Neuroprotective Effects of Astaxanthin in Preclinical Models of Alzheimer's Disease

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BACKGROUND

Alzheimer's disease (AD) is a debilitating neurodegenerative disease with a global population burden projected to triple by 2050. AD is the most common cause of dementia, and it accounts for about 70% of all dementia cases. The pathological manifestations of Alzheimer's disease include aggregation of misfolded protein fragment beta-amyloid outside neurons called plaques, hyper-phosphorylation of protein tau inside neurons called tangles, neuronal loss, synaptic degeneration, and neuroinflammation. Until date, there are no disease-modifying therapies available. Astaxanthin, a lipid-soluble xanthophyll beta-carotenoid synthesized by many microorganisms, has been reported to exhibit anti-inflammatory and neuroprotective functions. In this study we investigated the effects of astaxanthin on synaptic degeneration, autophagy, neuronal loss and neuro-inflammation as pathological hallmarks of AD using two cell culture models. Our data suggest astaxanthin to be a good candidate for the treatment of AD, although further analyses of its *in vivo* effects have to be performed to validate observed *in vitro* results.

MATERIALS AND METHODS

Primary mouse hippocampal neurons and organotypic brain slice cultures were treated with either amyloid beta ($A\beta_{1-42}$) or lipopolysaccharides (LPS) and co-incubated with astaxanthin (ASX) or dexamethasone (DEXA). DEXA is an anti-inflammatory agent used as reference substance. Expression levels of relevant markers were examined on mRNA level by quantitative real time polymerase chain reaction (qRT-PCR) and immunofluorescent labeling techniques. Cytokine release was determined using an immunosorbent assay (Mesoscale Discovery).

RESULTS

Astaxanthin Increases PSD95 and Effects LAMP2A Signaling in $A\beta_{1-42}$ Treated Primary Hippocampal Neuronal Cells

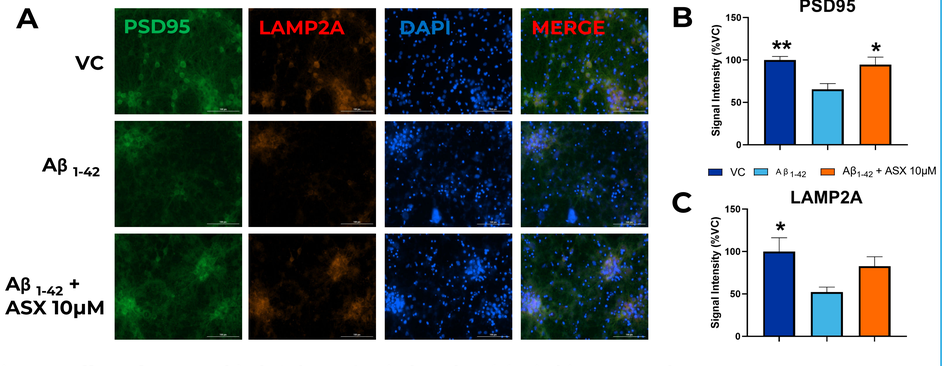

Figure 1. Effect of astaxanthin (ASX) on $A\beta_{1-42}$ induced toxicity in hippocampal neurons.
Representative images (A) and signal quantification of post synaptic (PSD95) and chaperone-mediated autophagy (LAMP2A) markers (B,C) in vehicle, $A\beta_{1-42}$ and $A\beta_{1-42}$ in combination with ASX treated primary hippocampal neurons. One-Way ANOVA with Dunnett's multiple comparisons test vs. $A\beta_{1-42}$. Mean + SEM; n=6-12. *p<0.05, **p<0.01.

Astaxanthin Partially Rescues Neuronal Loss in $A\beta_{1-42}$ Treated Primary Hippocampal Neuronal Cells

