



Article Health Consequences of Overexposure to Disinfectants and Self-Medication against SARS-CoV-2: A Cautionary Tale Review

Hassan Hashemi¹, Shiva Ghareghani^{2,*}, Nasrin Nasimi³, Mohammad Shahbazi⁴, Zahra Derakhshan¹ and Samuel Asumadu Sarkodie⁵

- ¹ Research Center for Health Sciences, Institute of Health, Department of Environmental Health Engineering, School of Health, Shiraz University of Medical Sciences, Shiraz 71348-14336, Iran
- ² Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Tehran 14176-13151, Iran
- ³ Nutrition Research Center, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz 71348-14336, Iran
- ⁴ Department of Behavioral and Environmental Health, School of Public Health Initiative, Jackson State University, Jackson, MS 39217, USA
- ⁵ Nord University Business School (HHN), P.O. Box 1490, 8049 Bodø, Norway
- Correspondence: shv_ghareghani@yahoo.com

Abstract: To control and prevent the spread of the infectious agents in the environment and body, various measures have been taken, including the use of disinfectants for hands and surfaces, use of detergents, self-medication by herbal concoctions, and dietary supplements. Although these actions may have a therapeutic effect or reduce the viral load, incorrect use (abuse or overuse) could have negative health repercussions. Therefore, public awareness in this context is essential. The purpose of this narrative review was to evaluate the health consequences of overexposure to disinfectants and self-medication against infectious agents, specially SARS-CoV-2. The literature search for this review was conducted using related keywords in PubMed, Web of Science (WOS), and Scopus databases. This review found a significant number of reported poisoning cases during the pandemic as a result of the overuse of alcoholic hand sanitizers, household bleach products, and detergents. This paper also provides an integrated systemic overview of the possible toxic effects of self-medication, alcohol consumption, and self-administration of dietary supplements and herbs during the COVID-19 pandemic. The present review indicated that the main adverse effects associated with the overuse of popular preventative actions against contagious respiratory illnesses specially COVID-19 and Influenza (flu) were methanol intoxication, skin damage, respiratory problems, gastrointestinal ulcers, nausea, vomiting, epigastric pain, and liver injury. Due to the significant increase in the use of these preventative measures, it is essential to raise public awareness of the side effects of their excessive and unnecessary use.

Keywords: SARS-CoV-2; alcoholic disinfectants; bleach; detergents; dietary supplements; drugs; herbal remedies

1. Introduction

The emergence of a new strain of virus leading to an epidemic and/or pandemic has constantly threatened the overall public health [1]. In the early stages of the COVID-19 pandemic, there were no vaccines or approved measures to immunize the population or any drugs to treat the disease, similar to the beginning of other recorded epidemics/pandemics. It is acknowledged that validated pathogen prevention protocols played a pivotal role in maintaining public health [2]. Therefore, certain healthcare guidelines against COVID-19, such as hand washing, use of alcohol-based hand sanitizers (ABHS), wearing face masks, and consumption of dietary supplements, were recommended by the World Health



Citation: Hashemi, H.; Ghareghani, S.; Nasimi, N.; Shahbazi, M.; Derakhshan, Z.; Sarkodie, S.A. Health Consequences of Overexposure to Disinfectants and Self-Medication against SARS-CoV-2: A Cautionary Tale Review. *Sustainability* **2022**, *14*, 13614. https://doi.org/10.3390/ su142013614

Academic Editor: Mihajlo (Michael) Jakovljevic

Received: 7 August 2022 Accepted: 17 October 2022 Published: 20 October 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). Organization (WHO) [3,4]. At the same time as early public health measures taken by different local, national, and global health agencies, some studies assessed the effects of available antiviral medications and investigated the development of vaccines and new medicines for the treatment of COVID-19. Furthermore, some medications previously approved by Food and Drug Administration (FDA) for other purposes were used to treat COVID-19 [5,6].

Although numerous studies have been published on the use of disinfectants, detergents, and dietary supplements as the main or complementary measures to protect against COVID-19, SARS, MERS, etc. [7–9], few investigations have evaluated the toxic effects of these substances on human health during this global biological disaster. Furthermore, a limited number of comprehensive articles have been published that simultaneously address all the recommended protective measures during infectious disease outbreaks, epidemics and pandemics, as well as their toxic effects on human health. Thus, the current narrative review was designed to investigate the adverse effects of frequently used substances, including disinfectants and detergents, alcohol consumption, self-medication, and self-administration of dietary supplements and herbal medicine, which could cause toxicity to the human body, in order to provide a more comprehensive review for easier and faster reference.

The literature search of this narrative review was conducted using the keywords "poisoning" of ("detergents" OR "sanitizers" OR "disinfectants" OR "alcohol" OR "dietary supplements" OR "herbal medicine" OR "drug", OR "ivermectin") AND ("COVID-19" OR "SARS-CoV-2") in PubMed, Web of Science, and Scopus databases. The relevant articles were selected from studies that evaluated the poisoning effects of the suggested COVID-19 preventive substances from the beginning of the pandemic. The toxic impacts of all the measures were also assessed in order to determine the adverse side effects of these substances on the human body. Since only a limited number of studies directly investigated the relationship between the toxic effects of some of these materials and their inappropriate usage during the COVID-19 pandemic, the previously published articles evaluating their toxicity that best matched the subject were also included. We retrieved about 400 articles and included more than 90 of them in this paper. The selected articles were reviewed for toxic side effects, and articles with duplicated information were excluded.

In this review, it was found that the most common causes of poisoning during the infectious pandemic including COVID-19 were poisoning with disinfectants (such as ABHS [10–17]), bleach, and household cleaners [11,13,17,18], detergents [13,16,18], self-medication [13,18], and alcoholic beverages (spiritus) [19–26].

2. Excessive Use of Disinfectants

It has been indicated that coronaviruses could survive on surfaces made of metal, glass, and plastic for several hours to days. In order to control the transmission chain, there has been a dramatic increase in the use of disinfectants.

A recent study showed that 41.4% of the participants had health problems in at least one organ (skin dryness, obsession, skin itching, coughing, hand redness, headache, eye itching, lung and throat burning) due to the increase in detergent and disinfectant application during the COVID-19 pandemic [27]. Another study compared the poisonings attributed to the increased use of disinfectants in the first six months of 2019 and 2020. The number of cases of intoxication by surface disinfectants and hand sanitizers in 2020 was found to be higher than that in 2019 [28]. Furthermore, the results of another study demonstrated that the number of calls to the poison center has dramatically increased as a result of enhanced exposure to bleach (42%), hand sanitizers (25%), chlorine gas (21%), and chloramine gas (2%) [29].

2.1. Overexposure to Alcoholic Hand Sanitizers

To prevent the spread of COVID-19, ABHS is the most favorable and effective alternative sanitizer for hand washing, especially when soap and water are not available [30]. Due to the high use of ABHS in these critical circumstances, numerous issues are emerging that, if not addressed, may lead to other crises in the public health domain [31]. The possible adverse effects of excessive ABHS use on the human body are described in more detail in the following.

2.1.1. Ethanol and Methanol Poisoning

One of the negative aspects of alcohol-based products is that they are produced with non-standard formulas. Ingestion of these compounds is linked with extremely high morbidity and mortality rates because the accumulation of low molecular weight agents (such as methanol) increases the osmolal gaps at a level that is often higher than that seen in ketoacidosis, lactic acidosis, and renal failure in critically ill patients [32]. When methanol is absorbed into the human body (from oral, dermal, and industrial inhalation pathways), it is metabolized to formaldehyde and formic acid by the dehydrogenase enzymes. These final products are toxic and may lead to metabolic acidosis, cardiovascular instability, blindness, brain injury, or even death. In addition, compared to ethanoic-based products, alcoholbased sanitizers containing methanol are reportedly more hazardous to the human skin and can cause injury or contact dermatitis [33]. Due to their curious nature and tendency to discover new things via touching and testing, unintended ingestion of ABHS by children can also lead to alcohol poisoning and has attracted much attention. After the emergence of the new coronavirus, ABHS was widely used to help control the spread of the infection via hands and surfaces [34]. Therefore, it seems that the ingestion of ethanol from household hand sanitizers can cause poisoning and hypoglycemia in children. Moreover, it has been observed that even older children ingested hand sanitizers. Consecutively swallowing more than a few mouthfuls of ABHS-containing ethanol has been shown to cause alcohol poisoning as well [35].

