

## EDITORIAL

## Phytochemicals and COVID-19: Two years of knowledge

## 1 | INTRODUCTION

On 31 December 2019, the World Health Organization (WHO) formally reported the occurrence of 'viral pneumonia' in Wuhan, China. Since then, the disease, later identified as COVID-19 has affected millions of individuals worldwide. As of 9 January, over 304 million confirmed cases and over 5.4 million deaths have been reported globally (WHO, weekly epidemiological update). The present virtual issue represents an update of a previous online issue (<https://onlinelibrary.wiley.com/doi/toc/10.1002/1099-1573.Plant-Compounds-for-COVID19>, Adhikari et al., 2021; Ahmad, Rehman, Ahmad, & Alkharfy, 2020; Antonelli, Donelli, Maggini, & Firenzuoli, 2020; Bahrami, Kamalinejad, Latifi, Seif, & Dadmehr, 2020; Boozari & Hosseinzadeh, 2021; Brendler et al., 2021; Chrzanowski, Chrzanowska, & Graboń, 2021; Cui, Xin, Tao, Mei, & Wang, 2021; Dave et al., 2020; Derosa, Maffioli, D'Angelo, & Di Pierro, 2021; Fakhri, Nouri, Moradi, & Farzaei, 2020; Ganguly & Bakhshi, 2020; Habtemariam et al., 2020; Haq et al., 2020; M. T. Islam et al., 2020; M. N. Islam et al., 2021; Kim et al., 2020; Lima, Brito, & da Cruz Nizer, 2021; Masiello, Novelli, Beffy, & Menegazzi, 2020; Omotuyi et al., 2021; Parida, Paul, & Chakravorty, 2020; Pawar & Pal, 2020; Rocha & de Assis, 2020; Roy et al., 2020; Thota, Balan, & Sivaramakrishnan, 2020; Tutunchi, Naeini, Ostadrahimi, & Hosseinzadeh-Attar, 2020; Upadhyay et al., 2020; F. Yang et al., 2020; Zahedipour et al., 2020; Zaman, Saqib, Ullah, Ayaz, & Ye, 2020; Q. Zhang et al., 2020) and covers the most significant discoveries published in Phytotherapy Research in the 2021 year. Below, a summary on the main findings are reported.

## 2 | TRADITIONAL MEDICINE

Traditional medicine is believed to be an opportunity in the fight against COVID-19. Data from traditional medicine may serve as a rich data bank and as a guiding principle for researchers involved in COVID-19 research (Adhikari et al., 2021; Ali et al., 2021; M. N. Islam et al., 2021; Jadhav & Karuppayil, 2021; Jalali, Dabaghian, Akbrialiabad, Foroughinia, & Zarshenas, 2021; Merarchi, Dudha, Das, & Garg, 2021; Mukherjee et al., 2021; Sangtani, Ghosh, Jha, Parmar, & Bala, 2020; Shah et al., 2021; N. A. Singh, Kumar, Jyoti, & Kumar, 2021; Tan et al., 2020).

Concerning Traditional Chinese Medicine (TCM), a systematic review concluded that TCM combined with conventional Western medicine was a potential treatment option for increasing clinical effective rate, improving the clinical symptoms, and preventing disease

progression in COVID-19 patients (Jiang et al., 2021). Also, a network pharmacology analysis was used to explore the active ingredients, targets, and potential mechanisms of Yinqiao powder in COVID-19 (Lin et al., 2021). Also, another study showed that Xiyanning injection (a Chinese herbal medicine used in the clinic to treat respiratory infection and pneumonia) was safe and effective in improving the recovery of patients with mild to moderate COVID-19 (X. Y. Zhang et al., 2021).

Traditional Indian Medical (TIM) practices include Ayurveda, Siddha and Unani. A systematic review of TIM identified some potentially-important herbs such as *Ocimum tenuiflorum*, *Tinospora cordifolia*, *Achyranthes bidentata*, *Cinnamomum cassia*, *Cydonia oblonga*, *Embelin ribes*, *Justicia adhatoda*, *Momordica charantia*, *Withania somnifera*, *Zingiber officinale* and *Kabusura kudineer* (R. S. Singh, Singh, et al., 2021). The antiviral properties of *Andrographis paniculata* were reviewed in a different report (Jadhav & Karuppayil, 2021).

Brazil has been a global epicentre for COVID-19. A review of secondary metabolites related to Brazilian herbal medicines followed by in silico evaluations indicated 19 potential anti-SARS-CoV-2 compounds, mainly triterpenes and phenolic compounds. The indicated compounds showed a high affinity with proteins considered as the main molecular targets against SARS-CoV-2 (Amparo et al., 2021).

