Dear Editor,

Curcumin is an herbal spice and coloring food additive extracted from *Curcuma longa* that has been evaluated as a complementary tool in the scenery of COVID-19\(^1-8\). *C. longa* (turmeric) is a plant used as a traditional Indian medicine with antiviral, analgesic, antimicrobial, antiproliferative, and anti-inflammatory properties\(^1-8\). Moreover, turmeric is one of the most popular spices worldwide, mainly in India\(^1,2,5,7,8\). Curcumin chemoprotection and cytoprotection are due to the free radicals scavenging, and also to the antioxidant, anti-inflammatory, anticancer, and antimicrobial actions\(^1-8\).

Moreover, it can exert antithrombotic effects via the inhibition of thrombin and FXa, and might be a complementary option to prevent post-Covid thromboembolism\(^2,3,5,8\). Curcumin can modify pro-inflammatory cytokines, apoptotic proteins, cyclooxygenase, endothelin-1, malondialdehyde, phosphorylase kinase, glutathione, prostaglandin, C-reactive protein, pepsinogen, transferrin receptor, and the transforming growth factor\(^1\). Curcumin can regulate molecules related to the inflammatory mechanisms, including cellular pathways, transcription factors, chemokines and cytokines, kinases, enzymes, and regulators of inflammasomes\(^2,3,6,8\). Curcumin has usefulness to counteract toxic manifestations of medicines as anti-tuberculosis, chemotherapy, analgesics, psychiatric and anesthetic drugs; as well as substances heavy metals, insecticides, nicotine, benzopyrene, alcohol, and aflatoxins\(^1\). Researchers have been actively seeking for some really effective prophylaxis and treatment to employ in SARS-CoV-2 infection\(^2,8\). Until consistent data of the studies on a definite treatment schedule for COVID-19, the evidence suggests curcumin as a promising alternative prophylactic management\(^2,8\).

Curcumin may have antiviral activity against SARS-CoV-2 by the envelope disruption; action in viral membrane proteins; inhibition of proteases; antiviral responses induction; and targeting the NF-kB, inflammasome, IL-6 trans-signaling, and HMGB1 pathways\(^2\). The novel genome research utilizing ClusteredRegularly Interspaced Short Palindromic Repeats Cas9 (CRISPR-Cas9) revealed that the High Mobility Group Box 1 (HMGB1) is a significant pro-viral host factor in SARS-CoV-2 infection\(^8\). This non-histone nuclear protein can bind with DNA and regulate transcription; its major role in danger-related molecular patterns is to enhance the inflammatory responses by binding to Toll-like receptors and the activation of the inflammasome\(^2,8\).

The severity of COVID-19 is directly related to cytokine release syndrome (CRS), and authors have described the role of inflammasome activation involved in driving CRS\(^2\). Many studies confirmed the potency of curcumin to block inflammasome activation; this property is due to curcumin (diferuloylmethane), the most abundant bioactive pharmacological of curcuminoids; bisdemethoxycurcumin, or demethoxycurcumin\(^2,6,8\). HMGB1 antagonists might be potential alternatives for protection against SARS-CoV-2.
infection, reducing HMGB1 expression and the mediated proinflammatory responses\textsuperscript{2}. Curcumin may inhibit SARS-CoV 3CL protease activity, vital for viral replication; and interacts with S protein and ACE2 protein intervening on the viral entry in lung cells\textsuperscript{2,8}. Then, it may protect from COVID-19 by down-regulating the ACE2 expression\textsuperscript{2,4,5,7,8}. As a promising agonist of transcription factor NRF2, curcumin can activate the NRF2 pathway in the lung of mice, an indication of antiviral activity against SARS-CoV-2\textsuperscript{2}. The increased survival of infected mice treated with curcumin was related to lower levels of interleukins (IL-1beta and IL-6) and tumor necrosis factor alpha in bronchopulmonary and blood samples\textsuperscript{3}. Curcumin is an adjuvant to control risk factors for COVID-19 as immunosuppression; diabetes; hypertension; heart, lung, cerebrovascular, and renal diseases; and cancer\textsuperscript{1,3-6}. Worth of note, curcumin may be also effective against human influenza A virus, Respiratory Syncytial virus infection, SARS-CoV \textit{in vitro}, as well as other acute and chronic respiratory disorders and in sepsis, by mechanisms involving the oxidative stress\textsuperscript{2}.

Pawar \textit{et al.} studied the effects of associated curcumin/piperine in the management of COVID-19; and the evolution of 70 controls under conventional COVID-19 treatment and probiotics was compared to that of 70 patients receiving the conventional treatment plus association twice daily\textsuperscript{3}. The authors concluded that curcumin/piperine can improve the COVID-19 management, and their use reduced the time of hospitalization and the number of deaths\textsuperscript{3}. Saber-Moghaddam \textit{et al.} performed a nonrandomized trial about the use of curcumin in hospitalized COVID-19 patients\textsuperscript{4}. During 2 weeks 41 patients were evaluated: 21 used nano-curcumin (curcuminoids 40 mg as nanomicelles, two capsules twice daily), and 20 patients of the control group\textsuperscript{4}. No patients died in both groups as well as none of the treatment group had clinical deterioration, which occurred in 40% of those of the control group during follow-up\textsuperscript{4}. The authors commented that over 300 clinical trials showed protective effects of curcumin on cardiovascular, pulmonary, metabolic, and liver diseases, besides cancer\textsuperscript{4}. They concluded that nano-curcumin can be useful to COVID-19 control without significant adverse reactions, and contribute to the reduction of hospital permanence of mild to moderate cases\textsuperscript{4}.

Based on the data here commented, authors suggest more clinical trials to evaluate the curcumin preventive and therapeutic role as an alternative or complementary medication against COVID-19.

1. \textbf{References}