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Dietary Supplements and Nutrcaceutical Remedies for COVID-19

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SUMMARY

The World Health Organization (WHO) declared that novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV- 2/COVID-19), is a global pandemic. Covid-19 is a respiratory virus that infects people of all age groups. The symptoms are mild to asymptomatic in most of the patients. Those who are aged, having a weakened immune system or suffering with varied comorbidities may present with severe and life-threatening infections. The phytochemicals obtained from medicinal plants and dietary supplements, have been used as supplementary therapies for several disease conditions, including viral infections. Proper use of these supplementary remedies with antiviral proprieties may be useful in the treatment and/or prophylaxis of COVID-19 for speedy and higher recovery rate under medical supervision

INTRODUCTION

COVID-19 is a positive sense, single-stranded ribonucleic acid (RNA) enveloped virus belongs to the corona virus family called Coronaviridae, subfamily *Coronavirinae*. It is mainly transmitted through droplets generated when an infected person coughs, sneezes, or exhales. These aerosolized droplet particles are too heavy to hang in the air, and quickly fall on floors or surfaces. Clinical presentation of the infection ranges from no symptoms to mild upper respiratory tract infections to severe multi-organ failure and death. The specific physiopathology behind why COVID-19 produces such an extensive range of disease remains unknown; however, an aggravated inflammatory cascade has been implicated in the most severe of syndromes. To date, a combination of remedies including anti-inflammatory, antiviral, and other medications with unique pharmaceutical properties have been assessed for use in the treatment and/or prevention of COVID-19. Hippocrates said that "Let food be thy medicine, and let medicine be thy food" and another famous quote by Thomas A.Edison was " the doctor of the future will no longer treat the human frame with drugs, but rather will cure and prevent disease with nutrition. All over the history and Indian Ayurveda, functional foods and nutraceuticals, such as a variety of phytochemicals obtained from medicinal plants and dietary supplements, have been used as supplementary therapies for several disease conditions, including viral infections. Proper use of these supplementary remedies with antiviral proprieties may be useful in the treatment and/or prophylaxis of COVID-19 for speedy and higher recovery rate. Plant based natural products or extracts and isolation of nutraceuticals from the plant origin remains an important source of modern drug discovery and development of active pharmaceutical ingredient to treat novel diseases. Nutraceutical foods were defined by De Felice in 2002 as "a food (or part of) that provides medical or health benefits, including the prevention and/or treatment of diseases. Nutraceuticals include active phytochemicals isolated from plants, food for special dietary use, food for special medical purpose, functional foods with medicinal properties. Supplementary use of these agents may also prove to be beneficial in reducing the manifestations of COVID-19. These nutraceuticals include "immune boosting" foods and nutrients such as zinc, vitamins, garlic, turmeric, ginger, selenium, etc.

Table 1.Common medications are presently being assessed for treatment of COVID-19 infections (Subedi, L. et al., 2021 and Amit Verma et al., 2020).

Medication	Mode of action
Remdesvir (GS-5734)	Nucleotide analog that may inhibit virus replication
2-deoxy-D-glucose (2-DG)	Effects on the glycolytic pathway, anti-inflammatory action, and interaction with viral proteins.
Bamlamivimab	IgG1 monoclonal antibody against the spike protein of SARS-CoV-2, blocking the attachment to ACE2 receptors
Dexamethasone	Potent corticosteroid with predominantly glucocorticoid activity
Tocilizumab	Recombinant humanized monoclonal antibody against the IL-6 receptor Treatment of cytokine storm induced by SARS-CoV-2

Chloroquine/hydroxychloroquine	Prevents viral infection by blocking viral-cell fusion through alteration of the endosomal pH and glycosylation of cellular receptors. Enhances host immune modulation
Azithromycin	Macrolide antibiotic that may have antiviral properties and immunomodulation properties, decreasing cytokine release
Dipyridamole	Decreased SARS-CoV-2 replication in cells, clinical improvement potentially seen in cases of COVID-19 patients
Lopinavir/ritonavir	Protease inhibitor that may inhibit viral replication
Ribavirin	Guanosine analog that inhibits viral RNA synthesis
Nitazoxanide	Antiprotozoal and antiviral agent that inhibits the SARS-CoV-2
Baricitinib	Selective Janus kinase (JAK) 1 and 2 inhibitor
Penciclovir	Reduced SARS-CoV-2 replication
Nelfinavir	Protease inhibitor that inhibits viral replication

Table 2.Nutritional Supplements are presently being used for treatment of COVID-19 infections (Pecora F et al., 2020**).**

Nutrients	Inflammatory and innate immune response	Adaptive immune response
Vitamin -A	• Integrity of epithelia • Differentiation and function of NK-cells • Promotion of Foxp3+ Treg generation • Inhibition of Th1/Th17 generation • Phagocytic and oxidative burst activity of macrophages • Secretion of the pro-inflammatory cytokines IL-12 and IL-23	• Growth and differentiation of B cells • Production of Antibodies • Immunoregulatory function of Treg cells
Vitamin-C	• Barrier integrity • Scavenger of ROS • Chemotactic ability and anti bacterial activity of neutrophils • Apoptotic process of neutrophils • Reduction of formation of neutrophil extracellular traps (NETs)	• Differentiation and Proliferation of B- and T-cells • Immunostimulator of antibody production (IgM and IgG) • T-cells maturation via epigenetic mechanisms
Vitamin-D	• Production of anti microbial peptides • Modulation of macrophages/monocytes and dendritic cells function • Limits over production of pro inflammatory cytokines from macropages(IL1,TNF alfa)	• Limits over production of pro inflammatory cytokines from T cells (INFgamma, IL2, IL8, IL6) • Th1 to Th2 shift, increases Th2 cytokines (IL4, IL10) • Induces differentiation of Treg • Reduces excessive antibody production
Zinc	• Maintenance of membrane barrier integrity • Direct antiviral effects • Deceases oxidative stress	• Limits excessive release of pro inflammatory cytokines (IL2, IL6 and TNF-alfa) • Enhances the number of Teg
Omega 3FA	• Structures of cell membranes • Inhibition of cytokine production • Inhibiting neutrophil migration • Clearance of Polymorphonuclear leukocytes.	• Specialized pro-resolving mediators (SPM's) • Treg cells formation • B cells activation