Despite the fact that proper hand washing is sufficient as an effective preventative measure, the demand for ethanol increased among consumers [36], and some profit-seeking individuals changed the appearance of methanol and sold it as ethanol. Shortly after the outbreak of COVID-19, alcohol poisoning became an emergency in Iran in addition to COVID-19. Therefore, the number of alcohol poisoning cases in some areas increased to the point that the death rate due to poisoning was higher than COVID-19-related deaths [36]. Methanol poisoning was reported in all provinces of Iran, and 26 out of 31 provinces recorded fatalities. Since the beginning of the coronavirus epidemic, 924 and 998 morbidity cases of alcohol poisoning and 104 and 79 mortality cases occurred in Fars and Khuzestan Provinces, respectively [36]. Mahdavi et al. reported that 22 children and adolescents died of methanol poisoning in Iran during the first four months of the COVID-19 pandemic [37]. Hassanian-Moghaddam et al. also recorded 534 methanol deaths in Iran (23 February to 2 May 2020) [24]. Data from the Iranian Legal Medicine Organization (ILMO) showed that more than 700 deaths were caused by alcohol poisoning (20 February to 8 April 2020) [38]. In another study, Pirnia et al. reported that approximately 5000 people were poisoned by alcohol, and around 550 people died [39]. Shokoohi et al. showed a significant escalation in methanol-related morbidity and mortality, with over 5000 people poisoned and over 500 confirmed deaths [20]. Methanol poisoning was common throughout the world during the COVID-19 pandemic. White et al. also reported that the number and rate of alcohol-related deaths increased by approximately 25% in the first year of the COVID-19 pandemic [40]. In the United States, between May and June 2020, four adult patients in Arizona and New Mexico ingested alcohol-based hand sanitizers and subsequently died [14]. Moreover, a methanol poisoning outbreak was reported in Turkey, with 63 deaths within 11 days [37].

Incorrect information about materials that can supposedly cure or prevent COVID-19 can be just as perilous as the virus itself. It is important to emphasize that people should follow the suggested medical advice to prevent infection in themselves and their families. Lastly, it is worth noting that ethanol has previously been proven to suppress the immune system, and those with COVID-19 have a weak immune system [41]. Ethanol can change inherent immunity by altering the function of inherent immune cells. In addition, it can alter the activation of immune cells by specific interactions with cell-membrane molecules [42].

Therefore, ethanol therapy is not only an inconsequent treatment for COVID-19 but also an extremely perilous one.

2.1.2. Effects on Skin

Frequent use of hand sanitizers can lead to chronic irritation and skin injury. Hygiene products can lead to the denaturation of stratum corneum proteins, changes in intercellular lipids, reduction in corneocyte cohesion, and changes in the water-binding capacity of the stratum corneum. In addition, this type of skin injury may result in changes in the skin flora, which can lead to the destruction of the beneficial symbiotic bacteria, which are the first line of skin defense against various germs. It has been suggested that sanitizer-related skin reactions are categorized into two main types [30,33]: The first group includes irritant contact dermatitis, which is the most common one, and is identified by the feeling of dryness, itching, irritation, scaling or cracking, and even bleeding. This condition occurs as a result of repeated use of hygiene products, such as alcohol sanitizers or any other similar substance. The potential of each sanitizer to cause irritant dermatitis varies considerably based on its active ingredients and the frequency of usage. The second type is allergic contact dermatitis, which occurs scarcely and varies from mild to severe reactions. The most common agents of contact allergies are preservatives and fragrances.

2.1.3. Imbalance of Normal, Symbiotic Microbiota

The total population of microorganisms that colonizes a particular location is called microbiota. Microbiota consists of bacteria, fungi, viruses, and protozoa [43]. Evidence suggests that having normal, healthy microbiota has a noticeable impact on human health [44]. Excessive use of hand sanitizers has been shown to kill symbiotic microorganisms located on the skin and digestive system. Thus, there would be an imbalance between beneficial and detrimental bacteria [30]. This, in turn, may contribute to intestinal symptoms (abdominal pain and diarrhea), inflammatory bowel disease [45], obesity and diabetes [46], liver disease, chronic heart disease [47], autism [48], and colorectal cancer [49].

2.1.4. Developing Alcohol-Resistant Microorganisms

Alcoholic sanitizers are known as an effective killer of both Gram-positive and Gramnegative bacteria, as well as different viral families, including influenza A, rhinovirus, hepatitis A virus, HIV, and coronaviruses. In contrast, alcoholic sanitizers have no considerable activity against protozoan oocytes, bacterial spores, and non-enveloped (non-lipophilic) viruses [50,51]. Researchers have concluded that alcoholic antiseptic solutions do not have an adequate effect on all the introduced pathogens, as it seems that the impact of a single alcohol-based sanitizer (without additional stable compounds) is just limited to SARS-CoV-2. This may contribute to selection pressure on ethanol-resistant microorganisms, resulting in a new crisis, especially in hospitals or health centers [30].

2.2. Overexposure to Household Bleach Products

It has been proposed that proper and frequent disinfection of objects and surfaces touched by numerous individuals in households and public places (such as hospitals, offices, marketplaces, and transportation systems, among others) is one of the most significant methods of preventing the spread of the virus. Accordingly, there has been a considerable increase in the purchase and use of bleach (chlorine), a common surface disinfectant, mainly consisting of sodium hypochlorite [52]. Studies on the negative health effects of exposure to disinfectants and cleaners have demonstrated that bleach products may cause irritation to the skin, eyes, and respiratory system and trigger asthma and allergic rhinitis symptoms in some individuals [53]. In addition, the production of toxic halogenated volatile organic compounds, such as carbon tetrachloride, chloroform, chlorobenzene, 1,1-dichloroethane, and 1,1-dichloroethene, in indoor air as a result of bleach misuse and combining other cleaning agents or cleaning targets can be one of the significant methods of inhalation exposure [53].

2.3. Excessive Use of Detergents

Detergents have been commonly used for proper sanitation against microorganisms [54,55]. The first line of defense against coronavirus was hand washing with water and soap. During the COVID-19 pandemic, the toxic effects of detergent overuse on human health have been ignored. In general, detergent products are highly alkaline and destructive to our exposed body cells. Overexposure to detergents is associated with different side effects, such as irritant contact dermatitis, respiratory problems, namely allergies, asthma aggravation, damage to epithelial cells, and optical problems (corneal irritation and damage) [56–59]. Furthermore, the entering of dishwashing liquids or other detergents into the stomach and their residues can lead to gastrointestinal disorders, diarrhea, and tissue damage in epithelium cells [60].