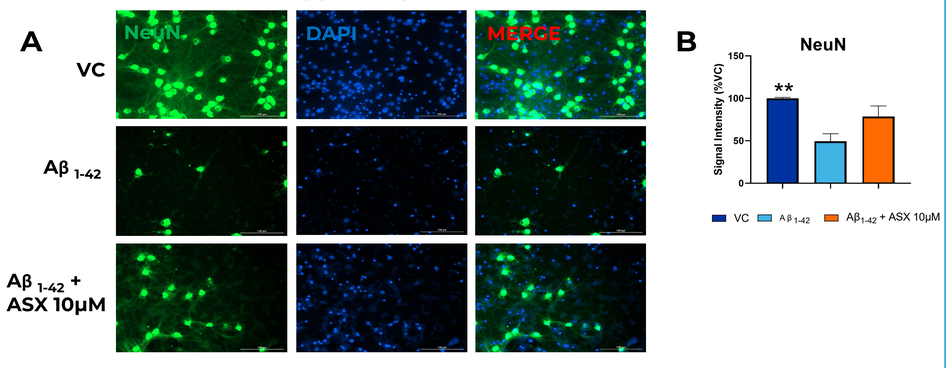

Figure 2. Effect of astaxanthin (ASX) on $A\beta_{1-42}$ induced toxicity in hippocampal neurons.
Representative images (A) and signal quantification (B) of neuronal marker (NeuN) labelling in vehicle, $A\beta_{1-42}$ and $A\beta_{1-42}$ in combination with ASX-treated primary hippocampal neurons. One-Way ANOVA with Dunnett's multiple comparisons test vs. $A\beta_{1-42}$. Mean + SEM; n=6. **p<0.01

RESULTS

Astaxanthin Reduces the Secretion of Cytokines in LPS-stimulated Organotypic Hippocampal Brain Slices

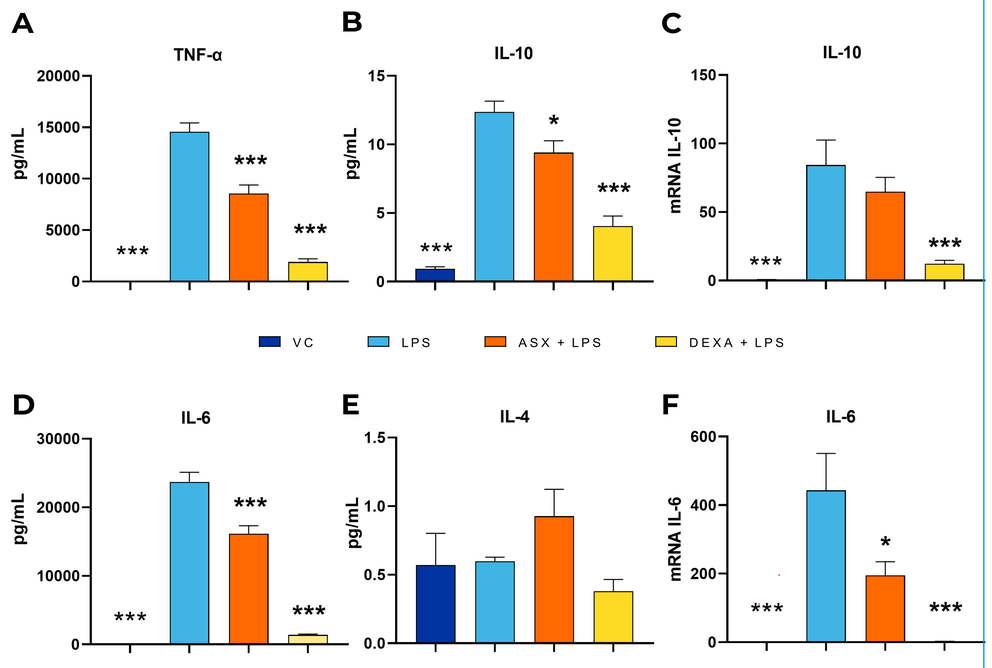

Figure 3. Effect of astaxanthin (ASX) on cytokine release in lipopolysaccharide (LPS)-stimulated brain slices.
Organotypic hippocampal brain slices were incubated with 10 ng/ mL LPS as well as with 10 ng/mL LPS in combination with 50 µM ASX or 10 µM dexamethasone (DEXA) for 24 h followed by detection of cytokine release into the supernatant by MSD and mRNA quantification of relevant pro-inflammatory markers by qRT-PCR. One-Way ANOVA with Dunnett's multiple comparisons test vs. LPS. Mean + SEM; n=5-9. *p<0.05, ***p<0.001.

CONCLUSION

Our data suggest that astaxanthin might be a therapeutic candidate by ameliorating pathophysiological manifestations associated with Alzheimer's disease.

For more information about the model please visit: www.qpsneuro.com
or send us an e-mail: office-austria@qps.com