Interim Report on a Live Review of Systematic Reviews of Natural Health Products and Natural Therapies in the Prevention and/or Treatment of COVID-19

Iva Lloyd,[1] **Kieran Cooley,**[2] and **Daniella Remy**[3]

ABSTRACT

Objective: This living review of systematic reviews investigates the types and volume of research pertaining to natural health products and therapies as they relate to the prevention and/or treatment of COVID-19 and post-COVID syndrome.

Methods: A monthly search for published peer-reviewed systematic reviews of the topic was initiated May 2022 and is ongoing. Using a systematic keyword search strategy with clear inclusion and exclusion criteria, a summary of the types of studies included, the overall outcome and treatment focus were assessed.

Results: A total of 225 systematic reviews encompassing 5,636 studies of randomized controlled trials (49.8%, *n*=112), observational studies (21.3%, *n*=48), clinical studies (20.4%, *n*=46), and other studies (12%, *n*=27) were included. Of those, 28.9% (*n*=65) of the systematic reviews focused on prevention, 67.6% (*n*=152) on treatment, and 3.1% (*n*=8) on post-COVID. The natural health products reviewed included herbal medicine, vitamins, minerals, other natural health products, and other therapies, with 83.5% (*n*=188) of all systematic reviews stating a positive outcome and beneficial potential of the natural treatment or therapy investigated.

Conclusion: This living systematic review concludes that there is a growing interest in research pertaining to natural health products and therapies with respect to the prevention of COVID-19 infections and addressing disease severity and mortality, especially in adjunct to conventional medical intervention. Nonetheless, there is a lack of high-quality evidence and consistency in outcome reporting across the large breadth of natural treatment and management options.

Key Words Living systematic review, post-COVID, natural therapies, vitamins, minerals, herbal medicine.

INTRODUCTION

The World Health Organization announced the presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in March of 2020.[1] SARS-CoV-2 was believed to be a novel virus with no known treatment to the array of symptoms generally referred to as COVID-19.[1] As the ensuing pandemic spread globally, the search for treatments and preventive strategies, both within conventional medicine and within the realm of traditional and complementary medicine (T&CM), became a focus internationally.

In March 2020, the World Health Organization (WHO) brought together ten T&CM non-governmental organizations, including the World Naturopathic Federation (WNF), to discuss the role of T&CM in addressing SARS-CoV-2.[2] In follow-up to that meeting, the WNF worked with naturopathic researchers globally to compile and publish ten rapid reviews on the role that specific natural health products (NHPs) might play in the prevention and/or treatment of COVID-19.[3] As outlined in this paper, T&CM researchers and organizations have contributed a tremendous body of research outlining the role of specific NHPs in the prevention and/or treatment of COVID-19 or the management and treatment of post-COVID syndrome.

In May of 2022, the WNF, in collaboration with the Canadian College of Naturopathic Medicine (CCNM), initiated a living review highlighting systematic reviews that had been published with respect to the role of NHPs and/or therapies in the prevention and/or treatment of COVID-19 or the management and treatment of post-COVID syndrome.[4] This interim report provides a summary of the data collected between May and December 2022. Updated information on this Living Review can be found on the WNF website[4]: https://worldnaturopathicfederation.org/live-review-of-natural-health-products-nhps-researched-with-respect-to-the-covid-pandemic/.

Correspondence to: Dr. Iva Lloyd, ND, 53 Snapdragon Drive., Toronto, ON M2J 4X5, Canada.
E-mail: i.lloyd@worldnaturopathicfederation.org

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Aim

This report is an interim narrative review of the systematic reviews that have been conducted with respect to NHPs and natural therapies in the prevention and/or treatment of COVID-19 and/or the management/treatment of post-COVID syndrome. The aim is to highlight the growing interest in NHPs in this area and to list the research on specific types of treatments and therapies that have been investigated within the realm of T&CM.

METHODS

Design

This study is a continual and active high-level monitoring of all systematic reviews on NHPs and natural treatments for the prevention and management of COVID-19 and post-COVID. With the aim of including any new important evidence on a condition that it is new to the world, monthly searches were conducted and up-to-date communication about research status was provided via the WNF website to answer the question: what T&CM products and therapies are being researched with respect to the treatment and/or management of COVID-19 and post-COVID syndrome.

