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Discussion about AHCC[®] on cytokine storm

Amino Up Co., Ltd.

AHCC[®], a standardized extract of cultured *Lentinula edodes* mycelia, has been reported to have protective effects against various bacterial and viral infections including West Nile virus, influenza virus, avian influenza (H5N1) virus, and human papillomavirus (HPV), shown in many animal and human clinical studies ¹⁻³). AHCC is considered to show such protective effects against infections via activation of innate immune response. At the same time, AHCC is also reported to suppress overproduction of proinflammatory cytokines in a lymphocyte-driven model of inflammatory bowel disease ⁴), and suppress excessive inflammatory response in hepatocytes stimulated with interleukin-1 β (IL-1 β) ⁵). Therefore, it is suggested that AHCC does not only activate, but modulate immune system, as a safe functional dietary ingredient.

As of April 5, 2020, coronavirus disease 2019 (COVID-19) has been confirmed in 1,133,758 people worldwide, carrying a mortality of approximately 5.5% ⁶), and it is suggested that cytokine storm is observed in a subgroup of patients with severe COVID-19 ⁷). Cytokine storm is a severe immune reaction in which the body releases excessive amount of proinflammatory cytokines into the blood. Cytokine storm sometimes get severe and lead to multiple organ dysfunction ⁸).

Under the circumstances, a specific concern was raised if AHCC promotes cytokine storm as it works on immunity. To address such concern, we asked experts who have been studying AHCC about its anti-inflammatory effects and the molecular mechanisms, and their technical comments are below.

- In B lymphocytes cell model and guinea pig model with viral infections, AHCC suppressed over expression of IFN- α in transcription level. It was suggested that AHCC may control progression toward cytokine storm by suppressing overproduction of cytokines caused by viral infection ⁹).

[Prof. Tominori Kimura, MD PhD, College of Pharmaceutical Sciences, Ritsumeikan University]

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- Cytokine storm is observed clinically in sepsis (blood poisoning) caused by bacterial and viral infections, and experimentally in endotoxemia model. In a rat endotoxemia model study, sepsis along with hepatic failure was caused by hepatectomy and LPS administration. Overproduction of proinflammatory cytokines (TNF- α , CXCL1, IL-6 and IL-1 β) observed in this model, considered as cytokine storm, leads to death of most rats within 48 hours. By AHCC supplementation (with LPS), elevations of serum liver enzymes (AST and ALT) were suppressed, those cytokines productions and iNOS expression were suppressed in liver, and the survival rate of rat was improved. In AHCC group, IL-10, an anti-inflammatory cytokine concentration was significantly increased in serum ¹⁰⁾. [Prof. Mikio Nishizawa, MD PhD, Department of Biomedical Sciences, Ritsumeikan University]
- These reports suggest that AHCC is likely to inhibit cytokine storm in bacterial and viral infections, by suppressing overproduction of type I interferons and proinflammatory cytokines. [Professors. Kimura and Nishizawa]

Currently, the development mechanism of cytokine storm is not clearly understood. Meanwhile, there is no report that continuous intake of AHCC causes overproduction of proinflammatory cytokines, and AHCC has been validated for its protective effects against various infections, and with those comments from experts, it is suggested that AHCC does not lead to cytokine storm.

References

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