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Food science and COVID-19

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ABSTRACT

Theories proposing a role of specific dietary components or food supplements in the prevention or treatment of COVID-19 have received extensive social media coverage.

A multitude of scientific publications have also pointed to the importance of food and nutrition in combating the COVID-19 pandemic. The present perspective critically addresses the question of what food science can actually contribute in this context.

Animal studies suggest that micronutrients, food bioactives or functional foods may carry the potential to augment viral defense. However, the specific roles of food components in viral infectious diseases in humans remain unclear. Rigorous research assessing the efficacy of food compounds in counteracting infections would require long-term randomized controlled trials in large samples. While no foods, single nutrients or dietary supplements are capable of preventing infection with COVID-19, a balanced diet containing sufficient amounts of macronutrients and diverse micronutrients is a prerequisite of an optimally functioning immune system. High-energy diets and obesity are major risk factors for a more severe course of COVID-19.

Therefore, population-wide body weight control and weight reduction in overweight people are important preventive measures. Diet may play a beneficial role in maintaining a healthy body weight and preventing non-communicable conditions.

1. Introduction

A previously unknown coronavirus, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in December 2019 and is the cause of the novel infectious coronavirus disease 2019 (COVID-19) [1]. COVID-19 was declared a global pandemic by the World Health Organization (WHO) in March 2020 [2]. The development of specific, effective and safe preventive and therapeutic measures against COVID-19, including vaccines, anti-viral agents and passive immunotherapy, is likely to face numerous obstacles and may see little success in the foreseeable future [3].

Food and nutrition play pivotal roles in the promotion of long-term health and the prevention of chronic disease [4]. Adequate nutrition is critically important for an optimally functioning immune system, and both consistent malnutrition and over nutrition can adversely affect immune responses. A PubMed literature search using the keywords "(food OR nutrition) AND (COVID-19 OR SARS-CoV-2)" found over 1 000 articles published up until July 31, 2020. The multitude of papers seem to suggest an important role of food and nutrition in the prevention of SARS-CoV-2 infection and the management of COVID-19. Moreover, countless news stories and reports on websites and social media platforms convey the message that dietary supplements or specific foods can prevent the spread of the novel coronavirus. The present perspective critically addresses the question of what food science can and cannot contribute in the times of the COVID-19 pandemic.

2. Nutrients, food compounds and COVID-19

Available evidence underlines a significant link between diet, immunity and disease susceptibility. Nutritional deficits in energy, protein and micronutrients can impair the immune system and resistance to infection [5,6]. Specific nutrients and combinations of nutrients may exert effects on immune functions through cell activation and modification of both gene expression and production

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of signaling molecules [7]. Dietary ingredients can also influence immune responses through their effects on gut microbiota composition [8].

The deleterious effects of disease-related malnutrition are well-known [9] and can be prevented or contained by prompt nutritional supplementation [10]. Based on the experience that, on admission to hospital, most patients with COVID-19 present with anorexia and severe inflammation resulting in a marked decrease in food intake, a nutritional support protocol for the prevention of the consequences of malnutrition in non-critically ill patients has been suggested; this protocol requires further evaluation [11].

A large number of functional food plants, such as ginger, garlic, turmeric, black pepper, liquorice, pomegranate and elderberry, have been claimed to have potentially immunomodulatory and anti-viral properties [12]. However, the evidence base for the efficacy of these food plants in humans is weak or non-existent, and some of them may produce toxic effects if taken in large amounts.

Polyphenols and carotenoids are food bioactives thought to have antiviral efficacy. Polyphenols, for example, have been shown to influence the regulation of immune cells, the synthesis of pro-inflammatory cytokines and the suppression of pro-inflammatory gene expression [13]. A mechanism underlying potential antiviral properties of resveratrol may be the upregulation of the angiotensin-converting enzyme 2 (ACE2), which has been demonstrated to be a functional SARS-CoV receptor [14,15] necessary for host cell entry and subsequent viral replication. The ACE2 receptor is also involved in the entry of SARS-CoV-2 to cells [16,17]. Hypotheses regarding antiviral benefits of carotenoids [18] and polyphenols [19] are based mainly on studies in cell cultures and animal models. However, controlled interventions using food bioactives in human have not been conducted, and any beneficial effects of food bioactives in regard to viral infections in humans are questionable.

Probiotics can activate multiple immune mechanisms and exert effects on host immunological networks [20,21]. They have been found to enhance immune responses [22] and to modestly decrease the incidence and duration of viral respiratory tract infections [23,24]. The administration of probiotics to strengthen the immune system has been recommended in COVID-19 guidelines [25]. While microbial dysbiosis with a reduction in *Lactobacillus* and *Bifidobacterium* has been observed in some people with COVID-19 [26], the efficacy of conventional probiotics in the prevention or therapy of COVID-19 is unknown. The effects of SARS-CoV-2 on gut microbiota should be investigated in more detail [27].