2.4. Alcohol Overdoses and Drug Abuse during Quarantines

A growing body of evidence indicates a strong relationship between quarantine or social isolation and an increase in alcohol consumption and drug abuse [61–63]. The experience of isolation and loneliness, economic repercussions, job loss, and stress or fear of the COVID-19 pandemic may lead to substance abuse and overdose as a coping mechanism. Subsequently, this may result in an elevation in the prevalence of substance use disorders (SUDs) and other hazardous associated problems [64–68]. SUDs include opioids, methamphetamine, and other psycho-stimulants, alcohol, nicotine, and tetrahydrocannabinol use disorders. Evidence shows that people with SUD (who smoke, vape, or use certain drugs) are more vulnerable to lung infections and diagnostic delay of this disease, resulting in more severe consequences, because an atypical presentation of COVID-19 may be mistaken as substance consumption or withdrawal [69]. In addition, the unofficial and illegal production of alcoholic drinks has been reported in many parts of the world, especially in countries where alcohol consumption is prohibited, such as Iran. The most dangerous complication associated with these drinks is methanol poisoning [21,70–72]. Moreover, access to detoxification centers, such as hospitals or other health services, has become increasingly difficult for people with SUDs, overdose cases, or those with methanol poisoning, which may increase mortality. Thus, health organization interventions and governmental support are needed to cope with social isolation without the use of any substance or alcohol [73].

2.5. Self-Administration of Dietary Supplements and Self-Medication

Self-medication/self-administration of different drugs was one of the greatest health issues during the COVID-19 pandemic [74]. Overconsumption of dietary supplements to support the immune system (such as vitamin D, vitamin C, zinc, and selenium supplements [75,76]), hydroxychloroquine (HCQ) and chloroquine (CQ), anti-inflammatory drugs, corticosteroids (such as dexamethasone), and ivermectin has become an important issue during the COVID-19 pandemic [77–79]. Since there are many published papers that suggest the consumption of these medications as a valid preventative measure against COVID-19, reviewing the toxic effects of their overuse seems to be necessary. Given that most of the toxic effects of dietary supplements and anti-inflammatory drugs, and herbal medicines are not severe, there is no published report of their direct poisoning during this pandemic. Thus, in this paper, their toxic effects were reviewed based on previously published reports.

2.5.1. Dietary Supplements: Vitamins C and D, Zinc, and Selenium

Vitamin D supplements: Evidence demonstrates that vitamin D plays a vital role in calcium homeostasis and bone mineralization and is implicated in regulating many physiological systems and pathways, including immune system strengthening, cardiovascular health, and cancer prevention as a sterol hormone [80]. It is estimated that more than 1.5 billion individuals suffer from vitamin D deficiency worldwide. However, despite the fact that obtaining adequate serum vitamin D levels is not out of reach, vitamin D deficiency has become a global health concern [81]. During the COVID-19 pandemic isolation

and quarantine, due to an imbalanced diet and lack of exposure to sunlight, vitamin D deficiency could become severe [82].

Evidence indicates that there is a relationship between vitamin D deficiency and different infectious diseases, mainly viral infections [83]. Moreover, it has been reported that patients with vitamin D deficiency exhibit poor responses to standard treatments. Various clinical trials have shown that vitamin D deficiency may increase the risk of pulmonary infections, including COVID-19, via different mechanisms, such as a negative regulatory impact on the renin-angiotensin signaling pathway [84,85]. Despite its wide therapeutic index, vitamin D poisoning can occur as a result of inappropriate use of dietary supplements. Vitamin D poisoning may occur due to iatrogenic factors, such as manufacturing errors and prescriptions written without laboratory diagnosis or excessive self-administration [86]. Previous research has indicated that hypervitaminosis D contributes to hypercalcemia and hypercalciuria, which may lead to various eye and skin disorders, as well as musculoskeletal, gastrointestinal, renal, cardiovascular, and central nervous system problems [87,88].

Vitamin C supplements: Vitamin C or ascorbic acid is a safe essential micronutrient for humans and serves as an antioxidant. It has been reported that vitamin C supports various cellular functions of the immune system, which may decrease the susceptibility of cells to various viral infections. Vitamin C may also impact inflammation [89]. It is believed that daily prophylactic intake of vitamin C via foods or supplements can help protect individuals against COVID-19. However, considering all the benefits, overdose and chronic overconsumption of vitamin C can lead to renal toxicity through a hyperoxaluric state. Vitamin C is considered to contribute to oxalate nephropathy at doses less than 2 g/day. Since vitamin C is a water-soluble vitamin, some authors have proposed that the recommended daily intake of vitamin C is almost 75 to 90 mg [90].

Zinc supplements: Zinc is a necessary element involved in numerous biological processes, including enzymatic reactions, transcription, and regulation of cellular pH [91]. It has been suggested that zinc deficiency is identified by impaired T-cell function, neurosensory injury, and slowed the healing process. One of the current concerns in the COVID-19 pandemic is potentiating the immune system against viral infection with zinc supplements [73]. However, Zn overdose due to self-medication may lead to zinc toxicity, which changes mitochondrial metabolism and contributes to a decrease in ATP production via mitochondria in the human body as an aerobic organism [92,93].

Selenium supplements: Evidence shows that selenium prevents the virus from entering the cytoplasm of healthy cells by limiting the expression of protein sulfhydryl groups (-SH) [94]. In addition, Jaya Warden et al. (2020) suggested that selenium supplementation prevents the development of influenza and polio viruses, which proves the hypothesis that selenium boosts the immune system [95]. It has been demonstrated that selenium decreases the development of thrombosis in blood vessels, suggesting that the use of sodium selenite in anticoagulation therapy can decrease the risk of blood clot creation in patients with COVID-19 [96]. Despite all these benefits, high-dose consumption of selenium supplements in order to prevent COVID-19 may be harmful in both acute and chronic phases. Selenium toxicity symptoms are reported to be nausea, vomiting, nail discoloration, brittleness, or even hair loss, fatigue, and foul breath odor, commonly known as "garlic breath" [97–99].

2.5.2. Drugs and Medicinal Products

CQ and HCQ: The identification of new candidates for the treatment or inhibition of COVID-19 enhances the potential risks of self-medication. At the beginning of the pandemic, despite the absence of firm evidence for the effectiveness of CQ and HCQ, attempts to prophylactically self-medicate with these drugs were observed among the general public, predominantly in Nigeria and the USA [100]. It has been reported that the overconsumption of HCQ may cause life-threatening side effects, including severe cutaneous adverse reactions, fulminant hepatic failure, and ventricular arrhythmias (especially when used concomitantly with azithromycin). Finally, CQ and HCQ overdoses are very hazardous and challenging to treat [101]. Ivermectin: Ivermectin is a cheap medicine mainly used for the treatment of parasites (such as intestinal parasites) in animals and scabies in humans around the world, especially in regions where parasitic infections are more prevalent. In addition to antiparasitic effects, ivermectin has been shown to affect mycobacteria, flavivirus, and nematodes via different mechanisms. Its antiviral properties and immunomodulatory impacts on the host have intrigued people to consume it as a preventative drug against COVID-19 (particularly in America), and many researchers have begun to study its efficacy or safety for the treatment and prevention of COVID-19 [102,103]. Although randomized and controlled trials have found no effect of ivermectin in the treatment or prevention of COVID-19, the use of this drug has risen in some countries. Self-medication/improper use of ivermectin may lead to toxic effects and poisoning symptoms, such as confusion, ataxia, weakness, gastrointestinal distress, hypotension, seizures, dizziness, rash, and visual defects [104].

Corticosteroid drugs: Corticosteroids are a group of drugs commonly prescribed to treat chronic inflammatory conditions, such as rhino-sinusitis, chronic respiratory disease (asthma and chronic obstructive pulmonary disease (COPD)), and autoimmune disorders including rheumatoid arthritis, Crohn's disease, and ulcerative colitis. According to some researchers, the use of corticosteroids against COVID-19 can help patients by limiting the cytokine storm and the inflammation induced by the uncontrolled immunologic response to the virus [105]. However, numerous studies have indicated that corticosteroids are no longer recommended due to their immune-suppressive effects. To defend against SARS-CoV-2, the human body needs activated T cells and specific antibodies, which are limited by corticosteroids [106]. One example of corticosteroids is dexamethasone (DXM), which is a synthetic corticosteroid approved by the FDA in 1958 and is recommended in some cases to control the cytokine storms in COVID-19 patients admitted to the hospital. However, as soon as it was declared as a potential anti-COVID-19 drug, some individuals started its prophylactic use for infection treatment without a prescription or supervision, which may lead to more susceptibility to viral infections, hyperglycemia, peptic ulcers, cataracts, glaucoma, bone metabolism, and osteoporosis if not controlled [107].

