Quercetin Supplementation and COVID-19

Abstract
Quercetin is an antioxidant, detox, and anti-inflammatory agent, which may help lower inflammation as well as reduce toxic effects. It has been argued that vaccines have potential risks of local and systemic inflammatory responses and toxic effects of synthetic nucleosides and components for vaccine delivery. Administration of substances such as Quercetin may then mitigate these effects. It has similarly been argued that substances such as Quercetin may reduce the efficacy of vaccines, which works in building an immune response to produce antibodies. Under this other perspective, the assumption of Quercetin should be avoided when receiving vaccines. The purpose of this paper is to analyze the information available to understand if Quercetin may mitigate the damage from novel coronavirus disease 2019 (COVID-19) vaccines, or also reduce their efficacy.

Keywords
mRNA vaccines, DNA vaccines, Quercetin, Quercetin supplementation

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To the Editor
There is the possibility that quercetin may interfere with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) replication as well as reduce the inflammation and toxic effects of coronavirus disease 2019 (COVID-19) vaccines. Despite the scientific evidence being limited in the first case and unavailable in the second, given that there are no risks with moderate supplementation, quercetin is recommended.

Quercetin acts as an antioxidant, detox, and anti-inflammatory agent. Quercetin is the most abundant dietary flavonoid that is found in many plants and foods, such as onions, apples, grapes, berries, broccoli, citrus fruits, cherries, green tea, coffee, red wine, and capers, Ginkgo biloba, St. John’s wort, American elder, Buckwheat tea and others. Quercetin has low bioavailability and supplements may include other compounds to increase absorption. Quercetin works better combined with other supplements, such as resveratrol, genistein, and catechins. Quercetin from food is likely to be safe. Optimal doses of quercetin as supplements have not been established for any condition and there are no risks with moderate supplementation.

Quercetin is an antibacterial agent, an antioxidant, a protein kinase inhibitor, an antineoplastic agent, a ribosyl dihydro nicotine dehydrogenase (quinone) inhibitor, a phytoestrogen, a radical scavenger, a chelator, and an Aurora kinase inhibitor. Quercetin-treated neutrophils exhibited suppression in inflammatory genes. It mostly helps to combat free-radical damage. Many therapeutic uses of quercetin are being prompted. It may alleviate oxidative damage, cadmium-induced autophagy inhibition, and may induce cancer cell death.

Several works have suggested that quercetin may interfere with COVID-19 replication and so this makes its use as a supplement interesting. Figure 1 summarizes the studies of quercetin for COVID-19 infection. There is an 87% improvement associated with the uptake of quercetin. Quercetin helps in the early stages of COVID-19 infection. Similarly based on a small RCT, quercetin also helped in prophylaxis. A similar positive was found in a small prospective study without a control group.

It has been argued that vaccines have the potential risks of local and systemic inflammatory responses and toxic effects of synthetic nucleosides and components for vaccine delivery. Administration of quercetin may then mitigate these effects. Considering how many people have been infected by SARS-CoV-2 also after having received the COVID-19 vaccines (see the cases in the UK or Seychelles), a natural compound that is potentially helpful against infection may have an even larger appeal if effective against side effects of vaccines.

The Australian Therapeutic Goods Administration (TGA) periodically reports the adverse events from the administration of COVID-19 vaccines. The vaccines adopted in Australia are predominantly Comirnaty (Pfizer), which is mRNA, and Astra Zeneca, which is DNA. Both vaccines require 2 shots. The latest report mentions a percentage of side effects of 0.56%, with dizziness and fainting the most common short-term side effects following vaccination. The previous report mentioned 210 accounts of deaths following the administration of 3.6 million doses of the vaccines, corresponding to 0.01%. Hence, there are significant side effects also in the short term associated with the administration of COVID-19 vaccines.
An mRNA vaccine works by providing the body with genetic information as a form of mRNA to produce viral proteins. In the case of SARS-CoV-2, they are the spike proteins found on the surface of the virus. These proteins trigger an immune response and the production of specific antibodies, preparing the body to fight off the infection when coming into contact with the pathogen. The vaccine works causing an immune response. The mRNA vaccine only carries the information needed to make a small part of the virus, but it does not contain the SARS-CoV-2 virus and it does not cause COVID-19. The DNA vaccine transmits the virus’s genetic information to the messenger RNA (mRNA) molecule. Thus, the DNA vaccine follows the same principle, but it is only one step behind. mRNA vaccines have potential risks of local and systemic inflammatory responses and toxic effects of synthetic nucleosides and components for vaccine delivery. As quercetin is an antioxidant and anti-inflammatory agent, it may help lower inflammation as well as reduce the toxic effects of COVID-19 vaccines. While there is no evidence yet that quercetin can limit this damage, the opportunity that quercetin can interfere with the vaccines’ downregulation of the immune response is extremely unlikely. While more research is certainly needed to limit damage from mRNA and DNA vaccines with quercetin, there are no risks with moderate supplementation.

In conclusion, there is evidence that COVID-19 vaccines have toxic effects, and do not prevent infection. There is also evidence that quercetin may have antiviral properties against COVID-19 infection and it may work as an antioxidant, detox, and anti-inflammatory agent. Quercetin may likely help to lower inflammation as well as reduce the toxic effects of COVID-19 vaccines, also reducing the chances of being infected. All these reasons support quercetin supplementation before and after the COVID-19 vaccination.