Search Strategy

Starting in May 2022, the researchers performed monthly literature searches. As per Cochrane Guidelines,[5] monthly meetings were held to review the research design and search terms used in all databases and make modifications as needed to ensure all new evidence was included for an accurate and complete collection of relevant evidence without any change to the aim or scope of the living review. These monthly meetings also were used to review the articles collected each month to determine whether they met the inclusion and exclusion criteria. This was a necessary part of the process to make sure the collection of articles was continually updated, and that the search incorporated all relevant new evidence on the natural prevention and/or treatment of COVID-19 and post-COVID syndrome available at that time, following the Cochrane guidelines for living systematic reviews.[5] Because it was a living review, other researchers in this field were asked to submit papers they may have come across, ensuring any articles not published in PubMed or Google Scholar would be included.

PubMed and Google Scholar databases were used, with search terms such as "natur*," "herb*," "nutraceutical," "botanical," "medicinal plant," "Ayurvedic," "Chinese medicine," "herbal patent formula," "vitamin," "mineral," combined with "prevention," "prophylaxis," "deficiency," "treatment," "management," and "*COVID*," "Coronavirus," "SARS-CoV-2." Additionally, individual herb names, compounds, vitamins, and minerals cited in the literature were searched. Though this report has drawn a line in the sand in December 2022 to publish the results thus far, monthly updates on published systematic reviews on the topic will continue.

The current absence of statistical analysis is deliberate and reflective of the abundance of new systematic reviews. Once the number of published articles declines significantly, this living review will likely be transitioned into a systematic review including an analysis of the quality of evidence available.

Inclusion and Exclusion Criteria

Only systematic reviews were included, with no restrictions regarding publication language. Articles were therefore included if the researchers used a structured search of databases, were transparent about their methodological criteria for their study inclusion/exclusion criteria, and presented a summary of conclusions about cumulative outcomes.

Excluded were narrative reviews, secondary analyses, literature reviews, editorial discussions, best practice guidelines, and book chapters. On occasion, a title or abstract stated the paper was a systematic review, but it did not provide the details of databases searched, inclusion/exclusion criteria, or other methodological rigour, so was ultimately excluded.

Table 1 summarizes the PICO eligibility criteria requirements for study inclusion of systematic reviews.

Data Mining

An online spreadsheet was used to collate included studies and extract relevant data. For each paper, the full reference, abstract link, full text link, year of publication, country of the primary author, WHO Region of the primary author, number of studies included in the systematic review, type of studies included, number of participants, short summary of findings, conclusion of the findings, treatment focus, and details of treatment focus were extracted. Keywords were used to itemize included topics relevant to NHPs and approaches (see Table 2).

Data Management

The data collected from each study was based on the information outlined by the authors in each systematic review for each analytic analyzed. The types of studies were grouped into randomized controlled trials (RCTs), clinical trials, observational studies, and other (which included other qualitative and quantitative studies on humans or animals, case reports, guidelines and other reviews, *in vitro*, and *in silico* studies). Studies were categorized as having a positive, neutral, or negative outcome. The outcome recorded was based on the authors' interpretation of their study. There were three options for the treatment category—prevention, treatment, or post-COVID—as outlined in the abstract. The categories for treatment focus included herbal medicine, vitamins, minerals, other NHPs (e.g., quercetin, probiotics, fish oils), and other therapies (e.g., Ayurveda, Qi Gong, nutrition, exercise). Details of the treatment focus included a listing of each specific herb, nutrient, or treatment provided. As outlined in

Table 1 PICO inclusion criteria

Population	Clinical or observational (humans of any age or gender, and in any setting), *in vivo* (including animal studies), *in vitro,* or *in silico* (including molecular docking)
Intervention	Any natural health product or approach
Comparison	No limitation for comparator studies
Outcome	Any symptom, biological marker, diagnostic criteria, or viral traits related to severe acute respiratory syndrome or viral respiratory tract infections of the coronavirus or COVID-19.

Table 2, if a paper included multiple terms for the same nutrient (e.g., Vitamin C, Ascorbic acid, ascorbate) only the main term was included in the list.

Data Analysis

Using standard Excel counting formulas, the number of occurrences for each defined word was counted and summary data tables were compiled. Descriptive statistics were prepared for each analytic (i.e., frequency). It was possible for systematic reviews to include more than one treatment focus or individual treatment, hence the totals included in those categories is greater than the total number of systematic reviews for that category.

