

Peer Review

Review of: "Can Urolithin A Help in Curing COVID-19 Infection?"

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This commentary explores the potential role of Urolithin A (UA), a gut microbiota-derived metabolite, as a possible supportive therapeutic agent in COVID-19 infection. The topic is scientifically interesting and relevant, particularly given the increasing attention toward nutraceuticals, host-microbiome interactions, and immunomodulatory compounds in infectious disease management. The manuscript provides a concise overview of UA biogenesis, biological functions, and mechanistic pathways, including antioxidant activity, anti-inflammatory effects, and mitochondrial quality control via mitophagy. These mechanisms are plausibly linked to pathological processes observed in COVID-19, such as cytokine dysregulation, oxidative stress, and mitochondrial dysfunction.

The article is well-structured and readable, and it effectively introduces UA to readers who may not be familiar with microbiome-derived metabolites. The integration of evidence from experimental and clinical studies investigating UA's systemic benefits strengthens the conceptual foundation of the commentary.

However, several important limitations should be addressed to improve scientific rigor. First, the central hypothesis linking UA to COVID-19 management remains largely speculative and is not supported by direct experimental, clinical, or epidemiological evidence. The manuscript would benefit from a clearer distinction between mechanistic plausibility and demonstrated therapeutic efficacy. Second, comparisons with supplements such as vitamin C, vitamin D, and zinc are presented without sufficient critical discussion of differences in evidence quality or clinical validation. Third, the manuscript would benefit from a more comprehensive discussion of pharmacokinetics, dosing considerations, bioavailability variability, and safety profiles of UA supplementation in infectious disease settings.

Additionally, the article could be strengthened by including discussion of potential antiviral mechanisms, interaction with immune signaling pathways specific to SARS-CoV-2 pathogenesis, and possible

limitations related to gut microbiome variability among individuals. Expanding the discussion toward future research directions, such as experimental models or clinical trial design, would also enhance translational relevance.

Overall, this commentary provides an interesting conceptual hypothesis linking Urolithin A with potential therapeutic or supportive roles in COVID-19 infection. While the biological rationale is promising, stronger evidence-based analysis and clearer delineation of speculative versus established findings are necessary to improve scientific credibility and clinical applicability.

Declarations

Potential competing interests: No potential competing interests to declare.