2.6. Self-Medication by Herbal Remedies

Some researchers claim that numerous herbs exhibit immunomodulatory and antiviral effects on the human body. Therefore, they could be used as antiviral agents by coating on masks and fumigation by boiling in a pot, as air-disinfectants (essential oils) to stop aerosol transmission, and as surface sanitizing agents to prevent infection and strengthen immunity [7]. These medicinal plants contain different antiviral compounds, including catechins, phenols, alkaloids, and terpenoids [108,109]. However, their overconsumption might lead to various adverse effects on human health. Based on previous studies on other viral infections, some of the most common herbs used against COVID-19 and the possible toxic effects of their overconsumption are listed in Table 1.

| Herbs | Ref. | English Name | Possible Toxic Effects of High Dose Consumption | Ref. |
|--------------------------------|-----------|--------------|--|-------|
| Alium stivum. L. | [110] | garlic | Vacuolation of liver cells of treated rats near the organ surface. RBCs and WBCs aggregation and alveoli thickening at very high doses. Significant edema in several places of the lung. | [111] |
| Zingiber officinalis Roscoe | [108,110] | Ginger | Cytotoxic effects against the promyelocytic leukemia cells might be possible. Mutagenic effects have been seen over pregnancy. Negative reproductive effects on male rats also have been reported. | [112] |

Table 1. The most common herbs consumed against COVID-19 for prevention or treatment.

| Herbs | Ref. | English Name | Possible Toxic Effects of High Dose Consumption | Ref. |
|------------------------|-------|--------------|--|-----------|
| Piper nigrum L. | [108] | Black Pepper | Increase in serum aspartate aminotransferase and ALP and decrease in serum protein led to liver damage. Increase in aflatoxin B1 binding to calf thymus. Damage to sperm function. | [113] |
| Glycyrrhiza glabra | [114] | Licorice | Based on consumption dose and time Hypertension, visual problems, pseudo -hyperaldosteronism, cardiovascular disorders, neurological syndrome can occur. Capability of causing mutagenicity, carcinogenicity, and genotoxicity has been reported. | [115,116] |
| Thymus vulgaris L. | [117] | Thyme | Nausea and vomiting, tachypnea, hypotension, allergy, headache and dizziness, heartburn, antityrotropic effects, liver toxicity, and bradycardia. | [118] |
| Eucalyptus polybractea | [110] | Eucalyptus | Irritation of the nasopharyngeal and lung epithelial cells, Because of its strong odor. Skin irritation, ataxia, muscle weakness, seizure, and slurred speech may occur in high doses. | [119] |

Table 1. Cont.

3. Conclusions

This review found that overuse of all Infectious diseases outbreaks including COVID-19 preventive interventions, such as detergents, disinfectants, alcohols, self-medication via herbal decoctions and medicines can cause more health problems. Overall, the major health effects of the overconsumption of these preventive measures are methanol intoxication, skin injury, respiratory problems, gastrointestinal ulcers, nausea, vomiting, epigastric pain, and liver injury. Moreover, the reported poisoning rate by different substances, such as disinfectants, alcohol sanitizers, household cleaners, and drugs, was elevated during the COVID-19 pandemic. Therefore, raising public awareness of the dangers of overusing disinfectants, detergents, and self-medication of dietary supplements, drugs, and herbal medicines seems completely necessary. Furthermore, excessive use of disinfectants, detergents, and self-administration of drugs, dietary supplements, and herbs during the COVID-19 pandemic not only has negative health effects but also might have several environmental and economic impacts. Therefore, a large number of medications, detergents, and disinfectants might enter the wastewater collection network and/or spill on the soil, contaminating the groundwater and surface water sources. In addition to the health effects, chemical drugs may be costly and lead to financial losses. In conclusion, many poisoning cases were reported due to incorrect consumption of chemical and herbal products, and therefore, this review can be beneficial for future studies. Further research is required to determine the validity of these findings and provide suitable strategies to reduce the poisoning cases caused by COVID-19 preventive measures.

Author Contributions: S.G.: Writing—Original draft preparation; H.H.: Supervision, Project administration; N.N.: Data curation; M.S.: Investigation, Analyzing; Z.D.: Methodology, Reviewing and Editing; S.A.S.: Reviewing and Editing. All authors have read and agreed to the published version of the manuscript.

Funding: This article was extracted from Shiraz University of Medical Sciences Grants (Approved NO. 22537, Ethical ID: IR.SUMS.REC.1399.1254).

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Shiraz University of Medical Sciences (Ethical ID: IR.SUMS.REC.1399.1254 and date of approval: 24 February 2021).

Informed Consent Statement: Not applicable.

Data Availability Statement: The datasets generated during and analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest: The authors report no conflict of interest. The authors alone are responsible for the content and writing of the article.