Limitations

The data collected from each systematic review was not assessed for a risk of bias nor quality grading. The aim of this study was to highlight the amount of new evidence emerging on a monthly basis to create awareness of options health practitioners could investigate for patient care. Articles labelled as finding positive, negative, or neutral results were based on the author's findings and conclusions. Some studies outlined that the NHPs and/or treatments studied were an adjunctive approach as opposed to independent interventions and hence direct conclusions about the NHPs and/or treatments are difficult to isolate.

Table 2 Keywords and their definitions, as used in the collection and analysis of the data

Keywords	Terms Included in the Keywords
Vitamins	
Vitamin A	Vitamin A, Retinol, Retinoid
Vitamin C	Vitamin C, Ascorbic acid, Ascorbate
Vitamin D	Vitamin D, Cholecalciferol, Hydroxycalciferol
Vitamin B	Vitamin B1, Thiamine, Vitamin B2, Riboflavin, Vitamin B3, Niacin, Vitamin B5, Pantothenic acid, Vitamin B6, Pyridoxine, Vitamin B7, Biotin, Vitamin B9, Folate, Folic acid, Vitamin B12, Cobalamin
Vitamin E	Vitamin E, Tocopherol
Carotene	Alpha Carotene, Beta Carotene, Carotenoid
Minerals	Listed individually by mineral name
Herbal Medicine	
Quinones	Quinone, Hydroxymethyl anthraquinone, Anthraquinone
Saponins	Saponin, Shikonin, Glycyrrhizic acid, Glycyrrhizin, Ruscogenin, Senegenin
Phenolic acids	Phenolic acids, Gallic acid, Vanillic acid, Syringic acids, Cinnaminic acid, Caffeic acid, Ferulic acid, Sinapic acid
Coumarin	Coumarin, Coumaric acid
Tannins	Tannin, Proanthocyanidin, Gallotannins, Ellagitannins
Turmeric	Curcuma longa, Curcumin, Turmeric
Patent Herbal Formula	Includes any herbal formula used in traditional Chinese, Korean, Ayurvedic or other medicine.
Note: Herbs are referred to by their first Latin name (e.g.: *Allium* = Garlic)	
Other NHPs	
Omega3	Omega3, EPA, DHA, Cod liver oil, Fish oil
Quercetin	Quercetin, Flavone
Probiotics	Probiotics, Symbiotics, Lactobacillus (coryniformis, paracasei, fermentum, casei, acidophilus, brevis, plantarum, reuteri, rhamnoses, and lactis), Bifidobacterium (lactis, bifidum, longum, short, animalis subsp. Lactis), Saccharomyces boulardii, Streptococcus thermophilus, Bacillus subtilis, Pediococcus pentosaceus
Polyphenols	Polyphenol, Resveratrol, Bergenin, Rosmarinic acid, Dicaffeoylquinic acid
Polysaccharides	Polysaccharide, Lectin, Glycoprotein, Glycans, Concanavalin A, Agglutinin, Fructo-oligosaccharides, Galacto-oligosaccharides
Terpenes	Terpene, Lactone, Euphorbia, Bisabolol, Picfeltarraenin, Jolkinolide, Anthocyanin
Glucosides	Glucoside, Glycoside, Salidroside, Ulinastatin, Forsythoside, Polydatin, Ginsenoside, Fraxin
Flavonoids	Flavonoid, Isoflavones, Hesperetin, Silymarin, Silibinin, Astilbin, Acacetin, Puerarin, Apigenin, Nobiletin, Tangeretin, Chalcone, Artemetin
Catechins	Catechin, Epigallocatechin gallate, EGCG
Steroids	Steroid, Steroidal compounds, Diosgenin
Other Therapies	
Nutrition	Nutritional interventions, Nutritional inadequacies, Diet, Fruit and vegetable intake, identification of specific diets, spices
TCM	TCM, Chinese herbal medicine, Korean herbal medicine, Oriental medicine, Chinese patent medicine
Acupuncture	Acupuncture, Electro-acupuncture

NHP = natural health product; TCM = traditional and complementary medicine.

This live review focused solely on systematic reviews, which means some NHPs and therapies may not have been included if they have not yet been studied at the level of systematic review. This applies especially to novel approaches for which primary research studies are being conducted. Similarly, reviews on post-COVID are limited, as this is a phenomenon still being unraveled and treatments for post-COVID are still being explored.

