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File: ■ Olive (*Olea europea*, Oleaceae) Leaf
■ Covid-19
■ Severe Acute Reparatory Syndrome Coronavirus-2

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RE: Olive Leaf Extract Improves Clinical Outcome Parameters and Length of Hospitalization in COVID-19 Patients After Five Days of Supplementation

Ahmadpour E, Toulabi T, Yadegarinia D, Yarahmadi S, Mohammadi R, Keyvanfar A. Efficacy of olive leaves extract on the outcomes of hospitalized covid-19 patients: A randomized, triple-blinded clinical trial. [published online October 29, 2022]. *Explore (NY)*. doi:10.1016/j.explore.2022.10.020.

Severe Acute Respiratory Syndrome Coronavirus-2, also known as SARS-CoV-2 or COVID 19, became a pandemic after its introduction to the world in December 2019. Since then, millions have been infected and died from COVID-19. Herbal medicine has traditionally been used to treat diseases and illnesses. Olive (*Olea europea*, Oleaceae) contains phenolic compounds and has antiviral, anti-inflammatory, antioxidant, and antibacterial activities. Trials have indicated that it increases the immune response against viruses by stimulating phagocytosis, and it has shown positive effects against human immunodeficiency virus and respiratory syncytial virus. The authors conducted a randomized, triple-blinded clinical trial to determine the effectiveness of olive leaf extract on hospitalized patients with COVID-19.

This study was conducted at the Labbafinejad Hospital, Tehran, Iran between July and December 2021. Inclusion criteria included patients hospitalized with COVID-19 between the ages of 18 and 72 with a Glasgow coma scale = 15 at admission to the hospital. Exclusion criteria included patients who received oleuropein supplements during the last three months, had comorbidities, were immunocompromised or taking immunosuppressive drugs, were hypersensitive to the trial product, had blood pressure < 70 mmHg at admission, required mechanical ventilation, were admitted to the intensive care unit, or died during the study.

Group A received 250 mg capsules of olive leaf extract to be taken orally every 12 hours for five days, and Group B received 500 mg capsules to be taken orally every 12 hours for five days. The third group received a placebo. The trial products and placebo were produced by Adonis Gol Darou Company, Tehran, Iran. The placebo content was not stated; however, it was stated the olive leaf extract was 30% oleuropein. Patients also received standard COVID-19 treatment which included dexamethasone, remdesivir, heparin, and supplemental oxygen with a simple mask. The primary outcomes were

body temperature, mean blood pressure, respiratory rate, pulse rate, and peripheral oxygen saturation, which were assessed daily by a trained professional. The secondary outcomes included laboratory tests and length of hospitalization. Laboratory tests were performed daily by a trained professional and included complete blood count, serum level of C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR).

Of the 165 patients assessed, 150 were selected with 50 in each group. Of the 150, 141 patients completed the study and follow-up. Reasons for leaving the study included admitted to intensive care unit (n = 5), declined to continue participation (n = 1), and death (n = 3). This left 48 in the 250 mg group, 46 in the 500 mg group, and 47 in the placebo group. The mean age of patients was 48.88 ± 11.96 years, and 72 patients were female. All baseline characteristics were similar other than myalgia ($P = 0.046$). All patients had imaging findings suggesting COVID-19 pneumonia.

After five days, the 250 mg group had significant positive effects on body temperature ($P < 0.001$), pulse rate ($P = 0.016$), respiratory rate ($P = 0.001$), and oxygen saturation ($P = 0.001$) compared to the placebo group. The 500 mg group also had similar significant positive effects compared to placebo for body temperature ($P = 0.001$), pulse rate ($P = 0.022$), respiratory rate ($P = 0.006$), and oxygen saturation ($P < 0.001$).

The 250 mg group saw significantly lower ESR ($P < 0.001$) and CRP ($P < 0.001$) compared to placebo; however, no other laboratory outcome was significantly different. The 500 mg group also saw a significant reduction compared to placebo for ESR ($P < 0.001$) and CRP ($P < 0.001$); however, no other laboratory outcome was significantly different. Post hoc test indicated that the 250 mg group and the 500 mg group were homogeneous groups for all primary and secondary outcomes and were significantly different compared to the placebo group ($P < 0.001$). Both the 250 mg group ($P < 0.001$) and the 500 mg group ($P < 0.001$) saw significantly shorter length of hospitalization compared to placebo.

The authors conclude olive leaf extract may mitigate the clinical status of patients with COVID-19 and decrease the length of hospitalization. The authors recommend trials with different doses of olive leaf extract, trials with variables such as underlying diseases, and more studies to verify these results.

—Dani Hoots

Referenced article can be accessed at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9617633/.