References

- 1. Jairoun, A.A.; Al-Hemyari, S.S.; Shahwan, M. The pandemic of COVID-19 and its implications for the purity and authenticity of alcohol-based hand sanitizers: The health risks associated with falsified sanitizers and recommendations for regulatory and public health bodies. *Res. Soc. Adm. Pharm.* **2021**, *17*, 2050–2051. [CrossRef]
- 2. Watkins, J. Preventing a COVID-19 pandemic. Br. Med. J. Publ. Group 2020, 368, m810. [CrossRef]
- 3. World Health Organization. Coronavirus Disease 2019 (COVID-19): Situation Report, 51; WHO: Geneva, Switzerland, 2020.
- 4. World Health Organization. *Water, Sanitation, Hygiene, and Waste Management for SARS-CoV-2, the Virus that Causes COVID-19: Interim Guidance, 29 July 2020;* World Health Organization: Geneva, Switzerland, 2020.
- Gao, K.; Nguyen, D.D.; Chen, J.; Wang, R.; Wei, G.-W. Repositioning of 8565 existing drugs for COVID-19. J. Phys. Chem. Lett. 2020, 11, 5373–5382. [CrossRef]
- 6. Scavone, C.; Brusco, S.; Bertini, M.; Sportiello, L.; Rafaniello, C.; Zoccoli, A.; Berrino, L.; Racagni, G.; Rossi, F.; Capuano, A. Current pharmacological treatments for COVID-19: What's next? *Br. J. Pharmacol.* **2020**, 177, 4813–4824. [CrossRef]
- 7. Panyod, S.; Ho, C.-T.; Sheen, L.-Y. Dietary therapy and herbal medicine for COVID-19 prevention: A review and perspective. *J. Tradit. Complement. Med.* **2020**, *10*, 420–427. [CrossRef]
- 8. Golin, A.P.; Choi, D.; Ghahary, A. Hand sanitizers: A review of ingredients, mechanisms of action, modes of delivery, and efficacy against coronaviruses. *Am. J. Infect. Control* **2020**, *48*, 1062–1067. [CrossRef]
- 9. Gupta, M.K.; Lipner, S.R. Hand hygiene in preventing COVID-19 transmission. J. Am. Acad. Dermatol. 2020, 82, 1215–1216.
- 10. Lebin, J.A.; Ma, A.; Mudan, A.; Smollin, C.G. Fatal ingestion of sodium chlorite used as hand sanitizer during the COVID-19 pandemic. *Clin. Toxicol.* **2021**, *59*, 265–266. [CrossRef]
- 11. Soave, P.M.; Grassi, S.; Oliva, A.; Romanò, B.; Di Stasio, E.; Dominici, L.; Pascali, V.; Antonelli, M. Household disinfectant exposure during the COVID-19 pandemic: A retrospective study of the data from an Italian poison control center. *Eur. Rev. Med. Pharmacol. Sci.* **2021**, 25, 1738–1742. [CrossRef] [PubMed]
- 12. Overbeek, D.L.; Watson, C.J.; Castañeda, N.R.; Ganetsky, M. A geographically distinct case of fatal methanol toxicity from ingestion of a contaminated hand sanitizer product during the COVID-19 pandemic. J. Med. Toxicol. 2021, 17, 218–221. [CrossRef]
- Chary, M.A.; Overbeek, D.L.; Papadimoulis, A.; Sheroff, A.; Burns, M.M. Geospatial correlation between COVID-19 health misinformation and poisoning with household cleaners in the Greater Boston Area. *Clin. Toxicol.* 2021, *59*, 320–325. [CrossRef] [PubMed]
- Yip, L.; Bixler, D.; Brooks, D.E.; Clarke, K.R.; Datta, S.D.; Dudley, S., Jr.; Komatsu, K.K.; Lind, J.N.; Mayette, A.; Melgar, M.; et al. Serious adverse health events, including death, associated with ingesting alcohol-based hand sanitizers containing methanol—Arizona and New Mexico, May–June 2020. *Morb. Mortal. Wkly. Rep.* 2020, *69*, 1070. [CrossRef] [PubMed]
- 15. McCulley, L.; Cheng, C.; Mentari, E.; Diak, I.-L.; Michele, T. Alcohol-based hand sanitizer exposures and effects on young children in the US during the COVID-19 pandemic. *Clin. Toxicol.* **2021**, *59*, 355–356. [CrossRef]
- 16. Mushtaq, S.; Terzi, E.; Recalcati, S.; Salas-Alanis, J.C.; Amin, S.; Faizi, N. Cutaneous adverse effects due to personal protective measures during COVID-19 pandemic: A study of 101 patients. *Int. J. Dermatol.* **2021**, *60*, 327–331. [CrossRef] [PubMed]
- Le Roux, G.; Sinno-Tellier, S.; Puskarczyk, E.; Labadie, M.; von Fabeck, K.; Pélissier, F.; Nisse, P.; Paret, N.; Descatha, A.; Vodovar, D.; et al. Poisoning during the COVID-19 outbreak and lockdown: Retrospective analysis of exposures reported to French poison control centres. *Clin. Toxicol.* 2021, 59, 832–839. [CrossRef] [PubMed]
- Le Roux, G.; Sinno-Tellier, S.; Descatha, A. COVID-19: Home poisoning throughout the containment period. *Lancet Public Health* 2020, 5, e314. [CrossRef]
- Neufeld, M.; Lachenmeier, D.W.; Ferreira-Borges, C.; Rehm, J. Is alcohol an "Essential Good" during COVID-19? Yes, but only as a disinfectant! *Alcohol. Clin. Exp. Res.* 2020, 44, 1906–1909. [CrossRef] [PubMed]
- Shokoohi, M.; Nasiri, N.; Sharifi, H.; Baral, S.; Stranges, S. A syndemic of COVID-19 and methanol poisoning in Iran: Time for Iran to consider alcohol use as a public health challenge? *Alcohol* 2020, *87*, 25–27. [CrossRef]
- Delirrad, M.; Mohammadi, A.B. New methanol poisoning outbreaks in Iran following COVID-19 pandemic. *Alcohol Alcohol.* 2020, 55, 347–348. [CrossRef]
- 22. Soltaninejad, K. Methanol mass poisoning outbreak, a consequence of COVID-19 pandemic and misleading messages on social media. *Int. J. Occup. Environ. Med.* **2020**, *11*, 148. [CrossRef]
- Arasteh, P.; Pakfetrat, M.; Roozbeh, J. A surge in methanol poisoning amid COVID-19 pandemic: Why Is this occurring? *Am. J. Med. Sci.* 2020, 360, 201. [CrossRef] [PubMed]
- 24. Hassanian-Moghaddam, H.; Zamani, N.; Kolahi, A.-A.; McDonald, R.; Hovda, K.E. Double trouble: Methanol outbreak in the wake of the COVID-19 pandemic in Iran—A cross-sectional assessment. *Crit. Care* **2020**, *24*, 402. [CrossRef] [PubMed]