Though some studies included the word "systematic review" in their title, they may have been excluded from the review because of their lack of transparency to the methodology and data analysis. It is recommended that researchers adhere to reporting guidelines for systematic reviews, such as the Cochrane or PRISMA Guidelines, to provide quality evaluations and summaries of all the available primary research. Nonetheless, our study did not assess the quality of the studies included, and publication bias was not assessed.

RESULTS

Study Selection

Between May and December 2022, a total of 225 systematic reviews focused on the role of NHPs or natural therapies with respect to the prevention and/or treatment of COVID-19, or post-COVID systems.[6-211] Of those, 28.9% focused on prevention, 67.6% on treatment, and 3.6% on post-COVID. In sum, 5,636 studies were reported as part of the systematic reviews, involving over 4 million participants and a reference list of 8,870 citations. With regard to the publication dates, 9.8% of the papers were published in 2020, 33.3% in 2021, and 56.9% in 2022.

Geographical Representation

With respect to geographical representation, 36.9% of the systematic reviews originated in the Western Pacific region, 18.2% in the European region, 15.6% in South-East Asia, 12.0% in the Eastern Mediterranean, 11.6% in the region of the Americas, and 5.8% in the African region. Our analysis indicated that systematic reviews on the prevention and/or treatment of COVID-19 have originated in 25 countries, with 21% (*n*=12) of those focused on prevention of COVID-19 originating in Iran, 11% (*n*=6) in the United Kingdom, and 9% (*n*=5) in both China and India. Of those focused on treatment of COVID-19, 33.6% (*n*=48) originated in China, 12.6% (*n*=18) in India, 8.4% (*n*=12) in Iran, and 7.0% (*n*=10) in Brazil.

Types of Studies

As outlined in Table 3, 49.8% of all systematic reviews were based on RCTs, 21.3% on observational studies, 20.4% on clinical or pre-clinical trials, and 12.0% included mixed designs and other types of studies. Of the systematic reviews focused on treatments, 59.2% (*n*=90) were based on RCTs, compared with 24.6% (*n*=16) focused on prevention. Among the pre-clinical trials, a total of 15 articles included *in vitro* or *in silico* studies to examine the effects a particular compound could have on SARS-CoV-2, while all animal and human studies were more focused on specific markers of disease (e.g., inflammatory markers, such as IL-6, TNF-alpha, etc.), clinical indicators of disease (e.g., blood oxygen levels, viral shedding, etc.), or symptoms of disease (e.g., fever, coughing, etc.).

Study Outcomes

The outcomes of the systematic reviews were recorded as positive, negative or neutral, or mixed based on the stated outcome of the authors. As such, 83.5% of all systematic reviews stated a positive outcome, 7.6% indicated a mixed response, and 6.8% a negative or neutral response. The percentage of positive outcomes between prevention and treatment reviews were 81.5% (*n*=53) and 84.9% (*n*=129), respectively. Of the prevention studies, 13.8% (*n*=9) stated a mixed outcome response, and 9.2% (*n*=14) of the treatment studies indicated a negative or neutral response.

Research Focus

As per Table 3, 41.8% of all systematic reviews researched herbal medicines, with 54.6% (*n*=83) focusing on herbal medicines as a treatment, versus 6% (*n*=4) as prevention. In comparison, 27% of reviews focused on vitamins as a form of treatment, but that percentage increased to 67.7% (n-44) in the systematic reviews focused on prevention. A total of 13.3% researched other therapies (including nutrition, breathing, exercise, etc.), 13.8% other NHPs, and 12.0% researched minerals.

As outlined in Table 4, the systematic reviews focused on prevention most researched Vitamin A (*n*=42), Vitamin D (*n*=42), Zinc (*n*=11), and Selenium (*n*=10). In the treatment studies, patent herbal formulas were the most common (*n*=50), followed by Vitamin D (*n*=32), Vitamin C (*n*=23), Turmeric (*Curcuma longa*) (*n*=11), and Zinc (*n*=11). The number of systematic reviews focusing on post-COVID is currently not sufficient to identify specific research focuses.

Nearly all (91%) of the publications focused on the benefit of natural treatments and therapies as adjunctive approaches to COVID-19. Research on natural treatments or therapies as independent interventions were limited to non-clinical studies to assess individual compounds and their specific molecular effects.

