

# Effect of Alcoholic Extract of the Olive Leaf on Clinical and Laboratory Outcomes of Patients with COVID-19: A Study Protocol

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## Study protocol

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The COVID-19 virus is swiftly spreading worldwide, resulting in a pandemic that challenges the competence of healthcare systems in developed countries [1]. The clinical characteristics of COVID-19 were diverse and unspecific, ranging from mild to severe respiratory, constitutional, and gastrointestinal signs and symptoms, progressing to severe acute respiratory infection and acute respiratory distress syndrome [2]. The diagnosis is confirmed with an approved real-time reverse transcriptase polymerase chain reaction (RT-PCR) test but with controversial sensitivity and even chest radiologic modalities [2]. Given that no effective treatments have been approved and the public health emergency persists, it is necessary to study the effectiveness of existing antiviral and herbal drugs against COVID-19 [3]. Studies indicate that further research is required on the effectiveness of Indian, Chinese, and Iranian medicinal plants in treating COVID-19 [4]. Phytomedicine refers to using roots, seeds, leaves, bark, and flowers for medicinal purposes [3].

Some of these plants have antiviral characteristics. Studies indicate that over 75% of the drugs used to treat viral diseases are obtained from botanical products [5]. Among the herbal medicines, one could mention olive [6]. Olive (*Olea Europaea*) is an Oleaceae family plant, encompassing 24 genera and 900 species [7].

Olive leaf's antiviral activity is likely due to its competence in preventing the entrance of viruses into cells, which is a result of olive leaf extract's ability to be combined with the cell membrane. The exact antiviral activity mechanism of the olive leaf is yet to be discovered; however, it might be as it prevents the virus from attaching to the cell, thus blocking the virus's entrance to the cells. The antiviral activity of the polyphenol in olive leaf has been witnessed in viral diseases, including hepatitis B virus, hepatitis C virus, papillomavirus, herpes simplex virus types 1 and 2, and influenza virus type A [8, 9]. Olive Leaf Extract (OLE) also improves immune system responses to the virus through phagocytosis stimulation. Various clinical studies conducted in European countries over

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the past 30 years have revealed the immunity of OLE. The results of clinical studies indicate that most patients tolerate the oral use of OLE, and no moderate or severe side effects have been reported. Published pharmacology and toxicology articles indicate that there is no immunity concern regarding the usage of this extract [10, 11]

A new clinical trial entitled "The effect of alcoholic OLE on clinical and laboratory outcomes of COVID-19 patients" is studying the effects of alcoholic OLE on COVID-19 patients. The Ethics Committee of the Lorestan University of Medical Sciences (IR.LUMS.REC.1399.262) approved the trial protocol and registered it at the Iranian Registry of Clinical Trials (IRCT20201128049520N1). This study is a three-blind clinical trial being conducted on 142 patients with the entrance criteria of being infected with COVID-19, diagnosed based on the standard diagnosis test (PCR test, as well as chest CT findings compatible with the COVID-19 pneumonia pattern) approved by an infectious disease specialist, ages ranging between 18 to 70, and a level of consciousness (LOC) equal to 15 based on the Glasgow coma scale (GCS); and exit criteria of having utilized mechanical ventilation tools, having background diseases, pregnancy and lactation, unwillingness to continue the cooperation, being discharged before the healing period completes, hypotension, hypoglycemia, incorrect and improper use of medication, and being allergic to the medication before or during the study. The researchers assign the population to 3 groups under treatment: OLE 250mg, OLE 500 mg, and placebo groups. Olive leaf extract will be made in 500 and 250 mg doses and placebo in capsules. The capsules are similar in color, shape, and size. Ten

