

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. ELSEVIER

Contents lists available at ScienceDirect

Medical Hypotheses



journal homepage: www.elsevier.com/locate/mehy

Letter to Editors

Bioactive compounds with possible inhibitory activity of Angiotensin-Converting Enzyme-II; a gate to manage and prevent COVID-19

Letter to editors

Till now, no treatment or vaccine has been characterized for COVID-19 [1]. Angiotensin-Converting Enzyme-II (ACE-II) receptor, most likely the COVID-19 target, plays essential roles in virus transmission to the alveolar cells [2]. Accordingly, agents with potential inhibition or regulation of ACE-II receptors might be effective in COVID-19 management [3].

Bioactive compounds are valuable for drug development and adjuvant therapy of such infection. These compounds can act either as preventive agents or treatment accelerators. Naringin (a flavanone-7-Oglycoside with potential inhibition of COVID-19 binding to ACE-II receptors), Naringenin and Hesperetin (flavanone), Hesperidin (flavanone glycoside), Baicalin and Neohesperidin (flavone glycoside), Nobiletin (O-methylated flavone), Scutellarin (a flavone), Nicotinamine (nonproteinogenic amino acid), Glycyrrhizin (saponin) and Emodin (6-methyl-1,3, 8-trihydroxyanthraquinone) are of most considerable natural ACE-II inhibitors [4–6]. The averting impact of Naringin on pro-inhibitory cytokines (increased in COVID-19 infection) including Cyclooxygenase-II, Interleukin-6 and -1 β , and Nitric oxide synthase is considerable [5]. Glycyrrhizin can inhibit COVID-19 S-protein binding to ACE-II receptors [7]. Emodin, a bioactive antiviral agent may prevent S-protein binding to ACE-II receptors. Thus, Emodin and probably Aloe-emodin can stave off the COVID-19 infection via competing with S-protein in binding to ACE-II [7]. *Rheum palmatum* L. and *Aloe vera* (L.) Burm.f. are rich sources of these compounds [8].

Based on this opinion (Fig. 1), concerned compounds could be applied in prevention and management of COVID-19 solely or combination with conventional interventions.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

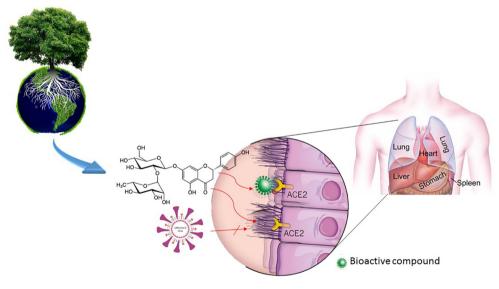


Fig. 1. Schematic view of bioactive compounds with ACE-II inhibitory activities.

Acknowledgment

Authors of this manuscript wish to express their appreciation to Tehran University of Medical Sciences (Project no: 99-1-104-47430).

References

- Bahbah EI, Negida A, Nabet MSJMH. Purposing Saikosaponins for the treatment of COVID-19. Med Hypotheses 2020;140:109782.
- [2] Zheng Y-Y, Ma Y-T, Zhang J-Y, Xie XJNRC. COVID-19 and the cardiovascular system. Nat Rev Cardiol. 2020;17(5):259–60.
- [3] Gheblawi M, Wang K, Viveiros A, et al. Angiotensin converting enzyme 2: SARS-CoV-2 receptor and regulator of the renin-angiotensin system. Circ Res 2020.
- [4] Chen H, Du QJP. Potential natural compounds for preventing 2019-nCoV infection. Preprints 2020.
- [5] Cheng L, Zheng W, Li M, et al. Citrus fruits are rich in flavonoids for immunoregulation and potential targeting ACE2. Preprints 2020.
- [6] Ho T-Y, Wu S-L, Chen J-C, Li C-C. Hsiang C-YJAr. Emodin blocks the SARS coronavirus spike protein and angiotensin-converting enzyme 2 interaction. Antiviral Res 2007;74(2):92–101.

- [7] Yan Y-M, Shen X, Cao Y-K, Zhang J-J, Wang Y, Cheng Y-X. Discovery of Anti-2019-
- nCoV Agents from Chinese Patent Drugs via Docking Screening. Preprint 2020.
- [8] Luo W, Su X, Gong S, et al. Anti-SARS coronavirus 3C-like protease effects of Rheum palmatum L. extracts. Biosci Trends 2009;3(4):124–6.

Farid Dabaghian^{a,b}, Mahnaz Khanavi^{a,c}, Mohammad M. Zarshenas^{b,d,e,*} ^a Department of Pharmacognosy, School of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

- ^b Medicinal Plants Processing Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
- ^c Faculty of Land and Food Systems, University of British Columbia, B.C., Canada
- ^d Epilepsy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
- ^e Department of Phytopharmaceuticals (Traditional Pharmacy), School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran E-mail address: zarm@sums.ac.ir (M.M. Zarshenas).

Medical Hypotheses 143 (2020) 109841