DISCUSSION

The growing number of systematic reviews and the wide range of NHPs and natural therapies researched with respect to the prevention and treatment of COVID-19 indicate a strong interest in the role of T&CM.

Growing Interest in the Role of NHPs and Natural Therapies in the Prevention and Treatment of COVID-19

The interest in the role of NHPs in the prevention and treatment of COVID-19 appears to be gaining momentum, with 17 systematic reviews being published in 2020, 75 in 2021, and at least 134 in 2022. The focus of the systematic reviews is broad and includes most vitamins, 6 minerals, a wide range of herbal medicines both as individual herbs and as patent herbal formulae, over 12 other individual NHPs (e.g., probiotics, flavonoids, quercetin, melatonin, etc.), and other therapies (i.e., Ayurveda, lifestyle, diet and nutrition, exercise, breathing, yoga, etc.). Studies on prevention

Table 3 Summary of the number of systematic reviews included, the geographical region, year of publication, type of studies included outcomes and area of study focus

WHO Region	Prevention	Treatment	Post-COVID	Totals
Number of papers	28.9% (*n*=65)	67.6% (*n*=152)	3.6% (*n*=8)	225
Number of studies	1983	3494	120	5,636
WHO Region				
African region	4.6% (*n*=3)	5.3% (*n*=8)	25% (*n*=2)	5.8% (*n*=13)
Americas	9.2% (*n*=6)	11.8% (*n*=18)	25% (*n*=2)	11.6% (*n*=26)
Eastern Mediterranean	20% (*n*=13)	9.2% (*n*=14)	0	12.0% (*n*=27)
European	32.3% (*n*=21)	11.8% (*n*=18)	25% (*n*=2)	18.2% (*n*=41)
South-East Asia	12.3% (*n*=8)	17.8% (*n*=27)	0	15.6% (*n*=35)
Western Pacific	21.5% (*n*=14)	44.1% (*n*=67)	25% (*n*=2)	36.9% (*n*=83)
Year of Publication				
2020	6.2% (*n*=4)	11.9% (*n*=18)	0	9.8% (*n*=22)
2021	41.5% (*n*=27)	30.9% (*n*=47)	12.5% (*n*=1)	33.3% (*n*=75)
2022	52.3% (*n*=34)	57.2% (*n*=87)	87.5% (*n*=7)	56.9% (*n*=128)
Type of Study				
RCT	24.6% (*n*=16)	59.2% (*n*=90)	75% (*n*=6)	49.8% (*n*=112)
Observational	40.0% (*n*=26)	13.8% (*n*=21)	12.5% (*n*=1)	21.3% (*n*=48)
Clinical	16.9% (*n*=11)	20.4% (*n*=31)	50% (*n*=4)	20.4% (*n*=46)
Other/mixed	24.6% (*n*=16)	6.6% (*n*=10)	12.5% (*n*=1)	12.0% (*n*=27)
Unspecified	7.7% (*n*=5)	4.6% (*n*=7)	0	5.3% (*n*=12)
Outcome				
Positive	81.5% (*n*=53)	84.9% (*n*=129)	75.0% (*n*=6)	83.5% (*n*=188)
Mixed	13.8% (*n*=9)	3.9% (*n*=6)	25.0% (*n*=2)	7.6% (*n*=17)
Negative/neutral	1.5% (*n*=1)	9.2% (*n*=14)	0	6.8% (*n*=15)
Treatment Focus				
Vitamins	67.7% (*n*=44)	27.0% (*n*=41)	37.5% (*n*=3)	39.1% (*n*=88)
Minerals	21.5% (*n*=14)	7.9% (*n*=12)	12.5% (*n*=1)	12.0% (*n*=27)
Herbal medicine	6.0% (*n*=4)	54.6% (*n*=83)	75.0% (*n*=6)	41.8% (*n*=94)
Other natural health products	6.1% (*n*=4)	1701% (*n*=26)	12.5% (*n*=1)	13.8% (*n*=31)
Other therapies	15.4% (*n*=10)	11.2% (*n*=17)	37.5% (*n*=3)	13.3% (*n*=30)

WHO = World Health Organization; RCT = randomized controlled trial.

tend to focus more on nutritional status and the use of vitamins and minerals, as well as lifestyle and diet. Studies focused on treatment most commonly focus on individual or patent herbal formulae. Both prevention and treatment studies focus on vitamins and minerals, but the prevention studies put a greater emphasis on Vitamin A, whereas the treatment studies focus on Vitamin C. Vitamin D is the most common vitamin researched. Treatment studies research a range of other NHPs, whereas the same trend is not found in the prevention studies.