capsules will be poured into similar envelopes, and the researcher, statistical analyst, and study participants will be unaware of the contents of the envelopes. The researcher will complete the demographic information questionnaires before starting the interventions. The medicine packets will be given to the participants and then assessed for general symptoms of COVID-19 (including cough, sore throat, sputum, rhinorrhea, muscle aches, fatigue, headache, abdominal pain, anorexia, breath shortness, anxiety, nausea, diarrhea, vomiting, and olfactory and taste changes), the pulse rate, respiratory rate, body temperature, mean atrial blood pressure, oxygen saturation (SpO<sub>2</sub>), and CPK, LDH, CRP, ESR, ALT, AST, CRE, BUN, ESR and CBC-diff laboratory tests before, during, and after the treatment). If the allergy or complications are severe, the intervention will be stopped, symptomatic treatment will be performed with the opinion of an infectious disease specialist, and only the complications will be reported.

Although the present study's findings would be out too late to help millions of people infected by the virus, it will yield valuable information regarding the possible reduction in symptoms through OLE during future COVID-19 outbreaks.

## **Declarations**

### **• Competing interests**

The authors declare that they have no competing interests.

### **• Acknowledgment**

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## **References:**

1. Agrawal M, Saraf S, Saraf S, Murty US, Kurundkar SB, Roy D, et al. In-line treatments and clinical initiatives to fight against COVID-19 outbreak. *Respiratory medicine*. 2020;106:192.
2. Vahedi A, Tabasi F, Monjazebi F, Hashemian SMR, Tabarsi P, Farzanegan B, et al. Clinical Features and Outcomes of ICU Patients with COVID-19 Infection in Tehran, Iran: a Single-Centered Retrospective Cohort Study. *TANAFOS (Respiration)*. 2020;19(4):300-11.
3. Huang F, Li Y, Leung EL-H, Liu X, Liu K, Wang Q, et al. A review of therapeutic agents and Chinese herbal medicines

- against SARS-COV-2 (COVID-19). *Pharmacological research*. 2020:104929.
4. Porembskaya O, Lobastov K, Pashovkina O, Tsaplin S, Schastlivtsev I, Zhuravlev S, et al. Thrombosis of pulmonary vasculature despite anticoagulation and thrombolysis: The findings from seven autopsies. *Thrombosis Update*. 2020;1:100017.
  5. Mirzaie A, Halaji M, Dehkordi FS, Ranjbar R, Noorbazargan H. A narrative literature review on traditional medicine options for treatment of corona virus disease 2019 (COVID-19). *Complementary Therapies in Clinical Practice*. 2020:101214.
  6. Chatfield K, Salehi B, Sharifi-Rad J, Afshar L. Applying an ethical framework to herbal medicine. *Evidence-Based Complementary and Alternative Medicine*. 2018;2018.
  7. Hung P-Y, Ho B-C, Lee S-Y, Chang S-Y, Kao C-L, Lee S-S, et al. *Houttuynia cordata* targets the beginning stage of herpes simplex virus infection. *PLoS One*. 2015;10(2):e0115475.
  8. Moradi M-T, Rafeian-Kopaei M, Karimi A. A review study on the effect of Iranian herbal medicines against in vitro replication of herpes simplex virus. *Avicenna journal of phytomedicine*. 2016;6(5):506.
  9. Toulabi T, Delfan B, Rashidipour M, Yarahmadi S, Ravanshad F, Javanbakht A, et al. The efficacy of olive leaf extract on healing herpes simplex virus labialis: A randomized double-blind study. *EXPLORE*. 2021.
  10. Şahin S, Samli R, Tan ASB, Barba FJ, Chemat F, Cravotto G, et al. Solvent-free microwave-assisted extraction of polyphenols from olive tree leaves: Antioxidant and antimicrobial properties. *Molecules*. 2017;22(7):1056.
  11. Dunne EF, Friedman A, Datta SD, Markowitz LE, Workowski KA. Updates on human papillomavirus and genital warts and counseling messages from the 2010 Sexually Transmitted Diseases Treatment Guidelines. *Clinical infectious diseases*. 2011;53(suppl\_3):S143-S52.