

Management of COVID-19 by Phytotherapy: A Pharmacological Viewpoint

At the beginning of 2020, the novel coronavirus has emerged as a global health problem. Despite the availability of effective vaccines for COVID-19, the disease is still recognized as a global emergency as researchers seek to find a way to treat and manage patients with COVID-19. The main route of transmission is the upper respiratory tract and it then affects different parts of the body.^[1] COVID-19 affects alveolar cells, the neural, immune, and cardiovascular system, liver, kidney, and even skin. Mortality is due to multiorgan failure, acute respiratory distress syndrome, heart failure, arrhythmia, renal failure, and shock.^[2,3] This necessitates specific attention to possible damage to these organs for the management of severe cases. The many previous clinical or preclinical studies have indicated medicinal plants and natural products can reveal their beneficial effects via multiple mechanisms in the treatment of diseases, including viral, cardiac, and inflammation.^[4] In this study, we aimed at introducing medicinal plants from the perspective of Persian Medicine to manage the symptomatic treatment of COVID-19^[5] such as anti-viral, antitussive, anti-inflammatory and boosting health of respiratory and cardiovascular systems [Table 1]. In line with the previous studies, the pivotal candidate medicinal plants listed in Table 1 can attenuate the most severe complication in viral pneumonia, such as rapidly developing cardiac infection, cough, and respiratory inflammation. Among these, the levels of inflammatory cytokines (including IL-6 and TNF- α) directly correlate with the magnitude of viral replication, respiratory and systemic symptoms in upper respiratory secretions.^[6,7] There is no immunity for those who are at risk for secondary COVID-19 infection.^[1] The most options in the management of COVID-19 treatment are reduction of virus replication and enhancing host immunity.^[4] Medicinal plants as an antiviral volunteer exert a unique preventive and therapeutic approach via inhibiting viral replication; the reduction of cytokine production leads to an improvement of symptoms [Table 1]. Besides, herbal remedy is often able to support physiological function in the host body and it boosts immune response through their active ingredients with multiple mechanisms and synergic effects in comparison with single/isolated molecules that may not be more effective [Table 1]. Most of the plants are listed in Table 1; they contain polyphenols, flavonoids, polysaccharides, and terpenoids, which possess anti-inflammatory, antioxidant, antiapoptotic, antiviral, and immunomodulatory properties due to activation or inhibition of many signaling pathways, cytokines, enzymes, and mitochondria repairing in each organ of the host or virus [Table 1]. Thus, phytotherapy by various beneficial pharmacological effects of herbals can be applied as a complementary remedy in the management or prevention of COVID-19 and this could reduce the adverse effects of conventional drugs.

Author's contribution

Mahdieh Eftekhari and Ayesheh Enayati: data collection and article preparation; Aref Salehi: article review; Ayesheh Enayati: article review and submission.

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Conflicts of interest

The authors declare that they have no conflict of interest.

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Table 1: Recommended medicinal plants based on Persian Medicine in management of COVID-19