The focus of the systematic reviews is common to what T&CM practitioners have historically used in the treatment of upper respiratory tract infections. The therapies highlighted in the rapid reviews conducted by the WNF in May 2020 supported the findings of the systematic reviews as of the end of 2022. That is, the most common natural therapies to consider in the prevention and treatment of COVID-19 and post-COVID include Vitamin C,[212] Vitamin D,[213] multivitamins,[214] Zinc,[215] Quercetin,[216] N-Acetyl-cysteine (NAC),[217] essential oils,[218] and the herbs *Echinacea,*[219] *Hedera helix,*[220] and *Sambucus nigra.*[221]

Despite the mounting volume of research on natural approaches for the prevention and treatment of COVID-19, there has been limited acknowledgement by or interest from governments with respect to the role of T&CM either adjunctively or individually with respect to the prevention and/or treatment of COVID-19 and/or post-COVID.

Global Contribution

The contribution of systematic reviews focused on the role of NHPs and treatments in the prevention and management of COVID-19 has been global, with 25 countries spanning all WHO regions contributing to the body of knowledge. Researchers from China have contributed the highest number of systematic reviews, with a primary focus being on the use of traditional Chinese herbal patents in the treatment of COVID-19. The high number

Table 4 Details of natural health products and natural therapies that were researched in the systematic reviews

Natural health product or natural therapy	Prevention	Treatment	Post-COVID	Total
Herbal Medicines				
TCM herbal patents*		32.9% (*n*=50)		22.2% (*n*=50)
Turmeric (*Curcuma longa*)		7.2% (*n*=11)		4.9% (*n*=11)
Licorice (*Glycyrrhiza glabra*)		4.6% (*n*=7)	25.0% (*n*=2)	4.0% (*n*=9)
Ginger (*Zingiber officinale*)		3.3% (*n*=5)		2.2% (*n*=5)
Andrographis (*Andrographis paniculate*)		2.6% (*n*=4)		1.8% (*n*=4)
Echinacea (*Echinacea angustifolia*)	1.5% (*n*=1)	2.0% (*n*=3)		1.8% (*n*=4)
Garlic (*Allium sativum*)		2.0% (*n*=3)		1.3% (*n*=3)
Ginseng (*Panax ginseng*)		2.0% (*n*=3)		1.3% (*n*=3)
Ashwagandha (*Withania somnifera*)		1.3% (*n*=2)		0.9% (*n*=2)
Essential oils		0.6% (*n*=1)	12.5% (*n*=1)	0.9% (*n*=2)
Individual herbs*	4.5% (*n*=3)	2.6% (*n*=4)	25.0% (*n*=2)	4.0% (*n*=9)
Vitamins				
Vitamin A	64.6% (*n*=42)	2.6% (*n*=4)	12.5% (*n*=1)	20.9% (*n*=47)
B Vitamins	6.1% (*n*=4)	3.3% (*n*=5)		4.0% (*n*=9)
Vitamin C	9.2% (*n*=6)	15.1% (*n*=23)		12.9% (*n*=29)
Vitamin D	64.6% (*n*=42)	21.0% (*n*=32)		20.9% (*n*=47)
Vitamin E		3.9% (*n*=6)		2.7% (*n*=6)
Minerals				
Zinc	16.9% (*n*=11)	7.2% (*n*=11)	12.5% (*n*=1)	10.2% (*n*=23)
Selenium	15.4% (*n*=10)	3.9% (*n*=6)		7.1% (*n*=16)
Iron	9.2% (*n*=6)			2.7% (*n*=6)
Calcium	4.6% (*n*=3)	0.6% (*n*=1)		1.8% (*n*=4)
Magnesium	4.6% (*n*=3)			1.3% (*n*=3)
Phosphorus	3.1% (*n*=2)			0.9% (*n*=2)
Other NHPs				
Probiotics		5.9% (*n*=9)		4.0% (*n*=9)
Flavonoids		5.9% (*n*=9)		4.0% (*n*=9)
Polyphenols		4.6% (*n*=7)		3.1% (*n*=7)
Quercetin		3.9% (*n*=6)		2.7% (*n*=6)
Melatonin		3.9% (*n*=6)		2.7% (*n*=6)
Propolis		3.9% (*n*=6)		2.7% (*n*=6)
Polysaccharides		1.3% (*n*=2)		0.9% (*n*=2)
Omega 3	.5% (*n*=3)	1.3% (*n*=2)		2.2% (*n*=5)
N-acetylcysteine (NAC)		1.3% (*n*=2)		0.9% (*n*=2)
Other NHPs**	1.5% (*n*=1)		37.5% (*n*=3)	1.8% (*n*=4)
Other Therapies				
Ayurveda		5.9% (*n*=9)		4.0% (*n*=9)
Lifestyle	6.1% (*n*=4)			1.8% (*n*=4)
Diet	6.1% (*n*=4)			1.8% (*n*=4)
Homeopathy		1.3% (*n*=2)		0.9% (*n*=2)
Pulmonary rehabilitation/ breathing			12.5%(*n*=1)	0.4% (*n*=1)
Acupuncture		0.6% (*n*=1)	12.5%(*n*=1)	0.9% (*n*=2
Exercise/physical therapy		0.6% (*n*=1)	12.5%(*n*=1)	0.9% (*n*=2)
Ozone		0.6% (*n*=1)		0.4% (*n*=1)

