

# Beneficial Effects of novel *Aureobasidium Pullulans* strains produced Beta-1,3-1,6 Glucans on Interleukin-6 and D-Dimer levels in COVID-19 patients; results of a randomized multiple-arm pilot clinical study

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## Abstract

**Objective:** Cytokine storm and Coagulopathy have been implicated as major causes of morbidity and mortality in COVID-19 patients. A black yeast *Aureobasidium pullulans* AFO-202 strain produced beta 1,3-1,6 glucan has been reported to offer potential immune enhancement and metabolism balancing, as well as mitigation of coagulopathy risks. The N-163 strain produced beta glucan is an efficient anti-inflammatory immune modulator. In this pilot clinical study, we report the beneficial effects of these two beta glucans on the biomarkers for cytokine storm and coagulopathy in COVID-19 patients. **Methods:** A total of 24 RT-PCR positive COVID-19 patients were recruited (Age range: 18~62; 17 males and 7 females). Patients were randomly divided into three groups (Gr): Gr. 1 control (n=8); Gr. 2: AFO-202 beta glucan (n=8); and Gr. 3, a combination of AFO-202 and N-163 beta glucans (n=8). All three groups received the standard care while groups 2 and 3 received additional supplementation of beta glucans for 30 days. In addition to basic clinical parameters, we periodically evaluated D-Dimer, IL-6, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), the neutrophil to lymphocyte ratio (NLR), the lymphocyte to CRP ratio (LCR) and the leukocyte-CRP ratio (LeCR). **Results:** The duration of hospital stay for all three groups was nearly equivalent. There was no mortality of the subjects in any of the groups. Intermittent oxygen was administered from day of admission for up to four to five days with mask (two to four Lpm) to two subjects in Gr. 2 and one subject in Gr. 3. None of the subjects required ventilation. The D-Dimer values in Gr. 1, which was on average 751 ng/ml at baseline, decreased to 143.89 ng/ml on day 15, but increased to 202.5 ng/ml on day 30, which in groups 2 and 3 decreased on day 15 and continued to remain at normal levels until day 30. IL-6 levels decreased on day 15 from an average of 7.395 pg/ml to 3.16 pg/ml in the control, 26.18 pg/ml to 6.94 pg/ml in Gr. 2 and 6.25 pg/ml to 5.22 pg/ml in Gr. 3. However, when measured on day 30, in Gr. 1, the IL-6 increased to 55.37 pg/ml while there was only slight marginal increase in Gr. 2 but within normal range, and the levels further decreased to less than 0.5 pg/ml in Gr. 3. The same trend was observed with ESR. LCR and LeCR increased significantly in Gr. 3. NLR decreased significantly in groups 2 and 3. There was no difference in CRP within the groups. **Conclusion:** In this exploratory study, consumption of *Aureobasidium pullulans* produced beta glucans for thirty

days, results in a significant control of IL6, D-Dimer and NLR, a significant increase in LCR, LeCR and marginal control of ESR in COVID-19 patients. As these beta glucans are well known food supplements with decades of a track record for safety, based on these results, we recommend larger multi-centric clinical studies to validate their use as an adjunct in the management of COVID-19 and the ensuing long COVID-19 syndrome.

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