		• Upregulate CCR5 expression

Table 3. Nutraceutical Supplements that may be beneficial for treatment of COVID-19 infections (Subedi et al., 2021**)**

Nutraceutical/Active Ingredient	Source	Predicted mode of action
Glycyrrhizin (triterpenoid saponins)	*Glycyrrhiza glabra; Glycyrrhiza uralensis* (licorice)	Inhibits viral replication and dsorption/penetration via induction of nitrous oxide synthase
Saikosaponin B2	*Bupleurum spp.; Heteromorpha spp.; Scrophularia scordonia*	Interferes with early-stage viral Replication
Tetrandrine Fangchinoline Cepharanthine	*Stephania tetrandra*	Inhibits viral replication as well as viral S and N protein expression to prevent viral entry
Indigo Sinigrin Hesperetin	*Isatis indigotica*	Inhibits viral replication by blocking the cleavage of the 3CLpro of SARS-CoV
Amentoflavone	*Torreya nucifera*	Inhibits viral replication by noncompetitively blocking cleavage of the 3CLpro of SARS-CoV
Herbacetin	Flaxseed	Inhibits viral replication by blocking the cleavage of the 3CLpro of SARS-CoV
Rhoifolin	*Rhus succedanea*	Inhibits viral replication by blocking the cleavage of the 3CLpro of SARS-CoV
Pectolinarin	*Cirsium chanreoenium*	Inhibits viral replication by blocking cleavage of the 3CLpro of SARS-CoV
Rhizoma cibotii	*Cibotium barometz*	Inhibits viral cytopathogenic effect and inhibits viral replication via effects on 3CLpro
Gentianae radix	*Gentiana scabra*	Inhibits viral cytopathogenic effect and inhibits viral replication via effects on 3CLpro
Discoreae rhizome	*Dioscorea batatas*	Inhibits viral cytopathogenic effect and inhibits viral replication via effects on 3CLpro
Cassiae semen	*Cassia tora*	Inhibits viral cytopathogenic effect and inhibits viral replication via effects on 3CLpro
Loranthani rhamus	*Taxillus chinensis*	Inhibits viral cytopathogenic effect and inhibits viral replication via effects on 3CLpro
Myricetin	*Ceratonia siliqua*	Inhibits viral replication by blocking the ATPase activity of the SARS-CoV helicase protein nsP14; may also have antioxidant properties
Secutellarein	*Scutettaria baicalensis*	Inhibits viral replication by blocking the ATPase activity of the SARS-CoV helicase protein nsP14
Aescin	*Aesculus hippocastanum* (horse chestnut tree)	Inhibition of viral replication via unknown mechanism; may also have anti-inflammatory properties
Reseprine	*Rauwolfia serpentine*	Inhibition of viral replication via an unknown mechanism
Juglanin	*Juglans regia*	Inhibits interaction between virus and host cells via blocking the 3a-protein channel

TGG	*Galla chinensis*	Interferes with viral cell fusion via effects on the S protein
Luteolin	*Veronicalina riifolia*	Interferes with viral cell fusion via effects on the S protein
Lycorine	*Lycoris radiata*	Inhibits viral cytopathic effect via an unknown mechanism
3_-friedelanol (triterpenoid)	*Euphorbia neriifolia L*	Inhibits viral activity via an unknown mechanism
Baicalin	*Scutellaria baicalensis*	Inhibits viral activity via an unknown mechanism
Ginsenoside-Rb1	*Panax ginseng*	Inhibits viral activity via an unknown mechanism
TSL-1	*Toona sinensis*	Inhibits viral activity via an unknown mechanism

The nutritional supplements and phytochemicals or nutraceuticals shown in table 2 and 3 cannot be recommended outside of clinical trials or research experiments, as further extensive research and approvals are required to confirm their potential therapeutic benefits in the cure and prevention of COVID-19.

CONCLUSION

Due to super spreading of disease, there is an emergency to control covid-19 on war footing basis, numerous active pharmaceutical ingredients and nutraceuticals are being evaluated to flatten the covid-19 curve across the globe. As vaccination process is underway and people continue to use many combinatorial strategies for treatment of COVID-19. Many functional foods, protein rich foods, Indian Ayurveda herbal extracts, Spices, phytochemicals, nutraceuticals, vitamin supplements have been consuming to fight against viral infections, including species of coronavirus. However, there is a lack of concrete evidence of safety and efficacy of nutraceuticals or herbal extracts regular use cannot be recommended with confidence. In addition to combinatorial therapies, other Covid-19 measures such as physical distancing, wearing of mask, use of hand sanitizer, home quarantine or isolation, and infection-control should continue to be followed as they are proven measures in control of corona virus spread.

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