TCM = traditional and complementary medicine; NHP = natural health product.
*Indicates the number of individual herbs that appeared in only one systematic review.
**Indicates the number of other natural health products that appeared in only one systematic review.

of studies originating from China may reflect the recognition of the Chinese government that both Traditional Chinese medicine and Western (or conventional) medicine can be used in combination to prevent and treat COVID-19.[222] With NHPs and natural therapies commonly used in North America, it is surprising to see the lack of research originating in this region. This may be due to the restrictions placed on T&CM healthcare workers with respect to the management of patients with COVID-19.

Positive Outcomes

Randomized control trials are recognized as the gold standard for evaluating the effectiveness of an intervention.[223] Over half of all the systematic reviews were based on RCTs and the systematic reviews focused on both prevention and treatment indicated positive outcomes, above 84% in the NHP and/or natural therapy that was being researched. More of the prevention studies (13.8%) indicated a mixed outcome, whereas 9.2% of the systematic reviews focused on treatment indicated a neutral or negative outcome. The high percentage of RCTs and the high rate of positive outcomes support further investigation of the role of natural therapies in the prevention and treatment of COVID-19.

None of the studies suggested that natural therapies or treatments should be used in isolation. Rather, they indicated use as a complement to conventional medicine. Integrative approaches to treatment or prevention included addressing nutrient deficiencies, combining medical care (e.g., adding an herbal or natural health product to pharmaceutical treatment), or managing symptoms (e.g., reducing inflammation or respiratory burden). Based on the abundance of research supporting the benefit of natural medicine as an adjunctive approach to COVID-19 treatment and prevention, the researchers see no grounds for inhibiting the use of T&CM as a general practice.

CONCLUSION

This live systematic review concludes that there is growing interest in research to support consideration of NHPs and therapies in the prevention and the treatment of COVID-19 in order to decrease disease severity and mortality, as an adjunctive therapy to conventional medical intervention, and that the range of NHPs and therapies studied is broad. Further research that follows consistent standard reporting is warranted.

AUTHOR AFFILIATIONS

[1]World Naturopathic Federation, Toronto, ON, Canada; Canadian College of Naturopathic Medicine, Toronto, ON, Canada; [2]Canadian College of Naturopathic Medicine, Toronto, ON, Canada; University of Technology Sydney, Ultimo, Australia; Pacific College of Health Sciences, San Diego, USA; National Centre for Naturopathic Medicine, Southern Cross University, Lismore, Australia; [3]World Naturopathic Federation, Toronto, ON, Canada; Canadian College of Naturopathic Medicine, Toronto, ON, Canada; Precision Health Alliance, Brisbane, Australia; Electronic Multinational Research Group – International Consulting, Inc, Toronto, ON, Canada.

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CONFLICTS OF INTEREST DISCLOSURE

We have read and understood the *CAND Journal*'s policy on conflicts of interest and declare that we have none.

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