- Sefidbakht, S.; Lotfi, M.; Jalli, R.; Moghadami, M.; Sabetian, G.; Iranpour, P. Methanol toxicity outbreak: When fear of COVID-19 goes viral. *Emerg. Med. J.* 2020, 37, 416. [CrossRef] [PubMed]
- 26. Dear, K.; Grayson, L.; Nixon, R. Potential methanol toxicity and the importance of using a standardised alcohol-based hand rub formulation in the era of COVID-19. *Antimicrob. Resist. Infect. Control* **2020**, *9*, 129. [CrossRef]
- Dindarloo, K.; Aghamolaei, T.; Ghanbarnejad, A.; Turki, H.; Hoseinvandtabar, S.; Pasalari, H.; Ghaffari, H.R. Pattern of disinfectants use and their adverse effects on the consumers after COVID-19 outbreak. *J. Environ. Health Sci. Eng.* 2020, 18, 1301–1310. [CrossRef] [PubMed]
- Babić, Ž.; Turk, R.; Macan, J. Toxicological aspects of increased use of surface and hand disinfectants in Croatia during the COVID-19 pandemic: A preliminary report. Arch. Ind. Hyg. Toxicol. 2020, 71, 261–264. [CrossRef]
- Yasseen Iii, A.; Weiss, D.; Remer, S.; Dobbin, N.; MacNeill, M.; Bogeljic, B.; Leong, D.; Wan, V.; Mosher, L.; Bélair, G.; et al. At-a-glance-Increases in exposure calls related to selected cleaners and disinfectants at the onset of the COVID-19 pandemic: Data from Canadian poison centres. *Health Promot. Chronic Dis. Prev. Can. Res. Policy Pract.* 2020, 41, 25.
- 30. Himabindu, C.S.; Tanish, B.T.; Kumari, N.P.; Nayab, S.N. Hand sanitizers: Is over usage harmful? *World J. Curr. Med. Pharm. Res.* **2020**, *2*, 296–300. [CrossRef]
- Mahmood, A.; Eqan, M.; Pervez, S.; Alghamdi, H.A.; Tabinda, A.B.; Yasar, A.; Brindhadevi, K.; Pugazhendhi, A. COVID-19 and frequent use of hand sanitizers; human health and environmental hazards by exposure pathways. *Sci. Total Environ.* 2020, 742, 140561. [CrossRef] [PubMed]
- 32. Pressman, P.; Clemens, R.; Sahu, S.; Hayes, A.W. A review of methanol poisoning: A crisis beyond ocular toxicology. *Cutan. Ocul. Toxicol.* **2020**, *39*, 173–179. [CrossRef]
- 33. Emami, A.; Javanmardi, F.; Keshavarzi, A.; Pirbonyeh, N. Hidden threat lurking behind the alcohol sanitizers in COVID-19 outbreak. *Dermatol. Ther.* **2020**, *33*, e13627. [CrossRef] [PubMed]
- 34. Khan, Z.; Ualiyeva, D.; Sapkota, S.; Khan, A.; Noor, Z.; Amissah, O.B.; Ahmad, U.; Zaman, N. The Potential Risk to Children Associated with Excessive use of Disinfectant Against Coronavirus Disease (COVID-19). *EC Microbiol.* **2021**, *17*, 01–06.
- Santos, C.; Kieszak, S.; Wang, A.; Law, R.; Schier, J.; Wolkin, A. Reported adverse health effects in children from ingestion of alcohol-based hand sanitizers—United States, 2011–2014. *Morb. Mortal. Wkly. Rep.* 2017, 66, 223. [CrossRef] [PubMed]
- Heidari, M.; Sayfouri, N. COVID-19 and alcohol poisoning: A fatal competition. *Disaster Med. Public Health Prep.* 2021, 89, 1–3. [CrossRef] [PubMed]
- Mahdavi, S.A.; Kolahi, A.; Akhgari, M.; Gheshlaghi, F.; Gholami, N.; Moshiri, M.; Mohtasham, N.; Ebrahimi, S.; Ziaeefar, P.; McDonald, R.; et al. COVID-19 pandemic and methanol poisoning outbreak in Iranian children and adolescents: A data linkage study. *Alcohol. Clin. Exp. Res.* 2021, 45, 1853–1863. [CrossRef] [PubMed]
- 38. Rostami, M. The coronavirus disease 2019 (COVID-19) and alcohol use disorders in Iran. *Am. J. Men Health* 2020, 14, 1557988320938610. [CrossRef] [PubMed]
- 39. Pirnia, B.; Dezhakam, H.; Pirnia, K.; Malekanmehr, P.; Soleimani, A.A.; Zahiroddin, A.; Eslami, M.R.; Sadeghi, P. COVID-19 pandemic and addiction: Current problems in Iran. *Asian J. Psychiatr.* **2020**, *54*, 102313. [CrossRef]
- White, A.M.; Castle, I.-J.P.; Powell, P.A.; Hingson, R.W.; Koob, G.F. Alcohol-related deaths during the COVID-19 pandemic. JAMA 2022, 327, 1704–1706. [CrossRef] [PubMed]
- 41. Qin, C.; Ziwei, M.P.; Tao, S.Y.; Ke, P.C.; Shang, M.M. Dysregulation of immune response in patients with COVID-19 in Wuhan, China; Clinical Infectious Diseases; Oxford Academic. *Clin. Infect. Dis.* **2020**, *71*, 762–768. [CrossRef]
- Goral, J.; Karavitis, J.; Kovacs, E.J. Exposure-dependent effects of ethanol on the innate immune system. *Alcohol* 2008, 42, 237–247. [CrossRef]
- 43. Sekirov, I.; Russell, S.L.; Antunes, L.C.M.; Finlay, B.B. Gut microbiota in health and disease. *Physiol. Rev.* 2010, *90*, 859–904. [CrossRef] [PubMed]
- Gevers, D.; Knight, R.; Petrosino, J.F.; Huang, K.; McGuire, A.L.; Birren, B.W.; Nelson, K.E.; White, O.; Methé, B.A.; Huttenhower, C. The Human Microbiome Project: A community resource for the healthy human microbiome. *PLoS Biol.* 2012, 10, e1001377. [CrossRef] [PubMed]
- De Gottardi, A.; McCoy, K.D. Evaluation of the gut barrier to intestinal bacteria in non-alcoholic fatty liver disease. *J. Hepatol.* 2011, 55, 1181–1183. [CrossRef] [PubMed]
- 46. Hooper, L.V.; Wong, M.H.; Thelin, A.; Hansson, L.; Falk, P.G.; Gordon, J.I. Molecular analysis of commensal host-microbial relationships in the intestine. *Science* **2001**, *291*, 881–884. [CrossRef]
- Thomas, C.M.; Hong, T.; Van Pijkeren, J.P.; Hemarajata, P.; Trinh, D.V.; Hu, W.; Britton, R.A.; Kalkum, M.; Versalovic, J. Histamine derived from probiotic Lactobacillus reuteri suppresses TNF via modulation of PKA and ERK signaling. *PLoS ONE* 2012, 7, e31951. [CrossRef] [PubMed]
- Burcelin, R.; Serino, M.; Chabo, C.; Blasco-Baque, V.; Amar, J. Gut microbiota and diabetes: From pathogenesis to therapeutic perspective. *Acta Diabetol.* 2011, 48, 257–273. [CrossRef]
- 49. Sherafat, S.J.; Azimirad, M.; Alebouyeh, M.; Amoli, H.A.; Hosseini, P.; Ghasemian-Safaei, H.; Moghim, S. The rate and importance of Clostridium difficile in colorectal cancer patients. *Gastroenterol. Hepatol. Bed Bench* **2019**, *12*, 358.
- 50. Widmer, A.F. Replace hand washing with use of a waterless alcohol hand rub? *Clin. Infect. Dis.* **2000**, *31*, 136–143. [CrossRef] [PubMed]