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**Trial Registration**

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**References**

1. Xu D, Hu MJ, Wang YQ, Cui YL. Antioxidant activities of quercetin and its complexes for medicinal application. *Molecules*. 2019;24(6):1123.
2. Terao J. Factors modulating bioavailability of quercetin-related flavonoids and the consequences of their vascular function. *Biochem Pharmacol*. 2017;139:15-23.
3. Kaşkıcı MB, Bağdatlıoğlu N. Bioavailability of quercetin. *Curr Res Nutr Food Sci*. 2016;4(October):146-151.
4. Pignatelli P, Pulcinelli FM, Celestini A, et al. The flavonoids quercetin and catechin synergistically inhibit platelet function by...
antagonizing the intracellular production of hydrogen peroxide. Am J Clin Nutr. 2000;72(5):1150-1155.
5. Scheepens A, Tan K, Paxton JW. Improving the oral bioavailability of beneficial polyphenols through designed synergies. Genes Nutr 2010; 5(1):75-87.
6. Quercetin SA. www.webmd.com/vitamins-and-supplements/quercetin-uses-and-risks, published 2021. (accessed May 27, 2021).
7. NIH PubChem. Quercetin. pubchem.ncbi.nlm.nih.gov/compound/Quercetin, published 2021 (accessed May 27, 2021).
8. Chuammitri P, Srikok S, Saipinta D, et al. The effects of quercetin on microRNA and inflammatory gene expression in lipopolysaccharide-stimulated bovine neutrophils. Vet World. 2017;10(4):403-410.
9. Dostal Z, Modriansky M. The effect of quercetin on microRNA expression: a critical review. Biomed Pap Med Fac Univ Palacky Olomouc. 2019;163(2): 95-106.
10. Li H, Chen FJ, Yang WL, et al. Quercetin improves cognitive disorder in aging mice by inhibiting NLRP3 inflammasome activation. Food Funct. 2021;12(2):717-725.
11. Derosa G, Mafstoi P, D’Angelo A, et al. A role for quercetin in coronavirus disease 2019 (COVID-19). Phytother Res. 2021;35(3): 1230-1236.
12. Gansukh E, Nile A, Kim DH, et al. New insights into antiviral and cytotoxic potential of quercetin and its derivatives—a biochemical perspective. Food Chem. 2021;334:127508.
13. Jia H, Zhang Y, Si X, et al. Quercetin alleviates oxidative damage by activating nuclear factor erythroid 2–related factor 2 signaling in porcine enterocytes. Nutrients. 2021;13(2):375.
14. Zhao Y, Li ZF, Zhang D, et al. Quercetin alleviates cadmium-induced autophagy inhibition via TFEB-dependent lysosomal restoration in primary proximal tubular cells. Ecotoxicol Environ Saf. 2021; 208:111743.
15. Wang ZX, Ma J, Li XY, et al. Quercetin induces p53-independent cancer cell death through lysosome activation by the transcription factor EB and reactive oxygen species-dependent ferroptosis. Br J Pharmacol. 2021;178(5):1133-1148.
16. Bastaminejad S, Bakhtiyari S. Quercetin and its relative therapeutic potential against COVID-19: a retrospective review and prospective overview. Curr Mal Med. 2021;21(5):385-391. DOI:10.2174/1566524020999200918150630
17. Agrawal PK, Agrawal C, Blunden G. Quercetin: antiviral significance and possible COVID-19 integrative considerations. Nat Prod Commun. 2020;15(12). doi.org/10.1177/1934578X20976293
18. Di Pierro F, Derosa G, Maffioli P, et al. Possible therapeutic effects of adjuvant quercetin supplementation against early-stage COVID-19 infection: a prospective, randomized, controlled, and open-label study. Int J Gen Med. 2021;14:2359-2366.
19. Di Pierro F, Iqtadar S, Khan A, et al. Potential clinical benefits of quercetin in the early stage of COVID-19: results of a second, pilot, randomized, controlled and open-label clinical trial. Int J Gen Med. 2021;14:2807-2816.
20. Arslan B, Uncu Ergan N, Topuz S, et al. Synergistic effect of quercetin and vitamin C against COVID-19: is a possible guard for front liners. SSRN Preprints. 2020. doi:10.2139/ssrn.3682517
21. Aguilar JF, Báez GAS, Galeano F. Oral quercetin in adult patients as a potential nutraceutical against coronavirus disease 2019 (COVID-19). J Adv Med. 2021;23(3):1-7.
22. Therapeutic Goods Administration (TGA). COVID-19 vaccine weekly safety report—. www.tga.gov.au/periodic/covid-19-vaccine-weekly-safety-report-03-06-2021, published 2021 (accessed June 3, 2021).
23. Therapeutic Goods Administration (TGA). COVID-19 vaccine weekly safety report—. www.tga.gov.au/periodic/covid-19-vaccine-weekly-safety-report-27-05-2021, published 2021. (accessed May 27, 2021).
24. Pardi N, Hogan MJ, Porter FW, et al. mRNA vaccines—a new era in vaccinology. Nat Rev Drug Discov. 2018;17(4):261-279.
25. Zhang C, Maruggi G, Shan H, et al. Advances in mRNA vaccines for infectious diseases. Front Immunol. 2019;10:p.594.
26. Jackson NA, Kester KE, Casimiro D, et al. The promise of mRNA vaccines: a biotech and industrial perspective. npj Vaccines. 2020;5(1):1-6.
27. Doulieris M, Papaefthymiou A, Kotronis G, et al. Does COVID-19 vaccination warrant the classical principle “ofelein imi vlapitn”? Medicina. 2021;57(3):p253.