Traditional Persian medicine (TPM) has recommended potential functional foods candidates to manage COVID-19. A clinical study demonstrated that Persian medicine herbal formulations (capsules and decoction) plus routine care significantly decreased duration of hospitalization, accelerated clinical improvement and decreased symptoms in the treatment group compared with standard-care group (Karimi et al., 2021).

A virtual screening among phytochemicals contained in plants used in traditional medical systems identified several compounds (e.g., ginkgolide, mezerein, tubocurarine, gnidicin, glycobismine A, sciadopitysin, gnididin, glycobismine A and sciadopitysin) as potential inhibitors of SARS-CoV-2 main protease (Sisakht, Mahmoodzadeh, & Darabian, 2021). Also, *Garcinia kola* and garcinic acid suppress SARS-CoV-2 spike glycoprotein S1-induced hyper-inflammation in human peripheral blood mononuclear cells through inhibition of NF- $\kappa$ B activation (Olajide et al., 2021).

Finally, other review articles highlighted traditional herbs or phytochemicals for the management of cardiovascular sign and symptoms (Mohammadi Pour, Farzaei, Soleiman Dehkordi, Bishayee, & Asgary, 2021) or to overcome stress, anxiety and improve mental

health associated with COVID-19 (Shahrajabian, Sun, Soleymani, & Cheng, 2021).

### 3 | POLYPHENOLS

Emerging data suggest polyphenols as potential immunomodulatory and/or antiviral agents against COVID-19. The present virtual issue contains review addressing the potential of flavonoids, curcumin, resveratrol and silibinin in attenuating lung injury and cytokine storm associated with the disease (Derosa et al., 2021; Di Petrillo, Orrù, Fais, & Fantini, 2021; El-Missiry, Fekri, Kesar, & Othman, 2021; Gour, Manhas, Bag, Gorain, & Nandi, 2021; Khezri, Saedi, Mohammadamini, & Zakaryaei, 2021; Palit, Mukhopadhyay, & Chattopadhyay, 2021; Pawar & Pal, 2020; Santana et al., 2021). Studies on specific polyphenols showed that (a) kaempferol inhibited the SARS-CoV-2 main protease (3CLpro) (Khan et al., 2021), (b) oroxylin suppressed the entrance of the SARS-CoV-2-spiked pseudotyped virus into ACE2 cells (Gao et al., 2021), (c) resveratrol inhibited the replication of SARS-CoV-2 in cultured Vero cells (M. Yang et al., 2021) and (d) silibinin interacted with SARS-CoV-2 main target proteins (e.g., spike protein RBD and Mpro residues) (Speciale et al., 2021). Clinical investigations showed the efficacy of nano-curcumin formulations in the management of mild to moderate hospitalized patients, being curcumin able to accelerate the recovery of the acute inflammatory phase (Hassaniazad et al., 2021; Saber-Moghaddam et al., 2021). Finally, a letter to the Editor discussed the interaction of fatty acids and resveratrol with angiotensin-converting enzyme 2 as well as immune system in COVID-19 (Hoang, 2020).

### 4 | CANNABINOID-RELATED MOLECULES

Specific reports are available for cannabidiol, a non-euphoric phytocannabinoid, and palmitoylethanolamide, a naturally occurring molecule related to the endocannabinoid anandamide. Pesce et al. (2020) analysed the antiinflammatory and immunomodulatory properties of palmitoylethanolamide in infectious and respiratory diseases and how these could translate to COVID-19 care. A different paper reported that cannabidiol inhibited SARS-Cov-2 spike (S) protein-induced enterotoxicity and inflammation through a PPAR $\gamma$ -dependent TLR4/NLRP3/Caspase-1 signalling suppression in intestinal cells (Corpetti et al., 2021).

### 5 | ALKALOIDS

Many alkaloids possess antiviral effects and, accordingly, they have been proposed as candidate for COVID-19. Pseudoephedrine was found to antagonize wild and mutated SARS-CoV-2 viruses by blocking virus invasion (Yu et al., 2021). A placebo-controlled study showed that a syrup containing propolis and *Hyoscyamus niger* L. extract

ameliorated the signs and symptoms of COVID-19 (Kosari et al., 2021). Finally, *Chelidonia majus*, a plant of the Papaveraceae family containing isoquinoline alkaloids, was believed to be a promising approach for the treatment of COVID-19, based on a 20-case series (Gardin & Braga, 2021).

Overall, it appears that the field regarding the potential use of plant-derived compounds in COVID-19 is advancing and thus far supplying the scientific community with its resources. The virtual issue is freely available at [https://onlinelibrary.wiley.com/doi/toc/10.1002/\(ISSN\)1099-1573.Phytocompounds-and-covid-19](https://onlinelibrary.wiley.com/doi/toc/10.1002/(ISSN)1099-1573.Phytocompounds-and-covid-19).

#### CONFLICT OF INTEREST

The Author declare no conflict of interest.

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