

The Role of Diet and Supplementation of Natural Products in COVID-19 Prevention

Amin Gasmi ¹ • Salvatore Chirumbolo ^{2,3} • Massimiliano Peana ⁴ • Sadaf Noor ⁵ • Alain Menzel ⁶ • Maryam Dadar ⁷ • Geir Bjørklund ⁸ •

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Abstract

Recently, a discussion has begun on the global management strategy against COVID-19 based on the hypothesis that individuals' macro- and micronutrient status combined with antiviral drugs and herbs can be an ally against the infection. The hypothesis is that people's nutritional and oxidative scavenging capacity may provide fundamental data to predict severe and acute pulmonary distress following SARS-Cov2 infection. Consequently, the scientific community has addressed the role of balanced diets, nutritional supplements, and micronutrients, including folk herbal formulations, in reducing hospitalization and the severity of pulmonary impact in COVID-19 by preventing the most serious forms of the infection. This led to an animated debate on the potential effectiveness of some vitamins, micronutrients, and traditional Chinese medicine in preventing COVID-19, with some authors convinced that plant extracts could act oppositely, exacerbating the effect of the infection. While current research is still far to assess the suggestions and issues raised in this short communication, it is undoubtedly true that determining an individual's current metabolic status, including macro- and micronutrients, is an essential factor in defining any individuals' deficiencies, which will need to be addressed urgently through a proper diet, specific personalized nutritional supplementation, and lifestyle changes.

 $\textbf{Keywords} \;\; \text{Immunomodulation} \; \cdot \text{COVID-19} \; \cdot \text{SARs-CoV-2} \; \cdot \text{Nutrients} \; \cdot \; \text{Vitamins} \; \cdot \; \text{Trace elements} \; \cdot \; \text{Natural products} \; \cdot \; \text{Dietary habits}$

The scientific community has recently addressed the role of balanced diets, nutrients from raw food and natural products,

- Société Francophone de Nutrithérapie et de Nutrigénétique Appliquée, Villeurbanne, France
- Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
- CONEM Scientific Secretary, Verona, Italy
- Department of Chemistry and Pharmacy, University of Sassari, Sassari, Italy
- Institute of Molecular Biology and Biotechnology, Bahauddin Zakariya University, Multan, Pakistan
- ⁶ Laboratoires Réunis, Junglinster, Luxembourg

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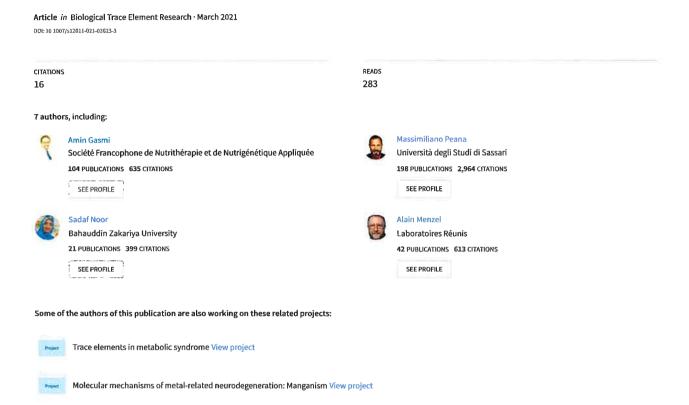
- Razi Vaccine and Serum Research Institute, Agricultural Research, Education and Extension Organization (AREEO), Karaj, Iran
- Second Council for Nutritional and Environmental Medicine (CONEM), Toften 24, 8610 Mo i Rana, Norway

and micronutrients, including folk herbal formulations such as Chinese medicine, in reducing hospitalization and the severity of pulmonary impact in COVID-19 by preventing the most serious and exacerbated forms of the infection [1, 2]. The general idea underlying this approach is that COVID-19 has an extraordinarily complex spectrum of clinical processes. These include the individual's ability to limit the severity of the infection's development through immunity, genetics, lifestyle, and environment. Therefore, people's nutritional and oxidative scavenging capacity may provide fundamental data to predict severe and acute pulmonary distress following SARS-Cov2 infection [3-6]. Despite some concerns about the possible toxicity of many xenobiotic compounds retrieved from plant extracts on the market, natural products in the diet may reduce COVID-19 exacerbation following viral infections [1]. Undoubtedly, COVID-19 remains a complex pathology where there is a significant association with metabolic disorders, particularly with obesity-related hypertension, usually associated with the elderly and the infection's course/ progression [7-9]. Therefore, a fundamental question would be: Does an optimized diet prevent the onset of COVID-19



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despite viral exposition? The challenge is to improve diet and lifestyle to reduce the impact of comorbidities related to metabolic imbalance [10–13]. A recent comment by Young and Zampella [14] addressed two areas of concern, including the discussion of the potential antiviral properties of some herbal products, such as *Withania somnifera L*. and some natural derived extracts [1]. The ability of withanolides from *Withania somnifera L*. (or ashwagandha), particularly withanoside 5, exhibits very high molecular docking properties and binding affinity against SARS-CoV2 components and makes promising use of some folk medicine to fight the clinical consequences of the COVID-19 outbreak [15].