A variety of micronutrients, e.g. vitamins and trace elements, play essential roles in both innate and adaptive immune responses, and micronutrient homeostasis is central to the maintenance of a healthy immune system [28]. While micronutrient deficiencies can decrease immunity to disease, supplementation has been found to improve immunity to viral infections [29]. For example, vitamin D deficiency appears to be associated with impaired immune responses and an increased risk of systemic infections [30]. Vitamin D supplementation may prevent respiratory infections through, among other mechanisms, a reduced production of pro-inflammatory cytokines and, thus, a consequent decrease in the risk of a cytokine storm leading to pneumonia [31].

The efficacy of micronutrients and other dietary interventions in infections can be affected by numerous factors, such as the type of pathogen, the dose and duration of administration and the age, genetics, lifestyle, immunological and nutritional status of the study participants [32]. In particular, immunosenescence during aging changes the impact of nutrition on immune function [33]. Furthermore, prolonged supplementation of food bioactives and micronutrients at high doses may have adverse effects and may even aggravate infectious diseases [34–36].

The search for individual nutrients capable of promoting optimal immune system functioning relies on a belief in magic bullets and an outdated model of disease pathophysiology. The expression 'magic bullet', coined by the German physician and Nobel laureate Paul Ehrlich more than a century ago, describes precisely targeted medical treatments [37]. The research strategy attempting to understand the functions of single nutrients and to examine their therapeutic efficacy individually is in accord with traditional pharmacological methodology. However, this approach is at odds with physiological processes, which require an intake of a wide range of nutrients in balance. This provides an explanation for the limited success of the administration of single nutrients.

3. Dietary habits, obesity and COVID-19

Recent studies have attempted to explain the highly variable COVID-19 case fatality ratios between countries with at least partially differing dietary habits [38,39]. For example, an examination of the correlation between average consumption of fermented vegetables and COVID-19 mortality across Europe, using information from the European Food Safety Authority Comprehensive European Food Consumption Database found that the national mortality risk for COVID-19 decreased by 35.4% for each g/day increase in the average intake of fermented vegetables such as sauerkraut [39]. Hypotheses explaining this association include antioxidant activity and effects of fermented vegetables on the microbiome. However, the correlational relationship does not necessarily equate with causation. The numerous factors likely to influence the mortality rates observed include demographic factors, extent of SARS-CoV-2 testing and assessment of death rates, trained immunity and cross-immunity of populations, public hygiene, characteristics and preparedness of health care systems, climatic and other environmental variations as well as other nutritional aspects.

Nevertheless, certain dietary patterns can have a detrimental effect on immune responses and can be involved in the development of various inflammatory diseases [40]. In animal models, western-type calorically rich diets have long been known to be capable of priming for augmented innate immune responses, e.g. they have been demonstrated to induce enhanced cytokine production to stimulation with lipopolysaccharide [41,42]. It has recently been shown that a western diet can also trigger innate immune reprogramming and lead to long-term changes of immune responses in mice; the NLRP3 inflammasome seems to play a critical role in these responses [43]. In summary, the consumption of a western diet can generate exaggerated immune responses to exogenous and endogenous triggers of inflammation and could contribute to inflammatory disease.

A link has been demonstrated between non-communicable diseases, such as obesity, type 2 diabetes and metabolic syndrome, and various infectious diseases, post-infection complications and mortality from severe infections [44,45]. Obesity, in particular, has been shown to have a substantial impact on pathogen defense and immunity. A characteristic of obesity is low-grade chronic inflammation, which can impair innate and adaptive immune responses and render the immune system more vulnerable to infections [46].

Non-communicable diseases may also increase the risk for adverse outcomes and mortality in individuals with COVID-19 [47–49]. Together with age and ethnicity, obesity has been found to be a key risk factor for COVID-19 [50]. The impact of obesity on COVID-19 may be mediated by its effects on pulmonary function, including a reduction in expiratory reserve volume, functional capacity and respiratory compliance [51,52]. Furthermore, adipose tissue produces cytokines and contributes to a pro-inflammatory milieu [53]. Elevated levels of pro-inflammatory cytokines may exacerbate inflammation in people with COVID-19, causing immune hyperactivation ("cytokine storm"), acute respiratory distress syndrome or multiple organ failure [54]. Metabolic dysfunction-associated fatty liver disease appears to be of particular importance, since the presence of obesity has been found to elevate the risk of severe COVID-19 approximately six fold [55–57].

