# Turmeric against Covid-19: too much of a coincidence?

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Dear Editor,

Although a worldwide phenomenon, severe acute respiratory syndrome (SARS)-coronavirus (Cov)-2 infection is apparently less severe in some parts of the world. However, some countries present a surprisingly low death toll (https://coronavirus.jhu.edu/map.html downloaded in March 22, 11:00 AM). Epidemiology is crucial to tackle this pandemic as well as the search for compounds to treat. Turmeric (Indian saphron), a much-appreciated spice has India is by far the greater producer, and consumer, together with Pakistan, Malaysia, Bangladesh, Sri Lanka, Taiwan, China, Burma (Myanmar), and Indonesia (http://www.fao.org/fileadmin/user_upload/inpho/docs/Post_Harvest_Compendium_-_Turmeric.pdf downloaded in March 21, 2020). Curcuma or curcuminoids isolated from Turmeric have long been reported to have anti-inflammatory and immunomodulatory activity. Due to its very low bioavailability, alternatives to improve turmeric absorption have been developed. That is not to say that edible consumption would be of no effect (Aggarwal, Gupta & Sung, 2003). A world coronavirus map reveals that countries in southeast Asia present very low numbers of SARS-Cov-2 infections. Although numbers of infected people may not be reliable, the death rate is hard to be hidden. We focused our list on the major turmeric consumers but Taiwan given the strict rules for isolation implemented there. As of March 26, the death covid-19 toll reported in Indonesia, Malaysia, India, Pakistan, Bangladesh, Sri Lanka, and Burma, that represent over one-quarter of the world population was 128, being 78, 23, 14, 8, 5, 0, 0, respectively. On the other hand, Iran, which was a greater consumer of Turmeric, has experienced a shortage of this product due to economic sanctions, and had 2,234 deaths in March 22 (https://economictimes.indiatimes.com/news/economy/foreign-trade/turmeric-exports-hit-by-us-sanctions-against-iran/articleshow/70446034.cms?from=mdr). Community isolation has been hard to be implemented in Iran, which probably has shortage of health facilities and supplies to face this epidemic. Faced with data from developing countries, the death coronavirus disease (covid)-19 toll from high curcumin consumers is apparently very low as compared to those from developed countries, some of them with severe rules restricting social activities and better health infrastructure to treat patients. Would this just be coincidental? There are claims that drugs acting in the angiotensin converting enzyme (ACE) pathway may worsen the clinical picture of patients affected by SARS-Cov-2 (https://www.acc.org/latest-in-cardiology/articles/2020/03/17/08/59/hfsa-acc-aha-statement-addresses-concerns-re-using-raas-antagonists-in-covid-19 downloaded in March 21, 2020). ACE blocking compounds may lead to upregulation of the ACE2 gene receptor expression. It follows that ACE2 receptors are used by SARS-Cov-2 as a cell entry. It has been previously shown that rats subjected to thioacetamide induced hepatotoxicity are protected by Curcumin administration, an effect that was associated with down-regulation of the ACE gene (Akinyemi et al., 2015). Further, rats subjected to induced systemic arterial hypertension were protected by pre-treatment with ginger and turmeric rhizome supplementation, that led to reduction in ACE activity (Fazal, Fatima, Shahid & Mahboob, 2015). Hence, it might well be that Curcumin, by down-regulating ACE gene expression, can be of help against covid-19 disease. Notwithstanding, previous reports have shown that curcumin presents both direct and indirect antiviral activity against the human immunodeficiency virus (HIV) by inhibiting virus

replication or via blocking inflammatory pathways operating in the acquired immunodeficiency syndrome (Prasad & Tyagi, 2015). Hard times pose hard problems that demand urgent policies. Health authorities worldwide are struggling to decide which is best to prevent people from getting covid-19 infection and, when the disease unleashes, which attitudes to preserve lives. There are various compounds being tested against covid-19. Hydroxychloroquine, given the safety profile of this well-known immunomodulating compound used in rheumatology for prolonged periods, is being indicated pending robust data to document its efficacy, if any, on the basis that it may be a non-expensive life-saving strategy posing no additional harm to an already affected SARS-Cov-2 patient (Touret & de Lamballerie, 2020). Using the best rationale to look for evidence about the therapeutic effects of turmeric in COVID19, we can do an exercise on Hill's causality criteria. The strength of the association is high, based on the incidence map, and has been a repeated pattern in many countries with similar consumption of turmeric. There is some consistency between epidemiological and laboratory findings given that Curcumin apparently down-regulates ACE2 gene receptor expression, a major pathway in covid-19 cell entry (see above). We cannot yet claim specificity or biological gradient (dose-response relationship). Temporality is guaranteed because the consumption of saffron has long been incorporated into the culture of those countries. Similarly, chloroquine appears to interfere with the terminal glycosylation of the ACE2 cell receptor (Touret & de Lamballerie, 2020). At this time, we do not believe a ginger tea or adding turmeric to our meal would be of any harm. If in vitro data prove curcumin to be effective, clinical studies could be then proposed.

## Declarations

**List of Abbreviations:** angiotensin converting enzyme (ACE); covid-19, coronavirus disease; severe acute respiratory syndrome (SARS)-coronavirus (Cov)-2. SARS-Cov-2.

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