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Letter to the Editor

Comment on "In Silico Comparison of Separate or Combinatorial Effects of Potential Inhibitors of the SARS-CoV-2 Binding Site of ACE2"

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Dear Editor-in-Chief

It was with great interest that we read the recent paper by Shakhsi-Niaei et al. (1). The authors demonstrated a better effect on viral RBD binding site for three natural products, including Saikosaponin A, Baicalin, and Glycyrrhizin, and proposed them as the compounds to inhibit the SARS-CoV-2 binding site of angiotensin-converting enzyme 2 (ACE2). We aim to discuss this case from another aspect.

Mortality in patients on angiotensin-converting enzyme inhibitors (ACEIs)/ angiotensin receptor blockers (ARBs) did not differ from that in other patients (2). Furthermore, among patients with diabetes and hypertension, lower mortality was documented in patients with COVID-19 on ACEIs/ARBs (2). In the meta-analysis, ACEIs/ARBs were not associated with the mortality risk in patients with COVID-19. However, ARBs and ACEIs may have protective advantages, particularly in patients with hypertension (3). In another meta-analysis on 30 studies involving more than 10,000 adults, Asian patients with COVID-19 on ACEIs/ARBs showed a lower risk of severe disease or death (4).

Natural products containing bioactive compounds by modulating ACE2 activity may prevent and mitigate the entry and fusion of SARS-CoV-2 (5). At the beginning of the ongoing pandemic, we proposed the potential use of Persian herbs in COVID-19 through inhibition of angiotensin-converting enzyme 2 and discussed the in vitro outcomes of phytochemical evaluation on 20 natural products conducted before the pandemic. The laboratory results showed the highest ACE-inhibitory effect for a list of plants (6). A study utilizing plant bioresources supported this hypothesis with different natural products (5).

In a pharmacological review study, several plants used in Traditional Persian Medicine (TPM) proposed for treatment of COVID-19 due to therapeutic activities, primarily through cytoprotective, anti-inflammatory, antiviral, anti-apoptotic, and antioxidant mechanisms (7). Considering our report (6) and the potential of TPM (7), randomized controlled trials are warranted to establish the efficacy of natural products potentially used as ACEI/ARB candidates in COVID-19.

Traditional remedies and medicinal plants have been commercialized during the COVID-19 pandemic (8); however, evidence is lacking even after approximately two years of the pandemic. Additionally, the risks of poisoning, abuse, and practicing pseudoscience should be considered

when discussing the potential use of TPM and herbs during a pandemic.

With the emergence of new viral strains (9) and the likelihood of living with COVID-19 for a long time (10), further evidence is necessary to determine the effectiveness of natural products against COVID-19. Policies should integrate TPM into the healthcare system, without conflicts of interest, focusing mainly on evidence and clinical trials instead of infodemics.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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