- 51. Wilder-Smith, A.; Chiew, C.J.; Lee, V.J. Can we contain the COVID-19 outbreak with the same measures as for SARS? *Lancet Infect. Dis.* **2020**, 20, e102–e107. [CrossRef]
- Chang, A.; Schnall, A.H.; Law, R.; Bronstein, A.C.; Marraffa, J.M.; Spiller, H.A.; Hays, H.L.; Funk, A.R.; Mercurio-Zappala, M.; Calello, D.P.; et al. Cleaning and disinfectant chemical exposures and temporal associations with COVID-19—National poison data system, United States, January 1, 2020–March 31, 2020. *Morb. Mortal. Wkly. Rep.* 2020, 69, 496. [CrossRef]
- 53. Samara, F.; Badran, R.; Dalibalta, S. Are disinfectants for the prevention and control of COVID-19 safe? *Health Secur.* **2020**, *18*, 496–498. [CrossRef]
- 54. Wilhelm, K.-P. Prevention of surfactant-induced irritant contact dermatitis. Prev. Contact Dermat. 1996, 25, 78–85.
- 55. Folletti, I.; Siracusa, A.; Paolocci, G. Update on asthma and cleaning agents. *Curr. Opin. Allergy Clin. Immunol.* **2017**, *17*, 90–95. [CrossRef]
- Wang, M.; Tan, G.; Eljaszewicz, A.; Meng, Y.; Wawrzyniak, P.; Acharya, S.; Altunbulakli, C.; Westermann, P.; Dreher, A.; Yan, L.; et al. Laundry detergents and detergent residue after rinsing directly disrupt tight junction barrier integrity in human bronchial epithelial cells. J. Allergy Clin. Immunol. 2019, 143, 1892–1903. [CrossRef]
- 57. Dumas, O. Cleaners and airway diseases. Curr. Opin. Allergy Clin. Immunol. 2021, 21, 101–109. [CrossRef]
- 58. Parks, J.; McCandless, L.; Dharma, C.; Brook, J.; Turvey, S.; Mandhane, P.; Becker, A.B.; Kozyrskyj, A.L.; Azad, M.B.; Moraes, T.J.; et al. Association of use of cleaning products with respiratory health in a Canadian birth cohort. *Cmaj* 2020, 192, E154–E161. [CrossRef]
- 59. Rosenman, K.D. Cleaning products-related asthma. Clin. Pulm. Med. 2006, 13, 221–228. [CrossRef]
- Suri, V.; Mahi, S.; Bhalla, A.; Sharma, N.; Varma, S. Detergents-uncommon household poisons. *Indian J. Med. Sci.* 2009, 63, 311–312. [CrossRef] [PubMed]
- 61. Schmidt, R.A.; Genois, R.; Jin, J.; Vigo, D.; Rehm, J.; Rush, B. The early impact of COVID-19 on the incidence, prevalence, and severity of alcohol use and other drugs: A systematic review. *Drug Alcohol Depend.* **2021**, *228*, 109065. [CrossRef] [PubMed]
- Hanafi, E.; Siste, K.; Limawan, A.P.; Sen, L.T.; Christian, H.; Murtani, B.J.; Adrian; Siswidiani, L.P.; Suwartono, C. Alcohol-and cigarette-use related behaviors during quarantine and physical distancing amid COVID-19 in Indonesia. *Front. Psychiatr.* 2021, 12, 622917. [CrossRef] [PubMed]
- Sallie, S.N.; Ritou, V.; Bowden-Jones, H.; Voon, V. Assessing international alcohol consumption patterns during isolation from the COVID-19 pandemic using an online survey: Highlighting negative emotionality mechanisms. *BMJ Open* 2020, 10, e044276. [CrossRef] [PubMed]
- 64. Chiappini, S.; Guirguis, A.; John, A.; Corkery, J.M.; Schifano, F. COVID-19: The hidden impact on mental health and drug addiction. *Front. Psychiatr.* **2020**, *11*, 767. [CrossRef] [PubMed]
- 65. Carrico, A.W.; Horvath, K.J.; Grov, C.; Moskowitz, J.T.; Pahwa, S.; Pallikkuth, S.; Hirshfield, S. Double jeopardy: Methamphetamine use and HIV as risk factors for COVID-19. *AIDS Behav.* **2020**, *24*, 3020–3023. [CrossRef] [PubMed]
- 66. Clay, J.M.; Parker, M.O. Alcohol use and misuse during the COVID-19 pandemic: A potential public health crisis? *Lancet Public Health* **2020**, *5*, e259. [CrossRef]
- 67. Shigemura, J.; Ursano, R.J.; Morganstein, J.C.; Kurosawa, M.; Benedek, D.M. Public responses to the novel 2019 coronavirus (2019-nCoV) in Japan: Mental health consequences and target populations. *Psychiatr. Clin. Neurosci.* 2020, 74, 281. [CrossRef]
- 68. Wang, Y.; Di, Y.; Ye, J.; Wei, W. Study on the public psychological states and its related factors during the outbreak of coronavirus disease 2019 (COVID-19) in some regions of China. *Psychol. Health Med.* **2021**, *26*, 13–22. [CrossRef]
- Chevance, A.; Gourion, D.; Hoertel, N.; Llorca, P.M.; Thomas, P.; Bocher, R.; Moro, M.R.; Laprévote, V.; Benyamina, A.; Fossati, P.; et al. Ensuring mental health care during the SARS-CoV-2 epidemic in France: A narrative review. *L'encephale* 2020, 46, 193–201. [CrossRef]
- 70. Mousavi-Roknabadi, R.S.; Arzhangzadeh, M.; Safaei-Firouzabadi, H.; Sharifi, M.; Fathi, N.; Jelyani, N.Z.; Mokdad, M. Methanol poisoning during COVID-19 pandemic; A systematic scoping review. *Am. J. Emerg. Med.* **2022**, *52*, 69–84. [CrossRef]
- 71. Iranpour, P.; Firoozi, H.; Haseli, S. Methanol poisoning emerging as the result of COVID-19 outbreak; radiologic perspective. *Acad. Radiol.* **2020**, *27*, 755–756. [CrossRef]
- 72. Simani, L.; Ramezani, M.; Roozbeh, M.; Shadnia, S.; Pakdaman, H. The outbreak of methanol intoxication during COVID-19 pandemic: Prevalence of brain lesions and its predisposing factors. *Drug Chem. Toxicol.* **2022**, *45*, 1500–1503. [CrossRef]
- Jothimani, D.; Kailasam, E.; Danielraj, S.; Nallathambi, B.; Ramachandran, H.; Sekar, P.; Manoharan, S.; Ramani, V.; Narasimhan, G.; Kaliamoorthy, I.; et al. COVID-19: Poor outcomes in patients with zinc deficiency. *Int. J. Infect. Dis.* 2020, 100, 343–349. [CrossRef] [PubMed]
- 74. Malik, M.; Tahir, M.J.; Jabbar, R.; Ahmed, A.; Hussain, R. Self-medication during COVID-19 pandemic: Challenges and opportunities. *Drugs Ther. Perspect.* 2020, *36*, 565–567. [CrossRef] [PubMed]
- Rugole, V.; Pucarin-Cvetković, J.; Milošević, M. Food supplements in healthcare professionals' diet during COVID-19 pandemic. Sestrin. Glas. 2021, 26, 82–91. [CrossRef]
- Keshavarz Shahbaz, S.; Naderi, Y.; Aali, E. A Promising Approach to Improving COVID-19 Symptoms: Using Antioxidant Supplements. J. Inflamm. Dis. 2021, 25, 105–126. [CrossRef]
- 77. Ağagündüz, D.; Çelik, M.N.; Çıtar Dazıroğlu, M.E.; Capasso, R. Emergent drug and nutrition interactions in COVID-19: A comprehensive narrative review. *Nutrients* **2021**, *13*, 1550. [CrossRef]

