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Astaxanthin and Coronavirus Disease 2019 (COVID-19)

Boosting the Immune System and Reducing Inflammation

Astaxanthin and COVID-19

About Astaxanthin

History and Background

Safety

Mechanism of Action

Synthetic vs. Natural Astaxanthin

Scientific Rationale: Immune Response, Inflammation, and COVID-19

Coronavirus Disease 2019 (COVID-19) can induce an extreme immune response characterized by the overproduction of immune cells and the uncontrolled release of pro-inflammatory cytokines. Exceedingly high levels of the cytokines IL-1, IL-6, IL-8, TNF-a, and CRP result in overt inflammatory symptoms that include mild to severe respiratory disease, high fever, and cough. In progressed disease this "cytokine storm" will circulate throughout the body to trigger a surge of active immune cells into the lungs resulting in acute lung injury and acute respiratory distress syndrome (ARDS) and may be particularly severe in immune compromised subjects such





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relatively early stage in alsease progression might be expected to stem the immune over-response and to slow or even prevent progression of symptoms leading to lung injury and ARDS. Importantly, an appropriate antiinflammatory intervention should not result in abnormal immune suppression but should target healthy immune homeostasis.

An anti-inflammatory treatment that resulted in the decrease of inflammatory cytokine signaling would seem a promising approach. Chinese researchers have identified IL-6 as a main driver of immune overreaction in COVID-19 patients and have already included elevated IL-6 levels as a biomarker of disease worsening. China's National Health Commission has updated its treatment quidelines for COVID-19 to include Roche's injected biologic, Actemra (tocilizumab), an inhibitor of the IL-6 receptor. Actemra, first approved by the U.S. FDA in 2010 for rheumatoid arthritis, can now be used in China to treat serious coronavirus patients with lung damage.

The Potential Role of Astaxanthin



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animal models of disease. (Further discussion and references are provided in the white paper, available for download.)

Results from the pre-specified interim review of the Company's ongoing CHASE (Cardiovascular Health Astaxanthin Supplement Evaluation) clinical trial demonstrated a statistically significant reduction in CRP (C-Reactive Protein, a measure of inflammatory health) in diabetics and a strong trend of CRP reduction in cardiovascular patients. The CHASE clinical trial is a double-blind, randomized, placebo-controlled clinical trial evaluating the effect of the Company's synthetic astaxanthin dietary supplement ZanthoSyn®, on cardiovascular health, as measured by C-Reactive Protein or "CRP" levels over 12 weeks in up to 120 subjects with documented cardiovascular risk factors. Pre-specified secondary cardiovascular/inflammatory health markers, safety parameters, exploratory endpoints, and pre-specified sub-groups are also being assessed. The trial includes an optional open-label extension through 48 weeks.

Collaboration Opportunities

Cardax is seeking strategic collaborations with appropriate academic, governmental, and/or





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has anacigonic extensive salety testing and has a long history of use in humans and animals.

Astaxanthin has demonstrated efficacy in models of inflammatory-mediated disease, including:

- Reduction of TNF- α levels equivalent to a steroid
- Reduction of cholesterol levels
- Reduction of elevated triglycerides
- Reduction in blood clot formation with no increase in bleeding
- Decrease in myocardial tissue damage following experimentally-induced myocardial infarction





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salmon from oxidative stress when they swim upstream to spawn – a taxing and traumatic event.

Identification and Study



Richard Kuhn

In 1938, Richard Kuhn identified and isolated astaxanthin from lobster. Kuhn had setup a laboratory on the banks of the Neckar River in Germany and quickly established his reputation as a leading experimentalist in organic chemistry. Astaxanthin was one of the earliest carotenoids to be examined by the broader research community.



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Safety

Commonly used anti-inflammatory drugs such as aspirin, ibuprofen, naproxen, COX-2 inhibitors, corticosteroids, and various biologics have risks of side effects including gastrointestinal bleeding, heart attacks, strokes, and severe infections. Prescription fish oil drugs, while safer than common anti-inflammatory drugs, also have risks of certain side



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stress that causes chronic inflammation, without affecting the normal function of





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