

The Potential of Topical Phytopharmaceuticals for the Management of COVID-19-Associated Cough from the Perspective of Traditional Persian Medicine

Dear Editor

The coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has developed into the most severe pandemic affecting millions of people worldwide. Pneumonia and severe hypoxemia due to SARS-CoV-2 infection could lead to acute respiratory distress syndrome (ARDS) and consequently increase the mortality rate.¹ It has been reported that the use of Chinese herbal medicine (CHM) could relieve cough, which is a typical symptom in COVID-19 patients.² Randomized controlled clinical trials and retrospective studies have shown that conventional western therapy is more effective when combined with CHM use, leading to increased recovery rate and reduction of the cough duration.² Similarly, besides oral medications, Traditional Persian Medicine (TPM) suggests topical phytopharmaceuticals (e.g., dermal application of *Viola odorata* L.) for acute cough.³ Five topical multi-component antitussives have been described in TPM manuscripts. They contain different combinations of seven medicinal plants, namely *Cinnamomum camphora* (L.) J.Presl., *Coriandrum sativum* L., *Cucurbita* spp., *Lactuca sativa* L., *Nymphaea lotus* L., *Santalum album* L., and *Viola odorata* L. These components are prepared as greasy ointments (semisolid dosage form) to achieve better absorbance.

The reported symptoms associated with COVID-19 are cough, pneumonia, shortness of breath, lung scarring, fever, inflammation, headache, insomnia, and catarrh. The Ayurvedic and Unani systems of medicine recommend the dermal application of *Viola odorata* L. (*V. odorata*) for dry cough and lung inflammation. Dermal use of plants containing mucilage and polysaccharides (e.g., *V. odorata*) reduces inflammation in the respiratory system. In a previous study, using an animal model, the anti-inflammatory activity of *V. odorata* aqueous extract was compared with hydrocortisone by evaluating the area of hemorrhage, alveolar wall thickness, rupture of the alveolar septa, and alteration of the epithelial lining of the bronchioles.⁴ It was shown that similar to hydrocortisone, the extract could partially prevent lung damage by significantly reducing alveolar wall thickness, septum rupture, and the area of hemorrhage. These effects may be associated with the salicylate and saponin content of the plant.⁴ Flavonoids, glycosides, stigmasterol, and alkaloids are other constituents of *V. odorata*. Another study demonstrated the relaxant effect of *V. odorata* on induced contractions in isolated rabbit tracheal preparations, indicating possible calcium channel blocking activities.⁵

Advantages of topical phytopharmaceuticals as antitussive agents are cough relief, ease of use, low risk of systemic adverse effects, and potentially increased efficacy due to longer contact time. In TPM, topical compounds are prescribed to treat dry cough, pulmonary inflammation, fever, and headache. Moreover, the use of topical phytopharmaceuticals improves the severity and frequency of cough. Despite these beneficial effects, little attention has been paid to topical phytopharmaceuticals, necessitating further research studies.

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Authors' Contribution

P.B: Conception of the study, interpretation of data, drafting and revising. F.E: Conception of the study and drafting. R.Ch: Conception of the study and revising. N.K.M: Conception of the study and revising. All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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