- 78. Younis, N.K.; Zareef, R.O.; Fakhri, G.; Bitar, F.; Eid, A.H.; Arabi, M. COVID-19: Potential therapeutics for pediatric patients. *Pharmacol. Rep.* **2021**, *73*, 1520–1538. [CrossRef]
- 79. Clinicaltrials.gov. Available online: https://clinicaltrials.gov/ (accessed on 6 August 2022).
- 80. Marcinowska-Suchowierska, E.; Kupisz-Urbańska, M.; Łukaszkiewicz, J.; Płudowski, P.; Jones, G. Vitamin D toxicity–a clinical perspective. *Front. Endocrinol.* **2018**, *9*, 550. [CrossRef]
- 81. Wimalawansa, S. Causes, benefits and consequences of vitamin D deficiency. J. Community Med. Health Res. 2019, 2, 122.
- 82. Boreskie, K.F.; Hay, J.; Duhamel, T. Preventing frailty progression during the COVID-19 pandemic. J. Frailty Aging 2020, 9, 130–131. [CrossRef]
- 83. Cannell, J.J.; Vieth, R.; Umhau, J.C.; Holick, M.F.; Grant, W.B.; Madronich, S.; Garland, C.F.; Giovannucci, E. Epidemic influenza and vitamin D. *Epidemiol. Infect.* 2006, 134, 1129–1140. [CrossRef]
- 84. Azmi, H.; Hassou, N.; Ennaji, M.M. Vitamin D immunomodulatory role in chronic and acute viral diseases. In *Emerging and Reemerging Viral Pathogens*; Elsevier: Amsterdam, The Netherlands, 2020; pp. 489–506.
- 85. Hadizadeh, F. Supplementation with vitamin D in the COVID-19 pandemic? Nutr. Rev. 2021, 79, 200–208. [CrossRef] [PubMed]
- Taylor, P.N.; Davies, J.S. A review of the growing risk of vitamin D toxicity from inappropriate practice. *Br. J. Clin. Pharmacol.* 2018, *84*, 1121–1127. [CrossRef] [PubMed]
- Millán-Oñate, J.; Rodriguez-Morales, A.J.; Camacho-Moreno, G.; Mendoza-Ramírez, H.; Rodríguez-Sabogal, I.A.; Álvarez-Moreno, C. A new emerging zoonotic virus of concern: The 2019 novel Coronavirus (SARS-CoV-2). *Infectio* 2020, 24, 187–192. [CrossRef]
- Han, Q.; Lin, Q.; Jin, S.; You, L. Coronavirus 2019-nCoV: A brief perspective from the front line. J. Infect. 2020, 80, 373–377. [CrossRef] [PubMed]
- 89. Milani, G.P.; Macchi, M.; Guz-Mark, A. Vitamin C in the Treatment of COVID-19. Nutrients 2021, 13, 1172. [CrossRef]
- 90. Sunkara, V.; Pelkowski, T.D.; Dreyfus, D.; Satoskar, A. Acute kidney disease due to excessive vitamin C ingestion and remote roux-en-y gastric bypass surgery superimposed on CKD. *Am. J. Kidney Dis.* **2015**, *66*, 721–724. [CrossRef] [PubMed]
- 91. Hambidge, M. Human zinc deficiency. J. Nutr. 2000, 130, 1344S-1349S. [CrossRef]
- 92. Lemire, J.; Mailloux, R.; Appanna, V.D. Zinc toxicity alters mitochondrial metabolism and leads to decreased ATP production in hepatocytes. *J. Appl. Toxicol. Int. J.* 2008, *28*, 175–182. [CrossRef]
- Piao, F.; Yokoyama, K.; Ma, N.; Yamauchi, T. Subacute toxic effects of zinc on various tissues and organs of rats. *Toxicol. Lett.* 2003, 145, 28–35. [CrossRef]
- 94. Kieliszek, M.; Lipinski, B. Selenium supplementation in the prevention of coronavirus infections (COVID-19). *Med. Hypotheses* 2020, 143, 109878. [CrossRef]
- 95. Jayawardena, R.; Sooriyaarachchi, P.; Chourdakis, M.; Jeewandara, C.; Ranasinghe, P. Enhancing immunity in viral infections, with special emphasis on COVID-19: A review. *Diabetes Metab. Syndr. Clin. Res. Rev.* **2020**, *14*, 367–382. [CrossRef] [PubMed]
- Fogarty, H.; Townsend, L.; Ni Cheallaigh, C.; Bergin, C.; Martin-Loeches, I.; Browne, P.; Bacon, C.L.; Gaule, R.; Gillett, A.; Byrne, M.; et al. COVID-19 coagulopathy in Caucasian patients. *Br. J. Haematol.* 2020, *189*, 1044–1049. [CrossRef] [PubMed]
- 97. Risher, J. Toxicological Profile for Selenium; Agency for Toxic Substances and Disease Registry: Atlanta, GA, USA, 2003.
- 98. Fan, A.; Kizer, K. Selenium. Nutritional, toxicologic, and clinical aspects. West. J. Med. 1990, 153, 160. [PubMed]
- 99. Sun, H.-J.; Rathinasabapathi, B.; Wu, B.; Luo, J.; Pu, L.-P.; Ma, L.Q. Arsenic and selenium toxicity and their interactive effects in humans. *Environ. Int.* 2014, *69*, 148–158. [CrossRef]
- Busari, S.; Adebayo, B. Nigeria Records Chloroquine Poisoning after Trump Endorses it for Coronavirus Treatment. CNN. 2020. Available online: https://www.cnn.com/2020/03/23/africa/chloroquine-trump-nigeria-intl/index.html (accessed on 24 July 2020).
- 101. Erickson, T.; Chai, P.; Boyer, E. Chloroquine, hydroxychloroquine and COVID-19. Toxicol. Commun. 2020, 4, 40-42. [CrossRef]
- Popp, M.; Stegemann, M.; Metzendorf, M.I.; Gould, S.; Kranke, P.; Meybohm, P.; Skoetz, N.; Weibel, S. Ivermectin for preventing and treating COVID-19. *Cochrane Database Syst. Rev.* 2021, 7, 1465–1858.
- 103. Heidary, F.; Gharebaghi, R. Ivermectin: A systematic review from antiviral effects to COVID-19 complementary regimen. *J. Antibiot.* **2020**, *73*, 593–602. [CrossRef]
- Temple, C.; Hoang, R.; Hendrickson, R.G. Toxic effects from ivermectin use associated with prevention and treatment of COVID-19. N. Engl. J. Med. 2021, 385, 2197–2198. [CrossRef]
- 105. Singh, A.K.; Majumdar, S.; Singh, R.; Misra, A. Role of corticosteroid in the management of COVID-19: A systemic review and a Clinician's perspective. *Diabetes Metab. Syndr. Clin. Res. Rev.* 2020, 14, 971–978. [CrossRef]
- 106. Isidori, A.; Arnaldi, G.; Boscaro, M.; Falorni, A.; Giordano, C.; Giordano, R.; Pivonello, R.; Pofi, R.; Hasenmajer, V.; Venneri, M.A.; et al. COVID-19 infection and glucocorticoids: Update from the Italian Society of Endocrinology Expert Opinion on steroid replacement in adrenal insufficiency. *J. Endocrinol. Investig.* 2020, 43, 1141–1147. [CrossRef]
- 107. Theoharides, T.; Conti, P. Dexamethasone for COVID-19? Not so fast. J. Biol. Regul. Homeost Agents. 2020, 34, 1241–1243. [PubMed]
- 108. Srivastava, A.; Chaurasia, J.; Khan, R.; Dhand, C.; Verma, S. Role of medicinal plants of traditional use in recuperating devastating COVID-19 situation. *Med. Aromat Plants* **2020**, *9*, 2167-0412.
- 109. Jahan, I.; Ahmet, O. Potentials of plant-based substance to inhabit and probable cure for the COVID-19. *Turk. J. Biol.* **2020**, *44*, 228–241. [CrossRef] [PubMed]

- 110. Villena-Tejada, M.; Vera-Ferchau, I.; Cardona-Rivero, A.; Zamalloa-Cornejo, R.; Quispe-Florez, M.; Frisancho-Triveño, Z.; Abarca-Meléndez, R.C.; Alvarez-Sucari, S.G.; Mejia, C.R.; Yañez, J.A. Use of medicinal plants for COVID-19 prevention and respiratory symptom treatment during the pandemic in Cusco, Peru: A cross-sectional survey. *PLoS ONE* 2021, *16*, e0257165. [CrossRef] [PubMed]
- 111. Hashemi, H.; Ghareghani, S.; Nasimi, N.; Shahbazi, M. A review of poisonings originating from self-administration of common preventative substances during COVID-19 pandemic. *Am. J. Emerg. Med.* **2022**, *epub ahead of print*. [CrossRef] [PubMed]
- 112. Chrubasik, S.; Pittler, M.; Roufogalis, B. Zingiberis rhizoma: A comprehensive review on the ginger effect and efficacy profiles. *Phytomedicine* **2005**, *12*, 684–701. [CrossRef] [PubMed]
- 113. Stojanović-Radić, Z.; Pejčić, M.; Dimitrijević, M.; Aleksić, A.; Kumar, N.V.A.; Salehi, B.; Cho, W.C.; Sharifi-Rad, J. Piperine-A Major Principle of Black Pepper: A review of its bioactivity and studies. *Appl. Sci.* 2019, *9*, 4270. [CrossRef]
- 114. Khan, T.; Khan, M.A.; Ullah, N.; Nadhman, A. Therapeutic potential of medicinal plants against COVID-19: The role of antiviral medicinal metabolites. *Biocatal. Agric. Biotechnol.* **2021**, *31*, 101890. [CrossRef]
- 115. Nazari, S.; Rameshrad, M.; Hosseinzadeh, H. Toxicological effects of Glycyrrhiza glabra (licorice): A review. *Phytother. Res.* 2017, 31, 1635–1650. [CrossRef]
- 116. Omar, H.R.; Komarova, I.; El-Ghonemi, M.; Fathy, A.; Rashad, R.; Abdelmalak, H.D.; Yerramadha, M.R.; Ali, Y.; Helal, E.; Camporesi, E.M. Licorice abuse: Time to send a warning message. *Ther. Adv. Endocrinol. Metab.* 2012, *3*, 125–138. [CrossRef]
- 117. Salem, M.A.; Ezzat, S.M. The use of aromatic plants and their therapeutic potential as antiviral agents: A hope for finding anti-COVID 19 essential oils. *J. Essent. Oil Res.* **2021**, *33*, 105–113. [CrossRef]
- 118. Basch, E.; Ulbricht, C.; Hammerness, P.; Bevins, A.; Sollars, D. Thyme (*Thymus vulgaris* L.), thymol. *J. Herb. Pharmacother.* **2004**, *4*, 49–67. [CrossRef] [PubMed]
- 119. Hu, Z.; Feng, R.; Xiang, F.; Song, X.; Yin, Z.; Zhang, C.; Zhao, X.; Jia, R.; Chen, Z.; Li, L.; et al. Acute and subchronic toxicity as well as evaluation of safety pharmacology of eucalyptus oil-water emulsions. *Int. J. Clin. Exp. Med.* **2014**, *7*, 4835. [PubMed]