On the contrary, some authors are convinced that plant extracts may exacerbate COVID-19 [14]. Natural products acting, for example, on such mechanisms exacerbated during COVID-19, such as pulmonary hypertension, notoriously borne by *Glycyrrhiza glabra* extracts, should be further examined in docking research to gather those compounds able to provide benefits in COVID-19 patients [16]. Important clinical trials are also planned to highlight which type of herbal extracts can address COVID-19 [17, 18]. The issue of using folk medicine is fundamental for at least two reasons. First, it is an approach highly adopted in South East Asian countries and China, where the COVID-19 outbreak began, and second it is a potential source of suggestions for new important therapeutic drugs against SARS-CoV2.

Very recently, Gasmi et al. discussed the individuals' macroand micronutrient status combined with antiviral medication and herbs in order to establish a comprehensive management strategy of both edible and pharmaceutical natural products to be used against COVID-19 [1]. The commonest micronutrients able to determine the clinical course of individual COVID-19 include vitamins D, A, and C, selenium, and zinc [12, 19]. However, more investigation is needed into other micronutrients, whose depletion or insufficient uptake may exacerbate COVID-19 [12]. There has been an animated debate on the role that vitamin D [20], essential amino acids, branched amino acids, polyunsaturated fatty acids (PUFAs), and other micronutrients play in COVID-19 prevention [21]. Furthermore, some medications and specific herbal products were recently discussed as potential therapeutic options according to their particular antiviral mechanism based on previous research about SARS-CoV and MERS-CoV [2, 22-24]. Agreement in this regard can be extremely hard to be achieved without further good-quality studies. For example, criticism was raised on the previous report [14] regarding the potential toxicity of substances such as Echinacea purpurea (purple coneflower), Astragalus (milkvetch), Pelargonium sidoides (African geranium), curcumin, propolis, Glycyrrhiza glabra (licorice) root, and glycyrrhizin [14], when these herbs have never been mentioned [1]. More than 85% of patients infected with SARS-CoV2 in China received certain types of traditional Chinese medicine (TCM) preparations as a part of their

treatment [25]. These remedies' allergic and anaphylactic potentials are poor and warrant their safety, though vigilance is mandatory [26]. China and South Korea released national guidelines for traditional medicinal treatment on COVID-19 [27]. They stress the possibility that herbal extracts could be noxious for patients with COVID-19 might be the logical consequence of a psychological attitude from the increasing belief that COVID-19 is worsening worldwide. Based on historical records and human evidence of SARS and H1N1 influenza prevention, the Chinese herbal formula could be an alternative approach for preventing COVID-19 in high-risk populations. Prospective, rigorous population studies are warranted to confirm the potential preventive effect of TCM. Despite this, there is mounting evidence that metabolic disorders, as a comorbidity of severe forms of COVID-19, are more frequent, therefore addressing diet and balancing them with supplementation, which may improve COVID-19 therapy [12].

For example, an individual with proven zinc insufficiency or deficiency could consider zinc supplementation as a sensible option to improve their micronutrient status during pandemics [28–31]. Zinc is fundamental to fight against SARS-CoV2 infection as this cofactor is of the utmost importance for ROS scavenging and reduction of the stress response, which can lead, particularly in the elderly, to exacerbated forms of pneumonia caused by COVID-19 [6, 32, 33].

Gasmi et al. [1] focused on the individual risk management strategy during this period without defined treatment for the general population. The determination of an individual's current metabolic status, including macro- and micronutrients, is essential. Any individuals' deficiencies need to be corrected through diet, nutrition, lifestyle, and environmental changes.

However, very few clinical trials or observational case or cohort studies are available to assess the suggestions and issues raised in this short communication [34–36]. The proper collection of dietary habits among different populations, with the available raw food and natural sources, is a major task of the WHO engagement to address the pandemic and manage the emergency. Physicians should advise for the better diet available to reduce the impact of pneumonia and better manage possible hospitalizations. The big concern of a correct dietary habit and lifestyle is not pleonastic and can address the coronavirus disease in a much more correct approach. Whereas most advertising about herbal medicine tends to discourage the use of natural products to prevent the onset of severe pneumonia, a correct diet optimizes both gut and lung microbiomes, allowing the subject to prevent any involutive course towards COVID-19 caused-ARDS. Utilizing new plant-derived drugs as a therapy against COVID-19 is still a long way from being realized. However, a thorough investigation of the immune-metabolic status of people who might be infected with SARS-Cov2, by studying their daily life habits and diets, based on their folk traditions and geographical distribution, is mandatory for science.



Data Availability Not applicable.

Declarations

Conflict of Interest The authors declare no competing interests.

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