exposing them to TNF or hydrogen peroxide for five days, which inhibited OPC differentiation. Protandim significantly promoted OPC differentiation under influence of ROS, but not TNF. Protandim, a combination of five herbal ingredients, potently induces antioxidants in oligodendrocytes and is able to protect oligodendrocytes against oxidative stress by preventing ROS-induced cell death and promoting OPC differentiation.

KEYWORDS:

Nrf2; antioxidant enzymes; multiple sclerosis; reactive oxygen species