NO.	Scientific name	Pharmacological effects				Ref.
		Anti-viral	Respiratory protection	Cardioprotection	Immunity	
1.	<i>Althaea Officinalis</i> L.	↓ Viral replication in initial stages	↑ Analgesic, antioxidant, mucosal repair	↑ Coronary flow, antioxidant, ↓ JAK/STAT pathway	↑ Anti-inflammatory, host monocytes to produce IL-6 and TNF- α cytokines, phagocytic activity of macrophages	[8-13]
2.	<i>Echium amoenum</i> Fisch. & C.A.Mey.	↓ Virus replication, infection, and fever	↑ Analgesic, antioxidant	↑ Antioxidant, vasodilator, anti-ischemic lipid peroxidation, VEGF, STAT1, and MCP-1	↑ Anti-inflammatory, antioxidant, IFN- γ ↓ Necrosis, iNOS, COX2, IL-1 β , IL-6, TNF- α , and cytokine levels	[14-16]
3.	<i>Glycyrrhiza glabra</i> L.	↑ Autophagy, anti-inflammatory, IFN- γ , β -chemokine induction, proliferation of T-lymphocyte ↓ Virus replication, virus polymerization, viral RNA/DNA, PKA, PKC, LPO, HMGB1 binding to DNA, CXCL10, IL-6, and CCL5 ↓ Virus replication	↑ Antioxidant, CAT, oxidant/antioxidant balance, cleaning the respiratory system (by increasing mucus production) ↓ Inflammatory cells diffusion, lung tissue fibrosis (collagen deposition), fibroblast proliferation, LPO levels, and hydroxyproline concentration	↑ Antioxidant	↑ Activation of T lymphocytes (increasing CD4 ⁺ and CD8 ⁺ levels), cytokine production, anti-inflammatory, secretion of IL-7, blood leukocytes, anti-apoptosis, and stimulation of macrophages ↓ Secretion of TNF- α , virus replication	[16,17-25]
4.	<i>Hyssopus officinalis</i> L.	↓ Virus replication	↑ Relaxant, regulating mucus secretion, smooth muscle proliferation ↓ Expression of MMP-9 and TIMP-1, collagen deposition	↑ Antioxidant ↓ Blood pressure	↑ Anti-inflammatory, regulation of IL-4, IL-6, IL-17, IFN- γ secretion, balancing Th1/Th2 ratio	[26-28]
5.	<i>Linum usitatissimum</i> L.	↓ Serine protease, virus replication	↑ Anti-inflammatory, antioxidant	↑ Antioxidant, HDL, anti-dyslipidemia ↓ Cholesterol, LDL, and blood pressure	↓ IgE, eosinophils ↓ Levels of TNF- α , IL-6, and cytokines	[29-31]
6.	<i>Malva sylvestris</i> L.	↑ Anti-inflammatory	↑ Anti-inflammatory, free radical scavenging	↑ Antioxidant, IL-10, NO ↓ LDH, CK-MB, TNF- α , IL-1 β , IL-6	↑ Anti-inflammatory, macrophage activation, IL-12, IFN- γ , regulation of CD14, MMP1, MIG ↓ Prostaglandins, thromboxane A2 (TXA2)	[32-36]
7.	<i>Matricaria chamomilla</i> L.	Antioxidant, free radical scavenging	Antioxidant, anti-inflammatory, anti-asthma, regulating Th1/Th2 ratio	Vasodilator, antioxidant, anti-ischemic, cardiac function, urinary creatinine, K ⁺ channels opener, sGC-cGMP signaling pathway, anti-hyperlipidemic, anti-hypercholesterolemic, and negative chronotropic effect ↓ Systolic and diastolic blood pressure, heart rate, blood pressure, ACE, Ca ²⁺ influx, LDH, CKMB, and Na ⁺ adsorption	Anti-inflammatory, free radical scavenging, anti-allergy, peripheral blood immune cells, and sensitivity of affected cells to auxiliary signals	[37-43]

Table 1: Continue

NO.	Scientific name	Pharmacological effects			Ref.
		Anti-viral	Respiratory protection	Cardioprotection	
8.	<i>Mentha pulegium</i> L.	↑ Anti-inflammatory, antioxidant	↑ Antioxidant, relaxant ↑ Heart rate (bradycardia), LDL oxidation	↑ Antioxidant, relaxant ↓ Heart rate (bradycardia), LDL oxidation	↑ Anti-inflammatory, antioxidant ↓ COX, JAK/STAT MAPK, iNOS, TNF- α , MCP-1, IL-6, NF- κ B, and production of thromboxane and leukotriene [44-46]
9.	<i>Origanum majorana</i> L.	↑ Anti-inflammatory ↓ Virus replication	↑ Anti-inflammatory, antioxidant	↑ Anti-ischemic, antioxidant, CAT, GPx, GST, SOD, heart function ↓ MDA, LDH, CK-MB	↑ Anti-inflammatory, Autophagy, MAPK, TGF- β ↓ Macrophage colony stimulation factor, MCP-1, VCAM-1, ICAM-1, I-TAC, MIG, collagen I and III, EGFR, MMP-1, PAI-1, TIMP1,2, TNF- α , IL-12 [47-51]
10.	<i>Viola odorata</i> L.	↓ Virus replication, virus receptor binding	↑ Anti-inflammatory, anti-cough, expectorant, regulating of mucus secretion, regulating of airway responses and eosinophilia, permeability of pulmonary arteries, protection of the inner mucous membranes of the mouth, throat, larynx, bronchi, and short-term agonists β_2 ,	↑ Antioxidant, relaxant, anti-dyslipidemia, NO, HDL, negative inotropic and chronotropic effect ↓ Blood pressure, calcium channel, atherogenic index, cholesterol, LDL	↑ Anti-inflammatory ↓ Total serum levels of IgE, IL-3, IL-4, bradykinin, proteases, and leukocytes [7,52-55]
11.	<i>Ziziphus jujube</i> Mill.	↓ Virus replication, serine protease, IFN- γ levels	↓ Pneumonia, mucositis, IgE, IL-3, IL-4 ↑ Antispasmodic, anti-inflammatory, levels of c-AMP, FOS, NO production ↓ Pulmonary smooth muscle thickening, regulating mucus production, Th2 cytokines (IL13, IL4, and IL5), pulmonary edema	↑ Antioxidant, anti-ischemic, anti-arrhythmic, SOD, CAT, and heart function ↓ MDA, LDH, apoptosis, creatine kinase, Ca ²⁺ -ATPase, Na ⁺ /K ⁺ -ATPase, and Mg ²⁺ -ATPase	↑ Anti-inflammatory, antioxidant, T-lymphocytes proliferation, CD4 ⁺ /CD8 ⁺ ratio, and natural killer cells (NK) [56-59]

↓: Inhibition or reduction. ↑: Activation or increase

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