

BETA-GLUCAN

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Introduction

β -glucans are naturally-occurring polysaccharides obtained from different sources such as oats, barley, bacteria, yeast, algae, and mushrooms. β -glucan derived from different sources have variation in their structure responsible for their specific biological properties.¹ There have been nearly 7,000 publications reporting the immune-modulating effects of β -glucans. Actions of β -glucan are not direct but rather due to β -glucan being a biological response modifier (BRM) to enhance immunity.

β -glucans are one of the main active components derived from mushrooms. There are some edible mushrooms with reported immunomodulatory actions. Lentinans are a specific class of β -glucans extracted from the edible mushroom *Lentinus edodes*, and are composed of a β -(1–3)-glucose backbone with two (1–6)- β -glucose branches of each five glucose units. There has been an increasing interest in their use for treating disease in animals and humans. McCarty and DiNicolantonio (2020) recently described the potential role of β -glucan as a natural nutraceutical for boosting type 1 interferon response to RNA viruses such as influenza and coronavirus.³ Findings showed that β -glucan from shiitake mushrooms (*Lentinus edodes*) demonstrated potential for the treatment of lung injury, reducing IL-1 β , IL-6 in an in vitro lung injury model, suggesting that it may ameliorate the cytokine storm that causes ARDS as seen in COVID-19.⁴

There is another specific β -glucan: a 1-3,1-6 β -glucan from a black yeast called *Aureobasidium pullulans* AFO-202 strain. It is a soluble β -glucan that contains both high and low molecular weight β -glucan. High molecular β -glucan (H-BG) has been found to stimulate the proliferation of lymphocytes with stronger effects and low molecular β -glucan (L-BG) component reduces the levels of inflammatory biomarkers (majorly cytokines), stimulates the cytokine and activates chemokine signaling pathways. This AFO-202 beta glucan decreases IL-6 levels. The increase in soluble Fas (sFas), which helps in regulating the immune response by immune suppression, will be highly valuable in regulating the cytokine storms and hyper-inflammation associated with COVID-19.⁵

Mechanism of Action

β -glucans are recognized by the immune system as a Pathogen Associated Molecular Patterns (PAMPs) which interact with Pathogen Recognition Receptors (PRRs) on innate immune cells, activating the immune response.

The most pronounced effect of β glucans consists of augmentation of phagocytosis and proliferative activities of professional phagocytes—granulocytes, monocytes, macrophages and dendritic cells.⁴ Here, macrophages are considered the basic effector cells in host defense versus bacteria, viruses, multicellular parasites, tumor cells and they play the most significant role.

When explored, β -glucan in one-way human mixed lymphocyte reaction (MLR) assay systems could activate suppressor cells—in particular, regulatory T cells (Treg)—and also induce the production of suppressive cytokines⁵ which will be helpful in suppressing the cytokine storm observed in COVID-19. While the immunological actions of the AFO-202 β -glucan are evident and will have potential use against COVID-19 infection by immunosuppressing pro-inflammatory cytokines, several studies have also reported that this β -glucan can enhance immunity by increasing the levels of cytotoxic cells such as NK cells and macrophages, which will be the actual line of defense against the viruses.

Clinical Studies

As of August 10, 2020, there are no studies registered on the use of β -glucans for COVID-19. Human trials are needed to test for its efficacy against COVID-19.

Recommended Dose

The dose has not yet been established for COVID-19.

Adverse Effects

The potential harms of β -glucan in COVID-19 still needs further investigation, however, as a nutraceutical, few adverse effects have been described and yeast β -glucan has been given the generally regarded as safe (GRAS) status.^{6,7}

Conclusion

The AFO-202 β -glucan has not yet been subjected to a clinical study in COVID-19 positive patients. The exact role in tackling COVID-19 has not been established.⁸

Further clinical studies are needed to refine β -glucan as a countermeasure for tackling cytokine storm that causes ARDS, as evident with COVID-19.⁴

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