Alginate oligosaccharide protects against endoplasmic reticulum- and mitochondrial-mediated apoptotic cell death and oxidative stress.

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Abstract
Oxidative stress is a major component of harmful cascades activated in neurodegenerative disorders. We sought to elucidate possible effects of alginate oligosaccharide (AOS) on H(2)O(2)-induced cell death and to determine the underlying molecular mechanisms in neuron-like PC12 cells. We found that AOS treatment protected PC12 cells against H(2)O(2)-induced endoplasmic reticulum (ER) and mitochondrial-dependent apoptotic cell death. AOS promoted Bcl-2 expression, while blocked Bax expression and inhibited H(2)O(2)-induced caspase-3 activation. It also blocked PARP cleavage. AOS acted on key molecules in apoptotic cell death pathway and reduced p53, p38, c-Jun NH2-terminal kinase phosphorylations, inhibited NFkB, and enhanced Nrf2 activation. These results suggest that treatment of PC12 cells with AOS can block H(2)O(2)-induced oxidative stress and caspase-dependent apoptotic cascades originating from both ER and mitochondria. Our in vivo experiments further confirm the neuroprotective potential of AOS against Aβ-induced neural damage. According to our data, the involvement of caspase-independent pathway in AOS-induced protection appears to be unlikely.

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