The increased risk of mortality from COVID-19 in obese people points to an important role of nutrition [58]. Food can influence the levels of gene expression of cytokines and thus modulate inflammation and oxidative stress [59]. Health-related consequences in populations affected by economic shutdowns, quarantines and curfews due to SARS-CoV-2 include psychological distress [60–62], which may be associated with an increase in energy intake [63] and a decrease in physical exercise [64], resulting in weight gain and increased rates of overweight and obesity.

Preventive interventions, such as weight reduction programs, may focus on obese individuals, with their greater risk for severe illness and mortality from COVID-19. However, risks for disease are quantitative and not categorical phenomena and constitute a continuous distribution. Prevention measures could therefore be introduced community-wide and may shift the population distribution of a risk. This approach may reduce the burden of disease more significantly than merely targeting people at high risk [65].

The United Kingdom has experienced the highest death rate from COVID-19 in Europe. As well as the relatively slow introduction of preventive measures and lockdowns, a potential causative factor may be the high prevalence of obesity and associated health conditions. In view of the increased severity of COVID-19 infection in obese people and the prospect of a second wave of the virus, the British government is planning to introduce a weight loss campaign [66]. The campaign to reduce body weight and to encourage healthier food choices to prevent future weight gain will include advertising on television and radio as well as in print and social media [67].

In summary, overweight and obese people are at high risk for severe or fatal outcomes of COVID-19. These individuals need special attention, with an emphasis on avoidance of infection and reduction in body weight.

4. Conclusion

Nutritional immune support has the potential to augment viral defense, as has been demonstrated in cell cultures and animal models. It is important to note that experimental evidence in support of beneficial effects of food compounds against infection stems from cell culture and animal research. The studies conducted in humans are observational, and interventional trials with robust controlled designs are lacking. In particular, findings of high-quality investigations in COVID-19 are not available, and the specific roles of food components in the prevention and therapy of viral infectious diseases in humans remains unclear. To no avail, food science has attempted for many years to find micronutrients, food bioactives or functional foods able to reliably improve immune functions. Scientifically rigorous research assessing the efficacy of food compounds in combating infectious diseases would require long-term randomized controlled trials in large samples, taking into account the participants' age, lifestyle, immune status and other relevant variables. Furthermore, it is becoming increasingly clear that the notion of single nutrients acting as magic bullets aimed at circumscribed physiological deficits within the immune system is outdated. In this respect, food science should not raise expectations that cannot be fulfilled (see Table 1).

At present, major targets of coronavirus research include a reduction in the number of infections with SARS-CoV-2 and the mitigation of severe cases of COVID-19. The important and urgent challenge facing governments and health care providers requires a focus on scientific strategies providing the most promising outcomes. While no foods or dietary supplements are capable of preventing infection with SARS-CoV-2, maintaining a balanced diet containing sufficient amounts of macronutrients and diverse micronutrients is important in supporting adequate immune functions. High-calorie "western diets" promote a pro-inflammatory state, and obesity is a major risk factor for a severe course of COVID-19. Therefore, population-wide body weight control and weight reduction in overweight and obese people are important preventive measures.

The most effective measure in preventing the spread of SARS-CoV-2 is unarguably the avoidance of exposure to the virus [68]. Dietary supplementation in relation to COVID-19, using micronutrients, food bioactives or functional food plants, is not evidence based and should not underlie decisions concerning prevention or treatment. While "let thy food be thy medicine "is of little relevance in the context of COVID-19, food and nutrition as a holistic concept may play a beneficial role, particularly in maintaining a healthy body weight and preventing non-communicable conditions.

Table 1
Contribution of food science to COVID-19.

No.	Contribution of food science
1	Experimental evidence in support of beneficial effects of food bioactives, functional foods and micronutrients against viral infection stems from animal and cell culture research.
2	The specific roles of food components in viral infectious diseases in humans remain unclear.
3	Many factors can affect the efficacy of micronutrients and food bioactives in infection (dosage, timing and duration of administration; age, health and nutritional status of target population).
4	Prolonged supplementation of food bioactives and micronutrients at high doses may have adverse effects and may even aggravate infectious diseases.
5	No foods, single nutrients or dietary supplements are capable of preventing infection with COVID-19.
6	Rigorous research investigating the efficacy of food compounds in counteracting infections requires long-term randomized controlled trials.
7	A balanced diet containing sufficient amounts of macronutrients and diverse micronutrients is a prerequisite of an optimally functioning immune system.
8	Obesity and high-energy diets are major risk factors for a more severe course of COVID-19.
9	Population-wide body weight control and weight reduction in overweight people are important preventive measures in COVID-19.
10	Diet may play a beneficial role in maintaining a healthy body weight and preventing non-communicable conditions.

Declaration of Competing Interest

The authors report no declarations of interest.

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