

Hypothetical Protective Effects of Crocin Carotenoid against Coronavirus-Induced Organ Damage: The Possible Role of the NF- κ B Signaling Pathway

Hypothesis

The coronavirus disease 2019 (COVID-19) pandemic is a major global medical and economic burden in that it had caused over 85 million infected cases and over 1.8 million deaths worldwide by the end of December 2020. Severe acute respiratory syndrome coronavirus (SARS-CoV-1) and Middle East respiratory syndrome coronavirus (MERS-CoV) are infectious diseases similar to COVID-19. However, unlike COVID-19, they did not create pandemics.¹⁻³ A major pathological hallmark of these infections is the so-called “cytokine storm”, which is an unregulated production of inflammatory cytokines inducing detrimental inflammation and causing organ injury and lethal multiple organ failure such as severe pulmonary, cardiovascular, and kidney failure in SARS-CoV-2 infection.^{4, 5} The coronavirus also induces inflammatory cascades, and thus, cause vasculopathy and coagulopathy, which might lead to lung cell degeneration and cardiovascular disease.^{4, 5} Mitochondrial dysfunction, oxidative stress, and inflammation and apoptosis pathways associated with COVID-19 might also induce multiple organ failure.^{4, 5} At the molecular level, the toll-like receptor 4 (TLR4)/toll/interleukin-1 receptor/resistance protein (TIR)-domain-containing adapter-inducing interferon- β (*TRIF*)/nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B) pathway is a common factor in activating cytokine production in infectious and inflammatory processes, including SARS-CoV-2 infection. Current data indicate the involvement of the cytokine inflammatory pathway, Janus kinase/signal transducers and activator of transcription, C-reactive protein, and the colony-stimulating factor in COVID-19-induced inflammatory events. Nonetheless, the clear role of the TLR4/TRIF/NF- κ B pathway in this regard is still unknown.^{6, 7}

Currently, there is no effective treatment for SARS-CoV-2 infection. A compound with potential for the treatment of SARS-CoV-2 infection is crocin carotenoid. Several studies have suggested the antiviral potential of crocin carotenoid in inhibiting the replication of several viruses similar to the coronavirus.⁸ Additionally, multiple experimental and clinical studies have reported the anti-inflammatory potential of crocin in various infectious and inflammatory disorders. Moreover, crocin carotenoid has properties both for protection against vascular damage and for the inhibition of thromboembolic events. Hence, its hypothetical protective effects against cardiovascular, cerebrovascular, and respiratory events.⁹ A preliminary study in humans has shown that at doses of 50 to 150 mg/kg, crocin carotenoid might have antiviral and anti-inflammatory effects during coronavirus-induced cytokine storms.⁹ On the other hand, preliminary results show that crocin carotenoid could not only modulate the TLR4/TRIF/NF- κ B pathway and thus, control cytokine production, vasculopathy, and coagulopathy in infections, but also mediate organ damage by inflammatory cascades.^{6, 7} Despite such properties, the protective effects of crocin carotenoid against coronavirus-induced inflammatory damage and its efficacy in the management of coronavirus replication have yet to be elucidated. Accordingly, we hypothesized that crocin carotenoid might confer antiviral and anti-inflammatory clinical benefits against SARS-CoV-2 infection, inhibit the vascular damage that leads to thromboembolic events after SARS-CoV-2 infection, and thus, protect the lung and cardiovascular systems. We welcome studies to further define the mechanism of action and potential clinical effects of crocin carotenoid in SARS-CoV-2 infection.

Conflict of Interest: None declared.

Please cite this article as: Gholami M, Nozarnezhad R, Motaghinejad M. Hypothetical Protective Effects of Crocin Carotenoid against Coronavirus-Induced Organ Damage: The Possible Role of the NF- κ B Signaling Pathway. *Iran J Med Sci.* 2021;46(3):228-229. doi: 10.30476/ijms.2021.88513.1921.

Mina Gholami¹, MD, PhD;^{ORCID} Rozhan Nozarnezhad², PharmD; Majid Motaghinejad³, PhD ^{ORCID}

¹School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran;

²Eastern Mediterranean University, School of Pharmacy, Famagusta, North Cyprus;

³Razi Drug Research Center, Iran University of Medical Sciences, Tehran, Iran

Correspondence:

Majid Motaghinejad, PhD;
 Razi Drug Research Center, Iran University of Medical Sciences, P.O. Box: 14496-14525, Tehran, Iran
Tel/Fax: +98 21 88622696
Email: motaghinezhad.m@iums.ac.ir
 Received: 14 October 2020
 Revised: 15 November 2020
 Accepted: 18 November 2020

References

- 1 Organization WH. Infection prevention and control guidance for long-term care facilities in the context of COVID-19: interim guidance, 21 March 2020. Geneva: World Health Organization; 2020.
- 2 Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *J Autoimmun.* 2020;109:102433. doi: 10.1016/j.jaut.2020.102433. PubMed PMID: 32113704; PubMed Central PMCID: PMC7127067.
- 3 Sharifian-Dorche M, Huot P, Oshero M, Wen D, Saveriano A, Giacomini PS, et al. Neurological complications of coronavirus infection; a comparative review and lessons learned during the COVID-19 pandemic. *J Neurol Sci.* 2020;417:117085. doi: 10.1016/j.jns.2020.117085. PubMed PMID: 32871412; PubMed Central PMCID: PMC7413162.
- 4 Becker RC. COVID-19-associated vasculitis and vasculopathy. *J Thromb Thrombolysis.* 2020;50:499-511. doi: 10.1007/s11239-020-02230-4. PubMed PMID: 32700024; PubMed Central PMCID: PMC7373848.
- 5 Mowla A, Sizardkhani S, Sharifian-Dorche M, Selvan P, Emanuel BA, Tenser MS, et al. Unusual Pattern of Arterial Macrothrombosis Causing Stroke in a Young Adult Recovered from COVID-19. *J Stroke Cerebrovasc Dis.* 2020;29:105353. doi: 10.1016/j.jstrokecerebrovasdis.2020.105353. PubMed PMID: 33039770; PubMed Central PMCID: PMC7518116.
- 6 Liu T, Zhang L, Joo D, Sun SC. NF-kappaB signaling in inflammation. *Signal Transduct Target Ther.* 2017;2. doi: 10.1038/sigtrans.2017.23. PubMed PMID: 29158945; PubMed Central PMCID: PMC5661633.
- 7 Dash P, Thomas PG. Host detection and the stealthy phenotype in influenza virus infection. *Curr Top Microbiol Immunol.* 2015;386:121-47. doi: 10.1007/82_2014_412. PubMed PMID: 25038940.
- 8 Kermanshahi S, Ghanavati G, Abbasi-Mesrabadi M, Gholami M, Ulloa L, Motaghinejad M, et al. Novel Neuroprotective Potential of Crocin in Neurodegenerative Disorders: An Illustrated Mechanistic Review. *Neurochem Res.* 2020;45:2573-85. doi: 10.1007/s11064-020-03134-8. PubMed PMID: 32940861.
- 9 Zeinali M, Zirak MR, Rezaee SA, Karimi G, Hosseinzadeh H. Immunoregulatory and anti-inflammatory properties of *Crocus sativus* (Saffron) and its main active constituents: A review. *Iran J Basic Med Sci.* 2019;22:334-44. doi: 10.22038/ijbms.2019.34365.8158. PubMed PMID: 31223464; PubMed Central PMCID: PMC6535192.